Pharmaceuticals and Medical Devices Agency, Japan

ANNUAL REPORT FY 2014

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(in the event of inconsistency, the Japanese text shall prevail).

THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2014 (April 2014 - March 2015)

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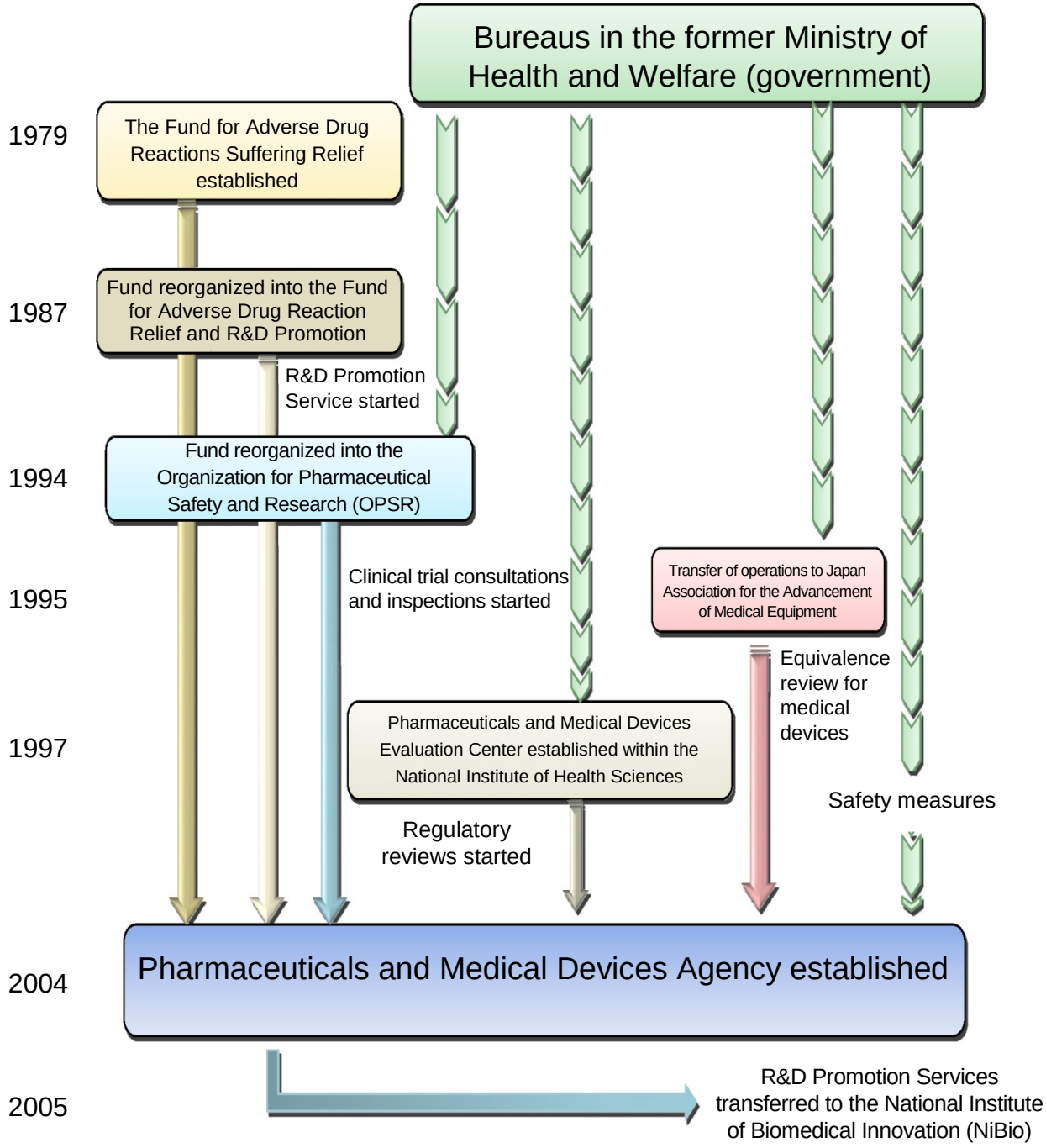
I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1 History and Objective of PMDA

- As a lesson learned from drug-induced health damage 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 the 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).
- In November 2012, PMDA started to provide benefits for sufferers of adverse health effects caused by cellular and tissue-based products (as a part of Relief Service for Adverse Drug Reactions and Relief Service for Infections Acquired through Biological Products).
- 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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145 of 1960, PMD Act) and based on the current scientific and technological standards, PMDA evaluates the efficacy, safety, and quality of drugs and medical devices for which applications have been submitted for regulatory approval. In addition, PMDA conducts re-examinations/re-evaluations of drugs, medical devices, and cellular and tissue-based products, medical device use-result survey, 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, Cartagena Law) (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 or 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), Good Post-marketing Surveillance Practice (GPSP), and the data integrity standards for product applications (GLP/GCP/GPSP Inspections).
- PMDA conducts on-site and document-based inspections to determine whether manufacturing facilities and manufacturing control methods for drugs, medical devices, and cellular and tissue-based products, etc., comply with the requirements of the Ministerial Ordinance on Good Manufacturing

Practices/Quality Management System, whereby products of appropriate quality can be manufactured. PMDA also inspects manufacturing sites of cellular and tissue-based products to determine whether their manufacturing facilities as well as manufacturing process and quality management system comply with the Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (Act No. 85 of 2013) (GMP/QMS/GCTP Inspections).

- PMDA conducts research for developing various standards, such as the Japanese Pharmacopoeia (JP), which is set forth in the PMD Act (Research for Standards Development).

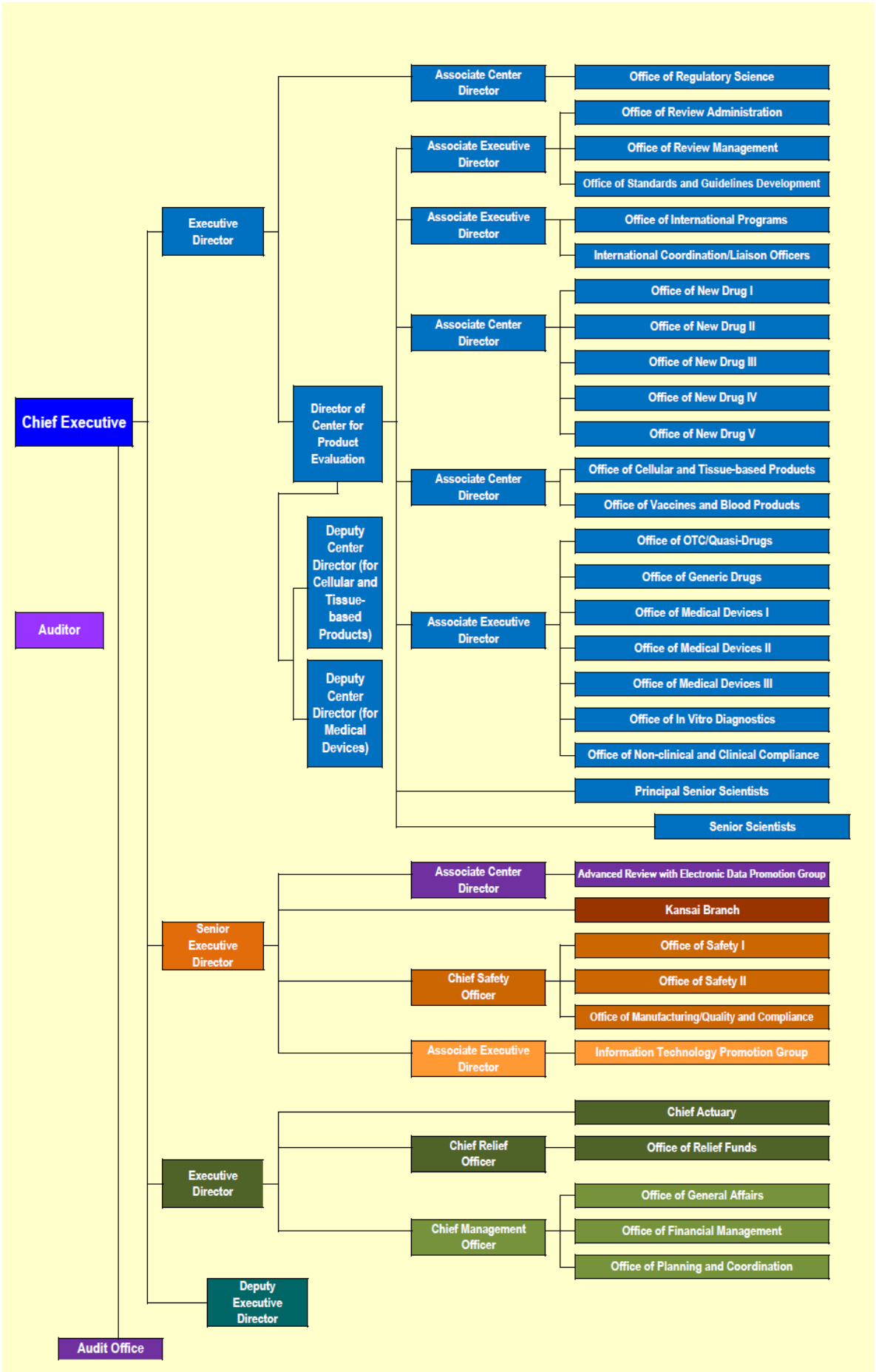
2.3. Safety Measures

- 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).

- PMDA also utilizes electronic medical records to quantitatively evaluate the risk of adverse events, to assess the effects on safety measures, to investigate the realities of drug prescription, and to develop medical information database, aiming to build a system that enables safety measures based on pharmacoepidemiological methods.

Structure of PMDA (as of March 31, 2015)



II. OPERATING PERFORMANCE FOR FY 2014

PART 1 Development of Fiscal Year 2014 Plan

1.1. Development and Implementation of Fiscal Year 2014 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 Third Mid-term Targets: April 2014 to March 2019). 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 2014, the fiscal year plan was developed at the end of FY 2013 based on the Third 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 2013

- It had been 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] prior to revision)
- On August 26, 2014, PMDA received the "Results of the Evaluation on Operating Performance for FY 2013" 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
- The "Results of the Evaluation on Operating Performance for FY 2013" was published on the PMDA website and reported to Advisory Council Meeting held on November 7, 2014.

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 2012 Performance	FY 2013 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	2	2
	A	Exceeding the level prescribed in the Mid-term Plan	16	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 endorsed the evaluation results in "Opinion on the Results of Evaluation on Operating Performance for Effective Period of Third Mid-term Targets" published on January 9, 2014.

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

- On August 26, 2014, PMDA received the "Results of the Final 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 previous 5 years, from FY 2009 to FY 2013. Among 18 evaluation items, "S" rating was given to "cost control efforts" and "expeditious operation and improvement of the system (drugs)" and "A" rating to 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

- The "Results of the Final Evaluation on Operating Performance for Effective Period of Mid-term Targets" was posted on the PMDA website and reported to Advisory Council Meeting held on November 7, 2014.

Results of PMDA's Final 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	2
	A	Exceeding the level prescribed in the Mid-term Plan	16
	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 the agencies under the new system/organization, and ensuring that employees of each agency perform their duties with pride and contribute to the growth of the economy or the improvement of people's living as much as possible. Based on this policy, the Act for Partial Revision of the Act on General Rules for Incorporated Administrative Agencies (Act No. 66 of 2014) and the Act for Arrangement of Relevant Acts Incidental to Enforcement of the Act for Partial Revision of the Act on General Rules for Incorporated Administrative Agencies (Act No. 67 of 2014) were promulgated on June 13, 2014 and came into effect on April 1, 2015. The Acts are intended to review the common system based on which incorporated administrative agencies are managed, so that the agencies can fulfill their duties of public accountability and exert their full policy-conducting functions in accordance with the primary objectives of the agencies.

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

- Measures to be taken for each agency

  [Pharmaceuticals and Medical Devices Agency (PMDA)]

  ○ It is a mid-term target management-type agency (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 agency 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) "Mid-term target management-type agency" conducts clerical and business operations while demonstrating significant independence/autonomy through mid-term target management, with the objective of improving the quality of its operations, such as services intended for the public. The Act on Pharmaceuticals and Medical Devices Agency was revised by the Act for Arrangement of Relevant Acts Incidental to Enforcement of the Act for Partial Revision of the Act on General Rules for Incorporated Administrative Agencies, and PMDA was defined as the mid-term target management-type corporate body provided in Article 2, Paragraph 2 of the Act on General Rules for Incorporated Administrative Agencies.

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

2.1. Efficient and Flexible Management of Operations

2.1.(1) Development of basic implementation policy for the Third Mid-term Plan

- To implement the Third Mid-term Plan in changing operational circumstances, the "Basic Policy for Implementation of the Third Mid-term Plan," clarifying the viewpoints to be predominantly considered, was determined in an Executive Directors' Meeting on November 25, 2014. PMDA is to steadily implement the Third Mid-term Plan by repeating PDCA cycle based on the Policy.

2.1.(2) 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 2014, 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.

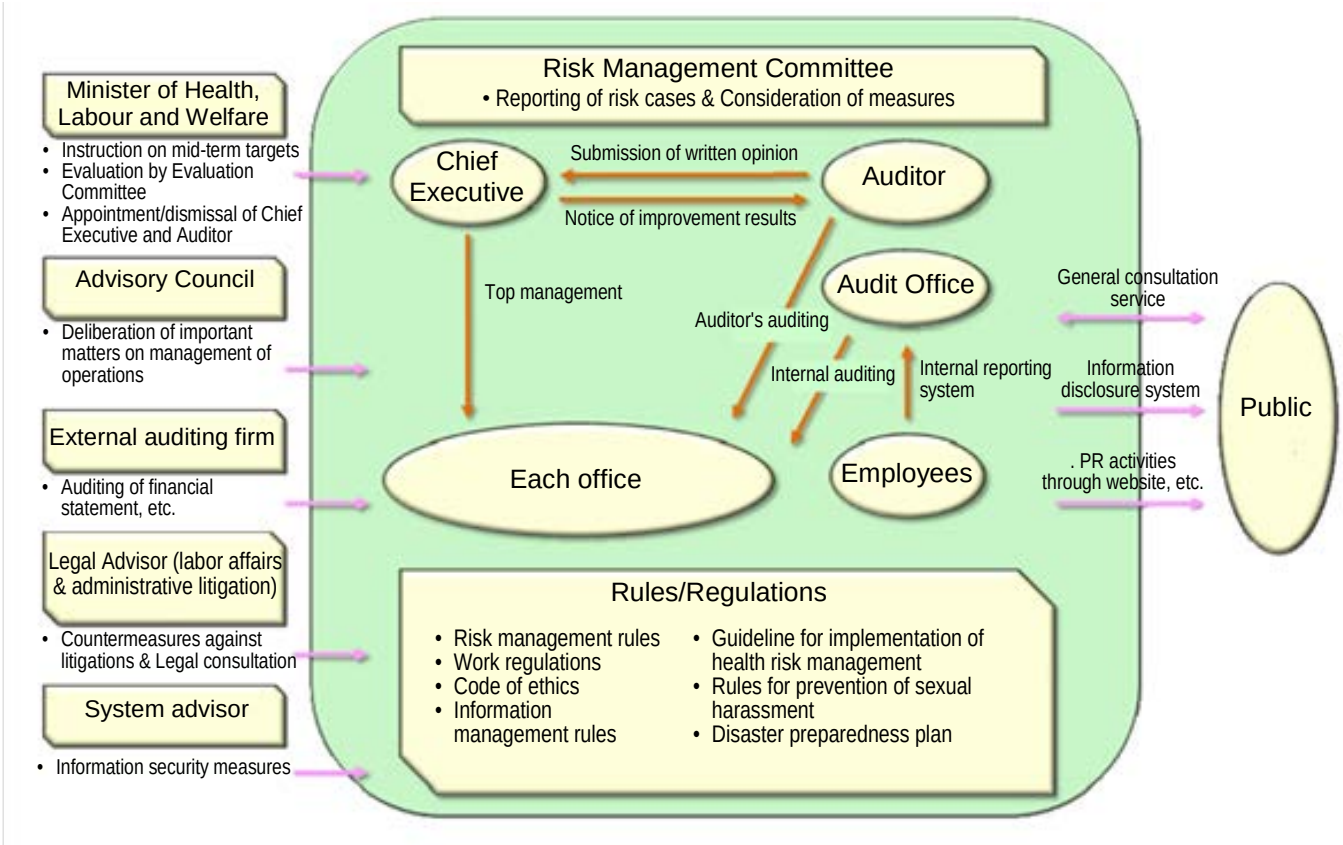
2.1.(3) Reinforcement of operational management system and top-down management

- 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, PMDA regularly (once a week, in principle) held "Board of Directors meetings," attended by executives and office directors, to ensure that the Chief Executive directly comprehends operational progress and provides necessary direction.
- Meetings of the "Steering Committee" were held to monitor the development status of optimization of operations and systems, and to hear opinions. Also, 3 meetings of the "Committee on Investment in Information Systems" were held to assess, from a comprehensive perspective, the necessity, cost-effectiveness, technical difficulty, etc., of new development and upgrading of the operations system. Then, well-planned and efficient investment options were selected.
- In order to regularly monitor the financial conditions to maintain sound financial performance and effective operations, the "Financial Management Committee," headed by the Chief Executive, held 12 meetings in FY 2014. The following information was reported to the meetings: user fees paid and cash flow analysis for each division for each month; and the declared amount of contributions.
- In March 2015, 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 with the pharmaceutical industry on new drugs (one session in October 2014) and on drug safety (one session in November 2014).

Also, regarding medical devices and *in vitro* diagnostics, PMDA helped the MHLW to manage and hold regular opinion exchange forum on regulatory affairs for medical devices (July 2014) and the Action Program Review Committee's meetings (July 2014).

- 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.
- The "PMDA Business Continuity Plan in the Event of Large-scale Disasters" was developed in March 2015 to define the scopes of important services that PMDA should maintain in the event of a large-scale disaster, such as an inland earthquake that directly hits the capital city.
- "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 public relations (PR) activities 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. Further, in consideration of the development of PMDA's philosophy, changing socioeconomic circumstances, etc., PMDA revised the Strategic Plan and determined to develop a PR plan every fiscal year based on the revised Strategic Plan, and to manage progress of PR plan to enable effective public relations designed separately for each stakeholder (came into force on April 1, 2015).
- 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 role of the International Strategy Meeting established in September 2012 (core members, executives) was transformed from a place for annual information and opinion exchange into a decision-making body that develops strategies (2 meetings were held before transformation and 6 after transformation). In the meetings, members discussed strategies toward establishment of the PMDA's position in international society, including matters such as new international strategies and policies for dealing with major international conferences. The contents were made widely known at the international liaison conference (held 11 times in FY 2014) intended for persons in charge in each division/department of their thorough dissemination.
- In response to a request for promotion of the "Kansai Innovation Comprehensive Global Strategic Special Zone," PMDA set up the Kansai Branch in Osaka City in October 2013. This office has conducted 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.(4) Advisory Council meetings

- In order to create opportunities for opinion exchange between knowledgeable individuals in various fields, PMDA holds meetings of the "Advisory Council" (chaired by Masataka Mochizuki, Professor, Faculty of Pharmaceutical Sciences, Tokyo University of Science), 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 Masataka Mochizuki, Professor, Faculty of Pharmaceutical Sciences, Tokyo University of Science) were also formed to discuss specialized operational issues. The dates of the meetings and specific agenda for FY 2014 were as follows.

[Advisory Council] (FY 2014)

Agenda for the 1st Meeting (June 26, 2014)

(1) Annual Report FY 2013
(2) Financial Report FY 2013
(3) Revision of the Statement of Operating Procedures (draft)
(4) Situations of recent main efforts
(5) Employment status of personnel from the private sector
(6) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(7) Others

Agenda for the 2nd Meeting (November 7, 2014)

(1) Selection of Chairperson and appointment of Acting Chairperson
(2) Results of evaluation of operating performance for FY 2013 and results of final evaluation of operating performance for the effective period of Mid-term Targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(3) Situations of recent main efforts
(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 (March 10, 2015)

(1) FY 2015 plan (draft) and PMDA Public Relations Strategic Plan (draft)
(2) Budget for FY 2015 (draft)
(3) Revision of the Statement of Operating Procedures (draft)
(4) Employment status and 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) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(8) Others

[Committee on Relief Services] (FY 2014)

Agenda for the 1st Meeting (June 25, 2014)

(1) Annual Report FY 2013
(2) FY 2014 plan
(3) PR on the Relief System for Adverse Health Effects
(4) Others

Agenda for the 2nd Meeting (December 10, 2014)

(1) Selection of Chairperson and appointment of Acting Chairperson
(2) Results of the evaluation of operating performance for FY 2013 and results of final evaluation on operating performance for the effective period of mid-term targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(3) Operating performance so far in FY 2014 and current situation of recent major initiatives
(4) Others

[Committee on Review and Safety Operations] (FY 2014)

Agenda for the 1st Meeting (June 26, 2014)

(1) Annual Report FY 2013
(2) FY 2014 plan
(3) Revision of the Statement of Operating Procedures on Reviews and Safety Measure Services (draft)
(4) Recent main situations
(5) Employment status of personnel from the private sector
(6) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(7) Others

Agenda for the 2nd Meeting (December 24, 2014)

(1) Selection of Chairperson and appointment of Acting Chairperson
(2) Results of the evaluation of operating performance for FY 2013 and results of final evaluation on operating performance for the effective period of the Mid-term Targets (Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(3) Operating performance so far in FY 2014 and issues to be addressed in the future
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions etc.
(6) Others

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

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 on reviews and safety measures. (1,304 external experts are commissioned as of March 31, 2015.)
- 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. (126 external experts are commissioned as of March 31, 2015.)
- 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). 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 payments received by external experts are disclosed immediately after confirmation of approval of designated products, implementation of safety measures, or development of approval standards for drugs or review guidelines, and 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 with advanced expertise in information systems and knowledge of pharmaceutical affairs as an information system advisor, to ensure consistency and coordination of services across 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

- Also in FY 2014, 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 PMDA website:

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 2014, PMDA designed and developed an integrated review system in part in response to the revision of the Pharmaceutical Affairs Act, built information systems that connect safety monitoring and relief services, upgraded existing IT systems, designed and developed the accounting system

and the personnel/salary system, and redesigned the PDMA website. The Agency also conducted research and reviews aimed at enhancing overall PDMA information management and IT control.

2.2. Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general and administrative expense

- PMDA has been making ongoing efforts to improve operations and increase management efficiency in order to attain the target of 15% or greater savings in the Mid-term Plan budget relating to general administrative expenses covered by administrative subsidies, as compared with that for FY 2014, by the end of the effective period of the Mid-term Plan/Targets (FY 2018).
- In FY 2014, PMDA promoted streamlining of efficiency of its services, such as optimization of systems and reduction of unnecessary expenditure. As in the previous fiscal year, PMDA made efforts to reduce procurement costs by conducting, in principle, general competitive bidding, resulting in a 27.7% reduction against budget.

2.2.(2) Cost control of operating expenses

- PMDA has been making ongoing efforts to improve operations and increase management efficiency in order to attain the target of 5% or greater savings in the Mid-term Plan budget relating to operating expenses covered by administrative subsidies, as compared with that for FY 2014, by the end of the effective period of the Mid-term Plan/Targets (FY 2018).
- In FY 2014, PMDA promoted streamlining of efficiency of its services, such as optimization of systems, promotion of computerization, and reduction of unnecessary expenditure. Similarly to the measures taken for general administrative expenses, PMDA made efforts to reduce procurement costs by concluding contracts through, in principle, general competitive bidding, resulting in a 14.2% reduction against budget

2.2.(3) Competitive bidding

- PMDA promoted bidding for all contracts by means of measures such as shifting to general competitive bidding based on the "Plan for Review of Optional Contracts etc. " In FY 2014, however, the ratio of competitive contract schemes, including competitive requests for proposals and invitations to bid, to total contracts decreased by 2.1% in terms of number of bids and by 35.5% in terms of monetary amount compared to the preceding fiscal year.

  The ratio of competitive contract in number decreased from FY 2013 to FY 2014 (-2.1%). This was due to a decrease of 2 competitive contracts and an increase of 3 non-competitive optional contracts. Other than contracts for office leases, there was an increase of 7 non-competitive optional contracts such as re-leasing contracts for leased properties with the specified contract party.

  Since FY 2014 is the first year of the effective period of the Third Mid-term Plan, PMDA entered into multi-year contracts for office leases, starting in FY 2014. Since the total contract amount for the multi-year contracts was included in the first fiscal year, the monetary amount for non-competitive operational contracts in FY 2014 increased by 71 million yen compared to the previous fiscal year, resulting in the decreased ratio in terms of the monetary amount for competitive contracts.

		FY 2013	FY 2014	Change
General competitive bidding (including competitive planning competition and invitations to bids)		135 bids (83.9%)	130 bids (91.8%)	-5 bids (-2.1%)
		5,838 million yen (76.8%)	6,240 million yen (41.3%)	402 million yen (-35.5%)
Non-competitive optional contracts		26 bids (16.2%)	29 bids (18.2%)	3 bids (2.0%)
		1,769 million yen (23.3%)	8,869 million yen (58.7%)	7,100 million yen (35.4%)
	Excluding contracts in relation to office lease	5 bids (3.1%)	12 bids (7.5%)	7 bids (-4.4%)
		35 million yen (0.5%)	321 million yen (2.1%)	286million yen (1.6%)
Total		161 bids 7,606 million yen	159 bids 15,109 million yen	-2 bids 7,503 million yen

Note: Since the figures are rounded off to the nearest number, the sum of the figures does not always match the sum of the totals.

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 2014, regarding the appropriateness of the contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 4 meetings in FY 2014 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

2014, the collection rates achieved for ADR contributions, infection contributions, and safety measure contributions were 99.7%, 100%, and 99.7%, respectively.

FY 2014 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	693	692	99.9%	3,852
	MAHs of pharmacy-compounded drugs	5,673	5,658	99.7%	6
	Total	6,366	6,350	99.7%	3,857
Infection contributions	MAHs of approved biological products	92	92	100%	93
Post-marketing Safety measures etc., contributions	MAHs of drugs	588	587	99.8%	1,035
	MAHs of medical devices	2,291	2,288	99.8%	256
	MAHs of drugs/ medical devices	224	224	100%	1,682
	MAHs of pharmacy-compounded drugs	5,673	5,658	99.7%	6
	Total	8,776	8,757	99.7%	2,977

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.

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

a. ADR contributions

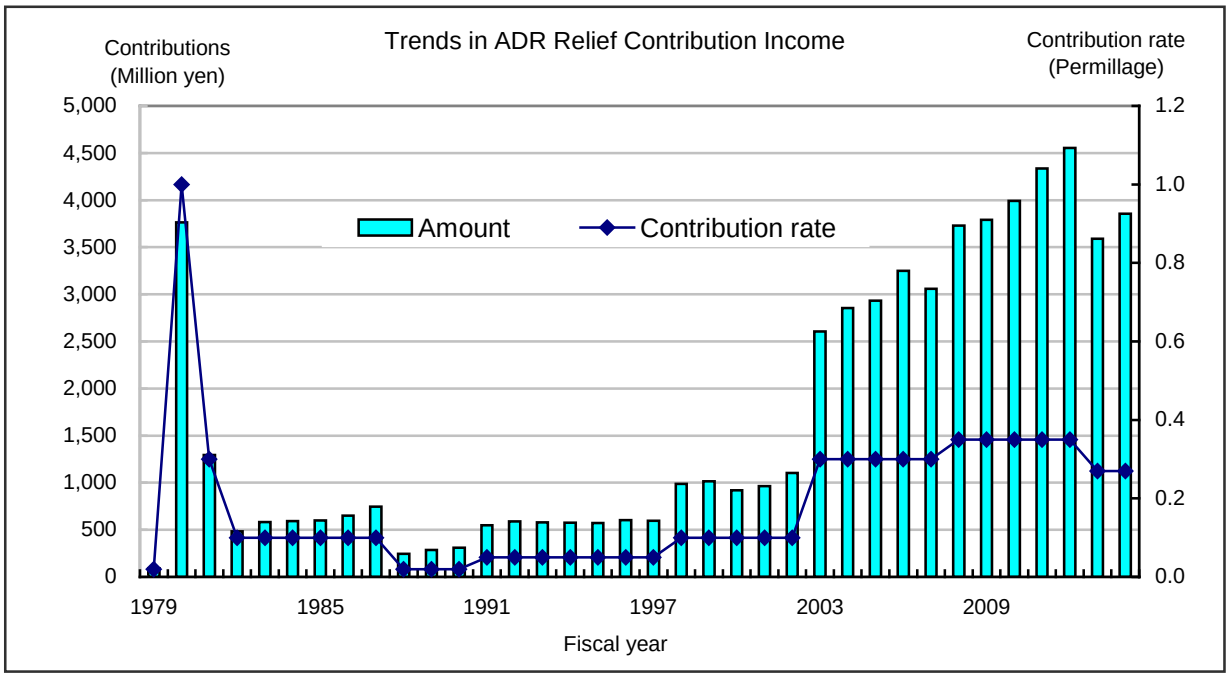
- In order to fund the relief service for adverse drug reactions, PMDA has collected ADR contributions from MAHs of approved drugs. In FY 2014, the contribution rate applied to such MAHs was set at 0.27/1000 and the collected amount was 3,857 million yen.

(Million yen)

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Contributions from MAHs of drugs	3,984 [716]	4,330 [713]	4,548 [688]	3,590 [688]	3,852 [692]
Contributions from MAHs of pharmacy-compounded drugs	7 [7,082]	7 [6,694]	6 [6,186]	6 [5,866]	6 [5,658]
Total amount	3,991	4,337	4,554	3,596	3,857
Contribution rate	0.35/1000	0.35/1000	0.35/1000	0.27/1000	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 2014, the contribution rate applied to such MAHs was set at 0.1/1000 and the collected amount was 93 million yen.

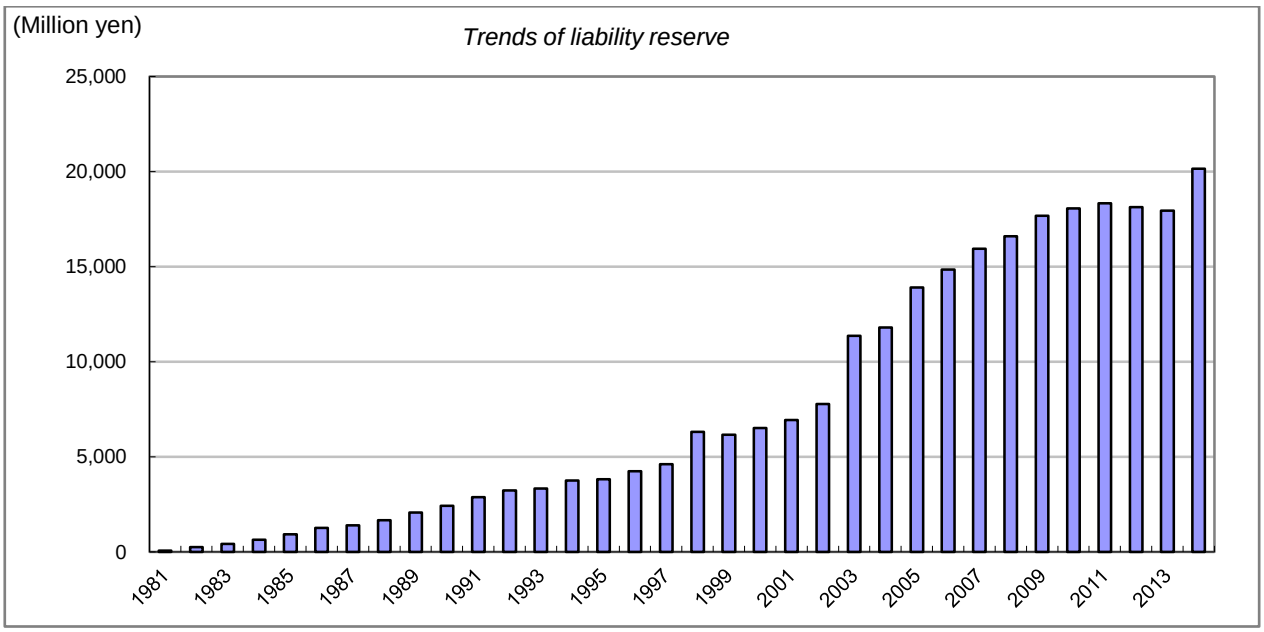
(Million yen)

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Contributions from MAHs of approved biological products	693 [93]	785 [92]	866 [92]	869 [94]	93 [92]
Contribution rate	1/1000	1/1000	1/1000	1/1000	0.1/1000

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 2014 was 20,141 million yen. In the settlement of accounts for FY 2014, 1,015 million yen of provision shortfall due to miscalculation of liability reserves in previous fiscal years was calculated as an extraordinary loss.



(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 2014, 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 2,977 million yen.

(Million yen)

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
MAHs of drugs/ medical devices	2,530 [2,922]	2,596 [2,974]	2,768 [2,970]	2,810 [3.023]	2,972 [3,099]
MAHs of pharmacy-compounded drugs	7 [7,082]	7 [6,694]	6 [6,186]	6 [5,866]	6 [5,658]
Total amount	2,537	2,603	2,774	2,816	2,977
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.
Since the figures for contribution amount are rounded off to the nearest million yen, the sum of the figures does not always match the sum of the contribution amounts.

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

- To steadily implement measures for "Reinforcement of efforts to reduce unnecessary expenditures" (formulated in FY 2009) under the Third Mid-term Plan, "Reinforcement of efforts to reduce unnecessary expenditures" was revised and, along with "Standard practice for taking more efficient cost-cutting measures", announced to 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 1,731 inquiries that PMDA received in FY 2014, 480 or approximately 30% of the total inquiries received were those relating to applications and consultations for drugs, medical devices, etc.

	Inquiry/ consultation	Complaint	Opinion/ request	Others	Total
FY 2014	1,604 (436)	10 (3)	117 (41)	0 (0)	1,731 (480)

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, medical devices, etc. 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 2014.
- 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 enhanced the content of its website. For example, new information and updates, etc. of existing content are sequentially posted on the website in order of requests from relevant departments.
- On March 16, 2015, PMDA integrated the "Medical Product Information" Web page (http://www.info.pmda.go.jp) into the Pharmaceuticals and Medical Devices Agency website (http://www.pmda.go.jp), and redesigned the whole website to make it more accessible to anyone.

  [Three ideas for improving the website to make required information more easily accessible for all users]

(1) Newly designed topics area to display the latest and most important information
(2) Newly designed navigation area to enable rapid access to target information (menu navigation by visitors, by products, and by services, and local navigation)
(3) Comprehensive provision of information on individual products and enhancement of search function for materials such as package inserts

2.3.(4) Proactive PR activities

- In line with the PMDA Public Relations Strategic Plan (July 11, 2008), developed from the perspective 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 2014, the following activities were implemented based on the Strategic Plan.

  In consideration of development of PMDA's philosophy, changing socioeconomic circumstances, etc., PMDA revised the Strategic Plan and determined to develop a PR plan every fiscal year based on the revised strategy and to manage progress of PR plan to enable effective public relations designed separately for each stakeholder (came into force on April 1, 2015).

  In FY 2014, PMDA distributed leaflets, which are designed 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 17 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., 29 times in Japan and 3 times overseas.

2.3.(5) Disclosure requests for agency documents

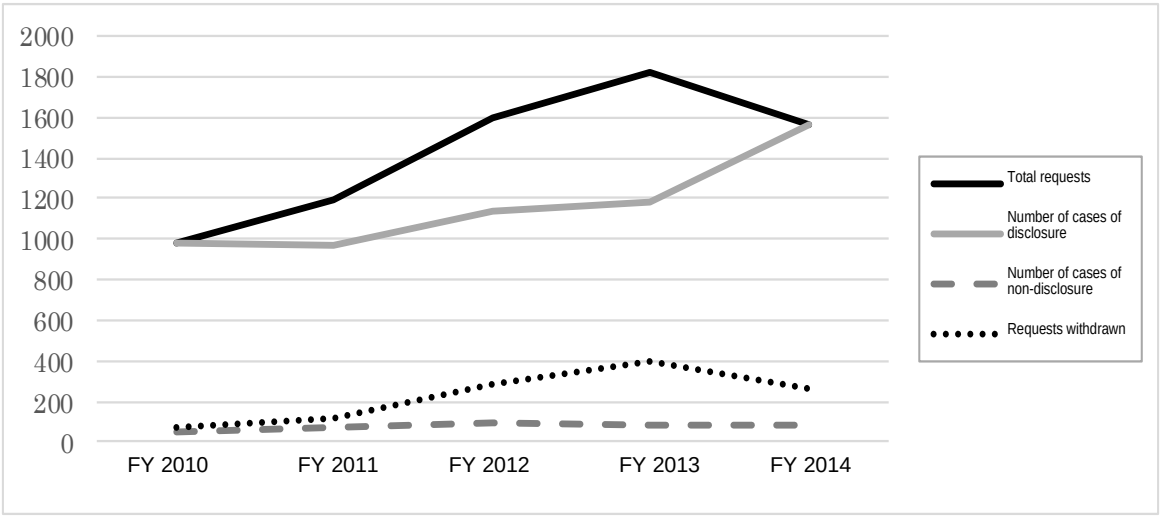
- The status of requests (over the last 5 years) for disclosure of documents under the Act on Access to Information Held by Incorporated Administrative Agencies is shown below. In FY 2014, the number of requests decreased by 14.3% and the number of disclosures increased by 32.5% compared to the previous fiscal year. PMDA appropriately processed requests 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 2015**
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
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
FY 2014	1,562	262	176	1,384	0	82	1	0	511

** 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 2015" 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 2010	FY 2011	FY 2012	FY 2013	FY 2014	Examples
Product application Review	902	1,046	1,410	1,675	1,457	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post-marketing Safety	78	139	176	131	97	ADR reports etc.,
Others	3	7	7	17	8	
Total	983	1,192	1,593	1,823	1,562	

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 2015
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
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	0
FY 2014	8	1	0	9	0	0	0	0	0

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 2014, PMDA conducted internal audits on the management status of documents, cash and cash equivalents, execution status of travel expenses, management status of competitive research funds, etc., and the status of compliance with rules restricting work assignments 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 2013, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2014 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 2013" on the website in August 2014.

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 Third Mid-term Plan (FY 2014 to FY 2018), PMDA also 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 2013 to March 2014 in pay raises etc., as of July 2014. 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) has been 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 has been conducted since 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.
- Thus to improve the quality of operations, PMDA needs to systematically provide training opportunities tailored to the objectives of each operation, for not only technical employees but also administrative employees who support organizational management. PMDA’s training programs are divided into 2 courses: General Training Course on important topics in light of the special nature of PMDA’s services (e.g., information technology and business manners) that employees should understand and address to fulfill their roles; and Specialized Training Course to develop expertise in quality, efficacy, safety evaluation, and other matters related to drugs, medical devices, etc. Employees systematically participate in both courses to learn about the knowledge and expertise.

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

  For implementation of each training course, the Training Committee formulated plans based on the needs of the employees. Various training programs, as listed below, have been implemented.

The training programs were evaluated and earned high marks in terms of participant satisfaction and acquisition of knowledge/skills.

1) General Training Course

(i) New recruit training was conducted between April and May 2014. 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 for follow-up, mid-level employees and management-level employees, as part of training programs by job level.

(iii) One-to-one English conversation lessons (e.g. practical business English for international conferences) and correspondence courses in English language were subsidized and TOEIC tests were administered to improve employees' English language skills.

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

(v) Three training program sessions were held, in which lecturers invited from organizations for adverse drug reaction sufferers and patient organizations delivered presentations.

(vi) In order to utilize electronic documents more efficiently, IT literacy training (Microsoft Office) was carried out for a total of 50 members through e-learning in which trainees learn at the personal computer on their own desk.

2) Specialized Training Course

(i) Training courses on the basic knowledge needed for review, safety, and relief services (case studies, medical writing training, etc.) were provided mainly for new recruits.

(ii) On-site training programs, such as visits to drug/medical device manufacturing facilities (8 facilities) and IRBs of medical institutions were provided. Hands-on training on medical devices was provided.

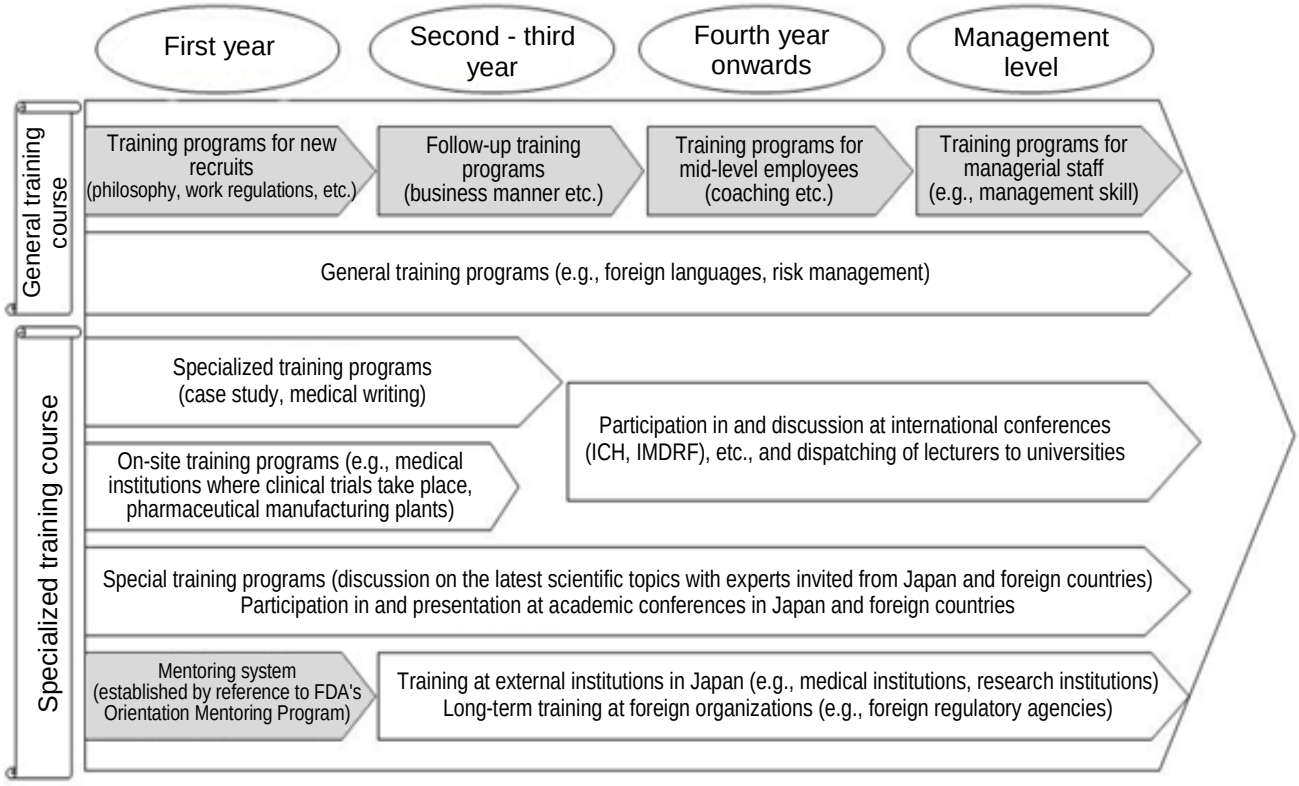
(iii) Experts invited from Japanese or overseas regulatory authorities, corporations, and universities provided special training in technical issues (24 sessions) and training in the regulatory system including the Pharmaceutical Affairs Act (2 sessions).Training in clinical study design to learn biostatistics (12 sessions) and in pharmacoepidemiology to learn features of pharmacoepidemiological study design (4 sessions) were also provided.

(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). For the acquisition of basic knowledge about medical devices, class I and II ME (Biomedical Engineering) technical trainings were also provided (19 employees).

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

(vi) One employee was dispatched to an accounting training course provided by the Accounting Center, Ministry of Finance and another employee to courses for internal auditors provided by the Board of Audit of Japan, to improve administrative processing skills. In addition, 5 employees attended Grade 2 or 3 bookkeeping courses. Also, 18 employees attended either an external logical thinking course, a management course, a labor management course, or a course for the Japanese business law examinations, as training for administrative staff members who are on main career tracks.

Training and Human Resource Development



Note: Training courses indicated in color are mandatory for all eligible employees.

2.4.(3) Appropriate personnel allocation

- In order to secure the expertise of staff members and operational continuity and make the best use of limited resources, in line with the basic policy of the Third Mid-term Plan, PMDA seeks to conduct appropriate personnel allocation.
  To achieve this target, PMDA deploys personnel taking into consideration the knowledge and work experience of individual staff members. PMDA conducts medium- and long-term rotation of personnel upon overall adjustment.
- Also in FY 2014, 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 Third Mid-term Plan, in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act, which reflects the content of the Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the final recommendations of the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Drug-induced Suffering, the target number of regular employees at the end of the period (end of

FY 2018) is set to be 1,065. 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 2014 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2014 *(as of April 1, 2015)*

1)	Technical (specialist) employees [open recruitment conducted twice]	
	Number of applicants	430
	Number of employments	68
2)	Administrative staff members who are on main career track [open recruitment conduced once]	
	Number of applicants	125
	Number of employments	11

FY 2014 Recruitment Activities

- Information sessions on career opportunities
  January and February: Two sessions in Tokyo and one session each in Osaka, Nagoya, Sapporo, and Fukuoka (total 371 participants)
  May: Two sessions in Tokyo and one session in Osaka (total 171 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 2016 ("My Navi 2016" and "Rikunabi 2016")

- Staff were recruited as needed for 10 job categories: toxicity, IT system, clinical medicine, biostatistics, epidemiology, clinical pharmacology/pharmacokinetics, information science[Note], GLP, GMP/QMS, and foreign language (English). As a consequence, 25 individuals were employed on an as-needed basis.

Note: Recruitment of information science staff was terminated in June 2014.

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	FY 2015 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	820	1,065
Review Department	350	389	415	438	460	492	532	
Safety Department	82	123	133	136	140	152	165	
Relief Department	32	34	34	33	33	33	36	

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 (excluding the one responsible for the Information Technology Promotion Group), Associate Center Directors (excluding the one 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 Drugs I to V, Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products, Office of OTC/Quasi-Drugs, Office of Generic Drugs, Offices of Medical Devices I to III, Office of In Vitro Diagnostics, Office of Non-clinical and Clinical Compliance, Chief of Kansai Branch, Consultation Division of Kansai Branch, Principal Senior Scientists, and Senior Specialists.

Note 3:The Safety Department consists of the Chief Safety Officer, Offices of Safety I and II, Office of Medical Infomatics and Epidemiology, Office of Manufacturing/Quality and Compliance, 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.
- As a set of countermeasures against power harassment in the workplace, a structure for efficient prevention and resolution of power harassment incidents has been developed, involving such measures as placing a counseling staff member in each office, based on the regulations relating to prevention of harassment and a manual on how to deal with issues related to power harassment.
- 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.

2.4.(6) Optimization of standards for remuneration

- PMDA compared its personnel remuneration system for FY 2013 against that for national government employees in order to facilitate public understanding of its remuneration levels, and released the results on its website.
- Based on the recommendations of the National Personnel Authority in FY 2014, PMDA revised the overall remuneration system, including narrowing the disparities in remuneration standards between PMDA and private sector (in particular, lowering of the remuneration standards for older employees).

2.4.(7) Development of better working environment

- Based on discussions in the Work-Life Balance Promotion Committee, PMDA has enhanced support measures for child-rearing by expanding the eligibility for "time off for sick/injured child care," "time for child care," and "early/late shift," and by introducing a separate leave category for the caring of children with school-infectious diseases.
- While promoting to generalize these child care support programs for employees, PMDA has also developed the General Business Owner Action Plan (third term) to address other issues, in order to support development of the next generation.

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 2014 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	70	800
Within PMDA		1,403

Note: The numbers of registered companies and issued certificates as of the end of March 2015

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

3.1. Relief Services for Adverse Health Effects

To ensure that the public is more widely informed 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 its relief fund services, takes the following measures to provide adequate and swift relief for those suffering from health damage caused by adverse reactions to drugs or cellular and tissue-based products and infections acquired through biological products or cellular and tissue-based 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. Every month, claims approved or rejected in the previous month are posted on the website.
  PMDA also distributes the information through its email service called "PMDA medi-navi" concurrently 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" on the web page and also distributed through "PMDA medi-navi" to further promote the proper use of drug products.
- The PMDA website contains a trial web page entitled "Patient's Report for Adverse Drug Reactions" in order to identify trends in occurrence of adverse drug reactions and collect other information, so that safety measures for drugs will be improved. The web page has a link to the "Relief System for Adverse Health Effects" web page.
- To make the administration of the relief system more transparent, PMDA released the operating performance until the end of September 2014 on the website.

(ii) Improvement of brochures etc.

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

  a) The leaflet for the general public is written in a conversational style instead of one-way statements. The setting used is as follows: First, a patient asks a health care professional, “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, the healthcare professional responds, “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 leaflet for healthcare professionals, it is stated “Please tell patients that a drug product may cause a serious health damage in rare cases even if they use it properly,” 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 leaflets are available on the website for users' convenience.

b) In association with the revised Pharmaceutical Affairs Act dated November 25, 2014, claim forms, including medical certificate, for medical expenses/allowances were revised. The revised forms and instructions are available on the website.

c) PMDA is making efforts to ensure users know that claim forms can be downloaded from the following website, to improve the convenience of users.
http://search.pmda.go.jp/fukusayo_dl/

d) The guidance for claims to be enclosed with claim forms and the checklists for claimants was revised, in accordance with the revision of amounts of payment as of April 1, 2015, 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.

Major activities conducted in FY 2014

(i) As a PR campaign on TV, a 15-second infomercial was aired through 30 nationwide TV stations to familiarize the general public with the relief system in accordance with the "Drugs and Health Week" from October 14 to 27, 2014.

(ii) An advertisement was placed in morning newspapers (5 national papers and 38 regional papers) for one day only in October 2014.

(iii) Web advertisements were placed on the website of Yahoo! Japan using the behavioral targeting advertising[*1] and search advertising[*2] methods for one month from October 17 to November 16, 2014.

(iv) PMDA renewed the home page and other pages of the special website for the relief system using PMDA's original character "Doctor Q."

(v) As transport advertising, digital signage (a still image on an upright LCD screen) that could attract the attention of train commuters was displayed at major stations nationwide for one week from October 20 to 26, 2014.

(vi) Posters were displayed and a commercial was shown on the monitors in 679 dispensing pharmacies nationwide from November 4 to December 3, 2014.

(vii) A 30-second commercial was aired 16 times a day from November 4 to 28 on the Hospital Channel shown on the monitors located in the waiting rooms of hospitals. In addition, PMDA placed an A4-sized leaflet racks in the waiting rooms and distributed 10,000 leaflets.

(viii) An advertisement was placed in 11 medical newspapers/journals for one day only in October 2014.

(ix) In collaboration with medical journals (Nikkei Medical, Nikkei Drug Information), publicity activities were conducted.

(x) PMDA placed a banner advertisement on the special website for nurses (Nurse Senka) for one month from November 1 to 30, 2014.

*1 A method to provide individual Internet users with advertisements that are relevant to their needs and interests based on the services they accessed via a browser or the keywords they entered into a search engine.

*[2] A method of placing online advertisements on web pages that match keywords an Internet user has entered on a search engine. Search advertising is mostly text-type.

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 on 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 this approach, medical institutions and other organizations requested training sessions; therefore PMDA has dispatched its staff members as lecturers to 30 medical institutions, 25 relevant organizations, and one government body to explain the relief system, and sent the PR materials to 159 medical institutions etc.

* Notification issued by Chief of the Office of Drug Induced Damages at General Affairs Division, Pharmaceutical and Food Safety Bureau, MHLW, dated November 29, 2013
"Enhancing public awareness of 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 academic conferences including the 6 occasions below:

- ◆ Booth presentations
  - Annual Meeting of the Japanese Dermatological Association
  - Annual Meeting of the Japanese Society of Pharmaceutical Health Care and Sciences
  - Annual Meeting of the Japanese Society for AIDS Research
- ◆ Distribution of booklets and brochures
  - Annual Meeting of the Japan Neurosurgical Society
  - Annual Meeting of the Molecular Biology Society of Japan
  - Annual Meeting of Japanese Society for Parenteral and Enteral Nutrition

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

PMDA informed 30 government bodies and relevant organizations, etc., of the current level of awareness of the relief system, and requested cooperation in publicity activities.

(iv) Others

At the 16th 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.

Others

(i) PMDA has continued to operate the special website, using its original character "Doctor Q."

(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.
The brochure in PDF format was posted on the PMDA 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 the 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. 319 (December 2014).”

(vi) With cooperation of the Federation of Pharmaceutical Manufacturers' Associations of Japan, PMDA placed 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". The leaflets enclosed in the brochures were distributed to relevant organizations etc.

(viii) Information on the relief systems was provided in a brochure "Useful Information on Medicines" (published by MHLW and the Japan Pharmaceutical Association) in the "Drug and Health Week."

(ix) An advertisement for the Relief System for Sufferers from Adverse Drug Reactions was placed in scientific 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). The advertisement and leaflet has the same design.

(x) PMDA continued to place the banner link to the special web page for the relief system on the home page of the website of the Japan Pharmaceutical Association, to raise the visibility of the banner.

(xi) PMDA inserted the website address of the relief system in the educational material entitled “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.

(xii) PMDA surveyed the level of awareness of the relief system among the general public and healthcare professionals, to understand how well the system is recognized and to make PR activities more effective.
Survey period: February 5 to February 23, 2015.

Home page of the special website

Tie-up with healthcare journals

◆Reproduced from December 2014 issue of Nikkei Medical

独立行政法人 医薬品医療機器総合機構

医薬品副作用被害救済制度を知る。

医薬品は有効性と安全性のバランスの上に成り立っているものであり、万全の注意を払ってもなお副作用の発生を完全に防止することは非常に困難である。副作用による健康被害を受けた患者をサポートするために、ぜひ知っておいていただきたい医薬品副作用被害救済制度について紹介しよう。

医薬品副作用被害救済制度は、医薬品の副作用により健康被害を受けた人々を速やかに救済することを目的に、1980年に設けられた公的制度だ。医療用医薬品や一般用医薬品を適正に使用したにもかかわらず発生した副作用によって入院治療が必要な程度の疾病や、日常生活が著しく制限される程度の障害などの健康被害が救済給付の対象となる。副作用救済給付には、医療費、医療手当、障害年金、障害児養育年金、遺族年金、遺族一時金、葬祭料――の7種類がある。同制度が設立して以来、請求件数は年々増加しており、2013年度は1371件となった（図1）。

適正に使用された場合が対象

救済給付が受けられるのは、医薬品の使用目的や方法が適正であり、入院治療が必要な程度の疾病や日常生活が著しく制限される程度の障害が生じた場合など。2009～2013年度では、5570件の決定のうち85%が支給決定されており、不支給決定は15%（839件）だった。

不支給決定となった理由は、「医薬品により発現したとは認められない（38%）」「使用目的または使用方法が適正とは認められない（29%）」「入院を要する程度または障害の等級に該当しない（16%）」など（別掲記事Q1参照）。このうち、「使用目的または使用方法が適正とは認められない」として不支給だったケースは、添付文書の使用上の注意に従わずに使用した場合などがある（Q2参照）。

書類作成に医師のサポートが必要

給付の支給決定には、まず発現した副作用の症状および経過とその原因と見られる医薬品との因果関係の証明が求められる。そのため、申請には原因薬を処方した医師の投薬証明書や、一般用医薬品の場合は購入した店舗の販売証明書が必要だ。また、副作用による疾患を治療した医師の診断書、さらに医療費・医療手当を請求する場合は、副作用の治療に要した費用を証明する受診証明書も必要となる。申請書類の作成には、医師の協力が不可欠だ。

それらの書類を、健康被害を受けた本人（死亡した場合には、その遺族のうち最優先順位の人）が記入した請求書とともにPMDAに提出する（図2）。請求書や診断書などのフォーマットは、給付の種類によって違うが、いずれもPMDAのホームページからダウンロードできる。

http://www.pmda.go.jp/kenkouhigai/fukusayo_dl/

"出前講座"で制度を知ってもらう

医薬品医療機器総合機構（PMDA）健康被害救済部では、医療関係者向けの"出前講座"を実施している（写真）。医薬品副作用被害救済制度の認知度を高め、請求手続に必要な書類作成に関与してもらうことなど制度利用への「橋渡し」となっていただくことを目的としている。

医療機関や地域の医療関係者の研修会など、講師を派遣し、制度の概要や請求手続、給付事例などを交え、1時間程度の講義を行う。受講した人たちからは、「必要とする患者さんに紹介したい」「万一の場合のために、医療者なら知っておくべき」といった意見が寄せられている。

（図1）救済給付件数、支給額の年次推移

（図2）請求から支給の可否の決定までの流れ

医療関係者に詳しく制度を知ってもらうための"出前講座"。

副作用救済給付の請求についての詳細は、PMDAにご覧ください。

独立行政法人 医薬品医療機器総合機構
救済制度相談窓口
受付時間：月～金（祝日・年末年始を除く）9時～17時
0120-149-931（フリーダイヤル）
http://www.pmda.go.jp/
Eメール：kyufu9@pmda.go.jp

詳しくは 副作用 救済 で 検索

Pharmacy vision; In-hospital vision

Pharmacy vision

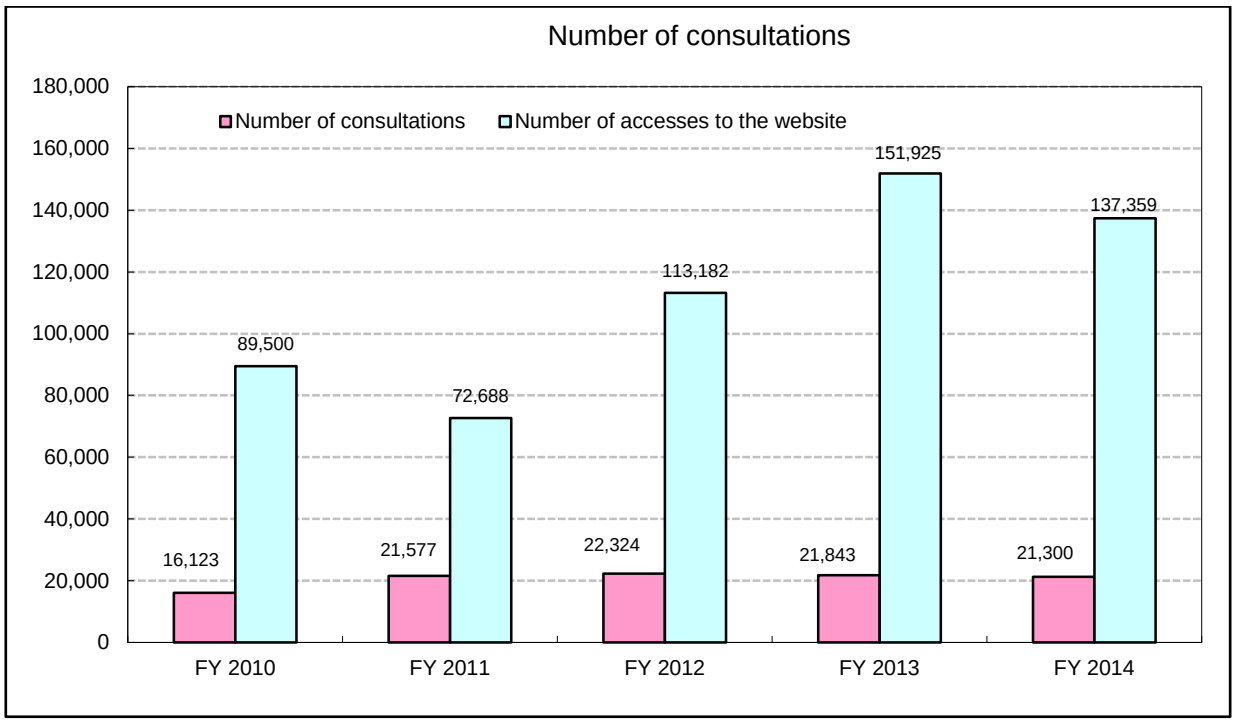
In-hospital vision

Transport advertising (digital signage in train stations)

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

- In FY 2014, the number of consultations at the Relief System Consultation Service was 21,300, with a ratio of 97.5% compared with the previous fiscal year (21,843 consultations).
- In FY 2014, the number of access to the website was 137,359, with a ratio of 90.4% compared with the previous fiscal year (151,925 access).
- The number of access to the web page of the relief system was 54,239, with a ratio of 77.9% compared with the previous fiscal year (69,616 access).
- PMDA tried to keep the people who seek consultation informed of the fact that claim forms can be downloaded from the website.

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	Compared with FY2013
Number of consultations	16,123	21,577	22,324	21,843	21,300	97.5%
Number of access to the website	89,500	72,688	113,182	151,925	137,359	90.4%



<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

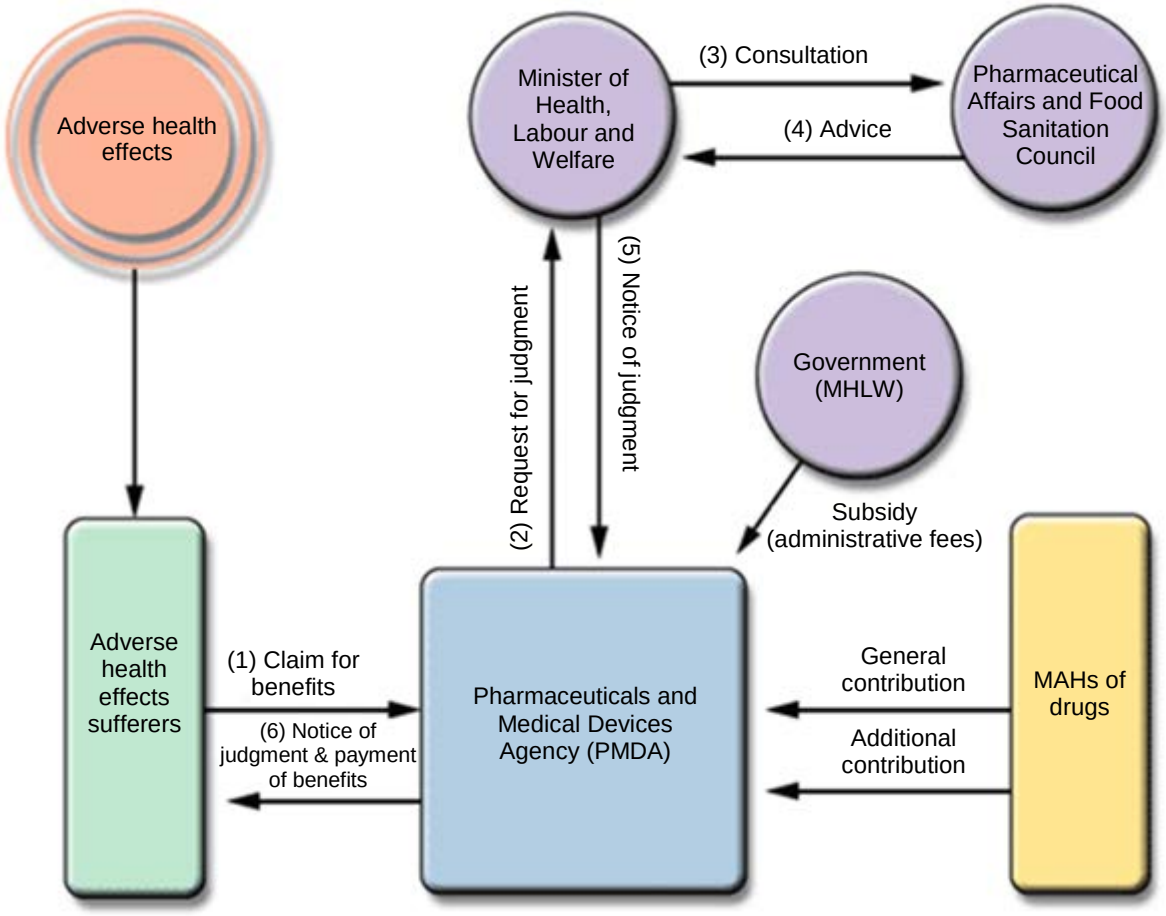
- To optimize the systems for Relief Services for Adverse Health Effects based on the Optimization Plan for Operations and Systems, the function of the relief benefits service system was enhanced, information on relief benefits were stored in a single database (several databases were integrated

into one database) to manage the information in a unified manner, and other measures were taken.

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 request the Minister of the MHLW to review the judgment.

- The Third Mid-term Plan specifies that, although the number of claims are expected to increase, at least 60% of claims that have been filed will be judged (approved or rejected) within 6 months, as before. In FY 2014, PMDA made efforts to judge at least 60% of claims within 6 months of filing.

  The number of claims filed increased from 1,371 in FY 2013 to 1,412 in FY 2014, and the number of claims judged also increased from 1,240 in FY 2013 to 1,400 in FY 2014. Furthermore, the number of claims judged within 6 months of filing was 867, which accounts for 61.9% of all claims filed and exceeds the annual target for FY 2014. This 867 in FY 2014 far exceeds 754 in FY 2013.

(i) Relief Service for Adverse Drug Reactions

PMDA provides 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, when caused by ADRs even though the drugs involved (or cellular and tissue-based products on or after November 25, 2014) were used properly.

a. Performance of Relief Service for Adverse Drug Reactions

The performance for FY 2014 is shown below.

Fiscal Year			FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of claims filed			1,018	1,075	1,280	1,371	1,412
Number of claims judged			1,021	1,103	1,216	1,240	1,400
	Approved		897	959	997	1,007	1,204
	Rejected		122	143	215	232	192
	Withdrawn		2	1	4	1	4
	Within 6 months	Number of claims	434	534	553	754	867
		Achievement rate[*1]	42.5%	48.4%	45.5%	60.8%	61.9%
Claims in progress[*2]			743	715	779	910	922
Median processing time [months]			6.4	6.1	6.2	5.8	5.7

*[*1] The percentages of the claims judged within 6 months of filing out of the total number of claims judged in each fiscal year.*

*[*2] The numbers of claims in progress at the end of each fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2014 by type of benefit are shown below.

Fiscal Year		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of claims filed		1,018	1,075	1,280	1,371	1,412
Types of benefit	Medical expenses	854	909	1,101	1,200	1,221
	Medical allowances	911	964	1,168	1,252	1,290
	Disability pensions	74	77	83	88	95
	Pensions for raising handicapped children	4	4	1	7	12
	Bereaved family pensions	46	47	46	49	41
	Lump-sum benefits for bereaved families	54	63	53	54	65
	Funeral expenses	100	107	98	105	103

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 2014 by type of benefit are shown below.

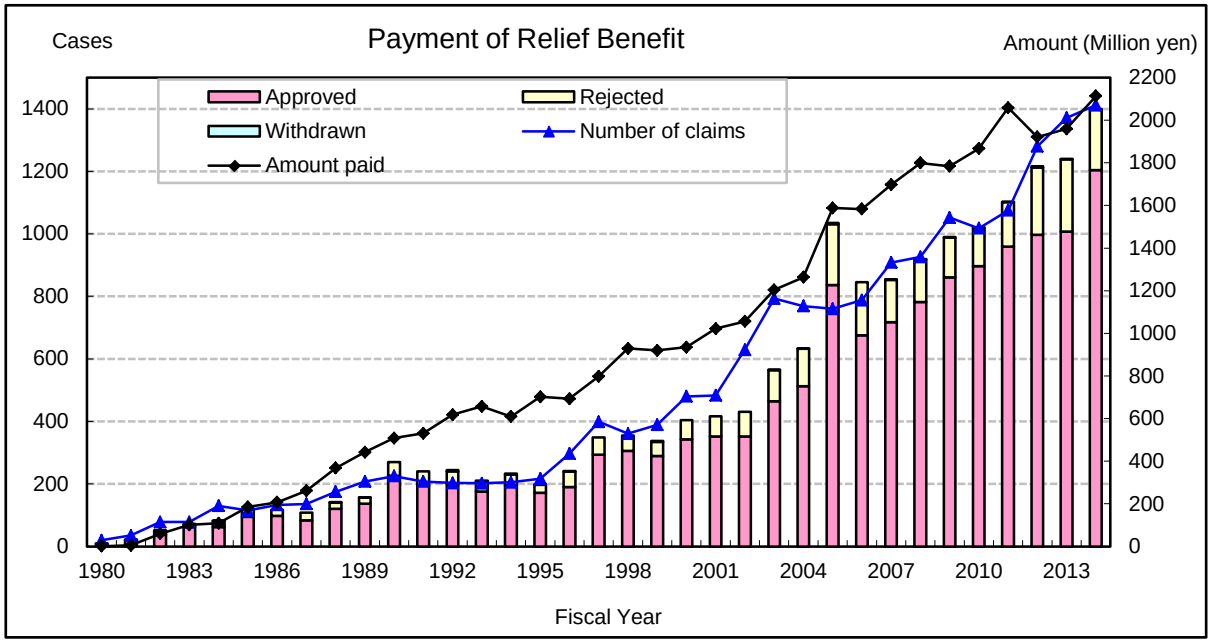
(Unit: Thousand yen)

Type	FY 2010		FY 2011		FY 2012	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	803	87,475	836	93,284	892	97,905
Medical allowances	837	71,142	895	75,198	947	75,326
Disability pensions	38	853,854	28	881,885	28	861,595
Pensions for raising handicapped children	5	44,210	6	49,906	0	43,744
Bereaved family pensions	31	583,501	35	614,318	32	602,068
Lump-sum benefits for bereaved families	29	214,081	47	328,093	32	227,696
Funeral expenses	63	12,927	80	16,006	62	12,438
Total	1,806	1,867,190	1,927	2,058,389	1,993	1,920,771

Type	FY 2013		FY 2014	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	886	95,025	1,108	123,987
Medical allowances	945	82,730	1,151	95,457
Disability pensions	39	905,233	37	943,939
Pensions for raising handicapped children	3	40,785	2	38,965
Bereaved family pensions	31	603,130	31	585,626
Lump-sum benefits for bereaved families	32	220,032	45	310,806
Funeral expenses	59	12,249	72	14,507
Total	1,995	1,959,184	2,446	2,113,286

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 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, when caused by infections even though the biological products involved (or cellular and tissue-based products on or after November 25, 2014) were used properly.

a. Performance of relief for infections

The performance for FY 2014 is shown below

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of claims filed	6	9	4	7	3
Number of claims judged	7	7	6	4	7
Approved	6	3	4	4	6
Rejected	1	4	2	0	1
Withdrawn	0	0	0	0	0
Claims in progress[*1]	2	4	2	5	1
Achievement rate[*2]	42.9%	100.0%	83.3%	100.0%	42.9%
Median processing time [months]	6.9	4.4	4.7	4.3	6.3

*[*1] Claims not judged at the end of each fiscal year.*

*[*2] The percentages of the claims judged within 6 months of filing out of the total number of claims judged during the fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2014 by type of benefit are shown below.

Fiscal Year		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of claims		6	9	4	7	3
Types of benefit	Medical expenses	5	6	2	6	2
	Medical allowances	5	8	4	7	3
	Disability pensions	1	0	0	0	0
	Pensions for raising handicapped children	0	1	0	0	0
	Bereaved family pensions	0	0	0	0	1
	Lump-sum benefits for bereaved families	1	0	0	1	1
	Funeral expenses	1	0	0	1	2

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 2014 by type of benefit are shown below.

(Unit: Thousand yen)

Type	FY 2010		FY 2011		FY 2012		FY 2013		FY 2014	
	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	5	425	3	213	2	83	3	258	5	336
Medical allowances	5	384	3	282	4	282	4	356	6	566
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,378	–	2,370	–	2,362	–	2,353	–	2,338
Lump-sum benefits for bereaved families	1	7,160	–	–	–	–	–	–	–	–
Funeral expenses	1	193	–	–	–	–	–	–	–	–
Total	12	10,540	6	2,865	6	2,726	7	2,967	11	3,239

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 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 by e-mail service named as "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 the 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 2014, PMDA summarized the operating performance for FY 2013, prepared an investigative research report, and conducted an investigative research in 83 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 (83 volunteers in FY 2014).

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 health problems 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 Problems 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 health care and on the use of welfare services to persons suffering from adverse health effects caused by adverse reactions to drugs, etc. or infections acquired through biological products, etc., and their families. In FY 2014, 44 consultations were performed.

(iii) Distribution of the benefit recipient card

For beneficiaries of adverse reaction relief benefits, in January 2010, PMDA started a service to issue a handy, credit-card sized certificate 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 2014, the card was issued to 657 persons.

(iv) Investigative research for improvements in the 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 the 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 2014, PMDA summarized the operating performance for FY 2013, prepared an investigative research report, and conducted research in 159 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 (159 volunteers in FY 2014).

Research Team

Team Leader: Kugahisa Teshima, Director, Graduate School of Social Service Management, 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

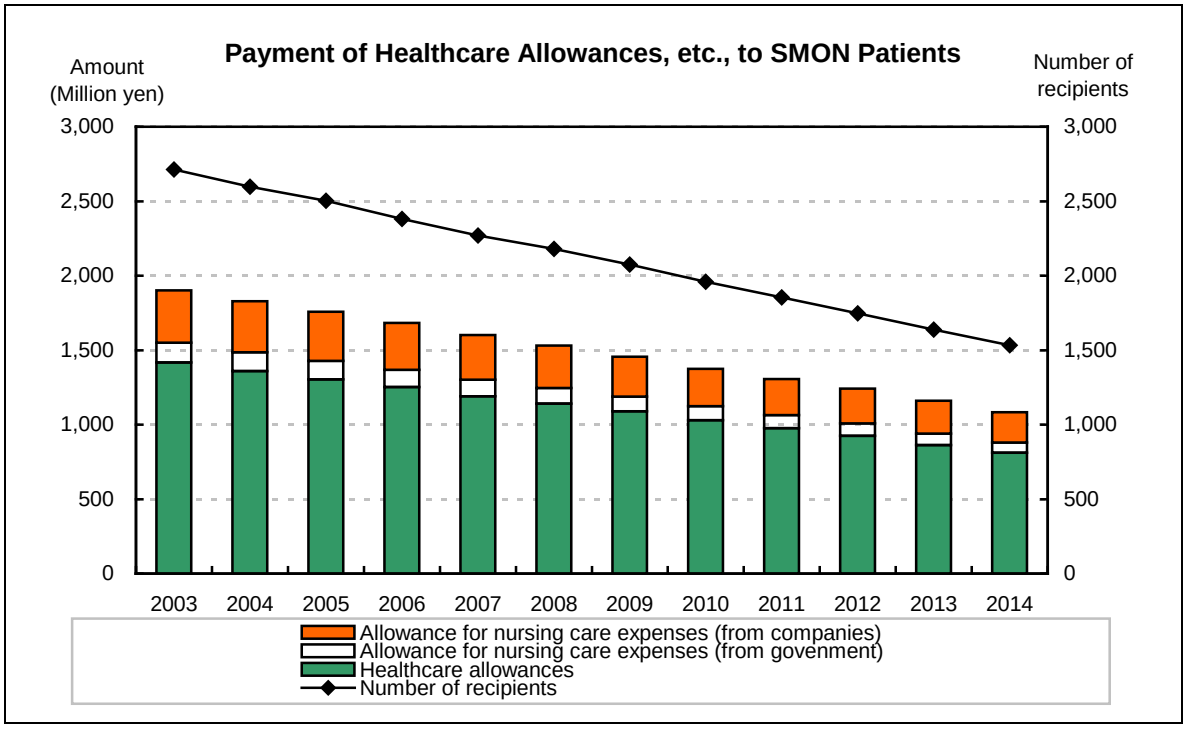
- PMDA appropriately provided healthcare allowances etc., to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

(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 2014, the number of patients receiving such allowances was 1,533, and the total amount paid in FY 2014 was 1,083 million yen.

Fiscal Year		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of recipients		1,960	1,855	1,748	1,639	1,533
Amount paid (thousand yen)		1,375,622	1,306,329	1,241,368	1,160,994	1,082,992
Break down	Healthcare allowances	1,031,376	975,567	924,669	864,462	811,727
	Allowance for nursing care expenses (from companies)	250,946	241,890	233,050	219,630	201,919
	Allowance for nursing care expenses (from government)	93,300	88,872	83,650	76,902	69,346

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)

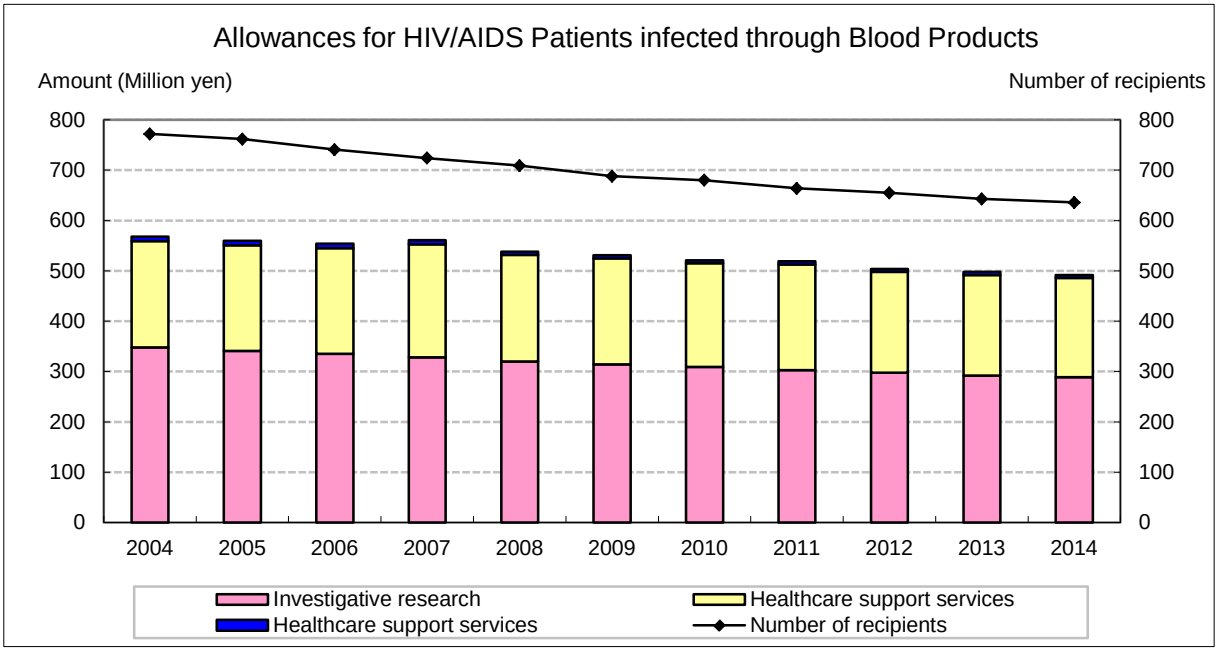
- PMDA provides allowances relating to the following 3 services for HIV-positive patients affected through blood products under commission of the relevant organization. In FY 2014, 524 HIV-positive patients received allowances relating to the investigative research, 110 AIDS patients received allowances 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 636, and the total amount paid in FY 2014 was 492 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 2010		FY 2011		FY 2012	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	562	309,355	547	302,763	540	297,790
Healthcare support services	116	206,100	115	210,000	112	199,500
Special allowance	2	6,300	2	6,276	3	6,362
Grand Total	680	521,755	864	519,039	655	503,652

Fiscal Year	FY 2013		FY 2014	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	529	292,349	524	288,736
Healthcare support services	112	199,650	110	197,400
Special allowance	2	6,232	2	6,190
Grand Total	643	498,230	636	492,325

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.



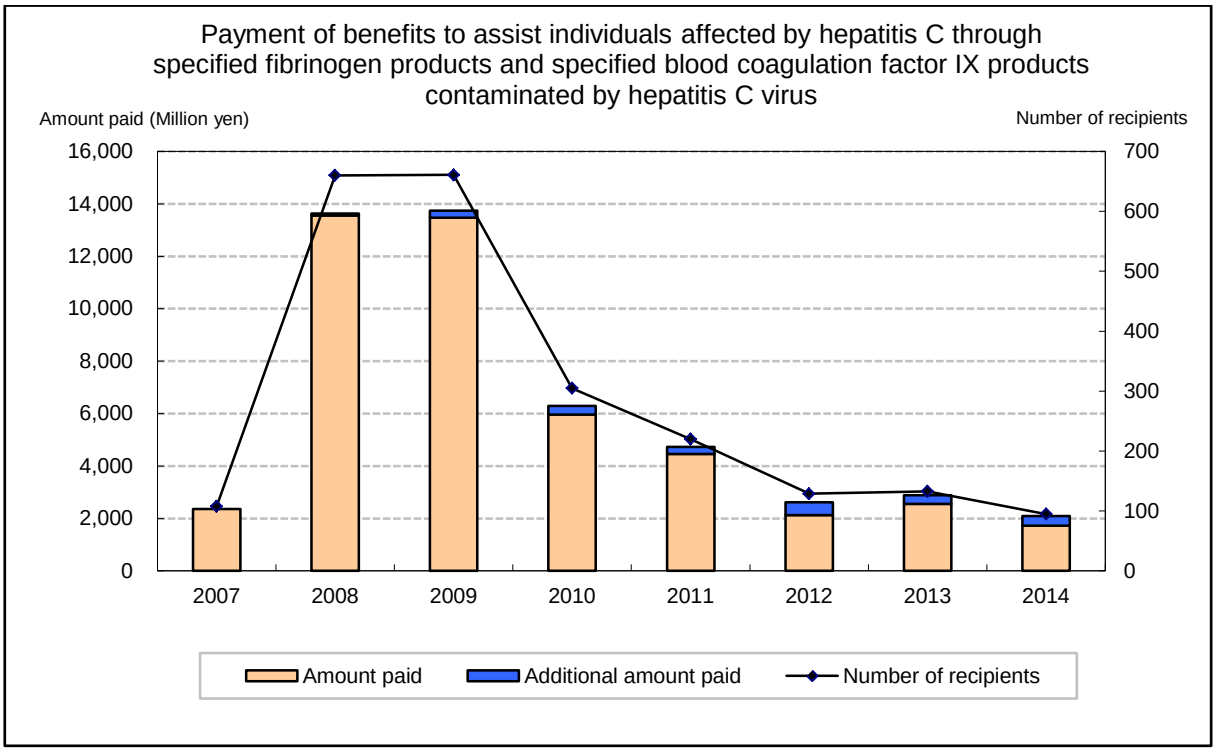
3.1.(9) Appropriate provision of the payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus

- 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 95, with 2,100 million yen as the total amount paid in FY 2014.

* 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 15, 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	FY 2014
Number of recipients	220	129	133	95
(Of which: number of recipients of additional payment)	(20)	(28)	(18)	(20)
Amount paid (thousand yen)	4,732,000	2,624,000	2,888,000	2,100,000
(Of which: amount of additional payment)	(268,000)	(488,000)	(332,000)	(368,000)
Number of consultations	674	982	473	660



3.2. Reviews and Related Services

Based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14, 2013), Healthcare and Medical Strategy (adopted by the Cabinet on July 22, 2014), the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Act), and Act on the Safety of Regenerative Medicine, etc., PMDA took the following actions in order to accelerate the review process, achieve "zero" review lag*, and upgrade the quality of reviews by investigating drugs, medical devices, and cellular and tissue-based products according to their respective characteristics, as well as to enhance pharmaceutical affairs consultations on R&D strategy with the aim of eliminating development lag*.

* Drug lag and device lag are roughly classified into two types of lags: "review lag," caused by the difference in the review period from application to approval) between the US and Japan; and "development lag," caused by the difference in time which medical companies apply to regulatory agencies in the US and Japan (quoted from the "Japan Revitalization Strategy"). Resolution of the issues associated with review lag and development lag will lead to the elimination of the overall lag in the approval process.

To deal with products using advanced science and technologies in a more appropriate 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 (reorganized and renamed the Science Board Management Office in FY 2014), were established in FY 2012. In FY 2014, 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 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 “Japan Revitalization Strategy - JAPAN is BACK-” and “Healthcare and Medical Strategy,” etc.

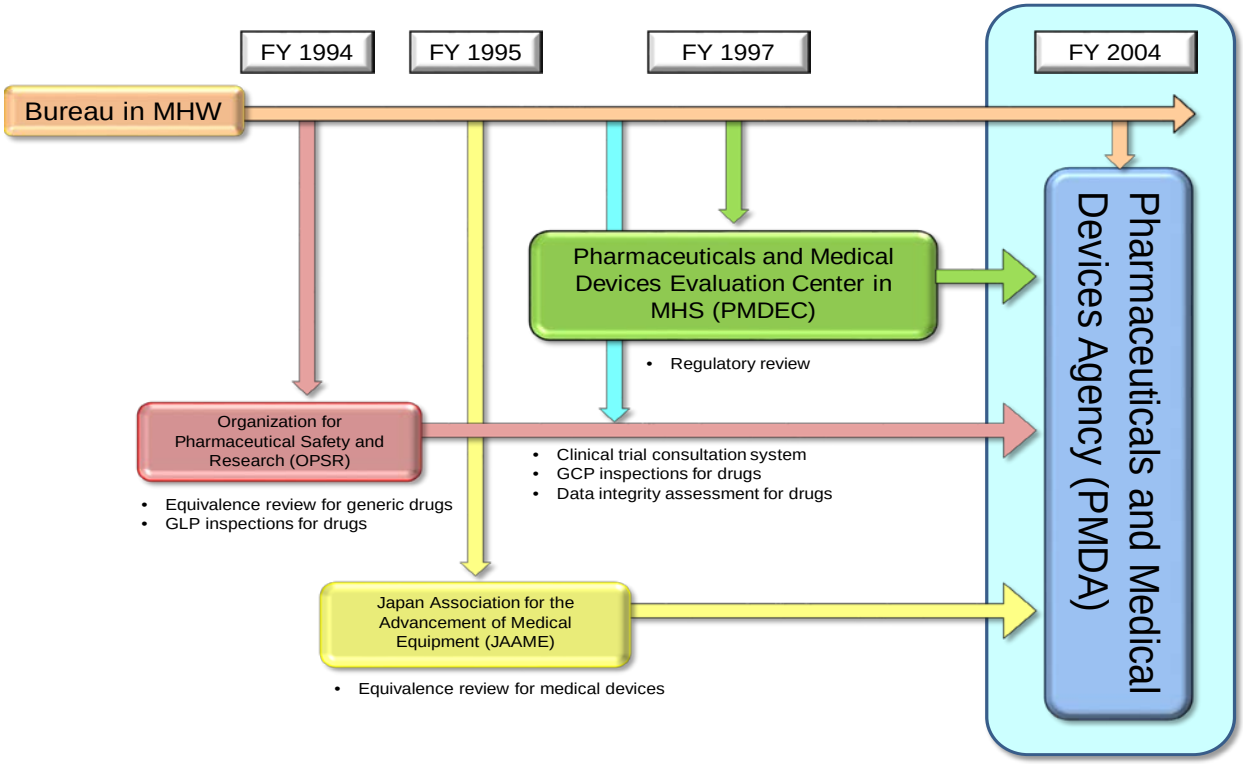
(i) Appropriate and prompt reviews

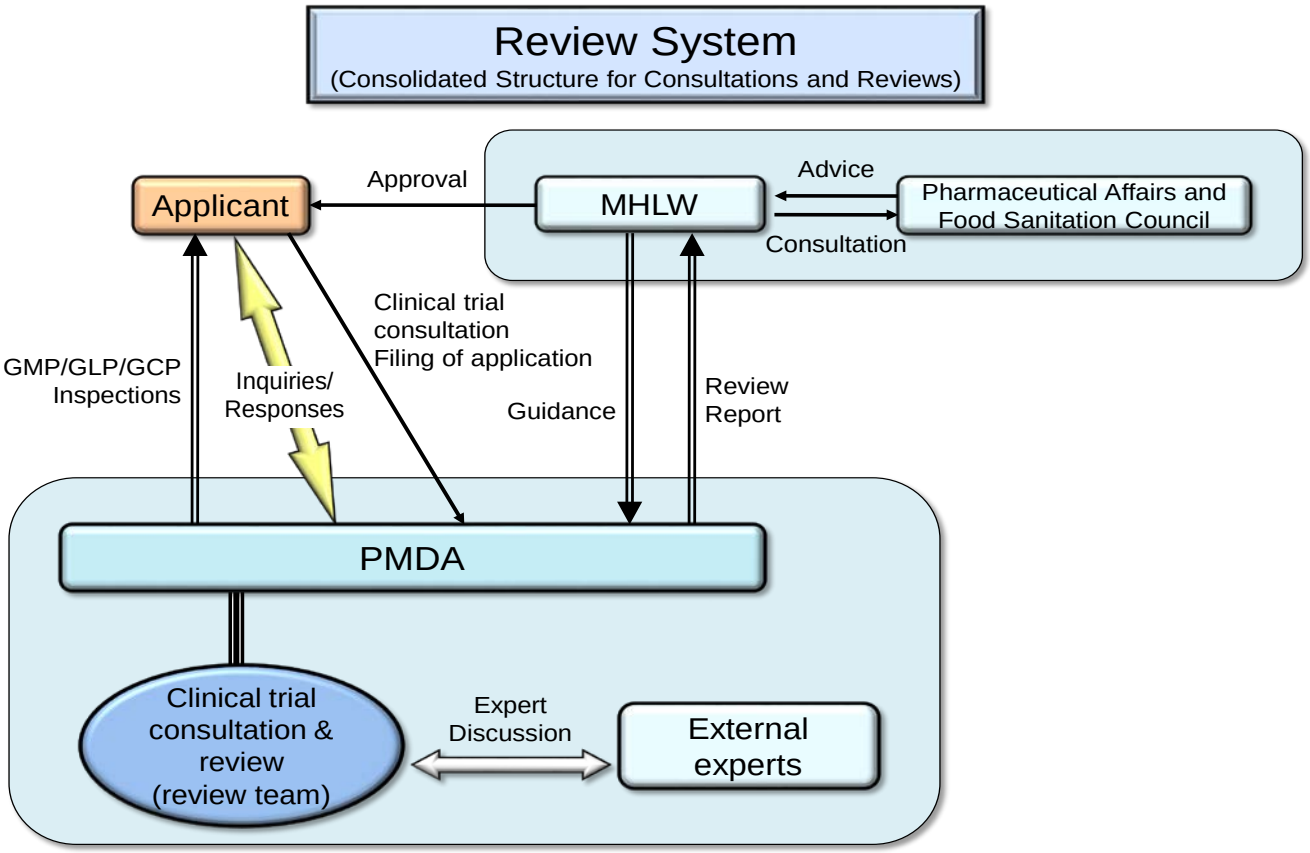
a. Structure for clinical trial consultations and reviews

- The review system for drugs and medical devices, etc. 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, etc. was left to the Ministry of Health, Labour and Welfare (MHLW). Further improvements in the review system were made by taking the following measures:

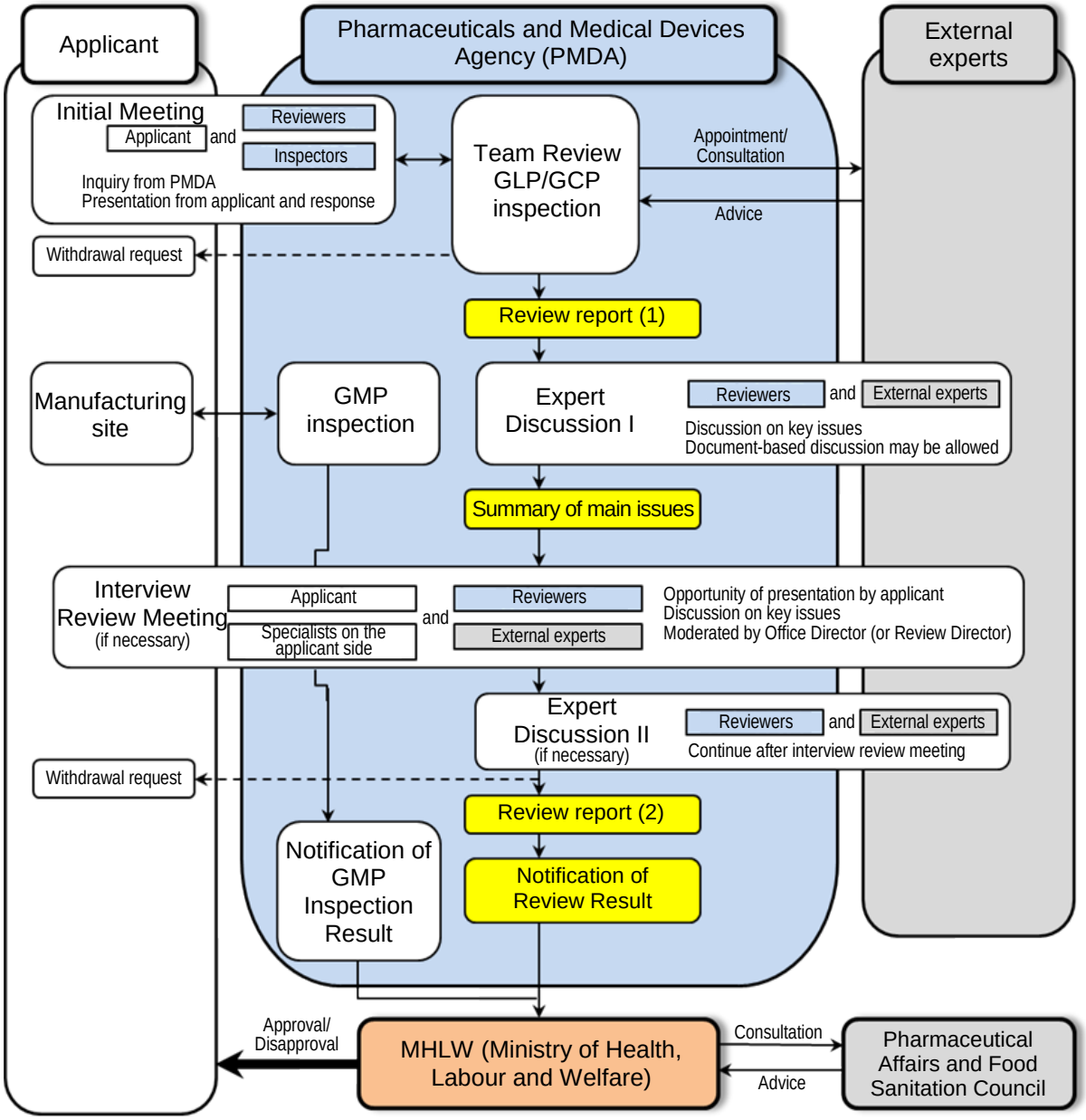
  1) In order to ensure the consistency and efficiency, the roles of three review-related agencies were re-examined thoroughly, and integrated into one agency as "incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency."
  2) Substantial increase in the number of staff including 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

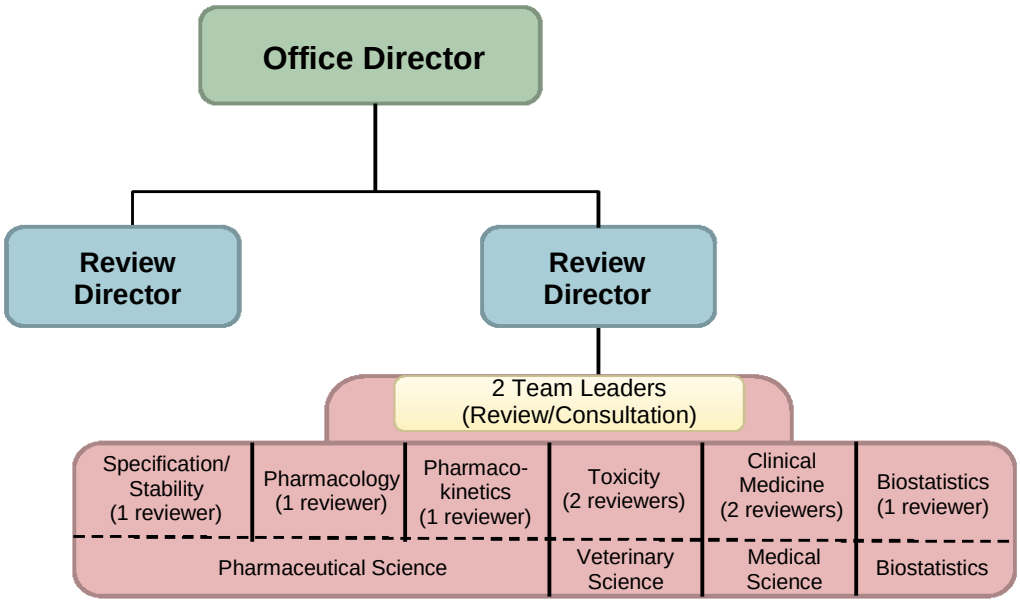


Review Performance for FY 2014 (drugs)

(1) Number of Expert Discussions conducted: 211 (151 document-based discussions, 60 meetings)
(2) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 80
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	Cell/tissue-processed products
	Gene therapy products	Gene therapy products among cellular and tissue-based products, Cartagena
	Bio-CMC	Quality of biologics, biosimilars
	Biological devices (quality)	Biological devices (quality)
Office of Vaccines and Blood Products	Vaccines	Vaccines (only those to be used for prevention of infection), 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 2014. 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 2014.)

  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. If reviewing a new drug application is difficult, review-related issues including reasons for the difficulty and the possibility of approving the drug are to be provided in writing to the applicant in accordance with the “Handling of New Drug Application and Total Review Time to Improve the Predictability of New Drug Approvals” (PFSB/ELD Notification No. 1006-1 and PFSB/CND Notification No. 1006-1 dated October 6, 2014), in order to increase the transparency of the review process.

c. Standardization of review

- To clarify 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, which provides basic considerations for review. The document is posted on the PMDA website. In addition, review times for priority review products and standard review products were presented for each review process in “Timeline in the Standard Process of New Drug Application” (PFSB/ELD/MHLW Administrative Notice dated January 30, 2015). This document is also 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 request 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 offers 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 the approval status at FDA and EMA,

and collected/organized evidence information etc., and then expanded the unapproved drug database to compare the approval status between Japan and the US or Europe. Of drugs with a new active ingredient approved by FDA or EMA in or after April 2009, 113 (FDA) and 84 (EMA) have not been approved in Japan as of March 2015. The list of the unapproved drugs is available on the PMDA website.

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.

  To further secure the consistency of clinical trial consultations etc., efforts to provide feedback information on previous clinical trial consultations were continued in FY 2014.

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 designated 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 2014, 86 products underwent re-examination; 139 products underwent re-evaluation for drug efficacy; and no product underwent re-evaluation for quality. Re-evaluation for drug efficacy had been completed for traditional Chinese medicines, non-steroidal anti-inflammatory agents, and antimetabolites by the end of FY 2014.

  Concerning products for which applications for re-examination are filed in or after FY 2014, PMDA is aiming to complete re-examination within 18 months (median) by FY 2018. For 102 products for which applications were filed in FY 2014, no notice of re-examination results was issued in FY 2014.

Number of Re-examinations/Re-evaluations Conducted

		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Products that underwent re-examination		115	81	50	121	86
Re-evaluations	Products that underwent re-evaluation for drug efficacy	0	0	0	0	139
	Products that underwent re-evaluation for quality	53	0	0	0	0

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

g. Development of the Japanese Pharmacopoeia

- In FY 2014, the Japanese Pharmacopoeia (JP) Draft Committee held a total of 79 meetings, and posted information on the PMDA website to seek public comments regarding 238 official monographs (56 new articles, 174 amendments, 8 deletions), 37 general tests (16 new tests, 19 amendments, 2 deletions), 9 ultraviolet-visible reference spectra, 15 infrared reference spectra, amendments to other General Notices, and partial revision of the General Rules for Preparations as a draft of the 17th edition of the Japanese Pharmacopoeia.

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

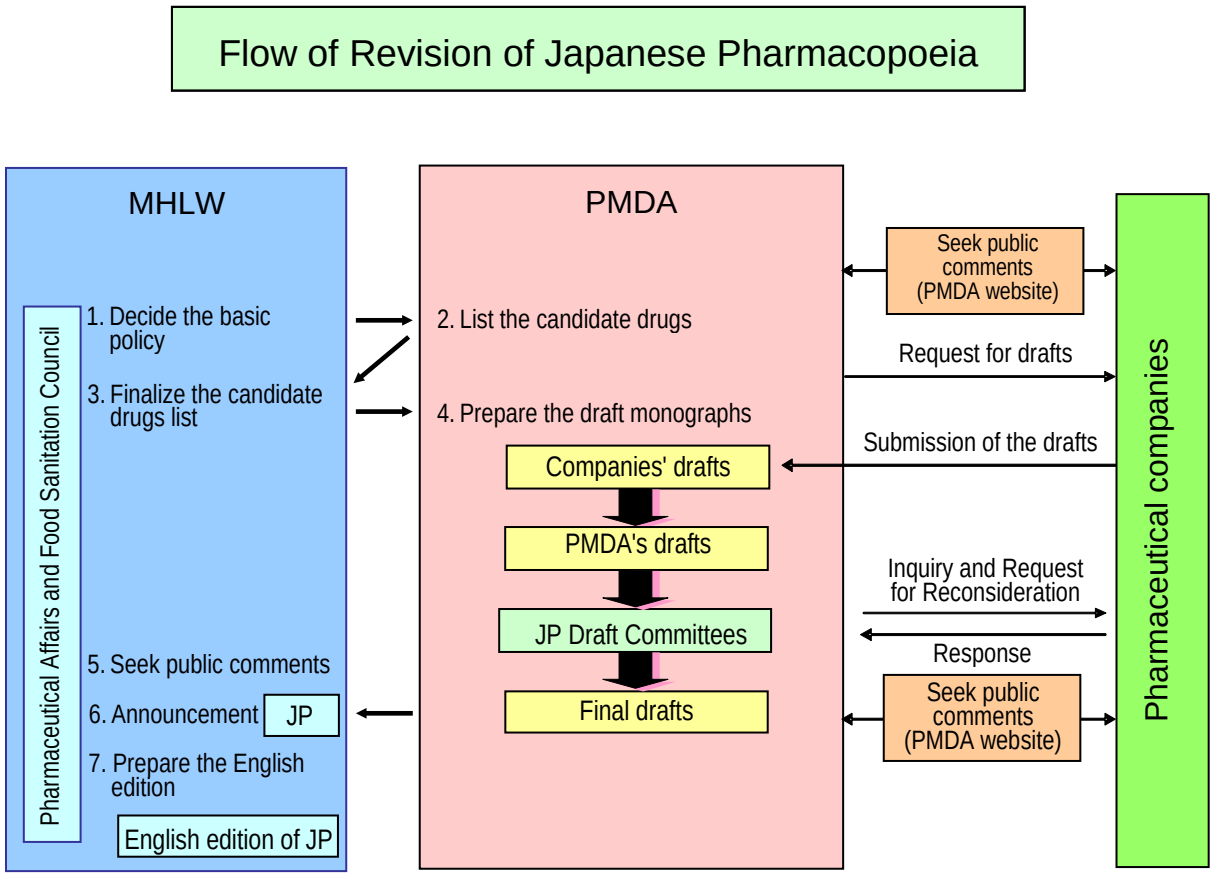
Month and year reported	Mar. FY 2007	Nov. FY 2008	Mar. FY 2009	Aug. FY 2009	Aug. FY 2010	Mar. FY 2012	Jan. FY 2013	Sep. FY 2013
New monographs	90	1	106	-	106	77	0	60
Amendments	171	1	122	2	330	176	1	172

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. The next draft to be reported is for the 17th edition of the Japanese Pharmacopoeia, and no draft was reported in FY 2015.

Ministerial Announcement on the Japanese Pharmacopoeia 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/english/rs-sb-std/standards-development/jp/0009.html)



h. Implementation of a workshop on the master file

- A pre-application checklist of application forms for master file registration was prepared and posted on the PMDA website, so that drug substance manufacturers, in-country representatives, MAHs, etc., would become familiar with overall pharmaceutical regulations including the master file registration system. In addition, one workshop was held to explain how to use the checklist, how to fill out the application forms, and how to respond to inquiries by PMDA after 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 2014, the request forms were separately received for consultations to be conducted in the first half and the second half of the fiscal year. PMDA made efforts to establish a consultation system to offer consultations upon request as much as possible. Consultations provided are broken down by review category, as follows.

  Review Category 2, 2 products (number of consultation categories, 7; the same applies hereinafter); Review Category 3-1, 3 products (16); Review Category 4, 2 products (5); Oncology drugs, 1 product (3); Vaccine, 1 product (1)

  (* 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. 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 2014, RMPs for 81 products were made public.

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

- The Advanced Review with Electronic Data Promotion Group (it was called Task Force for Advanced Review and Consultation with Electronic Data until the end of FY 2013) was set up in April, 2014 to consider issues related to the establishment of the system for advanced review and consultation with electronic data. The purposes of the system is to reduce the burden on applicants and improve the quality of reviews and consultations by electronically accumulating application data, analyzing the data using advanced methods, and utilizing the data.

  Toward the establishment of the system for advanced review and consultation with electronic data, PMDA continued to exchange opinions with the pharmaceutical industry regarding various issues, and cooperated on the issuance of "Basic Principles on Electronic Submission of Study Data for New Drug Applications" (PFSB/ELD Notification No. 0620-6 dated June 20, 2014) and Question and Answer Guide Regarding "Basic Principles on Electronic Submission of Study Data for New Drug Applications" (PFSB/ELD Administrative Notice dated June 20, 2014) based on the discussion with relevant industries and foreign regulatory authorities.
- A system developer was appointed in September 2015 to build and maintain the Electronic Application Data System, which allows companies to submit electronic data, stores submitted electronic data in PMDA, and performs statistical analysis processing.

  As in the previous fiscal year, a pilot program for the system was performed to receive electronic clinical study data on a trial basis, analyze the data, and investigate how to utilize the data in review process.
- The relevant personnel of PMDA were encouraged to participate in workshops held in and outside of PMDA about electronic data and usage of software to upgrade their skills.

(iii) Approaches to achieving "zero" review lag for drugs

- The targets for the total review time (from the application date to the approval date) for drugs for which applications were submitted on or after April 1, 2004, and approved in each fiscal year are 9 months for priority review products and 12 months for standard review products. PMDA aims to gradually increase the percentiles of products for which the targets are achieved to 80% by FY 2018. The regulatory authorities have been making efforts to achieve these targets while asking applicants for their cooperation.
- New drug applications (for drugs that are clearly different from approved drugs in terms of active ingredients, contents, administration, dosage, indications, efficacy, etc.) 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 2014 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")

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	9	9	9	9	9
Percentile	60	60	70	70	80

Results

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	60
Total review time [months] (Reference, 80th percentile) [months]	9.2 (12.6)	6.5 (9.2)	6.1 (9.0)	7.2 (9.1)	8.8 (9.2)
Number of approved applications	20	50	53	42	44

Reference

Regulatory review time [months]	4.9	4.2	3.8	3.6	4.0
Applicant's time [months]	3.4	2.0	1.5	3.8	5.0

Note 1:Products covered were those for which applications were filed in or after April 2004. The number of approved applications is based on active ingredients. For details, refer to the list of approved products included in the III SUPPLEMENTARY INFORMATION

Note 2: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

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	60
Total review time [months] (Reference, 80th percentile) [months]	12.0 (13.2)	9.2 (10.7)	9.0 (10.0)	8.0 (9.9)	8.9 (9.2)
Regulatory review time [months]	5.3	4.1	3.4	3.4	3.8
Applicant's time [months]	6.0	5.0	4.6	4.1	5.2
Number of approved applications	13	18	25	31	37

- 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 2014, 44 priority review products (including 7 public knowledge-based applications for the "Study Group on Unapproved and Off-label Drugs of High Medical Need") were approved.

- In FY 2014, 6 applications requesting priority reviews were submitted for drugs regarded as having particularly high medical needs, and 7 applications (including 1 application submitted in FY 2013) were judged as “applicable” and no applications were judged as “not applicable.”
- For priority review products approved in FY 2014, the total review time (60th percentile) was 8.8 months, achieving the target review time.

  The priority review products accounted for 38% of products approved in FY 2014, showing an increase from 30% in FY 2013.

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	12	12	12	12	12
Percentile	60	70	70	80	80

Results

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	60
Total review time [months] (Reference, 80th percentile) [months]	14.7 (22.7)	11.5 (15.7)	10.3 (11.9)	11.3 (12.3)	11.9 (12.3)
Number of approved applications	92	80	81	96	73

Reference

Regulatory review time [months]	7.6	6.3	5.7	6.7	6.8
Applicant’s time [months]	6.4	5.1	4.2	4.6	5.4

Note: Products covered were those for which applications were filed in or after April 2004. The number of cases is based on active ingredients. For details, refer to the list of approved products included in the III SUPPLEMENTARY INFORMATION

- For standard review products approved in FY 2014, the total review time was 11.9 months, achieving the target time.
- The number of applications under review at the end of FY 2014 was 105 (including 19 applications for orphan drugs and 5 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	109 (1)	0	29	2 [-1]
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	77 (1)	0	4	0 [-1]
FY 2009	106	87	1	18	0
FY 2010	116	105	0	11	0
FY 2011	130	128	0	2	0
FY 2012	140	135 (5)	0	5 (1)	0 [-5]
FY 2013	123	117 (81)	0	3 (3)	3 [-84]
FY 2014	130	30 (30)	0	0	100 [100]
Total	1,304	1,087 (118)	1	111 (4)	105 [9]

Note 1: Values in parentheses indicate those processed in FY 2014 (included in values on their left).
Note 2: Values in brackets [] indicate difference from the status reported in FY 2013.

(iv) 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 the following documents: "Basic Principles on Global Clinical Trials" (PFSB/ELD Notification dated September 28, 2007), “Basic Principles on Global Clinical Trials (Reference Cases)” (PFSB/ELD Administrative Notice dated September 5, 2012), and “*Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials*” (PFSB/ELD Administrative Notice dated October 27, 2014), which clarify basic concepts when conducting global clinical trials.

  Of 601 clinical trial notifications submitted in FY 2014, 178 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of notifications	134	121	130	169	178

- PMDA intends to take an active approach to global clinical trials. In FY 2014, PMDA carried out 67 consultations on global clinical trials for drugs with new active ingredients, meeting all the requests for consultations.

Number of Consultations on Global Clinical Trials with New Active Ingredients

Fiscal Year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Number of consultations	66	73	64	59	67

PMDA supported the efforts to promote global clinical trials in Asia based on the Multi Regional Clinical Trial Roadmap led by MHLW at APEC RHSC, and made a contribution in specialized fields by participating in the MRCT/GCP Inspection Workshop (in Qingdao in May) and the Steering Committee Meeting (in Beijing in August) as a champion of the roadmap project. Also, PMDA was appointed co-chair of the next RHSC meeting.

(v) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- In FY 2014, there were no requests for designation for priority consultations of drugs that are considered to have particularly high medical need. PMDA conducted no 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

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	390	447	387	354	411
Withdrawn	44	30	20	30	38
Total (conducted and withdrawn)	434	477	407	384	449

Number of Prior Assessment Consultations for Drugs

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	30	33	19	32	32
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	30	33	19	32	32

Number of Consultations on Pharmacogenomics/Biomarkers

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	1	1	0	0	0
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	1	1	0	0	0

Number of Consultations on Drug Product Eligibility for Priority Review

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	–	2	7	10	6
Withdrawn	–	0	0	0	0
Total (conducted and withdrawn)	–	2	7	10	6

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 2014, PMDA conducted a total of 411 consultations (including 38 withdrawals).
- To respond to 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 2014, PMDA provided a total of 373 consultations (including 38 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 2014, the target was achieved in 357 (98.3%) of 363 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 2014

Review category	Results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs etc.)	5	4	4	6	7	2	3	2	4	3	4	5	49
Category 6-2 (Hormone drugs)	3	1	3	4	2	1	2	0	1	2	4	2	25
Category 2 (Cardiovascular drugs)	5	1	4	7	2	7	2	4	7	3	2	2	46
Category 5 (Drugs for the urogenital system etc.)	4	2	2	1	0	0	0	1	4	0	4	1	19
Radiopharmaceuticals	1	0	0	0	0	0	0	0	0	2	0	0	3
In vivo diagnostics	1	0	0	1	0	0	1	0	1	0	0	0	4
Category 3-1 (Central nervous system drugs etc.)	3	3	6	10	2	8	6	0	4	2	1	7	52
Category 3-2 (Anesthetic drugs etc.)	1	2	1	4	0	2	1	4	1	1	2	3	22
Category 4 (Antibacterial agents etc.)	3	3	2	1	6	1	0	2	4	1	1	0	24
Category 6-1 (Respiratory tract drugs etc.)	3	2	2	1	4	4	6	6	2	5	2	3	40
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	1	1
Oncology drugs	10	2	7	7	3	4	4	6	13	3	4	8	71
Cellular and tissue-based products	0	0	1	1	0	2	1	0	0	0	-	-	5
Bio-CMC	1	4	4	1	1	4	3	3	2	1	2	1	27
Vaccines	1	1	2	2	1	2	0	1	0	0	0	4	14
Blood products	1	0	1	0	1	1	1	1	0	1	0	1	8
Generic drugs	0	0	0	0	0	0	1	0	0	0	0	0	1
[Re-listed] Prior assessment	2	0	0	6	6	11	0	3	0	0	0	4	32
[Re-listed] Drug product eligibility for priority review	0	2	0	1	0	0	0	0	0	1	1	1	6
Pharmacogenomics/biomarkers	0	0	0	0	0	0	0	0	0	0	0	0	0
GLP/GCP/GPSP compliance inspection	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	42	25	39	46	29	38	31	30	43	24	26	38	411
Withdrawal	3	3	5	7	0	2	2	2	3	3	3	5	38
Grand Total	45	28	44	53	29	40	33	32	46	27	29	43	449

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

Note 2: Consultations on cellular and tissue-based products for which applications were received on or after November 25, 2014 were counted as consultations belonging to the category of cellular and tissue-based products in the above table.

Note 3: 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 4: 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 5: Consultations on pharmacogenomics/biomarkers were conducted by the Omics Project Team.

Note 6: Consultations on GLP/GCP/GPSP compliance inspection were all conducted by the Office of Conformity Audit or Office of Manufacturing/Quality and Compliance, regardless of category.

d. Reclassification of consultation categories and their uses

- PMDA exchanged opinions with the relevant industries on clinical trial consultations and Pharmaceutical Affairs Consultations on R&D Strategy. As a result, PMDA started to offer a post-consultation meeting, in which PMDA provides advice on issues raised at a consultation within a rage requiring no additional data evaluation; what has been agreed in the meeting shall be

recorded in the minutes. Also, PMDA revised other consultation services and started providing such revised services in November 2014, including the provision of advice on plans for post-marketing clinical studies or use-results surveys and the expansion of consultation items covering evaluation for the review of approval conditions.

Taking into account requests from relevant industries, PMDA has completed detailed investigation of establishing a consultation service to assess the eligibility for minor change notifications based on data evaluation and another consultation service to evaluate application data for Sakigake designation products selected by MHLW for priority review.

(vi) Promotion of evaluation of new technologies

a. Utilization of external experts

- As PMDA is required to raise the expertise in the 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, 2015, the number of commissioned experts is 1,304 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2014 was 211 (151 through document-based discussions; 60 through meetings).

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

- PMDA integrated information on clinical trial consultations and reviews for nanomedicines and companion diagnostics through cross-sectional projects in order to maintain the uniformity of measures for nanomedicines and companion diagnostics, and used the comments made by external experts in the Expert Discussions for reviewing the applications of 3 products with companion diagnostics. The members of the Companion Diagnostics Working Group exchanged opinions with external experts on the development of genetic diagnosis technologies using next-generation DNA sequencers.

- PMDA has dispatched personnel to iPS cell research institutes such as the Center for iPS Cell Research and Application (CiRA) of Kyoto University through programs to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products and thereby collects the latest information in order to respond to the need to put innovative drugs and cellular and tissue-based products into clinical use.

b. Support for the development of national guidelines

- PMDA participated in the examination in a research project supported by Health and Labour Sciences Research Grants (Research on global health issues), which is titled "Research on Methods for Evaluating Quality, Efficacy, etc., of Travelers' Vaccines" 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 (Research on global health issues), 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. (In this research, “next-generation vaccines” are defined as vaccines developed using novel adjuvants such as nucleic acid adjuvants or genetic engineering technologies.)

- The team of the global clinical study project discussed an approach to the necessity of conducting a phase I clinical trial of an investigational product in the Japanese population before participating in a phase II or III global clinical trial, sorting out cases for reference. The project team cooperated in preparing “Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials" (PFSB/ELD Administrative Notice dated October 27, 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 “Items to Be Entered in the Manufacturing Method Section of the Application Form for Marketing Approval for Drugs and Quasi-Drugs Containing at least Three Active Ingredients” (PFSB/ELD Notification No. 0530-8 dated May 30, 2014).

- In addition to the above, about 10 or more notifications etc., were issued in FY 2014 with the cooperation of relevant review categories or offices in PMDA.

c. Preliminary reviews under Cartagena Act

- 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 Cartagena Act. PMDA set the target regulatory review time to be 6 months for approval of Type 1 Use and 2 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 2010	FY 2011	FY 2012	FY 2013	FY 2014
No. of preliminary reviews for Type 1 Use Median review time [months]	0 –	0 –	0 –	0 –	3 0.8
No. of preliminary reviews for Type 2 Use Median review time [months]	13 2.5	15 2.0	21 1.2	24 0.9	25 1.3

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 to universities, research institutions and venture companies that have promising seed-stage resources to provide guidance and advice concerning studies and clinical trials that are necessary at the initial stage of product development, in order to facilitate the development of innovative pharmaceuticals, medical devices, and cellular and tissue-based products in Japan. The number of consultations in FY 2014 is as shown in the table below.

- In FY 2014, a total of 122 on-site individual orientations were offered in Osaka, Kobe, Fukushima, Nagoya, Hiroshima, Fukuoka, etc., (included in the values on their left in the table below)

- Introductory consultations and pre-consultation meetings were also conducted in the Kansai branch of PMDA, which was established in October 2013.

- To promote the practical application of seed-stage resources originating in Japan, in November 2014 PMDA started to provide consultations, as a pilot scheme, on the development process (roadmap) to pharmaceutical companies, etc. and on investigator-initiated confirmatory clinical trial protocols.

Number of Pharmaceutical Affairs Consultations on R&D Strategy Conducted

Introductory consultations/pre-consultations	FY 2011[1]	FY 2012	FY 2013	FY 2014	Total
Introductory consultations (of which those conducted at the Kansai branch[2])	118	302	237 (20)	271 (63)	928 (83)
Pre-consultations (of which those conducted at the Kansai branch[2])	153	254	346 (26)	325 (57)	1,078 (83)

Face-to-face consultations on:	FY 2011[1]	FY 2012	FY 2013	FY 2014	Total
Drugs	20	28	66	48	162
Medical devices	6	5	38	16	65
Cellular and tissue-based products[3]	—	—	—	2	2
Quality and safety of cellular and tissue-based products[4]	5 [7]	7 [13]	19 [32]	18 [44]	49 [96]
Development plan[5]	—	—	—	1	1
Total	31 [33]	40 [46]	123 [136]	85 [111]	279 [326]

Note 1: Pharmaceutical Affairs Consultations on R&D strategy started in July 1, 2011.

Note 2: Consultations in Kansai branch started in October 1, 2013.

Note 3: Started in November 25, 2014 (before then consultations on cellular and tissue-based products had been included in consultations on drugs or medical devices).

Note 4: This category includes Consultations on R&D Strategy for Drugs conducted until November 24, 2014. Some consultations were divided into multiple sessions over several days, to confirm the quality and safety of cellular and tissue-based products before the submission of clinical trial notifications. The figures in [] indicate the total number of sessions.

Note 5: Started in November 25, 2014

Generic drugs, etc.

- PMDA took or examined the following measures to take measures to accelerate reviews for generic drugs, etc.

(i) Appropriate and prompt reviews

- PMDA established the Office of Generic Drugs in November 2014 and has made efforts to speed up reviews through more efficient operations.

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. Development of the Japanese Pharmacopoeia

- See 3.2.(1) **New drugs** (i)-g.

c. Implementation of master file workshop

- See 3.2.(1) **New drugs** (i)-h

d. Securing efficient and transparent reviews

- PMDA, in collaboration with industry associations, prepared a draft of a mock-up CTD to encourage the use of CTD/eCTD for marketing applications with the aim of performing more efficient reviews. Companies submitted a trial version of the CTD, if possible, for new applications filed in February 2015.
- To prepare review reports for new applications for generic drugs on a trial basis, PMDA discussed items to be included in a review report and examined a draft outline of review report for generic drugs.
- In order to discuss the development of a bioequivalence study guidance for drugs that cannot be evaluated by the existing guidelines for bioequivalence testing, PMDA first examined the past approval status of ophthalmic solutions. The results of the examination suggested that the bioequivalence of a generic drug should be evaluated based on more detailed investigation with consideration of the drug's pharmacological and pharmaceutical properties.

(ii) Approaches to shorten review times

- PMDA set up the following target regulatory review times for applications submitted on or after April 1, 2004 and approved in each fiscal year, and has made efforts to achieve these targets asking for cooperation of applicants.
- For prompt and accurate reviews of generic drugs, etc., PMDA carried out reviews in accordance with the Procedures for Review of Generic Prescription Drugs, which specify the review methods and procedures associated with reviews, and 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 held in FY 2014).

- The approval status of generic drugs in FY 2014 are as follows:

a. Review time for new application for generic drugs

Target

PMDA aims to achieve the following target for the 50th percentile (median) of products by FY 2018.

Product	Regulatory review time [months]
New generic drugs	10

Results

	FY 2014
Approved products	1,325
Of which those filed in or after April 2004	1,325
Median regulatory review time [months]	6.1

Note: The median was for the applications filed in or after April 2004.

b. Review time for partial change application for generic drugs, etc. (standard review products)

Targets

PMDA aims to achieve the following targets for the 50th percentile (median) of products by FY 2018.

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	15	14	13	12	10

Results

	FY 2014
Approved products	568
Of which those filed in or after April 2004	567
Median total review time [months]	15.7

Note 1: The median was calculated based on the applications filed in or after April 2004.

Note 2: Applications for partial change currently under submission are excluded from the table above.

c. Review time for partial change applications for generic drugs, etc. (excluding the products that fall under “b” above)

Targets

PMDA aims to achieve the following targets for the 50th percentile (median) of products by FY 2018.

Type	Total review time (months)
Applications for partial change (e.g., change of test methods)	6
Applications for partial change (expedited review)	3

Results

		FY 2014
Change of test methods, etc.	Approved products	1,233
	Of which those filed in or after April 2004	1,233
	Median total review time [months]	7.6
Expedited review	Approved products	158
	Of which those filed in or after April 2004	158
	Median total review time [months]	4.0

Note 1: The medians were calculated based on the applications filed in or after April 2004.

Note 2: Applications for partial change currently under submission are excluded from the table above.

Reference: Results obtained during the Second Mid-term Plan (Regulatory Review Time)

Generic drugs, etc.	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Approved products	3,271	2,633	3,091	3,421	3,504
Of which those filed in or after April 2004	3,245	2,590	3,046	3,388	3,502
Median regulatory review time [months]	7.5	6.9	6.5	5.9	5.3

Note 1: The number of approved products includes priority review products for which the standard regulatory review time is 6 months or less.

Note 2: The medians were calculated based on the applications filed in or after April 2004.

Note 3: Applications for partial change currently under submission are included in the table above.

Reviews and Related Services Conducted for Generic Drugs, etc. by Fiscal Year

Fiscal Year	Application	Approved	Withdrawn, etc.	Under review
FY 2010	3,062	2,633	224	3,454
FY 2011	2,893	3,089	165	3,093
FY 2012	4,077	3,421	190	3,559
FY 2013	3,893	3,504	343	3,605
FY 2014	3,452	3,447	214	3,396

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

Note 2: Applications for partial change currently under submission are included in the table above.

- The median regulatory review time for new generic drugs approved in FY 2014 was 6.1 months (target, 10 months), achieving the target. For partial change applications of generic drugs, the median total review time for standard review products was 15.7 months (target, 15 months), not achieving the target. This was because the median regulatory review time was 7.7 months while the median applicant's time was 7.9 months, suggesting that an even greater collaboration with applicants is needed in the review process. The median total review time for partial change applications (e.g., change of test methods) was 7.6 months (target, 6 months) and that for partial change applications (expedited review) was 4.0 months (target, 3 months). PMDA aims to achieve the targets by FY 2018 by taking measures such as increasing the number of reviewers from the next fiscal year.

Document-based Compliance Assessments for Generic Drugs by Fiscal Year

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Generic drugs	1,040	1,118	1,188	1,086	1,080

- For generic drugs, PMDA conducted 1,080 assessments to examine whether application data comply with GLP, GCP, GPSP, and other standards by checking the application data against raw data such as test records, laboratory notebook, and case report forms.

(iii) Efficient conduct of clinical trial consultations

- Regarding pre-application consultations for generic drugs, in January 2012, PMDA started to provide quality consultations for generic drugs and consultations on the bioequivalence of generic drugs on a trial basis, and 24 consultations were conducted in FY 2014. Since January 2015, PMDA has responded to all requests for consultations.

Number of Consultations for Generic Drugs

	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	3	10	17	24
Withdrawn	0	0	1	1
Total (conducted and withdrawn)	3	10	18	25

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

Number of Consultations for Generic Drugs by Consultation Category in FY 2014

Consultation category	Conducted	Withdrawn	Total (conducted and withdrawn)
Consultations on bioequivalence of generic drugs	15	1	16
Quality consultation for generic drugs	9	0	9
Total	24	1	25

Behind-the-counter (BTC) drugs, over-the-counter (OTC) drugs, and quasi-drugs

- PMDA took the following measures to promote public self-medication.

(i) Appropriate and prompt reviews

a. Reinforcement of the review system for BTC drugs and OTC drugs

- PMDA made efforts to improve post-marketing surveillance by allocating human resources with experiences in safety measures in order to respond to the establishment of the BTC drugs system. Personnel with experience in compliance assurance were also assigned to handle newly initiated document-based compliance assessments at the Office of OTC/Quasi-drugs.

  While reviewers for toxicity and clinical matters have not yet been assigned, PMDA took steps in collaboration with experts and sought their opinions as needed on issues associated with products for reviews or consultations.

- Reviewers actively participated in academic conferences, etc., held in and out of Japan, and exchanged opinions with healthcare professionals. The Agency conducted reviews and consultations, taking into account the information obtained in this manner.
- For the development of Japanese Pharmacopoeia, see 3.2.(1) **New drugs** (i)-g.
- PMDA made efforts to improve the quality of reviewers by exchanging opinions with experts in traditional Chinese medicines/crude drugs by having reviewers participate in the Japanese Pharmacopoeia Crude Drug Committee and also, as collaborative researchers, 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).

b. Reinforcement of the review system for quasi-drugs

- PMDA has accelerated reviews by increasing the number of reviewers and by newly allocating principle reviewers who specialize in the review of innovative products.
- PMDA supported the MHLW's process of the revision of Japanese Standards of Quasi-drug Ingredients by assisting MHLW to hold meetings of the "Review Committee on Japanese Standards of Quasi-drug Ingredients." In addition to that, PMDA prepared “Standards of Quasi-drug Excipients” to publicize the standards in the appendix, which are used mainly for approved quasi-drug cosmetics, in order to accelerate reviews and reduce the time and effort involved in making an application.
- PMDA has made efforts to improve the quality of reviewers by having them participate in training programs, academic conferences etc., in and out of Japan and exchange opinions with specialists. PMDA conducted reviews and consultations, taking into account the information obtained in this manner.

(ii) Approaches to shorten review times

- PMDA set up the target regulatory review times for applications for BTC drugs, OTC drugs, and quasi-drugs submitted on or after April 1, 2004, and has since conducted reviews toward the achievement of these targets.
- In order to review BTC drugs, OTC drugs, and quasi-drugs promptly and accurately, PMDA executed operations in accordance with the Procedures for Review of OTC Drugs, Procedures for

Review of Insecticides/Rodenticides, and Procedures for Review of Quasi-drugs, all of which specify the review methods and associated procedures, and also SOPs for various operations.

In addition, PMDA periodically collected data on the achievement level of the target review time, informed the reviewers of the level, and held meetings of the Progress Management Committee for Reviews and Related Services to monitor and examine operational progress. (4 meetings were held in FY 2014.)

- The approval status of BTC drugs, OTC drugs, and quasi-drugs in FY 2014 are as follows:

a. Review time for BTC drugs and OTC drugs

Target

PMDA aims to achieve the following target for the 50th percentile (median) of products by FY 2018.

Product	Regulatory review time [months]
BTC drugs, OTC drugs	7

Results

BTC drugs, OTC drugs	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Approved products	1,008	1,031	881	916	844
Of which those filed in or after April 2004	1,007	1,029	881	916	844
Median regulatory review time [months]	4.0	3.4	4.1	4.9	6.3

Note: The medians were calculated based on the applications filed in or after April 2004. These values were calculated excluding the period after completion of reviews up to notification of GMP inspection results from authorities such as prefectural governments.

b. Review time for quasi-drugs

Target

PMDA aims to achieve the following target for the 50th percentile (median) of products by FY 2018.

Product	Regulatory review time [months]
Quasi-drugs	5.5

Results

Quasi-drugs	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Approved products	1,976	1,938	1,968	2,028	1,779
Of which those filed in or after April 2004	1,976	1,938	1,968	2,028	1,779
Median regulatory review time [months]	5.2	5.0	4.9	4.9	4.9

Note: The medians were calculated based on the applications filed in or after April 2004. These values were calculated excluding the period after completion of reviews up to notification of GMP inspection results from authorities such as prefectural governments.

Reviews Conducted for BTC Drugs, OTC Drugs, and Quasi-drugs by Fiscal Year

Classification	Fiscal Year	Applications	Approved	Withdrawn, etc.	Under review
BTC drugs, OTC drugs	FY 2010	1,092	1,008	133	1,834
	FY 2011	1,130	1,031	92	1,841
	FY 2012	1,005	881	90	1,875
	FY 2013	1,013	916	63	1,909
	FY 2014	882	844	99	1,848
Quasi-drugs	FY 2010	2,297	1,976	142	2,013
	FY 2011	2,212	1,938	97	2,190
	FY 2012	2,117	1,968	79	2,260
	FY 2013	2,298	2,028	174	2,356
	FY 2014	1,828	1,779	125	2,280

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

Note 2: Partial tabulation errors were found for FY 2010, 2011, and 2012, and the numbers of reviews conducted for quasi-drugs have been corrected as follows:

Quasi-drugs

The value in the "Withdrawn etc., column" for FY 2010 was corrected from 135 to 142.
The value in the "Under review column" for FY 2010 was corrected from 2,030 to 2,013.
The value in the "Withdrawn etc., column" for FY 2011 was corrected from 82 to 97.
The value in the "Under review column" for FY 2011 was corrected from 2,222 to 2,190.
The value in the "Withdrawn etc., column" for FY 2012 was corrected from 74 to 79.
The value in the "Under review column" for FY 2012 was corrected from 2,297 to 2,260.
The value in the "Under review column" for FY 2013 was corrected from 2,393 to 2,356.

- The median regulatory review time for approved products in FY 2014 was 6.3 months for BTC drugs and OTC drugs (target, 7 months) and 4.9 months for quasi-drugs (target, 5.5 months), showing that the targets were achieved for both categories.

(iii) Efficient conduct of consultations

a. Improvement of pre-application consultations for BTC drugs and 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 decreased in FY 2012 as compared to that in the previous year, but markedly increased in FY 2013, and this increased number was maintained in FY 2014. PMDA intends to make efforts to further improve the consultation service.

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

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	23	17	4	21	21
Withdrawn	0	2	0	0	0
Total (conducted and withdrawn)	23	19	4	21	21

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2014

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

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

- PMDA exchanged opinions on specific issues with concerned parties such as the Japan Cosmetic Industry Association to start a new pre-application consultation system for quasi-drugs. PMDA continues to harmonize opinions aiming to implement the consultation system at an early date.

Medical devices

- Various measures were implemented or investigated to accelerate reviews for new medical devices, based on the "Cooperation Plan to Accelerate Reviews of Medical Devices" (March 2014) (the successor of "Action Program to Accelerate Reviews of Medical Devices" [December 2008]), "Japan Revitalization Strategy -JAPAN is BACK-", and "Healthcare and Medical Strategy".

(i) Appropriate and prompt reviews

a. Structure for clinical trial consultations and reviews

- In order to strengthen the review system and thereby achieve new targets, PMDA increased the number of reviewers allocated to the categories where a markedly greater number of new medical device applications were filed and the review process for such applications was likely to be prolonged.
- Under the guidance of an office director and a review director, reviews of new medical devices and improved medical devices were basically conducted by review teams consisting of experts who have academic degrees in engineering, pharmaceutical science, physical science, medicine, dentistry, veterinary medicine, statistics, etc.

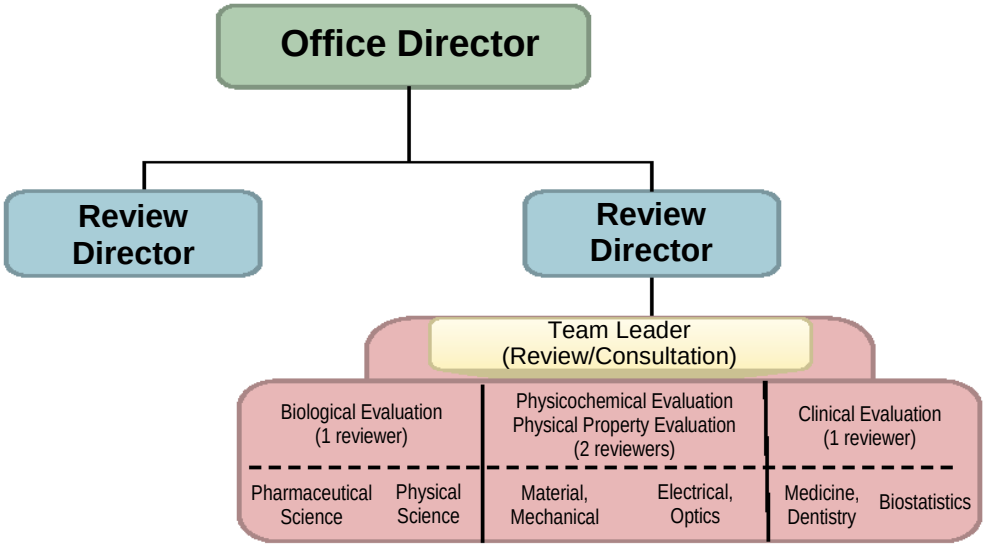
  The review team is typically comprised of team leader(s) and reviewers who specialize in biological evaluations, physicochemical/physical property evaluations, and clinical evaluations.

(Note) *New medical devices:*
- *Medical devices subject to re-examination, which have a clearly different structure, usage, indications, performance, etc., compared to existing approved medical devices or certified medical devices (definition under the Pharmaceutical Affairs Act).*
- *Medical devices for which marketing approval has been granted (medical devices that have been specified as being subject to use results assessment according to the provisions of Paragraph 1, Article 23-2-9 of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Act) at the time of approval, excluding those for which the survey period has not expired; hereinafter referred to as "approved medical devices") (definition under the PMD Act)*

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. (definition under the Pharmaceutical Affairs Act)*
- *Medical devices that do not fall under "new medical devices" or "generic medical devices" (definition under the PMD Act)*

Generic medical devices:
- *Medical devices that are regarded as substantially equivalent to existing approved medical devices in terms of structure, usage, indications, performance, etc. (definition under the Pharmaceutical Affairs Act).*
- *Medical devices that are regarded as equivalent to existing approved medical devices in terms of structure, usage, indications, and performance; that is, medical devices that are substantially equivalent to existing approved medical devices in terms of structure, usage, indications, and performance (definition from the PMD Act)*

Organization for New/Improved Medical Device Reviews



- New and improved medical devices were reviewed by teams designated based on the review categories shown 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 (Note)	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)

Note: Operations of Category 7 were transferred from the Office of Medical Devices II to the Office of In Vitro Diagnostics (a new office) on April 1, 2015.

- 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 2014 (medical devices and in vitro diagnostics)

(1) Number of Expert Discussions conducted: 51 (36 document-based discussions, 15 meetings)
(2) Applications deliberated at the Committees on Medical Devices and *in vitro* Diagnostics (under PAFSC): 12
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 321 (303 medical devices, 18 *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.

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 2014, PMDA promoted the system based on the experiences in the previous year.

c. Reinforcement and transparency 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 2014. In the meetings, information on the overall review status for new medical devices including QMS inspections etc., and associated issues were shared, and measures to address the issues and future approaches were examined (11 meetings were held in FY 2014).

  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 Executive Director, and the results of discussions of issues and improvement measures for products with a difficulty that required a prolonged review time were notified within review segments.
- In order to accelerate review times, timelines were strictly managed in accordance with the "On the Standard Review Timeline for New Medical Devices" (PFSD/ELD/OMDE Notification No. 1120-1 dated November 20, 2013), "On the Standard Review Timeline for Improved Medical Devices (with Clinical Data)" (PFSD/ELD/OMDE Notification No. 0328-4 dated March 28, 2014),

and "On the Standard Review Timeline for Improved Medical Devices (without Clinical Data) and Generic Medical Devices" (PFSD/ELD/OMDE Notification No. 0519-1 dated May 19, 2014).

- In accordance with the "Information Sharing about the Progress of Reviews of New Medical Devices and Improved Medical Devices" (PFSD/ELD/OMDE Notification No. 0530001 dated May 30, 2014), PMDA communicated the progress of reviews at each review stage to applicants, and the relevant office director held meetings with applicants upon their request to explain to them the progress status and outlook for their reviews.

d. Standardization and transparency of review

- To clarify review standards, PMDA posted on its website the following three documents on basic considerations for review: "Points to Consider in regard to Applications for New Medical Devices, etc.," "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 the guidelines at workshops to make them widely known. 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," "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)," and "Confirmation of Application Documents for Generic Medical Devices" 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 in the operation of the study group, and provided clinical trial consultations and reviewed product applications taking into account the results of investigations by the study group. Through this initiative, 7 medical devices were approved in FY 2014.

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. Efficient operation and implementation of the use-results evaluation system

- With the enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act (Act No. 84, 2013), PMDA worked on the efficient operation and implementation of the use-results evaluation system for medical devices, which was introduced on November 25, 2014, in accordance with "Basic Principles on Products Subject to Use-results Evaluation at the Time of Approval" deliberated and approved at the 6th meeting of the Committee on Medical Devices and In-vitro Diagnostics (MHLW) in FY 2014.

  Based on this principle, 30 medical devices (including 7 medical devices selected for use-results survey) were approved in FY 2014.

- In order to implement the new system smoothly, medical devices that had been designated as products subject to re-examination before the system revision were processed with greater collaboration with the division of surveillance (Office of Non-clinical and Clinical Compliance). As a result, 8 medical devices subject to re-examination were processed in FY 2014.

(ii) Introduction of new review systems

a. Introduction of prior assessment consultation

- To preliminarily evaluate the quality, efficacy and safety of medical devices in 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 2014, 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 3 products 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 19 products approved in FY 2014 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 5 meetings in FY 2014.

  The number of approval or certification standards reported to MHLW in FY 2014 to be established or revised was as follows. The number of certification standards reported to MHLW was 129 (including 20 revised standards) for designated controlled medical devices and 3 for designated specially controlled medical devices (all of them were classified as Class III for risk level).

FY (for reporting)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	Total
Approval standards	6	7	5	2	6	6	5	4	0	41
Certification standards (designated controlled medical devices)	0	14	86	64	294	84	67	82	129	820
Certification standards (designated specially controlled medical devices)	–	–	–	–	–	–	–	–	3	3
Review guidelines	0	1	2	6	0	0	0	0	0	9

The number of standards established by MHLW in FY 2014 based on the reports from PMDA is shown below. The number of certification standards established was 109 for designated controlled medical devices and 3 for designated specially controlled medical devices (all of them were classified as Class III for risk level).

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	FY 2014	Total
Approval standards	0	17	8	10	-2*	5	3	0	0	4	0	45
Certification standards (designated controlled medical devices)	363	9	24	0	17	68	274	67	2	3	109	936
Certification standards (designated specially controlled medical devices)	–	–	–	–	–	–	–	–	–	–	3	3
Review guidelines	0	0	0	0	3	1	4	0	0	0	0	8

** In FY 2008, 2 established approval standards were switched to certification standards, resulting in a negative number.*

List of Certification Standards for Medical Devices (FY 2014)

Established: Certification standards,112; Approval standards,0; Review guidelines, 0	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 404, dated November 5, 2014	Certification Standard for Insulin Pen (and other 1 certification standard)
MHLW Ministerial Announcement No. 445, dated November 25, 2014	Certification Standard for Programs for multipurpose Diagnostic X-ray Equipment (and other 107 certificate standards)
MHLW Ministerial Announcement No. 120, dated March 25, 2015	Certification Standard for Enteral Nutrition Pumps, etc. (and other 1 certification standard)

- 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 2014 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).
- In order to clarify the definition of substantial equivalence of generic medical devices based on the "Cooperation Plan to Accelerate Reviews of Medical Devices," PMDA held two meetings with related industry associations and strived to identify and summarize problems that needed to be resolved.

(iii) Efforts to achieve "zero" review lag for medical devices

- With respect to total review time for medical device applications filed on or after April 1, 2004 and approved in each fiscal year, PMDA has made efforts with the cooperation of applicants to achieve the targets "a" to "e," presented below, by FY 2018 by gradually increasing the target percentile.
- Progress management was reinforced for products under review in any application category (new, improved, or generic medical devices). PMDA endeavored to reduce the backlog of pending applications. Specifically, to promptly complete the prolonged review of applications filed years earlier, PMDA and applicants had discussions to analyze reasons for prolonged review and resolve relevant issues for each product. In addition, reminder notices were frequently sent to applicants if their responses to PMDA's inquiries were delayed. For products for which new applications have been submitted, progress management was enhanced to accelerate reviews.
- In order to eliminate review/development lag for medical devices being developed or to be developed in the near future, PMDA encouraged medical device-related industries, medical device companies, and academic institutions to take measures such as the proactive use of clinical trial consultations prior to regulatory submission, at academic conferences or periodic opinion exchange sessions with the industries. Moreover, PMDA provided specific examples of deficiencies often seen at the time of application for approval, at workshops, etc., to call for improvements to be made on the applicant's side.

- 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.
- 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. In FY 2014, PMDA participated in HBD Think Tank West (held in Washington D.C. in September 2014) and promoted global clinical development through activities supporting the Proof of Concept (POC) project. In addition, from the previous year, PMDA has been making ongoing 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 the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) conference held in Nagoya in July 2014 and the Cardiovascular Research Technologies (CRT) conference held in Washington D.C. in February 2015, to discuss issues such as the challenges in the development of new medical devices and methods of utilizing a post-marketing registry with industry, governments, and academic circles.
- 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 2014 was as follows:

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	10	10	10	10	10
Percentile	60	60	70	70	80

Results

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	60
Total review time [months] (Reference, 80th percentile) [months]	15.1 (19.7)	4.3 (12.8)	9.3 (20.8)	9.0 (10.0)	8.8 (8.9)
Number of approved applications	3	6	5	14	5

Reference

Regulatory review time [months]	5.3	2.9	7.2	5.1	4.0
Applicant's time [months]	10.7	1.3	3.4	3.5	3.3

Note: Products covered are those for which applications were filed in or after April 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 2014, 5 priority review products (all were new medical devices) were approved.

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

- The approval status of priority review products in FY 2014 was as follows: The total review time (60th percentile) was 8.8 months, and the achievement rate for the target total review time (10 months) was 100.0%, which was substantially higher than the target. The number of approvals was 5, which was close to the annual average.

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	14	14	14	14	14
Percentile	60	60	70	70	80

Results

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	60
Total review time [months] (Reference, 80th percentile) [months]	16.5 (21.6)	9.7 (17.8)	12.7 (15.5)	6.3 (14.8)	5.6 (10.6)
Number of approved applications	15	27	41	80	62

Reference

Regulatory review time [months]	7.1	5.1	5.4	4.0	3.5
Applicant's time [months]	8.2	3.4	5.0	1.6	2.2

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

- The approval status of standard review for new medical devices in FY 2014 was as follows: The total review time (60th percentile) was 5.6 months, and the achievement rate for the target total review time (14 months) was 98.4%, which was substantially higher than the target. The number of approvals in FY 2014 was 62, being the highest number next to FY 2013.

  This was probably because many applications for MRI-compatible pacemakers, ICD, etc., concentrated in FY 2014 as in FY 2013.

- The number of product applications under review at the end of FY 2014 was 78 (including 4 orphan medical devices and 3 non-orphan priority review medical devices).

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	4	0
FY 2010	28	24	2	2
FY 2011	42	40	2 (1)	0 [-1]
FY 2012	64	63 (1)	0	1 [-1]
FY 2013	72	65 (29)	0	7 [- 29]
FY 2014	99	30 (30)	1 (1)	68 [68]
Total	616	418 (60)	120 (2)	78 [37]

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 2014 (included in values on their left).

Note 4:Figures in brackets [] represent difference from the status reported in FY 2013.

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	10	10	10	10	10
Percentile	52	54	56	58	60

Results

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	52
Total review time [months] (Reference, 60th percentile) [months]	15.5 (17.5)	13.9 (18.0)	17.3 (19.8)	11.6 (13.2)	9.9 (10.5)
Number of approved applications	40	55	44	63	35

Reference

Regulatory review time [months]	7.6	7.0	7.9	5.7	5.0
Applicant's time [months]	7.6	7.2	8.8	5.5	5.0

Note 1: Products covered are those for which applications were filed in or after April 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 2014, the total review time (52nd percentile) was 9.9 months, and the achievement rate for the target total review time (10 months) was 57.1%, which was substantially higher than the target.

number of approvals in FY 2014 was 35, showing a decrease from the previous fiscal year but being nearly equal to the number of approvals in other fiscal years.

- This is due to the completion of the prolonged reviews of applications for improved medical devices (with clinical data) that were filed years earlier.

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	0
FY 2011	26	21	5 (2)	0 [-2]
FY 2012	42	39 (5)	2	1 [-5]
FY 2013	46	36 (21)	2	8 [-21]
FY 2014	45	8 (8)	0	37 [37]
Total	227	170 (34)	11 (2)	46 [9]

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 2014 (included in values on their left).

Note 4:Figures in brackets [] represent difference from the status reported in FY 2013.

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	6	6	6	6	6
Percentile	52	54	56	58	60

Results

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	52
Total review time [months] (Reference, 60th percentile) [months]	14.5 (17.3)	13.3 (14.9)	9.7 (11.1)	7.5 (9.2)	6.0 (7.4)
Number of approved applications	182	218	229	231	213

Reference

Regulatory review time [months]	8.0	5.6	4.8	3.7	3.3
Applicant's time [months]	6.2	6.5	4.7	3.7	3.4

Note 1:Products covered are those for which applications were filed in or after April 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 2014, the total review time (52nd percentile) was 6.0 months, and the achievement rate for the target total review time (6 months) was 52.6%, achieving the target. The number of approved

applications in FY 2014 was 213, showing a decrease from the previous fiscal year but being nearly equal to the number of approvals in other fiscal years.

- This is due to the completion of the prolonged reviews of applications for improved medical devices (without clinical data) that were filed years earlier.

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	15	0
FY 2010	165	140 (3)	24 (1)	1 [-4]
FY 2011	176	159 (4)	15 (2)	2 [-6]
FY 2012	210	198 (18)	10	2 [-18]
FY 2013	190	169 (84)	10 (7)	11 [-90]
FY 2014	261	100 (100)	0	161 [161]
Total	1,139	888 (209)	74 (10)	177 [43]

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 2014 (included in values on their left).

Note 4:Figures in brackets [] represent difference from the status reported in FY 2013.

e. Review times for generic medical devices

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	4	4	4	4	4
Percentile	52	54	56	58	60

Results

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Percentile	50	50	50	50	52
Total review time [months] (Reference, 60th percentile) [months]	11.0 (15.1)	5.0 (7.2)	4.0 (6.0)	3.9 (5.3)	3.9 (4.5)
Number of approved applications	1,391	907	1,216	958	920

Reference

Regulatory review time [months]	5.1	2.5	1.6	1.8	1.9
Applicant's time [months]	4.7	2.3	2.3	2.1	1.8

Note 1:Products covered are those for which applications were filed in or after April 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 2014, the total review time (52nd percentile) was 3.9 months, and the achievement rate for the target total review time (4 months) was 54.6%, which was substantially higher than the target.
- Although the number of applications has tended to decrease, the number of applications in FY 2014 was increased in association with the enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act. The number of approved applications in FY 2014 was 920, almost the same as that in FY 2013.The number of applications under review at the end of fiscal year was lower in FY 2014 than in FY 2013.
- Also, to further reduce the applicant's time for generic medical devices, PMDA requested applicants, at regular industry-PMDA dialogue meetings, to take following measures: i) To actively utilize 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 Generic Medical Devices by Fiscal Year of Application

Generic medical devices (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	1,126	1,037 (6)	84 (4)	5 [-10]
FY 2010	1,020	916 (21)	93 (6)	11 [-27]
FY 2011	995	923 (12)	61 (5)	11 [-17]
FY 2012	1,075	1,021 (23)	35 (7)	19 [-30]
FY 2013	921	846 (262)	18 (6)	57 [-271]
FY 2014	957	605 (605)	7 (7)	345 [345]
Total	6,094	5,348 (929)	298 (35)	448 [-10]

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 2014 (included in values on their left).

Note 4:Figures in brackets [] represent difference from the status reported in FY 2013.

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

Number of Consultations

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	105	136	165	162	196
Withdrawn	1	4	3	11	11
Total (conducted and withdrawn)	106	140	168	173	207

Number of Prior Assessment Consultations for Medical Devices (Among the Numbers Listed Above)

	FY 2010	FY 2011	FY 2012	FY 2013	Y 2014
Conducted	2	3	3	1	3
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	2	3	3	1	3

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

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	0	0	0	0	0
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	0	0	0	0	0

Note 1:The numbers of prior assessment consultations for medical devices and consultations on pharmacogenomics/biomarkers were counted on the basis of delivery dates of consultation documents to PMDA.

Note 2:Prior assessment consultations for medical devices are conducted for the categories of quality, non-clinical and clinical.

Number of Consultations for Medical Devices by Category in FY 2014

Consultations accepted by November 21, 2014

Consultation category	Conducted	Withdrawn	Total (conducted and withdrawn)
Pre-development consultation for medical devices	97	5	102
Safety consultation for medical devices (excluding biological medical devices)	2	0	2
Quality consultation for medical devices (excluding biological medical devices)	2	0	2
Safety consultation for biological medical devices	0	0	0
Quality consultation for biological medical devices	1	0	1
Performance testing consultation for medical devices	11	2	13
Clinical evaluation consultation for medical devices	12	1	13
Exploratory clinical trial consultation for medical devices	3	0	3
Clinical trial consultation for medical devices	27	1	28
Pre-application consultation for medical devices	5	0	5
Application procedure consultation for medical devices	3	0	3
Additional consultation for medical devices	2	0	2
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)	2	0	2
Total	168	9	177

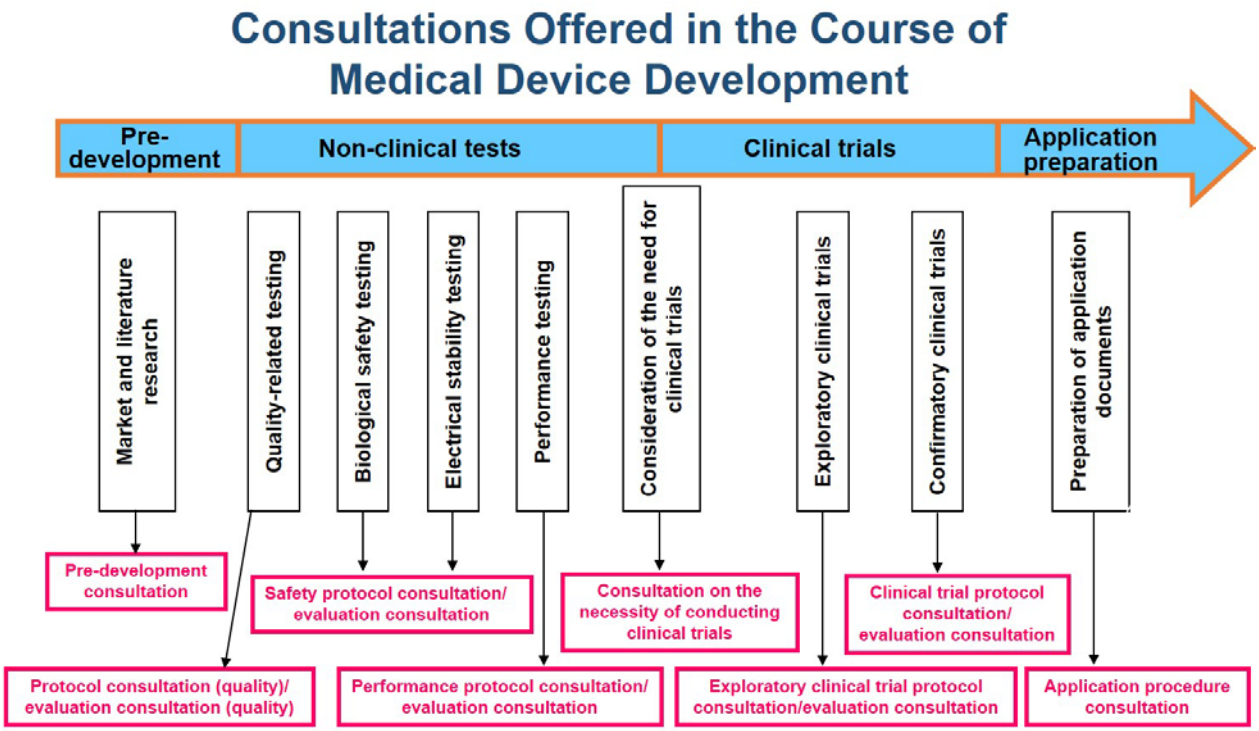
Consultations accepted on or after November 24, 2014

Consultation category*	Conducted	Withdrawn	Total (conducted and withdrawn)
Pre-development consultation for medical devices	8	0	8
Pre-development consultation for medical devices (preliminary consultation completed)	9	0	9
Protocol consultation for medical devices (safety) (4 or more trials) (preliminary consultation completed)	1	0	1
Protocol consultation for medical devices (exploratory clinical trial)	1	0	1
Protocol consultation for medical devices (clinical trial)	2	0	2
Protocol consultation for medical devices (clinical trial) (preliminary consultation completed)	3	0	3
Protocol consultation for medical devices (clinical trial) (additional consultation)	0	2	2
Data sufficiency/application category consultation for medical devices	1	0	1
Safety evaluation consultation for medical devices (4 or more trials) (protocol not evaluated)	1	0	1
Performance evaluation consultation for medical devices (4 or more trials) (protocol not evaluated) (preliminary consultation completed)	1	0	1
Evaluation consultation for medical devices (protocol not evaluated)	1	0	1
Total	28	2	30

** This table shows only the categories of the consultations implemented in FY 2014.*

c. Review of consultation categories

- Regarding clinical trial consultations for medical devices, PMDA reviewed consultation categories and improved consultation methods (implemented on November 25, 2014) in order to better accommodate a diverse range of needs in each stage of development and enhance the efficiency and effectiveness of consultations, taking into account the demands of industry and previous experience.
- In order to eliminate review/development lag for medical devices being developed or to be developed in the near future, PMDA encouraged medical device-related industries, medical device companies, and academic institutions, etc., to take measures such as the proactive use of clinical trial consultations prior to regulatory submission, at academic conferences or through periodic exchanges of opinions with the industry (reposted).



** 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

- As PMDA is required to raise the scientific level of its guidance and review, particularly in the fields of the latest technologies such as ICT and robotics, PMDA has continued to commission highly knowledgeable external experts to play the role of expert advisors to PMDA in order to obtain professional opinions on scientifically important matters at Expert Discussions for reviews and post-marketing safety measures (reposted). (As of March 31, 2015, the number of commissioned experts is 12 including experts in safety measures.)
- The number of Expert Discussions conducted in FY 2014 was 51 (36 document-based discussions, 15 meetings).
- In order to appropriately deal with medical devices developed with the latest scientific technologies, PMDA made efforts to strengthen the collaboration with academia and healthcare professionals and to collect relevant information at meetings of the Science Board (parent committee) and its Subcommittees on Application of Numerical Analysis to Non-clinical Evaluation and on Evaluation of Medical Devices in Pediatric Use.

b. Support for the development of national guidelines

- PMDA supported the preparation of the guidance documents for the evaluation of spinal implants for the maintenance of mobility and stability and orthopedic implants developed using three-dimensional layering technology, which were all included in “Publication of the Guidance Document for the Evaluation of Emerging Technology Medical Devices/Cellular and Tissue-based Products” (PFSB/ELD/OMDE Notification No. 0912-2 dated September 12, 2014), and released them on the PMDA website.

c. Preliminary reviews under Cartagena Act

- See 3.2.(1) **New drugs** (vi)-c.

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

- See 3.2.(1) **New drugs** (vi)-d.

e. 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 gives 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. In FY 2014, claims for fee subsidy were filed for 4 consultations/applications and all were subsidized.

In vitro diagnostics

(i) Appropriate and prompt reviews

- It is planned to establish the Office of In Vitro Diagnostics on April 1, 2015 in accordance with "Cooperation Plan to Accelerate Reviews of *In Vitro* Diagnostics" (March 2014).
- In order to encourage MAHs to develop *in vitro* diagnostics 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 was established in the MHLW in October 2006, and activities have been continuing. PMDA has cooperated in the operation of this Study Group.

Review Status of In Vitro Diagnostics

In vitro diagnostics (FY of submission)	Applications	Approved	Withdrawn	Under review
In or before FY 2003 ending Mar. 31, 2004	327	223	76	28
FY 2004	615	596	19	0
FY 2005	69	65	4	0
FY 2006	180	173	7	0
FY 2007	197	189	8	0
FY 2008	170	160	10	0
FY 2009	183	173 (1)	10	0 [-1]
FY 2010	164	157	7 (1)	0 [-1]
FY 2011	177	165 (3)	7 (2)	5 [-5]
FY 2012	165	153 (11)	8 (2)	4 [-13]
FY 2013	136	112 (45)	7 (5)	17 [-50]
FY 2014	163	49 (49)	2 (2)	112 [112]
Total	2,546	2,215 (109)	165 (12)	166 [42]

Note 1: Values in parentheses indicate those processed in FY2014 (included in values to their left)

Note 2: Values in brackets [] indicate difference from the status reported in FY 2013.

Note 3: Values are calculated based on the applications filed in or after 1994, when the equivalence review system was introduced (numerical values stored in the current application management system were used).

(ii) Expansion of consultation services

- Regarding clinical trial consultations for *in vitro* diagnostics, PMDA revised consultation categories (implemented on November 25, 2014) in order to better accommodate a diverse range of needs in each stage of development and enhance the efficiency and effectiveness of consultations, taking into account the demands of industry and previous experience.

Number of Consultations

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	7	5	8	7	25
Withdrawn	0	0	0	1	0
Total (conducted and withdrawn)	7	5	8	8	25

Number of Prior Assessment Consultations for In Vitro Diagnostics (Among the Numbers Listed Above)

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	0	0	0	0	0
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	0	0	0	0	0

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

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	0	0	0	0	0
Withdrawn	0	0	0	0	0
Total (conducted and withdrawn)	0	0	0	0	0

Note 1: The numbers of 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 2: Prior assessment consultations for in vitro diagnostics are conducted for the categories of quality, non-clinical, and clinical.

Number of Consultations for In Vitro Diagnostics by Category in FY 2014

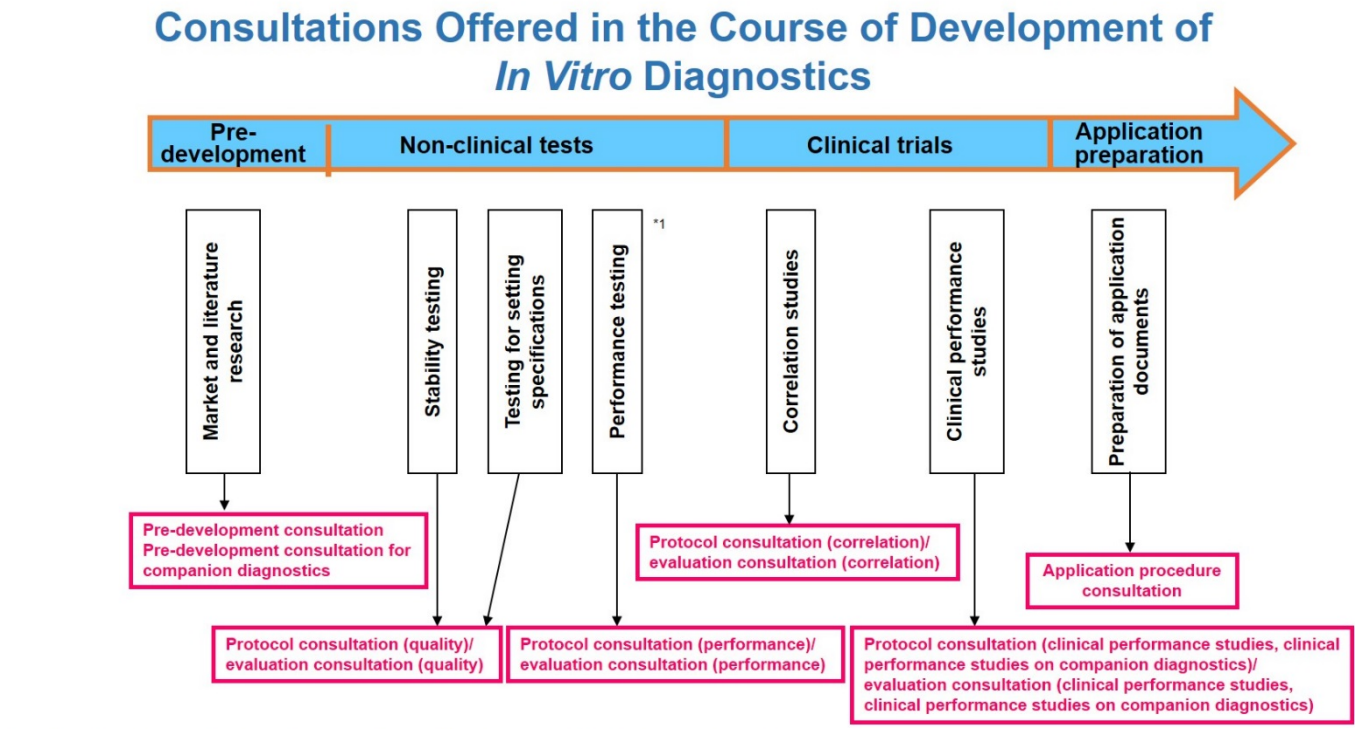
Consultations accepted by November 21, 2014

Consultation category	Conducted	Withdrawn	Total (conducted or withdrawn)
Pre-development consultation for *in vitro* diagnostics	5	0	5
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	7	0	7
Pre-application consultation for *in vitro* diagnostics	2	0	2
Application procedure consultation for *in vitro* diagnostics	1	0	1
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	18	0	18

Consultations accepted on or after November 24, 2014

Consultation category*	Conducted	Withdrawn	Total (conducted or withdrawn)
Protocol consultation for *in vitro* diagnostics (quality)	1	0	1
Protocol consultation for *in vitro* diagnostics (correlativity) (preliminary consultation completed)	1	0	1
Protocol consultation for *in vitro* diagnostics (clinical performance study)	1	0	1
Protocol consultation for *in vitro* diagnostics (clinical performance study of companion diagnostics) (preliminary consultation completed)	1	0	1
Application procedure consultation for *in vitro* diagnostics	1	0	1
Quality evaluation consultation for *in vitro* diagnostics (protocol not evaluated)	1	0	1
Evaluation consultation for *in vitro* diagnostics (other than quality) (3 or more trials) (protocol not evaluated)	1	0	1
Total	7	0	7

** This table shows only the categories of the consultations implemented in FY 2014.*



*1: Refers to quality control testing and tests excluding stability testing (e.g., operation and cross-reactivity testing)

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

Cellular and tissue-based products

(i) Introduction of new review systems and the conducting of appropriate and prompt reviews

- PMDA improved the review process for cellular and tissue-based products to appropriately address the introduction of a conditional and time-limited approval system for cellular and tissue-based products in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act. In order to ensure consistency between clinical trial consultations and reviews, PMDA flexibly organizes teams where necessary while maintaining communication between consultations and reviews and carries out reviews/consultations appropriately and promptly.

(ii) Setting of target review time

- The target standard regulatory review time from application to approval for cellular and tissue-based products approved in FY 2014 was set at 9 months, and review progress management was carried out based on this target review time. In FY 2014, 2 applications were filed for cellular and tissue-based products, but neither of them was approved.
- PMDA took the following measures to achieve the target:
  - (i) Accurate information on the progress of reviews was obtained and provided to each review team. The Progress Management Committee for Reviews and Related Services analyzed and examined operational progress to carry out progress management effectively.
  - (ii) When a problem was identified, the cause was analyzed and fed back to review teams, while, at briefing sessions for the industries, applicants were urged to exercise vigilance against the problem.
  - (iii) Questions and answers related to applications were prepared/renewed as appropriate to promote the transparency and efficiency of reviews.
- In order to enhance the transparency and efficiency of reviews and application-related questions and answers, PMDA coordinated the views of related industries and academic societies by the enforcement date of the Act for Partial Revision of the Pharmaceutical Affairs Act in November 2014 and supported the preparation/publication of ordinances and notifications related to review process for cellular and tissue-based products.

(iii) Efficient conduct of clinical trial consultations

- In order to conduct reviews promptly and efficiently, PMDA actively communicated with related parties and encouraged them to utilize consultations conducted by PMDA at meetings of academic societies such as the Japanese Society of Regenerative Medicine. Taking into account the characteristics of cellular and tissue-based products, consultations related to the quality, safety, and clinical trial protocols, etc., were established. Furthermore, consultation on cellular and tissue-based products was added to the menu of Pharmaceutical Affairs Consultation on R&D Strategy. PMDA informed related parties of these consultation services and started the services in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act enforced in November 2014.
- Pre-CTN (confirmation) application for gene therapy products was abolished and included in Pharmaceutical Affairs Consultations on R&D Strategy for quality and safety of cellular and tissue-based products.
- To make consultation more accessible to academic institutions and venture companies, in November 2014, PMDA started pilot consultation service to provide general advice on matters including development process (roadmap), as part of Pharmaceutical Affairs Consultations on R&D Strategy (Development Program Consultations on R&D Strategy). A dedicated consultation

category was established for cellular and tissue-based products, which had been treated as drugs or medical devices. The following consultations are offered under the category: Pharmaceutical Affairs Consultations on R&D Strategy for the quality or safety of cellular and tissue-based products; pre-consultations on cellular and tissue-based products, with minutes recorded; and other consultations.

Number of Consultations on Cellular and Tissue-based Products

	FY 2014
Conducted	6
Withdrawn	0
Total (conducted and withdrawn)	6

Note: The consultation categories for cellular and tissue-based products were established on November 25, 2014. The figure is the number of consultations conducted since then (before November 25, 2014, consultations for cellular and tissue-based products had been included in consultations for drugs or medical devices).

(iv) Promotion of evaluation of new technologies

a. Utilization of external experts

- PMDA proactively utilized the Science Board, in which highly knowledgeable external experts examined evaluation methods. In FY 2014, the CPC Subcommittee was established, and the members of the subcommittee discussed how to prepare a proposal on basic principles on quality assurance of cellular and tissue-based products.

  The viewpoints presented in the “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” finalized by the Science Board on August 20, 2013 were utilized in Pharmaceutical Affairs Consultations on R&D Strategy.

  At international academic conferences, etc., PMDA exchanged opinions with EMA and FDA, etc., about future international regulations on cellular and tissue-based products. In February 2015, PMDA and International Alliance for Biological Standardization (IABS) co-hosted an international conference on the global standardization of guidelines for the quality and safety of cellular and tissue-based products, and discussed the issues relating to the establishment of global standards with attendees from regulatory authorities, research institutions, and industries, in and out of Japan, that are involved in cellular and tissue-based products.

b. Collecting knowledge

- PMDA staff are dispatched to meetings held by relevant societies, including the Japanese Society for Regenerative Medicines, and to organizations facilitating development of cellular and tissue-based products (e.g., CiRA, Osaka University, Riken, Chiba University, and the Institute of Medical Science of the University of Tokyo). Through this, PMDA understands what is needed by medical institutions that develop cellular and tissue-based products and collects information on the practical application of such products.

c. Support to the development of national guidelines

- PMDA cooperated with MHLW in developing guidelines for evaluating products developed with the state-of-the-art technologies, such as cellular and tissue-based products, and in working on the initiative to facilitate development of innovative products. The results of these activities are described below.

- PMDA cooperated in developing seed-stage resources at each innovative development site and supported the study group for evaluating cellular and tissue-based products in developing guidelines, etc., and prepared drafts of 6 guidances, such as “Points to consider on the quality of human autologous iPS cells suitable for platelet induction (draft interim report)”, and drafts of 5 concept papers, such as “Concept paper on the treatment of sequelae of cerebral infarction with autologous bone-marrow-derived stem cells.”

  In the initiative to facilitate development of innovative products, PMDA, based on its experience in review, cooperated on the research that examined the standards for biological Ingredients to ensure the safety of raw materials for cellular and tissue-based products (Revision of Standards for Biological Ingredients; the notice was revised on September 26, 2014 and a related notice was issued on October 2, 2014).

- PMDA worked with MHLW to develop shared research reports "Research on detection/risk of abnormal prion in cellular/tissue-based products and biological drugs," "Research on bacterial endotoxin test methods," and "Research on standards for bovine-derived materials", which were partial research reports of "Research of the safety of innovative drugs against viruses and infectious agents" (General/Shared Research Report FY 2013), the research project on regulatory science for drugs, medical devices, etc. supported by the Health and Labour Sciences Research Grants. The results of the "Research on standards for bovine-derived materials," together with the results of the initiative to facilitate development of innovative products described above, were used as data to support the need to revise standards for biological ingredients. Based on the results of these research projects, PMDA is considering developing 3 high-level guidelines (for tests of sterility, mycoplasma, and endotoxin) related to cellular and tissue-based products.

- For the preparation of guidances for the evaluation of emerging technology medical devices and cellular and tissue-based products, PMDA cooperated with MHLW in establishing and issuing the guideline for cellular and tissue-based products (homologous iPS-cell-derived retinal pigment epithelial cells) issued as “Announcement of Guidance for the Evaluation of Emerging Technology Medical Devices/Cellular and Tissue-based Products” (PFSB/ELD/OMDE Notification No. 0912-2 dated September 12, 2014).

(v) Promotion of the use of Pharmaceutical Affairs Consultations on R&D strategy

- PMDA had conducted preliminary reviews of cellular and tissue-based products (including gene therapy products) prior to the initiation of clinical trials to determine whether the quality and safety of the products conform to the guidelines. The preliminary reviews were abolished and replaced by pharmaceutical affairs consultations on R&D strategy in July 2011 for cellular and tissue-based products and medical devices and in July 2013 for gene therapy products. PMDA has promoted the use of the Pharmaceutical Affairs Consultations on R&D strategy by doing the following activities: issuance of notifications to inform relevant parties of consultation services as well as the new consultation category of cellular and tissue-based products established in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act enforced in November 2014; and provision of relevant information at academic conferences. As a result, 9 clinical trials of cellular and tissue-based products, including investigator-initiated trials by academia, were started in FY 2014 with the support of PMDA [for the results of Pharmaceutical Affairs Consultations on R&D strategy, see 2. (1) (vi)-d].

- For preliminary reviews under the Cartagena Act, see 3.2.(1) **New drugs** (vi)-c.

Promotion of GLP/GCP/GPSP compliance assessments and clinical trials, etc.

- PMDA took the following measures to promote the proper conduct of laboratory tests and clinical trials for drug and medical device applications for approval to secure the reliability of application data.

(i) Efficient GLP/GCP/GPSP inspections and data integrity assessments for new drugs, etc.

- In collaboration with the Health and Labour Sciences Research Group conducting "Research on GCP-related activities for the vitalization of clinical trials," PMDA examined foreign compliance assessments to develop inspection methods in consideration of risk. As one such activity, a questionnaire survey was conducted targeting GCP-related regulatory authorities in Europe, and the results of the survey were documented.
- Office of Conformity Audit obtained information on products for which an application for approval was planned to file, at an earlier stage by having its staff participate in pre-review consultations introduced in FY 2014, and developed systems to exchange or share information of planned reviews/inspections with the relevant offices of the Review Division.
- In April 2014, PMDA conducted a questionnaire survey that asked companies how electronic records were being used and whether Clinical Data Interchange Standards Consortium (CDISC) standards had already been introduced. The results of the survey were presented at a GCP/GPSP workshop held in January 2015.
- With the cooperation of the Advanced Review with Electronic Data Promotion Group, Office of Clinical and Non-clinical Compliance started to investigate inspection methods using CDISC standard data (SDTM, ADaM) to be obtained by the Review Division and into risk-based methods, etc. In FY 2014, issues to be discussed were determined and prioritized.
- PMDA started a pilot inspection using the GCP Management Sheet (tentative name) in June 2014 with the participation of 12 companies that are major applicants for marketing approval as well as interested companies, and had investigated 19 products of 11 companies by the end of November 2014. In October 2014, PMDA exchanged opinions with industry associations about the adoption and effective use of the GCP Management Sheet (tentative name).

(ii) Efficient GLP/GCP/GPSP inspections and data integrity assessments for medical devices

- The Offices of Medical Devices and Office of Non-clinical and Clinical Compliance held joint meetings to share information on the progress of both reviews and inspections, and conducted GLP/GCP/GPSP compliance assessments in an appropriate and timely manner. In FY 2014, GCP on-site inspections were conducted for 5 new medical devices (including 4 priority review products) using appropriate procedures under the relevant system.
- PMDA participated in the Task Force for Medical Device Regulations to collect the industry's opinions on specific requirements for application, etc.
- From April 2014, applicants are required to submit a "checklist for application acceptance" when filing an application for generic medical devices. Office of Conformity Audit and Offices of Medical Devices started to discuss with medical devices industry which items, regarding the preparation of documents for GLP/GCP/GPSP compliance assessments, needed to be added to the "checklist for application acceptance".

(iii) Efficient GLP/GCP/GPSP inspections and data integrity assessments for cellular and tissue-based products

- In November 2014, PMDA established procedures and SOPs for GLP/GCP/GPSP compliance assessments of cellular and tissue-based products. In addition, PMDA established procedures for selecting studies to be reviewed and for selecting inspecting medical institutions for GCP on-site inspections.

(iv) Efficient GLP inspections and data integrity assessments

- A PMDA staff member became a vice chair of OECD Working Group on GLP. In addition, PMDA dispatched an employee to OECD as the person in charge of GLP, and thereby introduced PMDA's knowledge and know-how in international GLP-related activities.
- Toward the international harmonization, PMDA reviewed and revised the Procedures for GLP related to the categories of evaluation results, findings, test items, etc., and the revision was notified in November 2014.

(v) Efficient GLP/GCP/GPSP inspections and data integrity assessments for re-examination (including use-results evaluation)

- In collaboration with the pharmaceutical industry, PMDA took the following 2 measures to improve the efficiency of GLP/GCP/GPSP compliance assessments by shortening the inspection time and increasing the efficiency of inspection: (i) reduction of duplicated confirmation process by utilizing the results of past inspections; and (ii) continuation of a pilot assessment using the safety information management sheet (process inspection).
- PMDA shared problems revealed by inspections with the pharmaceutical industry in periodic opinion exchange sessions, and provided information obtained from these sessions at the GCP/GPSP workshop held in January 2015.
- In terms of medical devices, opinions were exchanged among MHLW, the Offices of Medical Devices, and the medical device industry about data that should be submitted when applying for a use-results survey and the implementation of GLP/GCP/GPSP compliance assessments. In addition, PMDA participated in the Task Force for Medical Device Regulations to facilitate the efficient operation of the relevant system.
- At the GCP/GPSP workshop held in January 2015, PMDA presented the issues revealed by GLP/GCP/GPSP compliance assessments for re-examination of medical devices.

(vi) Proper conduct of clinical trials, etc.

- Due to the enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act in November 2014, PMDA revised the procedures for consultations by taking the following measures: (i) consultations on GCP/GLP/GPSP and simple consultations on GCP/GLP/GPSP were introduced; (ii) new subcategories of consultation on GCP/GLP compliance for cellular and tissue-based products and consultations on GCP/GLP/GPSP were added to the existing category of consultation on GCP/GLP compliance; and (iii) contact point for consultation services, consultation procedures, and necessary forms were revised.
- PMDA held GCP/GPSP workshops in Tokyo and Osaka and presented findings frequently revealed by document-based GLP/GCP/GPSP compliance assessments, GCP on-site inspections, and GLP/GCP/GPSP compliance assessments for re-examination, to promote the proper conduct of clinical trials. Materials used for the workshops were posted on the PMDA website to make them known to all related parties. In addition, PMDA representatives gave lectures about GLP/GCP/GPSP compliance assessments at academic conferences attended by healthcare professionals, exchanging opinions with related parties.

- PMDA responded to any invitation for lecture on GCP/GLP/GPSP, etc., in so far as it could, to facilitate the understanding of GCP/GLP/GPSP compliance assessments.

Number of Participants in GCP Workshops

Venue	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Tokyo	1,048	1,086	1,254	1,189	1,242
Osaka	455	418	471	404	448
Total	1,503	1,504	1,725	1,593	1,690

Number of GLP/GCP/GPSP Compliance Assessments by Fiscal Year

		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Document-based assessments		2,359	2,437	2,737	2,610	2,396
	New drugs	251	280	286	364	370
	Generic drugs	1,040	1,118	1,188	1,086	1,080
	Medical devices	1,068	1,039	1,263	1,160	946
GCP on-site inspections		171	149	197	242	236
	New drugs	158	140	187	222	221
	Generic drugs	10	8	9	15	10
	Medical devices	3	1	1	5	5
Document-based assessments for re-examination		138	111	127	80	79
	New drugs	135	109	112	71	74
	New medical devices	3	2	15	9	5
GPSP inspections		135	109	112	71	74
	New drugs	135	109	112	71	74
	New medical devices	–	–	–	–	–
Document-based assessments for re-evaluation		–	–	–	–	–
GLP inspections		30	32	39	21	40
	Drugs	26	23	29	18	27
	Medical devices	4	9	10	3	13

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)

Promotion of GMP/GCTP/QMS inspections

(i) Efficient GMP/GCTP/QMS inspections

a. Background of GMP/GCTP/QMS inspections

- In accordance with the amended Pharmaceutical Affairs Act that came into effect in FY 2005, both manufacturing and quality control procedures used by manufacturing sites for drugs etc. must comply with the requirements specified in the Ministerial Ordinance on GMP for Drugs and Quasi-drugs[a] and/or Ministerial Ordinance on QMS for Medical Devices and *In vitro* Diagnostics[b], in order to satisfy regulatory requirements 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).

- In accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act, which came into effect in November 2014, "Pharmaceutical Affairs Act" was changed to "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Act)," in which the term “cellular and tissue-based products” was defined. Before the revision, a license was required to manufacture medical devices and *in vitro* diagnostics; after the revision only registration is required (change from license system to registration system).
- The Ordinance on QMS was also revised, and manufacturers were newly included in targets for QMS inspections. QMS inspections for medical devices with no certification standards, which had previously been conducted by prefectural governments, are now to be conducted by PMDA.
- GCTP Ordinance[c] and Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments for cellular and tissue-based products were established and came into effect in 2014. PMDA issued "Questions and Answers Related to Good Manufacturing Practice for Cellular and Tissue-based Products" (PFSB/CND Notification No. 0317-1 dated March 17, 2015) to promote the efficient conduct of manufacturing control and quality control at manufacturing sites.

[a] *Ministerial Ordinance on Good Manufacturing Practice (GMP) for Drugs and Quasi-drugs (MHLW Ministerial Ordinance No.179 of 2004)*
[b] *Ministerial Ordinance on Quality Management System (QMS) for Medical Devices and In vitro Diagnostics (MHLW Ministerial Ordinance No.169 of 2004)*
[c] *Ministerial Ordinance on Good Gene, Cellular, and Tissue-based Products (GCTP) (MHLW Ministerial Ordinance No.93 of 2014)*
Note 1: GMP (Good Manufacturing Practice):
Note 2: QMS (Quality Management System):
Note 3: GCTP (Good Gene, Cellular, and Tissue-based Products Manufacturing Practice)

b. Establishment of the inspection system

- PMDA had 47 GMP/GCTP/QMS inspectors (including inspectors in the Kansai Branch) as of April 1, 2014. In the areas of drugs and quasi-drugs, PMDA proceeded with building a system to supervise quality management, such as by setting up an inspection quality assurance group, based 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/GCTP/QMS inspections in FY 2014 is shown below:

GMP/QMS Inspections under the Pharmaceuticals and Medical Devices Act

	FY 2009				FY 2010			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	2,228	2,000 (297)	71	969	1,159	1,324 (131)	120	684
In vitro diagnostics	115	107 (3)	5	36	66	81 (0)	2	19
Quasi-drugs	3	3(0)	0	2	1	0 (0)	1	2
Medical devices	1,201	1,285 (66)	39	237	896	944 (54)	40	149
Cellular and tissue-based products	—	—	—	—	—	—	—	—
Total	3,547	3,395(366)	115	1,244	2,122	2,349 (185)	163	854

	FY 2011				FY 2012			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	1,538	1,283 (185)	31	908	1,582	1,593 (198)	40	821
In vitro diagnostics	73	85 (0)	1	6	64	48 (0)	0	16
Quasi-drugs	0	0 (0)	0	2	6	2 (0)	2	3
Medical devices	697	765 (36)	24	57	999	954 (81)	3	37
Cellular and tissue-based products	—	—	—	—	—	—	—	—
Total	2,308	2,133 (221)	56	973	2,651	2,597 (279)	45	877

	FY 2013				FY 2014			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	1,508	1,415 (168)	75	875	1,877	1,672 (163)	51	1,030 (0)
In vitro diagnostics	52	67 (1)	0	7	65	38 (1)	0	27 (0)
Quasi-drugs	3	3 (1)	0	4	5	6 (0)	0	2 (0)
Medical devices	988	883 (61)	11	193	755	512 (42)	18	225 (86)
Cellular and tissue-based products	—	—	—	—	0	0 (0)	0 (0)	0 (0)
Total	2,551	2,368 (231)	86	1,079	2,702	2,228 (206)	69	1,284 (86)

** 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 2014 are shown below:

Median Processing Time of GMP/QMS Inspections

	FY 2009		FY 2010		FY 2011	
	Total processing time (Median)	PMDA processing time (Median)	Total processing time (Median)	PMDA processing time (Median)	Total processing time (Median)	PMDA processing time (Median)
Drugs* (days)	162	91	118	63	147	77
In vitro diagnostics (days)	110	56	117	62	83	38
Quasi-drugs (days)	154	108	–	–	–	–
Medical devices (days)	142	56	145	69	113	21
Cellular and tissue-based products (days)	–	–	–	–	–	–
	FY 2012		FY 2013		FY 2014	
	Total processing time (Median)	PMDA processing time (Median)	Total processing time (Median)	PMDA processing time (Median)	Total processing time (Median)	PMDA processing time (Median)
Drugs* (days)	176	90	118	71	172	76
In vitro diagnostics (days)	100	36	106	66	147	102
Quasi-drugs (days)	219	71	272	71	166	96
Medical devices (days)	21	44	106	56	118	74
Cellular and tissue-based products (days)	–	–	–	–	–	–

** Excluding in vitro diagnostics.*

- The processing status of inspections of manufacturing facilities conducted in FY 2014 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. Since the enforcement the registration system in accordance with the PMD Act, no inspections of manufacturing facilities have been conducted for medical devices or *in vitro* diagnostics.

Number of Inspections of Buildings and Facilities for Domestic Manufacturing Sites

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs*	20 (19)	25 (19)	15 (9)	9 (4)	25 (11)
In vitro diagnostics	1 (1)	3 (3)	1 (1)	3 (3)	0 (0)
Medical devices	3 (3)	0 (0)	2 (1)	0 (0)	2 (2)
Cellular and tissue-based products	–	–	–	–	1 (1)
Total	24 (23)	28 (22)	18 (11)	12 (7)	28 (14)

** 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 at domestic manufacturers etc., under instructions from the MHLW. The number of for-cause inspections conducted in FY 2014 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs*	6	12	13	6	5
In vitro diagnostics	2	3	1	1	0
Medical devices	1	0	0	0	0
Cellular and tissue-based products	–	–	–	–	0
Total	9	15	14	7	5

** Excluding in vitro diagnostics.*

- PMDA conducts simple consultations on GMP/GCTP/QMS inspections. The number of simple consultations on GMP/GCTP/QMS inspections conducted in FY 2014 is shown below. There was an increase in number of simple consultations on QMS to accommodate the PMD Act.

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs*	36	44	38	44	32
In vitro diagnostics	0	0	0	0	0
Quasi-drugs	1	0	0	0	0
Medical devices	6	6	8	3	51
Cellular and tissue-based products	–	–	–	–	0
Total	43	50	46	47	83

** 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
FY 2014	20	3	51	0	74

Note: Breakdown of FY 2014:
Europe, France, Spain, Italy, Belgium, Austria, Germany, Turkey, Hungary, Cyprus, Latvia, Slovakia;
North, Central and South America, the United States (including Puerto Rico);
Asia, Oceania, China, India, South Korea, Taiwan, Thailand, Vietnam, Malaysia

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
FY 2014	5	5	19 (2)	0	29 (2)

Note: Breakdown of FY 2014:
Europe, Ireland, UK, Italy, India;
North, Central and South America, the United States (including Puerto Rico), Mexico;
Asia, Oceania, China, South Korea, Singapore, Taiwan, Malaysia

- The number of inspections of manufacturing facilities conducted in FY 2014 at foreign manufacturing sites based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below. Since the enforcement the registration system in accordance with the PMD Act, no inspections of manufacturing facilities have been conducted for medical devices or *in vitro* diagnostics.

Number of Inspections of Buildings and Facilities for Foreign Manufacturing Sites

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs*	230	579	530	383	384
In vitro diagnostics	27	60	68	79	23
Quasi-drugs	26	72	62	58	36
Medical devices	677	1,187	1,751	1,453	722
Cellular and tissue-based products	–	–	–	–	0
Total	960	1,898	2,411	1,973	1,165

** 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 at foreign manufacturers etc., under instructions from MHLW. The number of for-cause inspections conducted in FY 2014 is shown below:

Number of For-cause Inspections (Foreign Manufacturing Sites)

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs*	1	1	4	2	1
In vitro diagnostics	0	0	0	0	0
Medical devices	4	1	1	0	0
Cellular and tissue-based products	–	–	–	–	0
Total	5	2	5	2	1

** 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	FY 2014	Total
Europe	France	6	5	6	1	3	2	1	3	27
	Denmark	3	2	2	0	0	0	2	0	9
	Ireland	2	5	3	2	0	1	1	0	14
	UK	4	1	3	0	0	1	1	0	10
	Netherlands	1	1	5	0	0	2	0	0	9
	Spain	3	1	1	0	0	0	0	1	6
	Italy	2	5	3	2	0	1	2	3	18
	Belgium	1	2	4	3	1	0	2	3	16
	Austria	0	2	2	0	1	2	0	1	8
	Finland	0	0	2	0	0	1	0	0	3
	Germany	0	3	7	0	3	1	0	1	15
	Sweden	0	1	0	0	0	0	1	0	2
	Romania	0	1	0	0	0	0	1	0	2
	Czech	0	0	0	0	0	1	0	0	1
	Ukraine	0	0	0	0	0	1	0	0	1
	Lithuania	0	0	0	0	0	1	0	0	1
	Slovenia	0	2	1	0	0	0	0	0	3
	Portugal	0	0	0	3	0	0	0	0	3
	Greece	0	0	0	0	1	0	0	0	1
	Turkey	0	0	0	1	0	0	0	1	2
	Iceland	0	0	0	0	0	0	1	0	1
	Hungary	0	0	0	0	0	0	0	3	3
	Cyprus	0	0	0	0	0	0	0	1	1
	Latvia	0	0	0	0	0	0	0	2	2
	Slovakia	0	0	0	0	0	0	0	1	1
	Subtotal	22	31	39	12	9	14	12	20	159
North, Central and South America	USA	22	14	18	23	6	14	8	3	108
	Canada	0	2	2	1	0	0	1	0	6
	Mexico	0	1	0	0	1	0	0	0	2
	Argentina	0	2	0	0	0	0	0	0	2
	Brazil	0	0	0	0	0	0	1	0	1
	Subtotal	22	19	20	24	7	14	10	3	119
Asia/Oceania	China	5	11	25	10	20	16	18	23	128
	India	1	12	4	7	4	4	3	4	39
	Singapore	2	4	0	0	0	0	2	0	8
	South Korea	0	3	9	10	18	14	11	13	78
	Indonesia	0	0	0	0	0	1	0	0	1
	Taiwan	0	2	6	1	1	2	6	6	24
	Thailand	0	0	2	0	1	0	2	1	6
	Vietnam	0	0	0	1	1	0	0	3	5
	Israel	0	0	0	0	0	1	0	0	1
	New Zealand	0	0	1	0	0	0	0	0	1
	Malaysia	0	0	0	0	0	0	0	1	1
	Subtotal	8	32	47	29	45	38	42	51	292
Grand Total		52	82	106	65	61	66	64	74	570

Note 1: Excluded are for-cause inspections at foreign manufacturing sites under Article 75-4 of the PMD 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	FY 2014	Total
Europe	Ireland	0	6	0	4	1	3	0	1	15
	UK	0	1	0	0	1	0	1	2	5
	Italy	0	2	0	2	1	1	0	1	7
	Netherlands	0	1	0	1	0	0	0	0	2
	Switzerland	0	1	1	0	0	0	1	0	3
	Spain	0	1	0	0	0	1	0	0	2
	France	1	1	1	1	1	4	0	0	9
	Denmark	0	0	1	0	0	0	0	0	1
	Austria	0	0	0	0	0	1	0	0	1
	Belgium	0	0	0	0	0	1	0	0	1
	Turkey	0	0	0	0	0	0	1	0	1
	Subtotal	1	13	3	8	4	11	3	4	47
North, Central and South America	USA	10	16	27	19	12	21	8	4	117
	Mexico	0	1	0	0	1	0	0	1	3
	Brazil	0	0	1	0	0	0	0	0	1
	Canada	0	0	0	0	1	1	4	0	6
	Costa Rica	0	0	0	0	1	0	0	0	1
	Subtotal	10	17	28	19	15	22	12	5	128
Asia	China	0	0	3	0	0	1	1	6	11
	South Korea	0	0	0	1	0	0	5	8	14
	Thailand	0	0	0	0	0	1	0	0	1
	Singapore	0	0	2	0	0	0	2	1	5
	Philippines	0	0	0	0	0	2	0	0	2
	Israel	0	0	0	0	1	0	1	0	2
	Taiwan	0	0	0	0	0	0	1	3	4
	UAE	0	0	0	0	0	0	1	0	1
	Malaysia	0	0	0	0	0	0	0	1	1
	India	0	0	0	0	0	0	0	1	1
	Subtotal	0	0	5	1	1	4	11	20	42
Grand Total		11	30	36	28	20	37	26	29	217

Note 1: Excluded are for-cause inspections at foreign manufacturing sites under Article 75-4 of the PMDs Act.

Note 2: Puerto Rico was included in the USA.

d. Coordination between GMP/GCTP/QMS inspections and reviews

- During the review process for drugs, quasi-drugs, and cellular and tissue-based products, the Office of Manufacturing/Quality and Compliance holds periodic meetings with the Review Division (once a month with Offices of New Drug) to exchange information on the progress of reviews and the quality of reviews related to manufacturing control and quality control, and thereby ensures that inspections are conducted at the appropriate times in the review process.
- For applications for medical devices, QMS inspectors and reviewers share information at weekly meetings to check the progress of review and ensure that there are no discrepancies between the content of application documents and the specifications and test methods 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.

e. For-cause inspections of registered certification bodies

- As the regulatory authority governing registered certification bodies was transferred to PMDA from the MHLW, PMDA conducted for-cause inspections at 6 registered certification bodies on or after November 25, 2014.

(ii) Building of the inspection system based on the Act on Safety of Regenerative Medicine

a. Building of the inspection system

- In accordance with the Act on the Safety of Regenerative Medicine enacted in 2013 and enforced in 2014, the Office of Manufacturing/Quality and Compliance started to conduct inspections in order to ascertain conformity to the standards for buildings and facilities specified under Article 42 of the Act of Safety of Regenerative Medicine required for obtaining license/certification of manufacturing at cell processing centers, at the request of the Health Policy Bureau in MHLW or Regional Bureau of Health and Welfare. For-cause inspections are also to be conducted under instructions from the Health Policy Bureau of the MHLW.

  In FY 2014, on-site inspections of manufacturing facilities were started at Japanese cell processing centers that had submitted application for license/certification of manufacturing.

  To secure a sufficient number of inspectors, PMDA started to provide trainings in inspection methods to inspectors of the Office of Manufacturing/Quality and Compliance. PMDA is making efforts to obtain the number of inspectors needed in order to deal with all applications filed.

Number of Applications for License/Accreditation of Manufacturing Based on the Act on Securing of Safety of Regenerative Medicine, etc.

FY 2014				
	Application	Processed	Withdrawn	Under inspection
Application for license of manufacturing (in Japan)	19	0	0	19
Application for approval of manufacturing (in foreign countries)	0	0	0	0
Total	19	0	0	19

Administrative Processing Time for Inspection for License/Certification of Manufacturing

FY 2014		
	Median total processing time	Median PMDA processing time
Application for license of manufacturing (in Japan)	—	—
Application for approval of manufacturing (in foreign countries)	—	—

Number of For-cause Inspections Conducted by PMDA

Region	FY 2014
Japan	0
Foreign countries	0
Total	0

b. Establishment of inspection methods

With respect to standards for cell processing centers under Article 42 of the Act on the Safety of Regenerative Medicine, PMDA prepared a checklist that explains what is required to meet the standards and presents PMDA's viewpoints for inspection. The checklist is available on the PMDA website.

3.2.(2) Support for the initiative to facilitate the development of innovative drugs, medical devices, and cellular and tissue-based products

(i) Establishment and revision of review standards, etc., for innovative products

- Science Board was established in May 2012, in which PMDA reviewers exchange opinions with leading researchers in Japan about evaluation methods, etc., for advanced science and technologies. The Science Board completed activities for the first term at the end of FY 2014, and summarized the following 3 reports: "Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from induced Pluripotent Stem Cells (iPS) and iPSCs as Their Starting Materials," "Summary of Discussions on Non-clinical Pharmacology Studies on Anticancer Drugs," and "Summary of Discussion on the Assessment of the Current Status of Personalized Medicine Related to the Development and Regulatory Review."
- Based on the initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products (a project funded by MHLW), PMDA conducted personnel exchange and information sharing by accepting specially appointed experts from research institutions and dispatching employees of PMDA to such research institutions, and supported not only the establishment of methods to evaluate the safety and efficacy of innovative drugs, medical devices, and cellular and tissue-based products but also the conduct of research projects for the preparation of guidelines needed to accelerate reviews. In addition, PMDA has worked to develop human resources with expertise in innovative technologies and regulatory science both in academia and in the Agency.
- In order to properly conduct reviews, safety measures, and relief services for adverse health effects and to enhance the quality of these activities, PMDA is striving to promote regulatory science research on topics including the preparation of standards, guidelines and guidance, and research on how to conduct scientific prediction, evaluation, and judgment in PMDA's operations. Among regulatory science researches conducted by PMDA, those designated by the Chief Executive are carried out as part of PMDA's operations. Designation is based on research purpose, how research is related to PMDA's operations, and comments from the Regulatory Science Research Evaluation Committee. In FY 2014, 13 projects (7 new projects and 6 ongoing projects) were selected for designated research and the results of 2 of these projects were published in academic journals (reposted).
- In FY 2014, PMDA cooperated in the preparation of the government's evaluation guidelines through the activities of 11 standards development projects and working groups as the Projects Across Multi-offices in PMDA. These activities were intended to promote product development, facilitate international collaborations for review standards etc., and accelerate reviews by making clear scientific principles for reviews of drugs and medical devices. Specifically, PMDA cooperated in the issuance of one notification from the Post-approval Manufacturing Changes Project and one administrative notice from the Global Clinical Trial Project.
- In FY 2014, in order to share and investigate issues to be addressed by the Pediatric Drugs Working Group and Orphan Drug Working Group, which were Projects Across Multi-offices in PMDA, PMDA held teleconferences on a regular basis with experts from regulatory authorities in

the EU and the US. Members of the QbD Assessment Project participated in presentation sessions and panel discussions in workshops and international academic conferences, and thus explained how reviews and consultations are regarded in Japan and exchanged opinions with participants from foreign regulatory authorities toward international harmonization.

- In Vitro Companion Diagnostic Devices Working Group in the Companion Diagnostic and Omics Project (hereinafter referred to as “Companion Diagnostics Devices WG”) held a PMDA workshop entitled “Companion Diagnostics - Regulatory Perspective and Challenges in Development and Evaluation” on September 1, 2014 in association with the administrative notice issued in the previous fiscal year. With the aim of enhancing the efficiency of development and reviews, the regulatory agency, industry, and academia exchanged opinions and discussed proposals from academia and questions raised by companies.

  The Companion Diagnostics Devices WG also examined “Methodology in Clinical Trials Using Genomic Biomarkers and Selection of Patients (draft)” prepared in a project (Nagoya City University Graduate School of Pharmaceutical Sciences; cancer and personalized medicine) supported by the initiative to facilitate the development of innovative drugs, medical devices, and cellular and tissue-based products.

(ii) Expansion of Pharmaceutical Affairs Consultations on R&D Strategy

- Pharmaceutical Affairs Consultations on R&D strategy have been expanded since November 2014, and PMDA started to provide general advice on the development process (roadmap) and confirmatory clinical trial protocols to applicants including pharmaceutical companies on a trial basis. Furthermore, PMDA provided on-site introductory consultation and distributed brochures to relevant academic conferences for the purpose of publicity. Through collaboration between relevant offices, activities were carried out promptly and appropriately. Pharmaceutical Affairs Consultations on R&D Strategy were explained at relevant academic conferences by persons in charge from Tokyo Headquarters and the Kansai Branch.
- PMDA promoted the use of Pharmaceutical Affairs Consultations on R&D Strategy (introductory consultations and pre-application consultations) at Kansai Branch by providing relevant information at the first anniversary symposium of Kansai Branch of PMDA in November 2014 and other opportunities. Pharmaceutical Affairs Consultations on R&D Strategy continued to be conducted with collaboration between the offices in Tokyo and the Kansai Branch.
- In order to promote the establishment of an exit strategy at an early stage of development, in November 2014 PMDA started to offer consultations on R&D strategy for development program to advise on the development process (roadmap) on a trial basis, and thus enhanced the services offered by Pharmaceutical Affairs Consultations on R&D Strategy.

(iii) Implementation of approval system based on characteristics of cellular and tissue-based products

- In order to address the introduction of the conditional and time-limited approval system for cellular and tissue-based products, relevant offices collaborated in conducting Pharmaceutical Affairs Consultations on R&D Strategy, and provided relevant information at academic conferences, etc., and thus promoted the use of the system.

3.3 Safety measure services

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

- In order to improve the safety of marketed drugs, medical devices, and cellular and tissue-based products, and to enable patients and healthcare professionals to use them properly, PMDA

efficiently collects and examines safety information, rapidly processes such information, devises appropriate safety measures, and promptly provides easy-to-understand safety information, to ensure that reviews and safety measures function in an integrated manner.

- There were approximately 350,000 reports from companies on adverse reactions and infections attributable to drugs and approximately 32,000 reports on medical device malfunctions and infections attributable to medical devices submitted to PMDA from within and outside of Japan, and 17 reports on cellular and tissue-based product malfunctions and infections attributable to such products submitted to PMDA in FY 2014 (on and after enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics [PMD Act] on November 25, 2014). 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, in order to consider and evaluate PMDA's responses to products marketed in Japan on a daily basis, while reviewing academic literature for the purpose of analyzing, sharing and evaluating information on adverse drug reactions. In addition, PMDA is making efforts to implement comprehensive safety measures for drugs, medical devices, and cellular and tissue-based products in the post-marketing stage by enhancing cooperation between review offices and safety offices, and 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 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs	339	185	198	160	100
Medical devices	19	17	15	14	4
Cellular and tissue-based products	-	-	-	-	0[*1]
Medical safety[*2]	5	6	6	6	6

**1 Number of reports after enforcement of the PMD Act on November 25, 2014*

**2 "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 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs	Directions for revision to precautions in package insert	339	185	198	160	100
	Posting articles and cases on PMDSI	32	41	36	40	29
Medical devices	Directions for revision to precautions in package insert or issuance of notifications on self-check	3	5	4	3	2
	Posting articles on PMDSI	3	4	1	4	1
Cellular and tissue-based products*	Directions for revision to precautions in package inserts or issuance of notifications on self-checking	-	-	-	-	0
	Posting articles on PMDSI	-	-	-	-	0

** Number of reports after enforcement of the PMD Act on November 25, 2014*

- 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) in collaboration 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.) for new drugs, new medical devices, and new cellular and tissue-based products. 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 accordance with the PMD Act, PMDA started to organize and examine data on applications for relief benefits on November 25, 2014.
- In FY 2014, PMDA made the following efforts to appropriately collect, organize, and examine the reports on adverse drug reactions, 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 360 participants) to gather information
  d. Held regular liaison meetings on drugs, medical devices, and cellular and tissue-based products with MHLW (every week)

- PMDA's information management system for adverse drug reactions and the safety measures support system will need to comply with the ICH-E2B (R3) guideline, which is the next international data exchange standard for adverse drug reaction reporting. In FY 2014, PMDA continued developing the reception system from FY 2013. In addition, PMDA began modifying the safety measures support system in FY 2014.
- In accordance with the enforcement of Act for Partial Revision of the Pharmaceutical Affairs Act on November 25, 2014, PMDA was designated to receive reports from healthcare professionals on adverse reactions, infections, and malfunctions attributable to drugs or medical devices, and reports on adverse reactions associated with vaccination by healthcare professionals. PMDA developed the necessary system and structure for receiving such reports and made efforts to evaluate and discuss such matters more promptly.

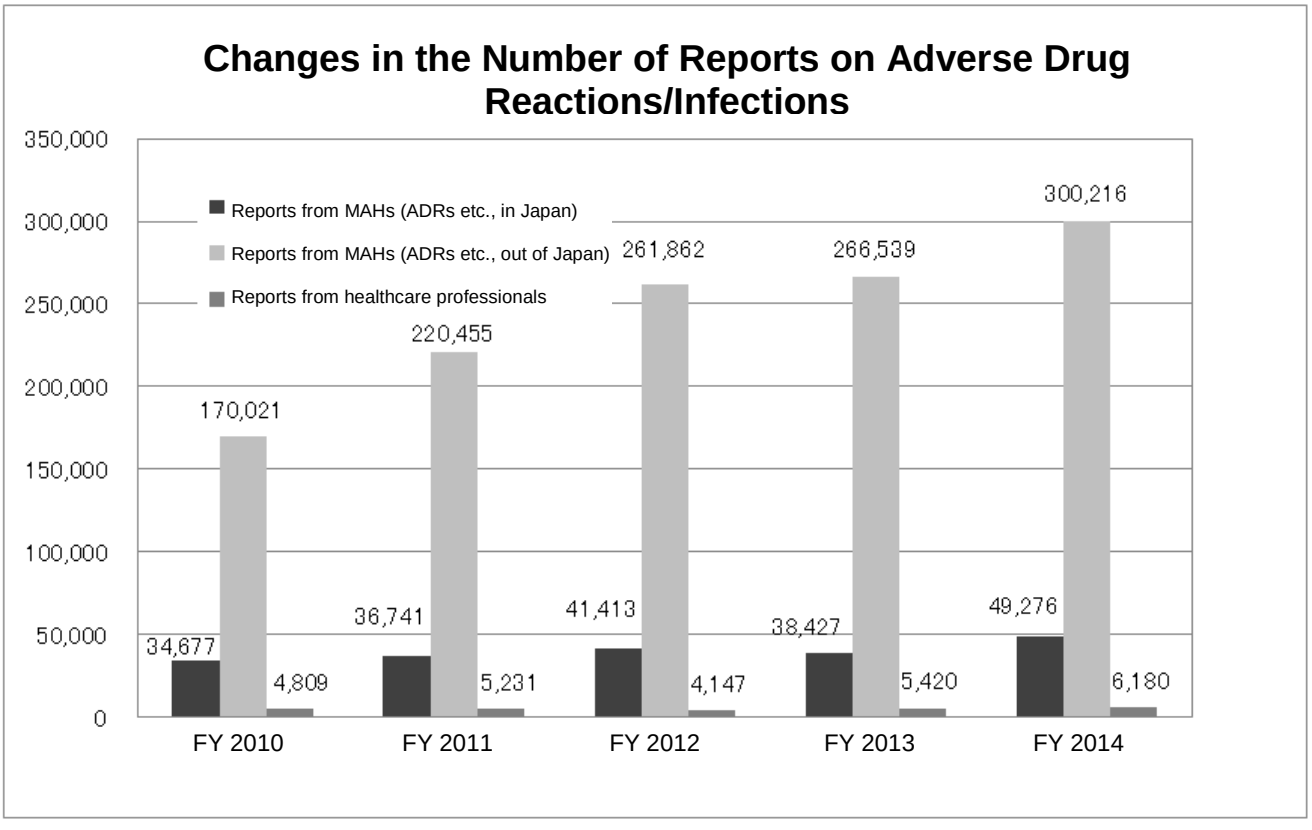
○ Collection of adverse reaction reports etc.

1-1) Number of reports relating to drugs

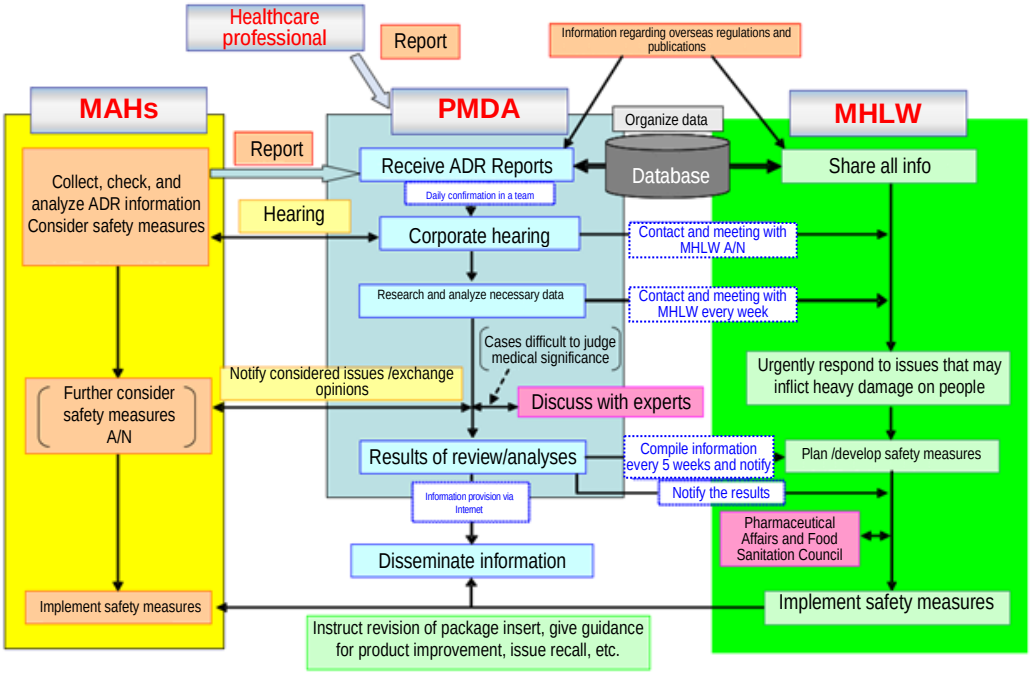
	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Reports from MAHs	207,772	260,473	306,410	308,383	352,908
(adverse drug reactions, in Japan)	(34,578)	(36,641)	(41,254)	(38,329)	(49,198)
(infections caused by drugs, in Japan)	(99)	(100)	(159)	(98)	(78)
(adverse drug reactions, out of Japan)	(169,994)	(220,410)	(261,823)	(266,506)	(300,191)
(infections caused by drugs, out of Japan)	(27)	(45)	(39)	(33)	(25)
(research reports)	(940)	(841)	(884)	(962)	(1,099)
(foreign safety measure reports)	(1,033)	(1,347)	(1,134)	(1,317)	(1,219)
(periodic infection reports)	(1,101)	(1,089)	(1,117)	(1,138)	(1,098)
Reports from healthcare professionals	4,809	5,231	4,147	5,420	6,180
(1) Safety information reporting system	3,656	3,388	3,304	4,067	4,782
(2) Vaccines*	1,153	1,843	843	1,353	1,398
Total	212,581	265,704	310,557	313,803	359,088

** For FY 2010 through 2012, the figures indicate the total numbers of reports on adverse reactions following vaccination with cervical cancer vaccine, Hib vaccine, pediatric pneumococcal conjugate vaccine, and influenza vaccines. From FY 2013 onward, the figures indicate the total numbers of reports on adverse reactions following vaccination with all vaccines.*

- PMDA began receiving individual case reports on adverse reactions attributable to quasi-drugs/cosmetics from April 1, 2014 and, up until the end of FY 2014, had received 561 reports on quasi-drugs and 116 reports on cosmetics.

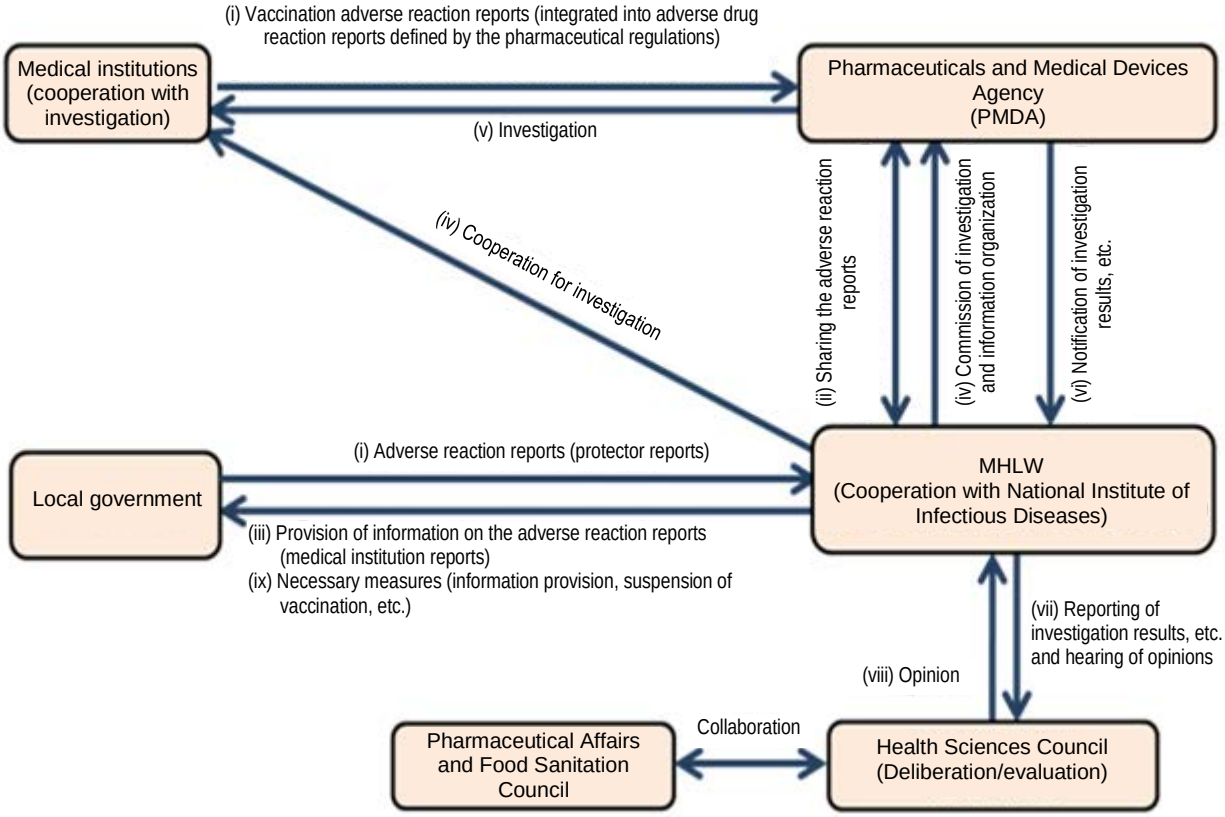


Flowchart for Processing Adverse Drug Reaction Reports



1-2) Reports on adverse reactions following vaccination based on the Preventive Vaccination Act

Pursuant to Article 14 of the Preventive Vaccination Act (Act No. 68 of 1948), PMDA has been conducting projects for investigating and organizing vaccination adverse reaction reports. As of November 25, 2014, vaccination adverse reaction reports are required to be submitted to PMDA in accordance with the revisions to the Preventive Vaccination Act and the Ministerial Ordinance for Enforcement of the Preventive Vaccination Act (see diagram, below). The number of vaccination adverse reaction reports received in FY 2014 was 1,398. Upon receiving vaccination adverse reaction reports, PMDA provides information to MAHs on suspect vaccines, and also issues directions on how to properly deal with such events under the PMD 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 reported by patients themselves 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. The purpose of those reports is to improve safety measures for drugs through such means 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 2014 is shown in the following table. In FY 2014, PMDA also released information on cases reported between April 2013 and March 2014. In October 2014, PMDA changed the display design of and added functions to the patient adverse drug reaction reporting system, based on results of a questionnaire survey of users of the system.

	FY 2011	FY 2012	FY 2013	FY 2014
Adverse drug reaction reports from patients (total number)*	30	154	122	91

** The number of reports is that at the end of each fiscal year. Reports may be withdrawn at the request of reporters. Reports on items not classified as adverse drug reaction reports from patients (i.e., items other than drugs and vaccine) are excluded.*

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.

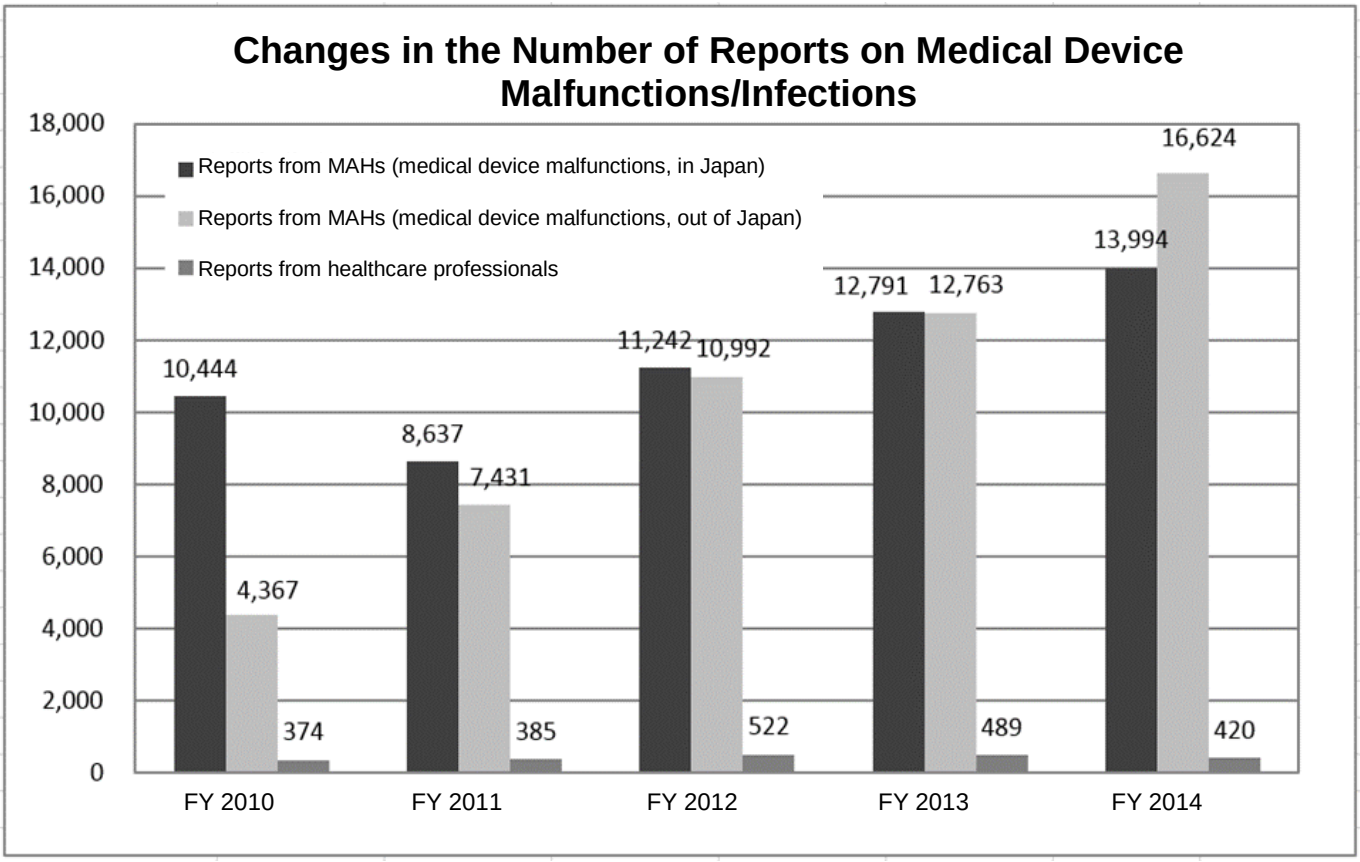
The number of cases investigated by PMDA by the end of FY 2014 is shown in the following table.

	FY 2012	FY 2013	FY 2014
Number of cases investigated by PMDA	663	862	1,067

For adverse drug reaction/infection reports investigated by PMDA through inquiries after being submitted by healthcare professionals to the Minister of Health, Labour and Welfare (and to PMDA from November 25, 2014 onwards), data on individual adverse reactions/infections in the reports were communicated, via the internet (dedicated server), to the MAHs of the primary suspect drugs.

2) Number of reports relating to medical devices

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Reports from MAHs	15,874	17,192	23,643	27,303	32,490
(medical device malfunctions, in Japan)	(10,444)	(8,637)	(11,242)	(12,791)	(13,994)
(medical device malfunctions, out of Japan)	(4,367)	(7,431)	(10,992)	(12,763)	(16,624)
(infections caused by medical devices, in Japan)	(0)	(0)	(0)	(0)	(0)
(research reports)	(27)	(2)	(3)	(5)	(20)
(foreign safety measure reports)	(978)	(1,060)	(1,337)	(1,669)	(1,779)
(periodic infection reports)	(58)	(62)	(69)	(75)	(73)
Reports from healthcare professionals	374	385	522	489	420
Total	16,248	17,577	24,165	27,792	32,910



3) Number of reports relating to cellular and tissue-based products

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Reports from MAHs	-	-	-	-	17
(product malfunctions, in Japan)	-	-	-	-	12
(product malfunctions, outside of Japan)	-	-	-	-	0
(infections caused by products, in Japan)	-	-	-	-	0
(infections caused by products, outside of Japan)	-	-	-	-	0
(research reports)	-	-	-	-	0
(foreign safety measure reports)	-	-	-	-	0
(periodic infection reports)	-	-	-	-	5
Reports from healthcare professionals	-	-	-	-	0
Total	-	-	-	-	17

** Reporting in respect of cellular and tissue-based products was initiated on November 25, 2014, the date of enforcement of the PMD Act. The figures for FY 2014 indicate the number of reports submitted on and after the date.*

(ii) Sophistication of safety measures

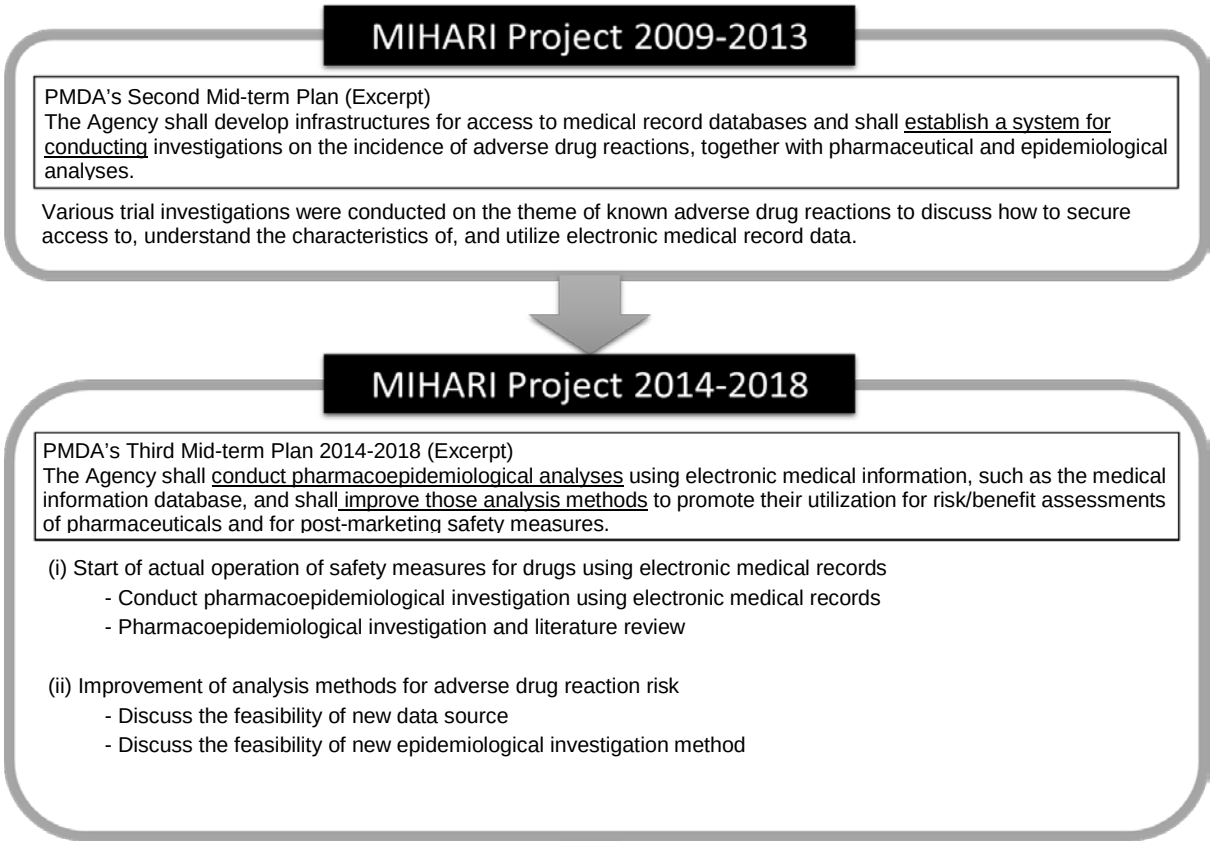
a. Use of electronic medical records etc.

- In accordance with the Third Mid-term Plan, PMDA intends to perform pharmacoepidemiological analysis using digitized medical information such as medical information database and to advance the analytical method, to utilize digitized information for risk-benefit assessment or safety measures for drugs.

  Accordingly, through the "MIHARI Project", starting in FY 2009, based on results obtained during the period of the Second Mid-term Plan, PMDA is promoting "(1) actual operation of safety measures for drugs using electronic medical records" and "(2) advancement of risk analytical methods for adverse drug reactions" during the period of the Third Mid-term Plan, to proactively

utilize investigation and analytical methods that use electronic medical records, including claims data and hospital information system data, for post-marketing drug safety evaluation (see figure below).

Direction of the MIHARI Project in the Third Mid-term Plan

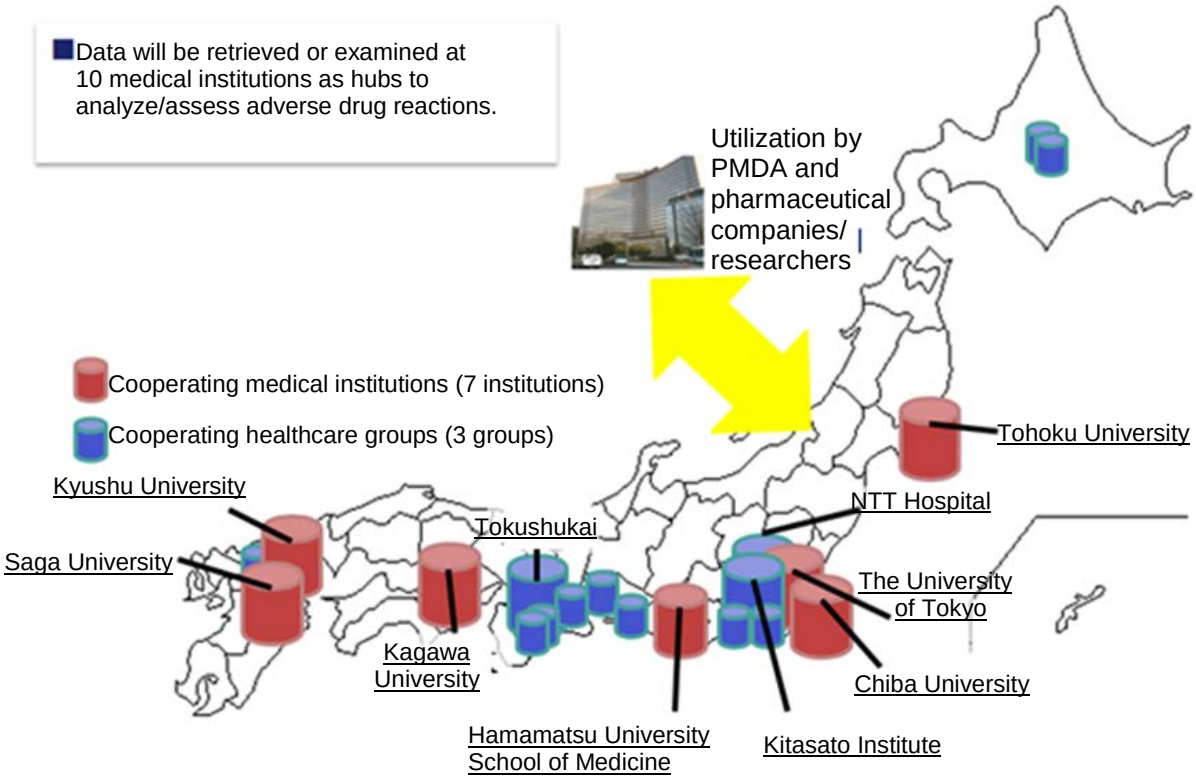


- For "(i) actual operation of drug safety measures using electronic medical records," PMDA will act to review literature on pharmacoepidemiology, investigation reports, etc. submitted by pharmaceutical companies, etc. regarding individual drug safety issues identified in the post-marketing phase, and to conduct investigations using electronic medical records as necessary, and to provide useful information for determination of safety measures to be implemented, such as revision of package inserts and issuance of notifications. In FY 2014, PMDA conducted an investigation to assess "risk of developing dyslipidemia after prescription of atypical antipsychotics" using claims data from health insurance societies. In addition, the Offices of Safety I & II and Offices of New Drugs collaboratively reviewed evidential literature submitted by pharmaceutical companies and investigated how drugs are actually prescribed.
- For "(ii) improvement of analysis methods for adverse drug reaction risk," PMDA will discuss utilization of a new database of electronic medical records and new pharmacoepidemiological methods. In FY 2014, PMDA planned a trial survey, "Comparison of cardiovascular risk by antidiabetic drug classes," using "National Claim Data" managed by the Health Insurance Bureau of MHLW as a new data source. PMDA asked the Bureau to provide claim data (special sampling), and gained the consent from the Bureau. Going forward, PMDA will receive, analyze, and evaluate the data.
- In FY 2014, PMDA redesigned the MIHARI Project pages (e.g., rearrangement of the archives) within the PMDA website to make them more user-friendly, and sequentially disclosed the reports on respective trial surveys conducted during the effective period of the Second Mid-term Plan.

Furthermore, in FY 2014, PMDA started to release “MIHARI Communication,” summaries of the survey results written in relatively simple language, as a communication tool so that healthcare professionals who are not specialized in pharmacoepidemiology could understand the pharmacoepidemiological studies conducted under the MIHARI Project.

- The purpose of the "Project for developing the medical information database infrastructure” is to build a database that collects electronic medical information from 10 cooperating medical institutions nationwide, such as university hospitals, selected by MHLW through open recruitment. The project aims to establish a linked system for medical information databases (MID-NET®) covering 10 million patients, nationwide. In this project, PMDA is responsible for establishing the system in the cooperating medical institutions. The Agency also intends to develop its internal analysis system so as to utilize this database for safety measures (see diagram).

Project for Developing the Medical Information Database



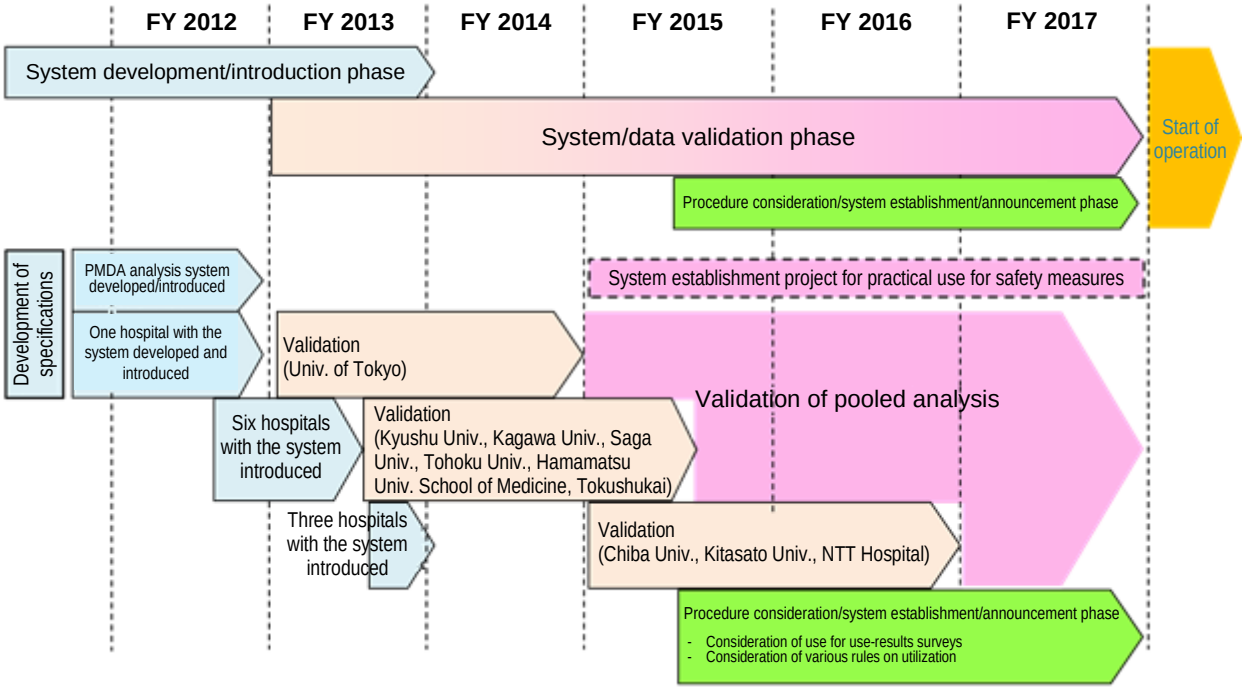
- Development of the medical information database system was initiated in FY 2011 and was completed at 10 cooperating medical institutions by the beginning of April 2014.

  In FY 2014, PMDA promoted data accumulation in the database introduced to the 10 medical institutions and took the lead in conducting verification to control and improve the quality of stored data based on the results of the validation project that was carried out in FY 2013 (see below). In FY 2015, PMDA will continuously conduct validation to control and improve the quality of data and will promote trial utilization of medical information stored in the database for practical application in safety measures. However, data quality issues were identified by validation, and a certain amount of time is required to address the issues and ensure data quality. PMDA therefore reviewed the

project plan with MHLW and changed the time for the full-scale launch of the medical information database, including the start of utilization by third parties such as pharmaceutical companies, from FY 2016 to FY 2018.

- In FY 2013, PMDA started a data validation project to sophisticate analytical methods for the medical information database. 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 will also lead to confirmation of the reliability of the medical information database toward full-scale utilization. In 7 medical institutions, validation starting in FY 2013 or FY 2014 will continue in FY 2015. In the remaining 3 medical institutions, validation will start in FY 2015.

Progress and Plan for Project for Development of the Medical Information Database Infrastructure



b. Collection of data on medical devices (implantable ventricular-assist devices [IVADs])

- In accordance with the Third Mid-term Plan, based on discussions held up until the effective period of the previous Mid-term Plan, PMDA intends to reinforce a post-marketing information collection system, such as construction of a patient registration system (registry) for confirming long-term safety, in collaboration with relevant academic societies, companies, etc.

- In FY 2014, PMDA continued with the "Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS)" project, which had been built and operated as a registry model project under industry-government-academia collaboration during the effective period of the previous Mid-term Plan. In FY 2014, PMDA began discussing with relevant academic societies, companies, etc. how the system will operate going forward. As of March 30, 2015, a total 449 patients (351 for IVAD, 98 for extracorporeal VAD) had been enrolled at 31 medical institutions participating in J-MACS. The number of enrolled patients, survival rates, and other data have been progressively updated on the PMDA website.

c. Evaluation of medical device malfunctions

- In accordance with the First and Second Mid-term Plans, PMDA intended to develop methods for evaluation of medical devices by ascertaining the incidence of device malfunctions that could unavoidably occur at a certain rate due to the nature of particular devices, rather than to structural defects, and it conducted pilot studies of an implantable central venous port system and coronary stents.
- In FY 2014, PMDA published the final report on analysis results of a pilot study of coronary stents, followed for 5 years, in a total of 15,792 patients undergoing percutaneous coronary intervention (13,592) or coronary artery bypass graft (2,200) who were enrolled in 26 medical institutions. The report was released on the PMDA website.
- In addition, based on the pilot studies of an implantable central venous port system and coronary stents, PMDA summarized the points to be considered in conducting a study to evaluate medical device malfunctions, and released the report on its website.

d. Building the patient registration system (registry) for cellular and tissue-based products

- In the "Project for developing a patient registration system for cellular and tissue-based products" at MHLW, a plan for building the "patient registration system" for registering information on patients using cellular and tissue-based products was prepared in order to enhance post-marketing safety measures for cellular and tissue-based products. To this end, under the Third Mid-term Plan, PMDA will build the patient registration system (registry) for verifying long-term safety in collaboration with relevant academic societies, companies, etc.
- In FY 2014, PMDA prepared the specifications for the patient registration system and began constructing the system.

(iii) Establishment of a post-marketing safety system through information feedback

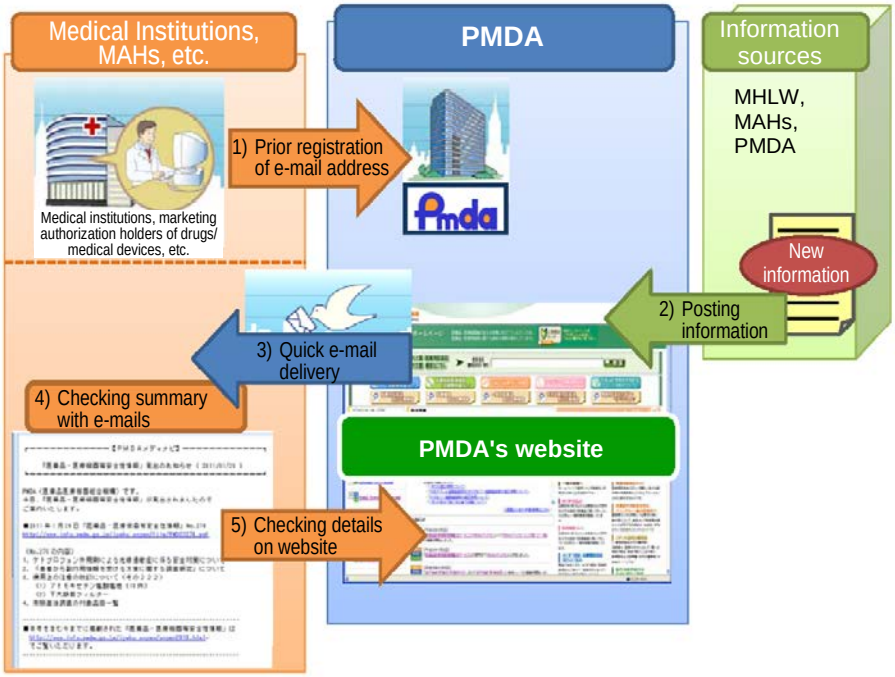
a. Provision of information via website and pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)

- PMDA promptly posts on its website important safety information issued on a daily basis, including revisions of precautions in package inserts, and distributes that information to healthcare professionals and relevant persons at companies by e-mail (PMDA medi-navi) upon issuance thereof. PMDA has also been making efforts to enhance and reinforce provision of information by posting various safety information, including package inserts, on its website. The PMDA Medical Product Information Web page, on which safety information had mainly been posted, was integrated into the PMDA website on March 15, 2015.
- In FY 2014, a new drug category of behind-the-counter (BTC) drugs was added, as an option, to the search page for package inserts, in accordance with enforcement of the revised Pharmaceutical Affairs Act in June 2014; therefore package inserts for BTC drugs are now available on the PMDA website. Furthermore, “BTC drugs” was added to “Risk Category” on the search page, so that BTC drugs can be searched.
- PMDA medi-navi provides safety information, by email, such as Dear Healthcare Professional Letters of Emergent Safety Communications, directions for revising precautions in package insert, and Class I recalls. To enhance public recognition of the service and increase the number of subscribers, PMDA reinforced PR activities by publishing articles on interviews with PMDA medi-navi users in professional journals, distributing an introductory video on PMDA medi-navi

operation, providing leaflets on practical training to pharmacy faculties at universities, distributing leaflets at the time of issuance of a pharmacist licenses., and conducting PR activities at academic conferences.

- Among 112,079 subscribers registered as of the end of FY 2014 (showing an increase of 9,289 in the course of FY 2014), approximately 36,400 were hospitals or clinics, 33,500 pharmacies, 7,300 dental clinics or other medical facilities, and 16,000 MAHs or distributors.
- In June 2011, PMDA began providing "My Drug List for Safety Update" as an additional function of PMDA medi-navi. As of the end of FY 2014, a total 7,974 subscribers had been registered.
- This service "My Drug List for Safety Update" enables a user to prepare a customizable drug list on the website. When the user registers particular drugs (My Drugs), a list of links to Web pages for package inserts, Interview Forms, Drug Guides for Patients, etc., for My Drugs is displayed. Additional functions include displaying a warning message when safety information (e.g., Dear Healthcare Professional Letters of Emergent Safety Communications) has been issued for any of My Drugs.

Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)



Breakdown of Contents of PMDA medi-navi Distributed in FY 2014

Contents of e-mails	Number of cases
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letter)	3
Recalls (Class I)	19
Pharmaceuticals and Medical Devices Safety Information	10
Drug Safety Update (DSU)	10
Revision of PRECAUTIONS of drugs	12
Revision of PRECAUTIONS of medical devices	2
Notification on self-check (medical devices)	0
PMDA Medical Safety Information	2
Approval information (medical devices)	6
Approval information (prescription drugs)	39
Notifications on drugs, Notifications on medical devices	35
Information on proper use of drugs	9
Information on drug risk under evaluation	10
Information on products submitted for public knowledge-based applications that are covered by insurance	4
Notice of decision on payment/non-payment of adverse reaction relief benefits	12
Risk Management Plan (RMP)	42
Others*1	20

**1 Except for RMP.*

Number of Information Documents Released on the PMDA's Web Page as of the End of FY 2014

		FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Package insert information[*1]						
	Prescription drugs	12,256	12,064	12,435	12,921	14,912
	Medical devices	13,979	15,584	17,539	19,309	20,504
	Cellular and tissue-based products	-	-	-	-	2
	OTC drugs	9,884	10,136	10,158	10,234	11,127
	BTC drugs	-	-	-	-	20
	In vitro diagnostics	3,984	3,994	4,054	4,076	4,247
Drug Guide for Patients[*1]		1,338 (2,311 products)	1,307 (1,951 products)	1,748 (2,453 products)	2,155 (3,409 products)	2,701 (4,842 products)
Guidance for persons who undergo vaccination[*1]		-	-	-	-	72 (74 products)
Safety information issued by MHLW		409	438	464	494	519
• Directions for revision of package inserts					257	272
• Pharmaceuticals and Medical Devices Safety Information					168	178
• Press release					69	69
Urgent safety information (by pharmaceutical companies)[*2]		24	24	25	27	30
Risk Management Plan (RMP)[*3]		-	-	-	6	117
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])		71	81	91	101	111
Notification of safety measures for medical devices						
	Notification on self-check	50	50	51	51	52
	Notification of revisions of labeling	33	41	45	48	50
	Other related notification	74	83	93	111	145
Information about case reports on suspected ADR		175,360	210,412	254,392	292,720	338,224
Information about case reports on suspected malfunction		51,169	62,898	73,012	84,766	98,407
Notification related to preventive measures for medical accidents		68	77	87	96	108
PMDA Medical Safety Information		22	29	36	43	45
Manuals for management of individual serious adverse drug reactions		63	75	75	75	75
Information on approved new drugs		513 active ingredients	592 active ingredients	666 active ingredients	700 active ingredients	834 active ingredients
• Review reports, summaries of product applications		(1,034 products)	(1,189 products)	(1,314 products)	(1,416 products)	(1,652 products)
Information on recalls of drugs or medical devices[*4]		1,977	2,299	1,907	1,913	1,817
Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)						
	E-mails issued[*5]	203	259	207	215	234
	Subscribers	35,719	55,372	84,146	102,790	112,079

*[*1] The numbers of package inserts and products are indicated. The numbers may decrease due to discontinuation of products.*

*[*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] Since the figures denote the total numbers of new or revised RMPs, the sum of the figures does not match the sum of the products.*

*[*4] Added as necessary; and deleted after two years, in principle*

*[*5] The figures are the total number of e-mails sent in each fiscal year. A single e-mail may contain several subject matters; therefore when counted according to the number of subject matters contained, the number of emails does not match the the figures in the columns.*

b. Provision of information on package inserts

- PMDA constructed a system for handling notifications of package inserts, in line with enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act on November 25, 2014. As for pharmacy-compounded drugs and medical devices, PMDA modified the system so that an MAH can carry out the whole process on-line, from submitting the notification through posting the package insert on the PMDA website for MAHs, and it began accepting such information in line with enforcement of the Act. As for BTC drugs and cellular and tissue-based products, PMDA accepts notifications delivered by hand or sent by post.
- By the end of FY 2014, PMDA had posted 14,912 package inserts for prescription drugs on its website. Upon issuance of notifications directing revisions of package inserts, PMDA posts such notifications on its website within 2 days and provides links to the corresponding package inserts.
- Instructions for use of medical devices have been available on the PMDA website since FY 2005, with 20,504 instructions at the end of FY 2014. The Agency has also posted notifications directing revisions of instructions for use in conjunction with the issuance of such information, and has provided links to the corresponding instructions for use.
- For cellular and tissue-based products, PMDA disclosed two package inserts following enforcement of the PMD Act on November 25, 2014.
- For OTC drugs, PMDA started posting package inserts for OTC drugs on its website in March 2007. A total of 11,127 package inserts were accessible on the website as of the end of FY 2014.
- For BTC drugs, PMDA started providing information on package insert for BTC drugs upon enforcement of the revised Pharmaceutical Affairs Act in June 2014. A total of 20 package inserts were accessible on the website as of the end of FY 2014.
- For *in vitro* diagnostics, information on package insert has also been accessible since FY 2008. A total of 4,247 package inserts could be accessed from the website as of the end of FY 2014.

c. Public release of adverse drug reaction cases and malfunction cases

1) Public release of adverse drug reaction cases

- Since January 2006, PMDA has sequentially and publicly released adverse drug reaction reports submitted by MAHs in and after April 2004 on its website. In March 2012, PMDA expanded the scope of data items and reports to be released in order that the content could be more easily utilized by relevant parties.

  Currently, PMDA discloses the following data from adverse drug reaction reports in Japan within approximately 4 months of receipt: fiscal year and quarter of a year reported, reporting category, type, job category of reporter, investigation status, gender, age, primary disease, body height, body weight, suspected drug/brand name, reason for use, route of administration, 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.

- Among adverse drug reaction/infection reports from healthcare professionals to the Minister of Health, Labour and Welfare (to PMDA on and after November 25, 2014), those investigated by PMDA (e.g., inquiries) are also published. By the end of FY 2014, PMDA had posted 338,224 reports submitted up until November 2014.
- In addition, in April 2012, PMDA started providing data sets of adverse drug reaction reports exported into the CSV format for public release, expanding the scope of data to be disclosed.

Until then, the database had only been available in line-listing format. As a result, the data can now be used for research and studies.

2) Public release of information on medical device malfunction cases

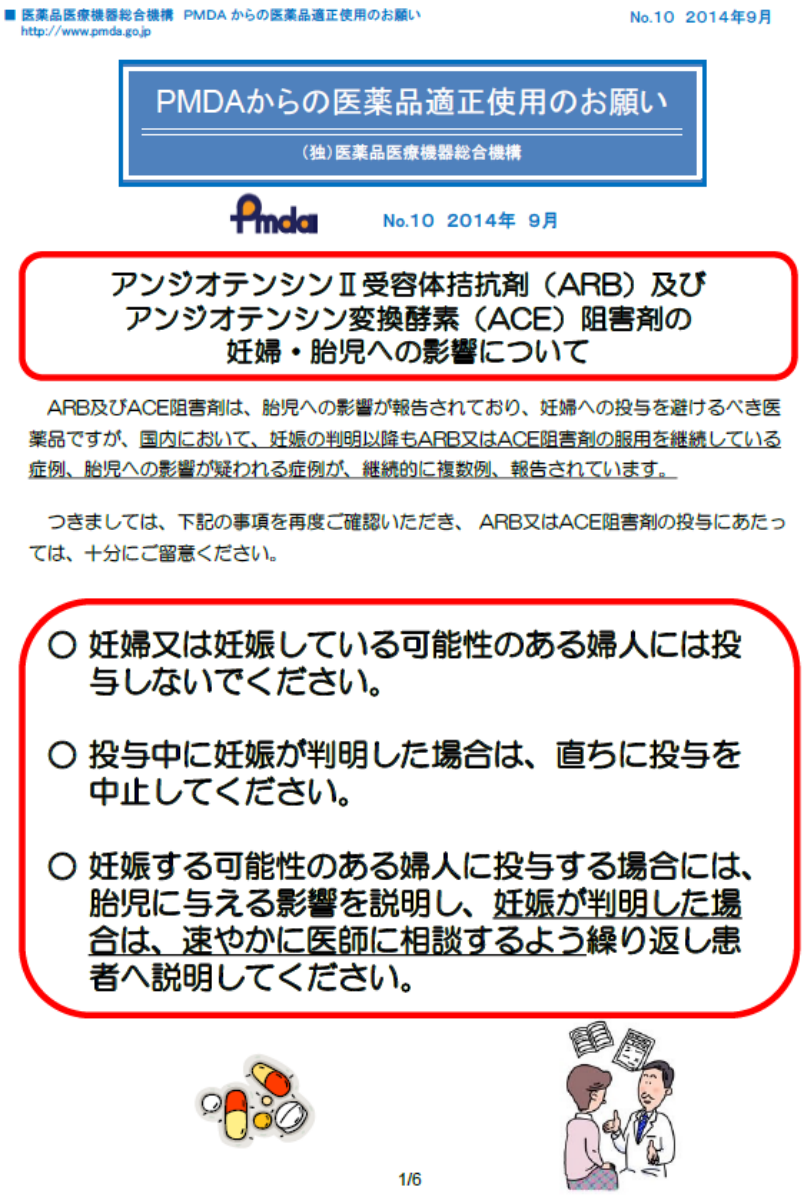
- For reports on medical device malfunctions submitted by MAHs in or after April 2004, the following data have been available on the PMDA website since March 2006: fiscal year reported, gender, age, outcome, generic name, condition of the medical device, and adverse events experienced by patient In total, 98,407 reports (submitted by September 2014) were published on the PMDA website by March 2014.

3) Access by MAHs to adverse drug reactions reports associated with their products

- PMDA investigates information on adverse drug reactions 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 MAHs through a system which enables the MAHs to access and download ICH-E2B-compliant SGML files on such adverse drug reactions from the PMDA website, so that the MAHs can analyze the information and take measures accordingly.

d. 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. PMDA provided one Request for Proper Use of Drugs in FY 2014.



■ 医薬品医療機器総合機構 PMDA からの医薬品適正使用のお願い
http://www.pmda.go.jp
No.10 2014年9月

PMDAからの医薬品適正使用のお願い

(独)医薬品医療機器総合機構

No.10 2014年 9月

アンジオテンシンⅡ受容体拮抗剤（ARB）及び
アンジオテンシン変換酵素（ACE）阻害剤の
妊婦・胎児への影響について

ARB及びACE阻害剤は、胎児への影響が報告されており、妊婦への投与を避けるべき医薬品ですが、国内において、妊娠の判明以降もARB又はACE阻害剤の服用を継続している症例、胎児への影響が疑われる症例が、継続的に複数例、報告されています。

つきましては、下記の事項を再度ご確認いただき、ARB又はACE阻害剤の投与にあたっては、十分にご留意ください。

○ 妊婦又は妊娠している可能性のある婦人には投与しないでください。

○ 投与中に妊娠が判明した場合は、直ちに投与を中止してください。

○ 妊娠する可能性のある婦人に投与する場合には、胎児に与える影響を説明し、妊娠が判明した場合は、速やかに医師に相談するよう繰り返し患者へ説明してください。

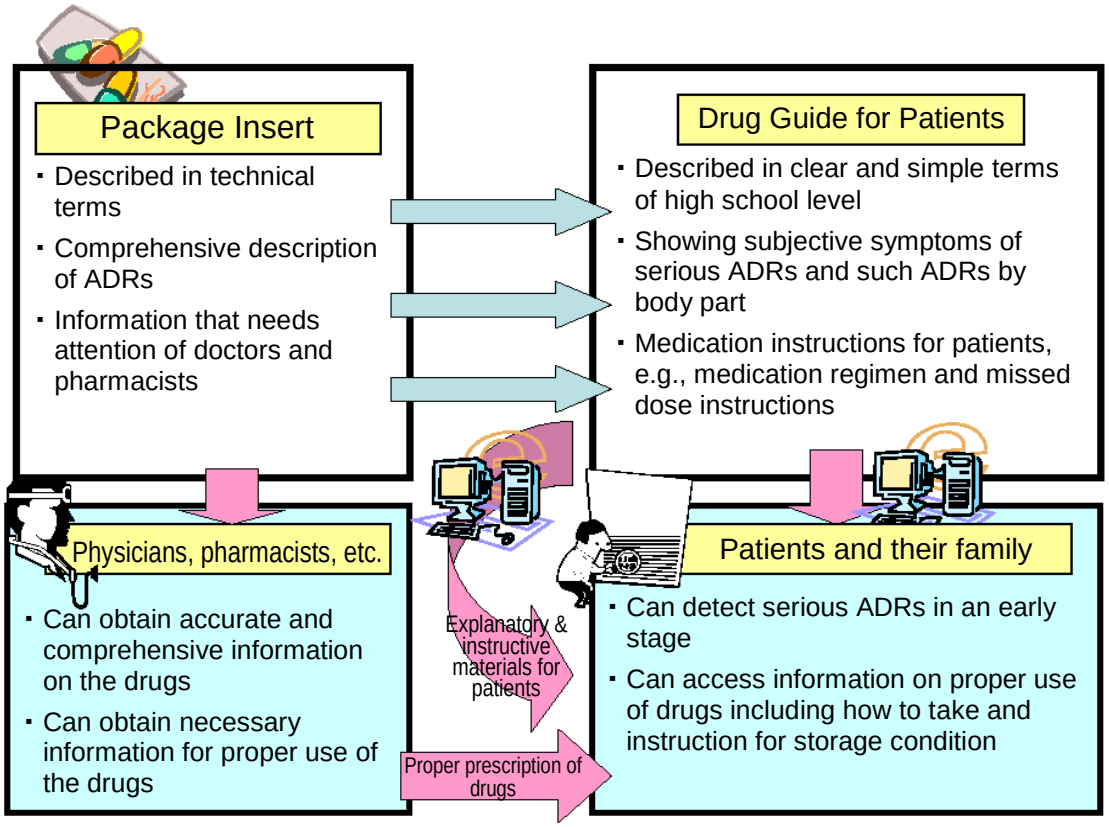
1/6

e. Provision of information such as Drug Guide for Patients and manuals for management of individual serious adverse drug reactions

1) Provision of Drug Guide for Patients

- In accordance with the "Guidelines for Developing the Drug Guide for Patients" (PFSB Notification No. 0630001 dated June 30, 2005), PMDA has reviewed and revised the Drug Guide for Patients while continuously obtaining advice from experts (a study supported by the Health and Labour Science Research Grants, titled "Research on how to provide patients and people with drug safety information").
- To promote proper understanding of prescription drugs among patients and to enable detection of serious adverse drug reactions at an earlier stage, the Drug Guide for Patients has been available on the PMDA website since January 2006. In FY 2014, 102 Drug Guides for Patients (including 13 for generic drugs) were prepared for products newly marketed or products that required preparation of Drug Guide for Patients due to a revision of precautions in the package insert. A total of 2,701 Drug Guides for Patients (4,842 products) were posted by the end of FY 2014.

Package Inserts for Prescription Drugs and Drug Guide for Patients



2) Provision of guide for persons who undergo vaccination

- In accordance with "Guidelines for Developing the Guide for Persons Who Undergo Vaccination" (PFSB Notification No. 0331-7 dated March 31, 2014), PMDA discussed the guide for persons who undergo vaccination while continuously obtaining advice from experts.
- "Guide for Persons Who Undergo Vaccination" has been available on the PMDA website since June 2014 to promote proper understanding of vaccines among persons who undergo vaccination and their families and to enable detection of serious adverse reactions at an earlier stage. In FY 2014, 29 Guides for Persons Who Undergo Vaccination were prepared for vaccines or toxoids against the following diseases or infections: influenza, yellow fever, mumps, polio (acute poliomyelitis), rabies, tuberculosis (BCG), diphtheria, varicella (chickenpox), meningococcal infection, Japanese encephalitis, pneumococcal infection, tetanus, Hib infection, rubella, measles, rotavirus gastroenteritis, hepatitis A, hepatitis B, diphtheria-pertussis-polio-tetanus combined vaccine (quadruple vaccine), diphtheria-pertussis-tetanus combined vaccine (triple vaccine), diphtheria-tetanus combined vaccine, and measles-rubella vaccine (MR vaccine). A total of 72 Guides for Persons Who Undergo Vaccination (74 products) were posted by the end of FY 2014.

3) 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 2014, but the manuals are being reviewed for a future revision.

f. Provision of medical safety information

- PMDA has been extracting, evaluating, and examining near-incident cases associated with drugs, medical devices, and cellular and tissue-based products 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 2014, 2,064 cases associated with drugs and 314 cases associated with medical devices were evaluated and the results were reported to MHLW. The details of 2,378 cases, for which deliberations had been completed by MHLW, were posted on the PMDA website and also shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 2,378 cases	2,064	314
1) Cases in which safety measures for the use of drugs, medical devices, or cellular and tissue-based products taken by MAHs, etc. were considered necessary or possible.	0	1
2) Cases in which measures have already been taken, or are currently under consideration, by the MAHs, etc.	18	35
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.	2,046	278

- 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 only text but also 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 2014, the following 2 issues of PMDA Medical Safety Information were posted on the web page.

No.	Posted on	PMDA Medical Safety Information titles
No.44	May 2014	Medication Errors in Prescription Orders
No.45	August 2014	Precautions in Handling of Indwelling Venous Needles

g. Release of information on drug risks under evaluation

- From the perspective 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 and (2) risk information which has attracted attention from foreign regulatory authorities, academic societies, etc. and is under evaluation by MHLW/PMDA. These types of information have been posted on the PMDA website, as appropriate, since July 2011, as preliminary information that could lead to implementation of safety measures such as revisions to Precautions.

h. Information provision in English

- In order to promote dissemination of information on safety measures to foreign countries, PMDA translated into English "Frequently Asked Questions," information on revision of Precautions, and safety-related documents issued by MHLW in relation to the PMD Act and posted the information on the 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.

i. Responses to consultation requests from MAHs

- In order to contribute to improvement of post-marketing safety measures by MAHs, PMDA provided various consultations (on drugs, medical devices, cellular and tissue-based products, 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 2014 is shown below:

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Drugs	752	670	704	776	869
Medical devices	171	163	179	95	325
Medical safety	83	59	80	31	72
Cellular and tissue-based products*	-	-	-	-	0

** The figure indicates the number of consultations following enforcement of the PMD Act on November 25, 2014.*

- Consultations for medical safety conducted in FY 2014 were mainly in respect of names of new drugs, packaging/labeling, and near-incident cases for drugs, medical devices, and cellular and tissue-based products. PMDA provided all consultations in an appropriate and prompt manner.

j. 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 2014, the number of persons receiving consultations was 11,556 (14,345 calls) for drugs and 370 (419 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

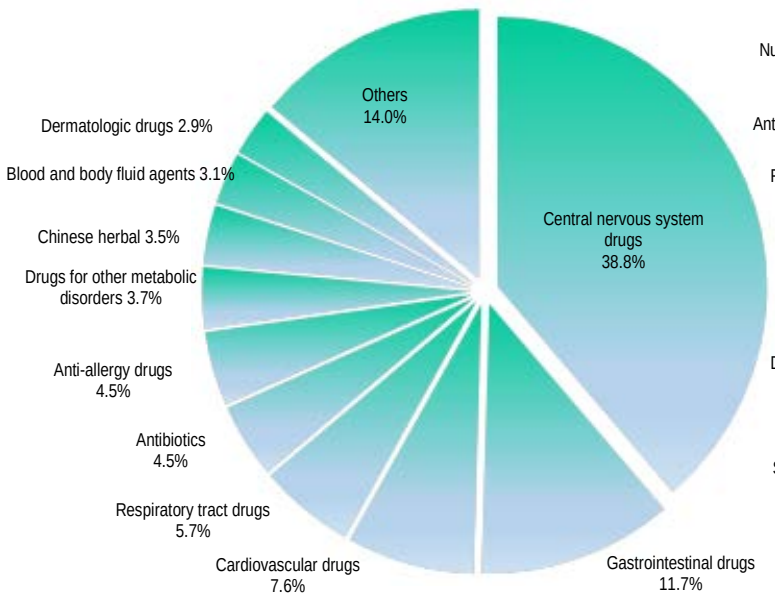
	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Consultations on drugs	8,846	8,945	9,679	10,244	11,556
[cases/day]	[36.4]	[36.7]	[39.5]	[42.0]	[47.4]
(of which consultations on generic drugs)	(617)	(453)	(493)	(626)	(543)
Consultations on medical devices	574	660	700	547	370
[cases/day]	[2.4]	[2.7]	[2.9]	[2.2]	[1.5]

Contents of Consultations on Drugs

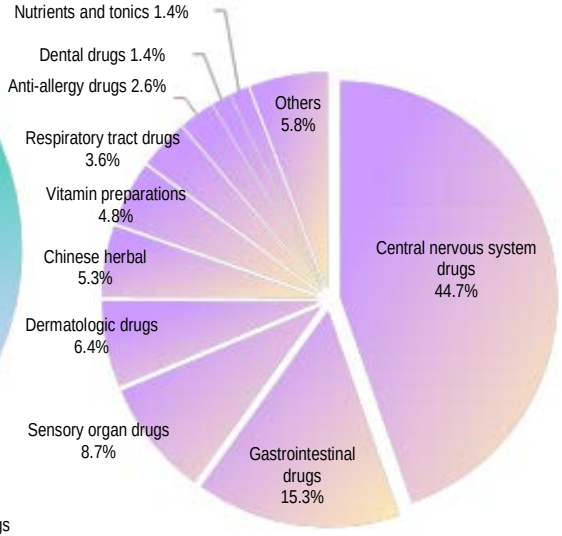
Contents of consultation	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
(1) Safety	5,553 (45.0%)	5,146 (41.3%)	5,267 (41.9%)	4,437 (35.2%)	5,401 (37.6%)
(2) Indications	890 (7.2%)	1.,147 (9.2%)	1,158 (9.2%)	1,302 (10.3%)	1,517 (10.6%)
(3) Dosage and Administration	784 (6.4%)	981 (7.9%)	1,259 (10.0%)	1,278 (10.1%)	1,345 (9.4%)
(4) Interactions	784 (6.4%)	986 (7.9%)	1,206 (9.6%)	1,426 (11.3%)	1,606 (11.2%)
(5) Ingredients	181 (1.5%)	199 (1.6%)	222 (1.8%)	255 (2.0%)	286 (2.0%)
Others	4,144 (33.6%)	4,014 (32.1%)	3,446 (27.5%)	3,919 (31.1%)	4,190 (29.2%)
Total	12,336 (100.0%)	12,473 (100.0%)	12,558 (100.0%)	12,617 (100.0%)	14,345 (100.0%)

Percentages of Consultations on Drugs by Therapeutic Category in FY 2014

Prescription drugs (n = 23,263)



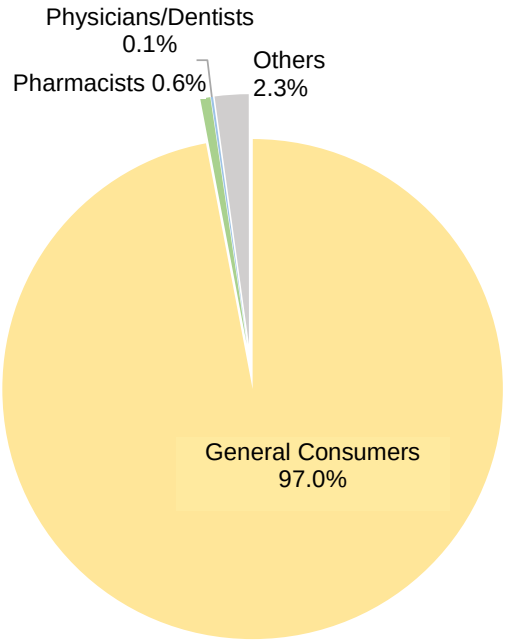
Over-the-counter drugs (n = 1,151)



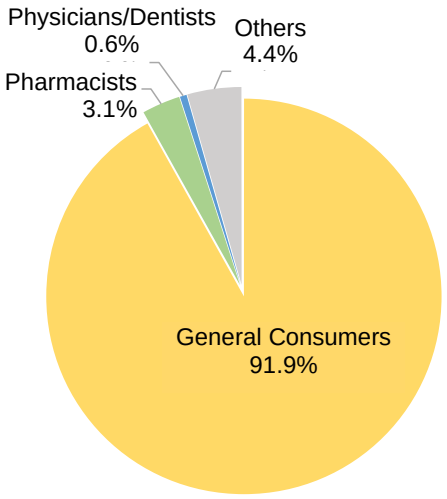
** Including BTC drugs*

Breakdown of Persons Receiving Consultations on Drugs in FY 2014 (by Profession etc.)

Consultations on drugs (n = 11,556)

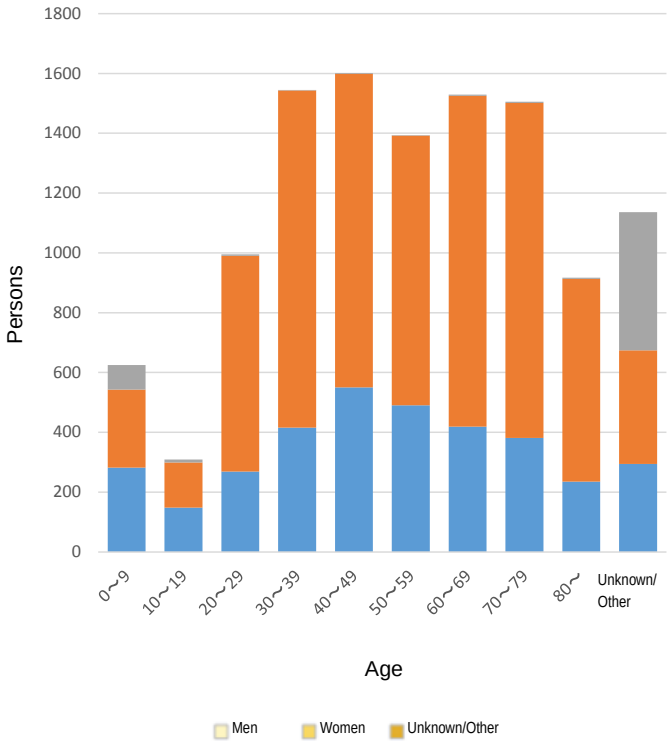


Consultations on generic drugs (n = 543)

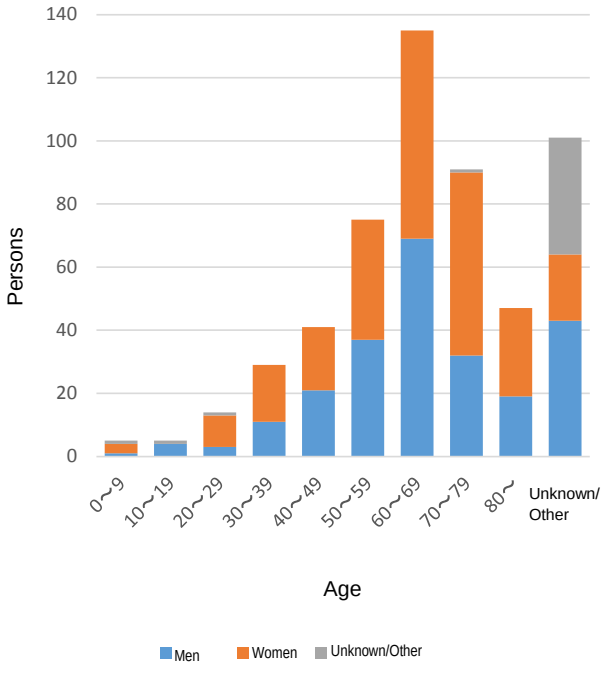


Breakdown of Persons Receiving Consultations on Drugs in FY 2014 (by Age/Gender*)

Consultations on drugs (n = 11,556)



Consultations on generic drugs (n = 543)

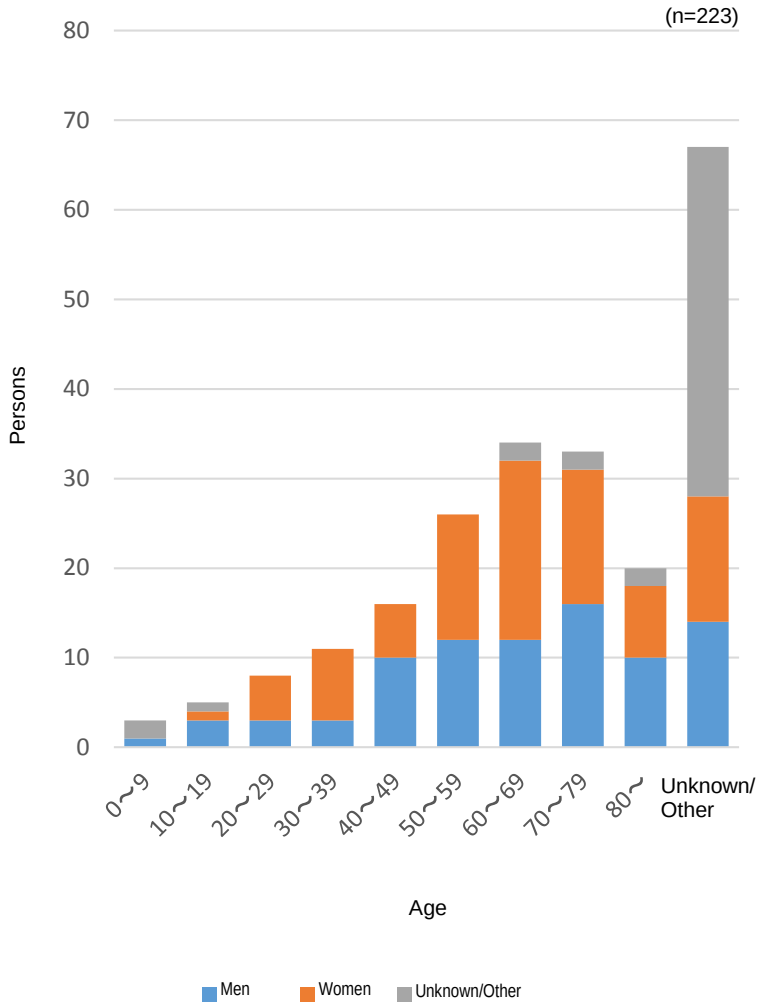


* Persons taking/using drugs were counted by age/gender

Contents of consultations on medical devices

Contents of consultation	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
(1) Safety	78 (12.5%)	85 (12.4%)	106(14.5%)	68 (11.5%)	48 (11.5%)
(2) Indications	61 (9.8%)	69 (10.1%)	62 (8.5%)	43 (7.3%)	64 (15.3%)
(3) Performance	17 (2.7%)	24 (3.5%)	36 (4.9%)	13 (2.2%)	9 (2.1%)
(4) Method of use	12 (1.9%)	10 (1.5%)	7 (0.9%)	9 (1.5%)	6 (1.4%)
Others	454 (73.0%)	498 (72.5%)	522 (71.2%)	458 (77.5%)	292 (69.7%)
Total	622 (100.0%)	686 (100.0%)	733 (100.0%)	591 (100.0%)	419 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2014 (by Age/Gender)**



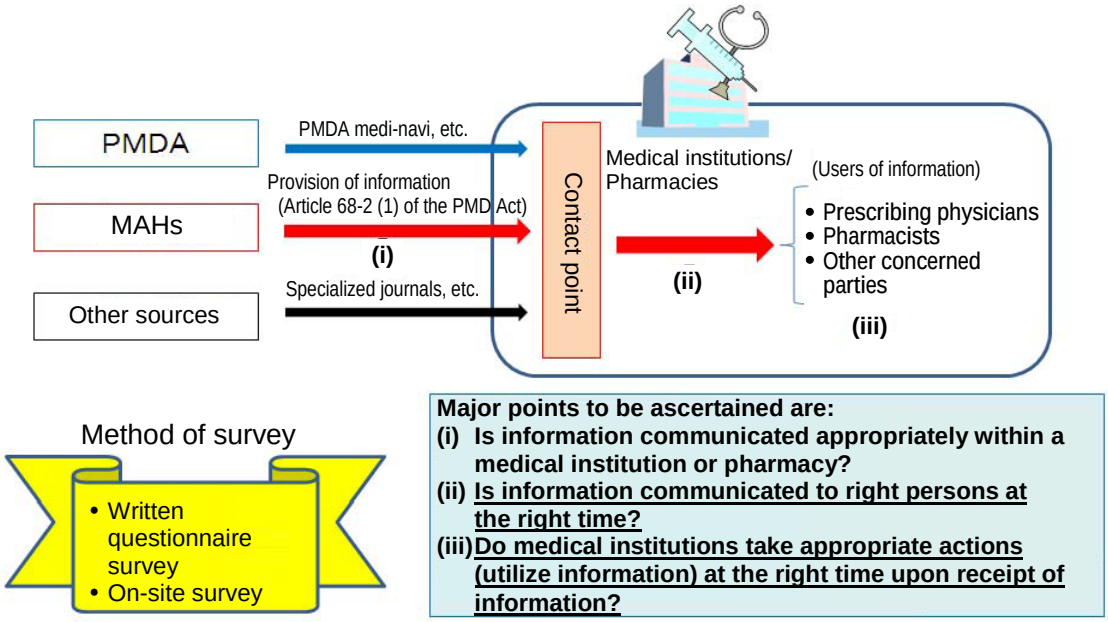
** Consultations from general consumers and consultations received via the national consumer affairs center of Japan were counted by age/gender.

k. Status of communication and use of transmitted safety information within medical institutions

- To promote proper use of drugs and medical devices, it is important that necessary safety information, such as safety measures to be taken is appropriately communicated to and used by healthcare professionals in clinical settings. Accordingly, in FY 2010, PMDA initiated a survey to ascertain the status of procurement, communication, and use of safety information in medical

institutions and pharmacies, and to discuss methods for providing information, and measures for procurement, communication, and use of information in clinical settings, in order that healthcare professionals in clinical settings can appropriately use such safety information. The survey results to date are available on the PMDA website, etc.

- Based on a survey on good practices related to the status of procurement, communication, and use of drug safety information conducted in FY 2013, PMDA in October 2014 produced a leaflet designed to raise awareness of appropriate management of drug safety information in hospitals, etc. and circulated it to some 9,000 hospitals and 49,000 pharmacies, as well as distributing it in the Agency's workshops, at academic conferences, etc.
- In FY 2014, PMDA conducted the following two surveys: 1) a survey on the status of procurement, communication, and use of drug safety information in hospitals nationwide (8,481 institutions), and 2) a survey on the statuses of procurement, communication, and use of medical device safety information in 500 randomly sampled general hospitals. PMDA plans to release the survey results upon completion of compilation and to use the results and materials to promote proper procurement, communication, and use of information at medical institutions.



Outline of surveys conducted to date

FY	Title	Target	Period	Remarks
2010	Survey on the status of communication and use of drug safety information	Hospitals nationwide (8,679 institutions)	January 13, 2011 to February 10, 2011	Questionnaire survey (response rate, 41.2%)
2011	Survey on the status of communication and use of drug safety information	Hospitals nationwide (8,640 institutions)	January 20, 2012 to February 10, 2012	Questionnaire survey (response rate, 25.9%)
2012	Survey on the status of procurement, communication, and use of drug safety information	Hospitals nationwide (8,541 institutions)	January 7, 2013 to February 28, 2013	Questionnaire survey (response rate, 53.4%)
		Half of all pharmacies nationwide (26,915 institutions)	January 7, 2013 to February 28, 2013	Questionnaire survey (response rate, 64.6%)
2013	Survey on the status of procurement, communication, and use of good practices on drug safety information	14 hospitals and clinics/pharmacies near the hospitals in Japan	October 2013 to February 2014	Door-to-door survey
	Basic survey on the status of procurement, communication, and use of medical device safety information	9 hospitals/clinics in Japan	October 2013 to February 2014	Door-to-door survey
2014	Survey on the status of procurement, communication, and use of drug safety information	Hospitals nationwide (8,481 institutions)	December 15, 2014 to March 13, 2015	Questionnaire survey (response rate, 57.8%)
	Survey on the status of procurement, communication, and use of medical device safety information	500 general hospitals (sampled randomly)	February 9, 2015 to March 13, 2015	Questionnaire survey (response rate, 40.0%)

I. 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 PMDA's web page, and PMDA's consultation services.

3.4. Promotion of regulatory science, internationalization, etc.

3.4.(1) Promotion of regulatory science

(i) Use of the Science Board

- The Science Board (parent committee) was established in May 2012 as an external body to deliberate on the scientific aspects of drug, medical device, and cellular and tissue-based product reviews in order to more appropriately review products that utilize advanced science and technologies, and to advance regulatory science and reinforce collaboration and communication with academia and medical professionals with a view to future promotion of healthcare innovation. Materials relating to individual products may be used for discussion; therefore, meetings are closed to the public. Members are external experts in such areas as medicine, dentistry, pharmacy, and engineering.
- The following three reports summarizing discussions were prepared and published in the First Term (up to March 2014) (reposted).
  1) 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
  2) Summary of Discussion on Non-clinical Pharmacology Studies on Anticancer Drugs
  3) Summary of Discussion on the Assessment of the Current Status of Personalized Medicine Related to Development and Regulatory Review

- In the Second Term, commencing April 2014, the parent committee determined issues to be discussed and new subcommittees were established according to the identified issues. As of March 31, 2015, 4 meetings of the parent committee had been held (2 of which were not actually meetings but document-based inquiries, and the following five subcommittees were established, in which specific discussions are being advanced.
  1) Subcommittee on Placebo-controlled Studies (3 meetings held)
  2) Subcommittee on Non-clinical Studies (4 meetings held)
  3) Subcommittee on Application of Numerical Analysis to Non-clinical Evaluation (3 meetings held)
  4) Subcommittee on Evaluation of Medical Devices in Pediatric Use (3 meetings held)
  5) CPC (Cell Processing Center) Subcommittee (5 meetings held)

- Minutes and materials of the subcommittee meetings are available on the PMDA website.

(ii) Enhancement of regulatory science research

- With respect to electronic submission of clinical trial data on new drugs, see 3. 2. (1) New Drugs (ii)-c.
- In order to properly conduct reviews, safety measures, and relief services for adverse health effects and to enhance the quality of these activities, PMDA is striving to promote regulatory science research on topics including the preparation of standards, guidelines, and guidance and how to conduct scientific forecasting, evaluation, and judgment. Among regulatory science researches conducted by PMDA, those designated by the Chief Executive are carried out as part of PMDA's operations. Designation is based on research purpose, how research is related to

PMDA's operations, and comments from the Regulatory Science Research Evaluation Committee. In FY 2014, 13 projects (7 new projects and 6 ongoing projects) were selected for designated research and the results of 2 of these projects were published in academic journals (reposted).

- Regarding innovative products, see 3.2. (2) (i).
- PMDA conducted regulatory science research in cooperation/collaboration with external organizations such as academic institutions (26 projects used public research funds, such as Health and Labour Science Research Grants).
- PMDA developed rules, formats, etc. for regulatory science research to match actual situations and established an ethical review board to improve the environment and systems for such research activities.
- In a global clinical trial project, based on the "Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials" (PFSB/ELD Administrative Notice dated October 27, 2014), a PMDA workshop "Global Clinical Trials – What Japan Can Do for Drug Development" was held in December 15, 2014. In the workshop, measures and issues to be considered in order for Japan to be able to participate in global clinical trials and to contribute to drug development in an effective and efficient manner were widely discussed among industry, government, and academia, based on specific cases.
- PMDA established a system for concluding comprehensive partnership agreements to develop and reinforce the collaborative graduate school program, and established a framework for promoting joint research activities with academia, etc. (See (iv) Promotion of interaction with outside researchers and collaboration on investigative research, c. Development and expansion of collaborative graduate school program)
- PMDA made presentations on the activities of the projects across multi-offices at academic conferences to publicize the activities and also exchanged opinions with experts regarding how to evaluate the activities.

(iii) Enhancement of staff training

a. Lectures and guidance given by experts

- In order to improve the quality of reviews and safety measures, PMDA provided its employees with the following training opportunities: special training programs including lectures in which experts invited from within and outside of Japan presented on product development activities at companies, and training in respective review parts with the cooperation of the National Institute of Health Sciences (NIHS) (24 sessions); training programs in laws and regulations, such as the Pharmaceutical Affairs Act, to learn about the regulatory system etc. (2 sessions); training programs in clinical study design, to learn biostatistics (12 sessions); and training programs in pharmacoepidemiology to learn features of pharmacoepidemiological study design (4 sessions).
- A total 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). For acquisition of basic knowledge concerning medical devices, Class I and Class II medical engineering (ME) technical training courses were also provided (19 employees).

b. Overseas dispatch

- In order to develop human resources with the abilities to take the initiative in global negotiations and conferences, and to cooperate with representatives of other countries on establishing

standards and guidelines, PMDA dispatched employees on long-term assignments to overseas institutions such as US FDA (5 employees).

- To provide opportunities to learn about actual situations regarding review and safety measures provided by overseas authorities, PMDA dispatched employees for short-term attendance at training seminars, etc. conducted by overseas regulatory authorities (12 employees).

c. On-site training

- PMDA conducted on-site training programs, including visits to drug and medical device manufacturing facilities (8 facilities), IRBs of medical institutions, etc.
- Product hands-on training using medical devices was provided (3 facilities).
- To enable learning about technical knowledge and skills in radioactivity, radioactivity training, including hands-on training such as radioactivity measurement, was provided (11 employees).
- To enable personnel to acquire knowledge about biological safety testing, training on biological safety testing, including hands-on training, was provided (4 employees).
- Five employees were dispatched to two medical institutions for practical training under hospital pharmacists in order to enable reviews and safety measures in line with the reality of clinical practice. In addition, 12 employees were dispatched to 2 medical institutions to observe testing procedures, treatments, etc. using medical devices.

(iv) Promotion of interaction with outside researchers and collaboration on investigative research

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

- PMDA works to develop personnel who are 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 also promotes cooperation on research projects concerning methods for evaluating the efficacy and safety of products developed using advanced technologies. In FY 2014, PMDA conducted personnel exchanges with 24 universities, etc., accepted 26 researchers as specially appointed experts (including non-regular staff), and dispatched a total 38 employees (including non-regular staff).

b. Promotion of collaborative graduate school program

- In order to contribute to diffusion of regulatory science and provision of information, PMDA continued the Joint Graduate School Program. PMDA had concluded joint graduate school agreements with 19 universities by the end of FY 2014.
- PMDA accepted 2 graduate students (one from the Gifu Pharmaceutical University Graduate School and the other from the University of Shizuoka Graduate School) as pre-doctoral fellows, to provide research education and guidance in accordance with “Implementation Guidelines for Acceptance of Pre-Doctoral Fellow at PMDA for FY 2014.” In a regulatory science promotion liaison meeting (July 2014), PMDA decided to accept students from joint graduate school without employment relationship under the new system.
- As a part of efforts to increase recognition of regulatory science, PMDA arranged to send PMDA staff members to give lectures upon request from universities (FY 2014: 27 universities, 56 lectures).

c. Development and expansion of collaborative graduate school program

- In order to develop and enhance education and research guidance systems conducted by directors and staff members, PMDA ascertained the status of doctoral degree acquisition by technical employees (July 2014).
- PMDA provided executives and employees with information on entrance examinations for joint graduate schools, via the Intranet.
- PMDA collected reference information on the support system of the National Personnel Authority (system for supporting acquisition of degrees, etc.).
- In a regulatory science promotion liaison meeting (January 2015), PMDA decided to go into partnership with the National Center for Global Health and Medicine and medical and research institutions that conduct high-quality clinical trials, in addition to universities, for the development of distinctive and varied collaborations under comprehensive agreements making the most of the advantages of individual institutions, in order to establish a broad cooperation and collaboration system beyond conventional research and educational activities. This was reported to the Advisory Council (March 2015).

3.4.(2) Action taken for internationalization

- PMDA should carry out international activities in a planned and systematic manner, being clearly aware of roles the Japanese regulatory agencies (MHLW and PMDA) should play, in order to fulfill the needs of the public in Japan and across the world. To this end, PMDA has been proactively promoting activities in line with the PMDA International Strategic Plan (developed in November 2011) clarifying the concrete goals to be attained in the next 5 to 10 years, and the "Road Map for the PMDA International Vision" (developed in April 2013) summarizing those concrete efforts. PMDA aims to steadily implement those efforts by following them up in a timely manner.

  In addition, in order to respond to the rapidly changing international situation, PMDA has been discussing a new international strategy incorporating the Plan and Vision, and aims to develop it in early FY 2015, maintaining consistency with the international strategy being discussed by MHLW.

(i) 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 authorities in the U.S. and the EU, PMDA, in collaboration with MHLW, has had discussions with the US FDA and the EC/EMA, gathered information on review systems, safety measures, etc., and also exchanged opinions on international cooperation.
- PMDA dispatched employees as liaison officers to the U.S. Pharmacopeial Convention, the EMA, and Swissmedic, in order to gather information and exchange views.
- PMDA dispatched 4 employees (2 employees for 3 months and 2 for 1 year) to the U.S. FDA to collect information and exchange opinions, and arranged dispatch activities for the following fiscal years.
- PMDA participated in the 2nd Meeting of the Global Coalition for Regulatory Science Research (GCRSR) held in Montreal (Canada) in August 2014, and exchanged opinions on regulatory science research with regulators and academia in relevant countries, including the U.S., Canada, and Australia.

- PMDA participated in the 8th International Summit of Heads of Medicines Regulatory Agencies held in Beijing (China) in November 2014 and exchanged opinions on regulatory affairs with regulators from relevant countries, including the US FDA and the EMA.
- In 2013, executives of regulatory authorities from various countries established the International Coalition of Medicines Regulatory Authorities (ICMRA), an international collaborative organization to strategically control/coordinate various issues relating to international cooperation and harmonization and to support enhancement of the capabilities of regulatory authorities. Dr. Kondo, Chief Executive of PMDA, served as vice-chair of the Management Committee, leading discussions on international cooperation at the level of the heads of the respective regulatory authorities.
- In April 2014, PMDA representatives visited the State of Bahrain and exchanged opinions on regulatory affairs with local regulators. At the same time, it was clarified that products approved in Japan would be covered by brief reviews in Bahrain.
- In May 2014, PMDA held the 2nd Indonesia-Japan Symposium and exchanged opinions on quality control, drug recalls, and international activities in both countries. Concurrently, the two regulatory agencies held a bilateral conference and agreed to continue to reinforce their cooperative relationship, as had been done in the 1st Symposium.
- In August 2014, PMDA held a Brazil-Japan seminar on regulations on pharmaceuticals and medical devices and exchanged views on improvement of review efficiency, GMP, pharmacopoeia, and opinions from industry. At the same time, a bilateral conference was held and both regulators agreed to the creation of a close collaborative relationship, going forward.
- In October 2014, PMDA held the 2nd Thailand-Japan Symposium and exchanged opinions on new drug reviews, GMP, pharmacovigilance, and pharmacopoeia. Concurrently, a bilateral conference was held and it was decided to discuss regulatory systems for drugs and medical devices, and to promote future cooperation.
- In October 2014, PMDA participated in the 2nd Joint Conference of Taiwan and Japan on Medical Products Regulation and exchanged opinions on regulations, such as drug and medical device regulations. At the same time, bilateral conference was held and continuous discussions on regulatory systems for drugs and medical devices and reinforcement of cooperative relationship were agreed.
- In March 2015, PMDA held the 1st Malaysia-Japan Symposium and exchanged opinions on regulatory systems, in particular on drug reviews, pharmacopoeia, bio-products, etc. Concurrently, a bilateral conference was held and representatives from both parties exchanged opinions on the reference pharmacopoeia system and the orphan drug system, and agreed to the creation of a close collaborative relationship, going forward.
- PMDA continued to have discussions with the regulatory authorities in countries participating in the above bilateral symposiums, using various opportunities such as meetings and conferences. Also, PMDA held bilateral conferences with US FDA, EMA in the EU, AIFA in Italy, MHRA in the UK, HSA in Singapore, TGA in Australia, MFDS in Korea, CFDA in China, etc., exchanged information and opinions, and discussed the status of progress on currently active cooperative projects and directions for further development.
- PMDA conducted overseas GCP inspections, accompanied where possible by representatives of the regulatory authorities of the investigated countries, which had been contacted by PMDA in advance. When regulatory authorities of foreign countries conducted GCP inspections in Japan, PMDA staff in the Office of Non-clinical and Clinical Compliance accompanied the inspections, and exchanged and shared information on GCP inspection methods, etc. PMDA exchanged

information with US FDA and EMA, centered on product issues in global clinical trials. PMDA discussed collaboration and improvement of circumstances regarding GCP through having employees in the Office of Non-clinical and Clinical Compliance participate in training programs, etc. conducted by US FDA and EMA.

- PMDA participated in the Third and Fourth International Meetings of World Pharmacopoeias, which were held by WHO in April and October 2014, respectively, and cooperated in the preparation of Good Pharmacopoeia Practice as a member of the draft formulation group.
- In November 2014, a bilateral conference between PMDA and the Chinese Pharmacopoeia Commission was held and both parties agreed to develop a mutual cooperative relationship on pharmacopoeia.

(ii) Strengthening of activities for international harmonization, etc.

- In FY 2014, PMDA continued to actively participate in international harmonization initiatives for drugs such as ICH. PMDA improved the consistency of Japanese standards with international standards (e.g., standards for data prepared for regulatory submission) agreed by Japan, the U.S., and the EU in ICH Meetings, thereby promoting further international harmonization.
- Toward development of international standards and 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 conference of the IPRF, which has been newly established for exchange of opinions/information among drug regulatory authorities, PMDA served as vice-chair and cooperated with the chair, Swissmedic, thereby 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
- In FY 2014, 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
    * ISO: International Organization for Standardization
    * IMDRF: International Medical Devices Regulators Forum
- For IMDRF, Japan has served as chair of Management Committee Meetings since January 2015 (tenure of 1 year), and PMDA's Associate Executive Director (for International Programs) has acted as a chair. In March 2015, PMDA hosted the 7th Management Committee Meeting at PMDA. The meeting adopted a resolution to start a new project, proposed by Japan, for internationally harmonizing terms for medical device malfunctions, with Japan acting as chair for the project.

- For HBD, PMDA supported the activities of each working group as a co-chair with U.S. academia, and contributed to regulatory harmonization on a practical level through teleconferences or meetings of respective working groups. Also, in September 2014, PMDA participated in the HBD West 2014 Think Tank Meeting held in Washington D.C. and delivered a presentation on activity results and future prospects. In addition, PMDA held HBD town hall meetings within academic conferences, including CVIT2014, TCT2014, and CRT2015, and provided presentations and discussion about the latest medical devices and technique. Through the HBD-derived project titled "Information Exchange with US FDA for Consultations and Reviews for Approval of Medical Devices," PMDA shared information with the US FDA regarding specific issues raised in the process of product reviews.

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: Minneapolis meeting and Lisbon meeting
    - Impurities: Guideline for Metal Impurities (Q3D)
    - Q&A on GMP for Active Pharmaceutical Ingredients (Q7 IWG)
    - Lifecycle Management (Q12)
    - ICH Medical Dictionary for Regulatory Activities (MedDRA) (M1PtC)
    - Electronic Standards for Transmission of Regulatory Information (M2)
    - CTD (Common Technical Document) 2.5.6 Enhancing the Format and Structure of Benefit-Risk Information (M4E [R2])
    - 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])
    - Good Clinical Practice (E6 [R2])
    - Statistical Principles for Clinical Trials (E9)
    - Clinical Investigation of Medicinal Products in the Pediatric Population (E11 [R1])
    - Multi-Regional Clinical Trials (E17)
    - Genomic Sampling Methodologies for Future Use (E18)
    - Clinical Safety Data Management: Periodic Benefit-Risk Evaluation Reports (E2C [R2])
* PDG: Pharmacopoeial Discussion Group: Rockville meeting and Strasbourg 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)*1: Taiwan meeting and Singapore meeting (*1: changed from Pilot to Program)
* 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): Qingdao meeting and Beijing meeting

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

* ISO
  - ISO/TC/276 (Biotechnology)
  - ISO/TC/194 (Biological and clinical evaluation of medical devices)
  - ISO/TC/150 (Implants for surgery)
  - ISO/TC/106 (Dentistry)
  - ISO/TC/210 (Quality management and corresponding general aspects for medical devices)

* IEC
  - IEC/TC62 (Electrical equipment in medical practice)

* 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)

- PMDA participated in the PDG meetings held in June and November 2014, at which 4 excipients and 1 general test resulted in new harmonization. In addition, PMDA sought public comments in Japan for 2 drafts proposed by PDG.
- PMDA held a total 5 Expert Discussion meetings on drug names and reported 68 Japanese accepted names (JAN) to MHLW. Five consultations on applications for international non-proprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in April and October 2014.
- PMDA participated in the International Generic Drug Regulators Pilot (IGDRP) meeting held in November 2014 and exchanged opinions on, in particular, the master file, handling of bioequivalence with the regulatory authorities. In addition, PMDA discussed the probability of harmonization of regulations on bioequivalence evaluation between Japan and overseas in a research project supported by Health and Labour Science Research Grants.
- PMDA participated in the 8th International Cooperation on Cosmetics Regulation meeting (ICCR-8) held in Canada in July 2014 and exchanged information on regulations of cosmetics with regulators from the U.S., Europe, Canada, Brazil, and China.
- For contribution to enhancement of the international status of the Japanese Pharmacopoeia through cooperation on international activities of pharmacopoeia conducted by WHO, etc., see 4. (2) (i).

- PMDA cooperated with the Medical Device International Standardization Strategy Promotion Project conducted by MHLW. The project was started in FY 2014 with the purpose of reinforcing PMDA's function in order to achieve more rapid and rational reviewing of medical devices by promoting international standardization. As the first step, PMDA conducted the following activities: 1) identifying the international standards and Japanese review groups that should be covered by this project; 2) preparing a list of international meetings and corresponding Japanese committees to be held to deliberate on standardization; and 3) developing the infrastructure for PMDA to participate in international meetings, such as collaborative arrangements with Japanese review groups. Specifically, PMDA participated in the 51 ISO-related committee meetings (4 international meetings) and 9 IEC-related committee meetings (2 international meetings) as well as committees of Japanese review groups that are essential for ISO/IEC activities. PMDA developed the project procedure and draft road map for conducting the project, in consideration of information such as the importance of standards obtained from these activities.
- In addition to assuming the position of vice chair of the Working Group on GLP of OECD, PMDA dispatched an employee to OECD as the person in charge of GLP, and thereby introduced PMDA's knowledge and know-how into international GLP-related activities.
- PMDA has conducted mutual acceptance of GLP investigation results based on the OECD's mutual data acceptance system.
- PMDA exchanged opinions with representatives from relevant industries on expanding the scope of data in English permitted for product application.

(iii) Promotion of personnel exchanges

- PMDA accepted 4 trainees from the Thai-FDA, 2 from Malaysia NPCB, and 1 from the US FDA. PMDA also hosted government research teams from China, Taiwan, and Vietnam, and explained PMDA's services, etc.
- For personnel from overseas regulatory authorities, PMDA held 2 training seminars on its services and case studies of regulatory review for drugs and medical devices.
- As preliminary research into whether or not PMDA should dispatch employees to Health Canada, the Head of the International Department of Health Canada visited PMDA for 4 days. During the visit, PMDA's operations in each office/division were explained to the Health Canada officer.

(iv) Development of internationally oriented human resources with excellent communication skills

- In order to develop human resources with the abilities to take the initiative in global negotiations and conferences, and to cooperate with representatives of other countries on establishing standards and guidelines, PMDA dispatched employees for long-term assignments to overseas institutions such as US FDA (5 employees).
- In order to improve employees' English language skills, PMDA subsidized one-to-one English conversation lessons (e.g. practical business English for international conferences) taken by 53 employees and correspondence courses in English language taken by 44 employees.

(v) Improvement and strengthening of international publicity and provision of information

- PMDA made efforts to provide information in English through such measures as posting monthly PMDA Updates on its English website.
- In order to provide information on its reviews and related services and safety measures to international audiences, PMDA prepares and releases English translations of review reports and

safety information on its website. In FY 2014, the Agency prepared and published English translations of 9 review reports. PMDA also prepared lists of approved new drugs/new medical devices in English, and released them approximately every quarter.

- At the DIA Annual Meetings, RAPS Annual Meetings, etc., held in Japan, the U.S., and Europe, PMDA speakers gave presentations on the Agency's reviews and safety measures to raise international recognition of PMDA's services, and also made booth exhibitions for the publicity of PMDA's services.
- Information on projects across multi-offices in PMDA is posted on the English website. An administrative notice "Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials" (in Japanese) was issued in October 2014. Within 15 days of issuance, an English translation was published on the PMDA website to provide timely information to overseas readers. PMDA provided information on the concept for reviews in Japan by occasionally uploading presentations on projects across multi-offices, in particular the QbD Evaluation Project, given at international academic conferences.

3.4.(3) Measures for intractable diseases and orphan diseases, etc.

- In the Orphan Drug Working Group, one of the projects across multi-offices in PMDA, the Agency has been discussing methods for promoting orphan drug development by collaborating with MHLW and by exchanging information with EMA.
- For efficient operation of notifications on companion diagnostics, see 2. (2) (i).
- In association with the establishment of Expert Working Group on the ICH E18 guideline "Genomic Sampling Methodologies for Future Use," the omics working group was newly restructured, centering on E18 members, to share information and exchange opinions within PMDA.

3.4.(4) Promoting provision of information such as review reports

a. Improving provision of information

- To promote proper use of drugs and medical devices and ensure transparency of reviews, PMDA releases information on reviews of new drug applications (e.g., review reports) on the PMDA website, in collaboration with MHLW and with the cooperation and understanding of relevant companies.

b. Releasing information related to review reports

(Review reports on new drugs)

- Based on submitted information, new drugs fall into 2 categories: those to be deliberated in the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (hereinafter referred to as "deliberation products"); and those 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. For "report products," "review reports" are subject to public release. These documents are published on the PMDA website after conferring with the relevant companies regarding the content to be released for each product, based on a Notification Issued by ELD, PFSB at MHLW.

- In FY 2014, PMDA released 130 review reports (median time from approval to release, 13 days; median adjustment time [Note], 21 days), 88 summaries of product applications (median time from approval to release, 56 days; median adjustment time, 32 days), and 40 re-examination reports (median time from result notification to release, 22 days; median adjustment time, 11 days).

Note: Adjustment time means the number of days from the date of receipt of a masked draft of release materials prepared by the applicant to the date on which the applicant is requested to submit the release materials after adjustment and confirmation.

The percentage of review reports released within 1 month after approval was 70% (99% in FY 2013) and the percentage of summaries of product applications released within 3 months after approval was 94% (95% in FY 2013).

(Review reports on new medical devices)

- In FY 2014, PMDA released 9 review reports (median time from approval to release, 62 days; median adjustment time, 35 days), 13 summaries of product applications (median time from approval to release, 136 days; median adjustment time, 78 days) and 6 re-examination reports (median time from result notification to release, 8 days; median adjustment time, 6 days).

  The percentage of review reports released within one month after approval was 44% (74% in FY 2013) and the percentage of summaries of product applications released within 3 months after approval was 38% (78% in FY 2013).

(Review reports on OTC drugs and quasi-drugs)

- In FY 2014, PMDA released 3 review reports, 4 summaries of product applications, and 3 re-examination reports for OTC drugs (which were retrospectively released for products with notification of results in and after FY 2009). PMDA also released 1 review report and 1 summary of a product application for a quasi-drug.

3.4.(5) Securing of impartiality in utilization of external experts

- It is necessary to secure impartiality and transparency of judgments made by commissioned external experts. The "Rules for Convening Expert Discussions etc., by the Pharmaceuticals and Medical Devices Agency" (December 25, 2008; revised on February 26, 2015) was set forth with the aim of ensuring transparency of PMDA's services by releasing review reports and information on conflicts of interest among commissioned external experts, thereby allowing outside parties to verify the decision-making process. In accordance with the rules, PMDA reports to the Advisory Council and the Committee on Review and Safety Operations regarding cash contributions and contract payments received by external experts commissioned by PMDA for Expert Discussions on reviews and safety measures.

3.4.(6) Provision of training in specially controlled medical device certification standards

- In association with the establishment of specially controlled medical device certification standards (3 standards), reviewers at the registered certification bodies were trained by PMDA to conduct product certification review and compliance assessments based on the standards.

3.4.(7) Improvement of quality of reviews/safety operations through enhancement of information systems

- On August 25, 2014, PMDA began operating an application/review system constructed based on the Optimization Plan for Operations and Systems. On November 25, 2014, PMDA began accepting applications for cellular and tissue-based products in accordance with enforcement of the PMD Act. In addition, on February 16, 2015, PMDA issued "Points to Consider for Reports on Post-marketing Adverse Drug Reactions and Reports on Clinical Trial Adverse Drug Reactions," for implementation of E2B/R3 and took actions for operation of the system.
- Final decision documents for regulatory approval of drugs, etc., clinical trial notifications for agents and devices, etc., were converted into digital image data to reduce storage space and enable long-term storage. Review process was streamlined and accelerated by using the search function for digital image data.
- With regard to the new eCTD viewer system, PMDA upgraded the hardware and software and modified the system related to collaboration with the application/review system. The modified system began to operate on August 25, 2014. For a secure environment in which external expert advisors can access eCTD data, PMDA renewed and verified the hardware and software to expand the available PC environment and improve convenience for expert advisors.
- PMDA published the implementation guide (draft) for eCTD ver. 4.0 under development by ICH and began seeking public comments and information. The eCTD ver. 4.0 was considered to pose difficulties in respect of manual creation of messages and viewing of messages visually due to characteristics of its specifications. PMDA made a simple tool to assist in making and viewing eCTD ver. 4.0 messages and uploaded it on the PMDA website (available for free download) to support the understanding of technical specifications.

III. SUPPLEMENTARY INFORMATION

Table 1. Products Approved in FY 2014: New Drugs

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Jul. 4, 2014	1	Dovobet Ointment (Leo Pharma K.K.)	Approval	(1) Calcipotriol hydrate/ (2) Betamethasone dipropionate	A new combination drug indicated for the treatment of psoriasis vulgaris.
1	Aug. 29, 2014	2	Rituxan Injection 10 mg/mL (Zenyaku Kogyo Co., Ltd.)	Change	Rituximab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of refractory nephrotic syndrome (for use in patients with frequent recurrence or steroid-dependent). [Orphan drug]
1	Sep. 19, 2014	3	Thymoglobuline for Intravenous Infusion 25 mg (Sanofi K.K.)	Change	Anti-human thymocyte immunoglobulin, rabbit	A drug with a new additional indication and a new dosage for the treatment of acute rejection after the liver, heart, lungs, pancreas, or small intestinal transplantation.
1	Sep. 26, 2014	4	Fomepizole Intravenous Infusion 1.5 g "Takeda" (Takeda Pharmaceutical Company Limited)	Approval	Fomepizole	A drug with a new active ingredient indicated for the treatment of ethylene glycol and methanol poisonings.
1	Dec. 26, 2014	5	Pariet Tablets 5 mg Pariet Tablets 10 mg (Eisai Co., Ltd.)	Approval Change	Rabeprazole sodium	A drug with a new additional indication and a new dosage in a newly-added dosage form, and a drug with a new additional indication and a new dosage for the prevention of recurrence of gastric ulcer or duodenal ulcer in patients treated with low-dose aspirin.
1	Dec. 26, 2014	6	Takecab Tablets 10 mg Takecab Tablets 20 mg (Takeda Pharmaceutical Company Limited)	Approval Approval	Vonoprazan fumarate	Drugs with a new active ingredient indicated for the treatment of gastric ulcer, duodenal ulcer, reflux esophagitis, prevention of recurrence of gastric or duodenal ulcer in patients treated with low-dose aspirin, prevention of recurrence of gastric or duodenal ulcer in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs), and aid to eradication of *Helicobacter pylori* in patients with gastric ulcer, duodenal ulcer, gastric MALT lymphoma, idiopathic thrombocytopenic purpura, *Helicobacter pylori* gastritis, and stomach after endoscopic treatment for early gastric cancer.
1	Dec. 26, 2014	7	Methylene Blue Intravenous Injection 50 mg "Daiichi Sankyo" (Daiichi Sankyo Company, Limited)	Approval	Methylthioninium chloride hydrate	A drug with a new active ingredient indicated for the treatment of toxic methemoglobinemia.
1	Dec. 26, 2014	8	Bepio Gel 2.5% (Maruho Co., Ltd.)	Approval	Benzoyl peroxide	A drug with a new active ingredient indicated for the treatment of acne vulgaris.
2	Jul. 4, 2014	9	Stalevo Combination Tablets L50 Stalevo Combination Tablets L100 (Novartis Pharma K.K.)	Approval Approval	Levodopa/ Carbidopa hydrate/ Entacapone	New combination drugs indicated for the treatment of Parkinson's disease [for use in patients having wearing-off phenomenon in the symptoms following administration of levodopa/carbidopa].
2	Sep. 19, 2014	10	Aricept Tablets 3 mg Aricept Tablets 5 mg Aricept Tablets 10 mg Aricept D Tablets 3 mg Aricept D Tablets 5 mg Aricept D Tablets 10 mg Aricept Fine Granules 0.5% Aricept Oral Jelly 3 mg Aricept Oral Jelly 5 mg Aricept Oral Jelly 10 mg Aricept Dry Syrup 1% (Eisai Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change Change	Donepezil hydrochloride	Drugs with a new additional indication and a new dosage for inhibiting progress of dementia symptoms in patients with dementia with Lewy bodies.
2	Sep. 26, 2014	11	Lixiana Tablets 15 mg Lixiana Tablets 30 mg Lixiana Tablets 60 mg (Daiichi Sankyo Company, Limited)	Change Change Approval	Edoxaban tosilate hydrate	Drugs with new additional indications and new dosages, and a drug with a newly-added dosage form indicated for prevention of ischemic stroke and systemic embolism in patients with non-valvular atrial fibrillation, or for the treatment and prevention of the recurrence of venous thromboembolism (deep vein thrombosis and pulmonary thromboembolism).
2	Nov. 18, 2014	12	Inderal Tablets 10 mg Inderal Tablets 20 mg (AstraZeneca K.K.)	Change Change	Propranolol hydrochloride	Drugs with a new additional indication and a new dosage for the prevention of hypoxic attack caused by right ventricular outflow tract obstruction. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	Feb. 20, 2015	13	Adempas Tablets 0.5 mg Adempas Tablets 1.0 mg Adempas Tablets 2.5 mg (Bayer Yakuhin, Ltd.)	Change Change Change	Riociguat	Drugs with a new additional indication for the treatment of pulmonary arterial hypertension.
2	Mar. 26, 2015	14	Opsumit Tablet 10 mg (Actelion Pharmaceuticals Japan Ltd.)	Approval	Macitentan	A drug with a new active ingredient indicated for the treatment of pulmonary arterial hypertension.
3-1	Jul. 4, 2014	15	E Keppra for I.V. Infusion 500 mg (UCB Japan Co., Ltd.)	Approval	Levetiracetam	A drug with a new route of administration indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizure (including secondary generalized seizure) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs. It is used as an alternative therapy for levetiracetam oral formulation in patients who are temporarily unable to be administered orally.
3-1	Aug. 29, 2014	16	Lamictal Tablets 25 mg Lamictal Tablets 100 mg (GlaxoSmithKline K.K.)	Change Change	Lamotrigine	Drugs with a new additional indication and a new dosage for use in the monotherapy for treatment of partial seizures (including secondary generalized seizure) and tonic-clonic seizures in patients with epilepsy.
3-1	Sep. 26, 2014	17	Belsomra Tablets 15 mg Belsomra Tablets 20 mg (MSD K.K.)	Approval Approval	Suvorexant	Drugs with a new active ingredient indicated for the treatment of insomnia.
3-1	Sep. 26, 2014	18	Midafresa Injection 0.1% (Alfresa Pharma Corporation)	Approval	Midazolam	A drug with a new additional indication and a new dosage in an additional dosage form indicated for the treatment of status epilepticus.
3-1	Feb. 20, 2015	19	E Keppra Tablets 250 mg E Keppra Tablets 500 mg E Keppra Dry Syrup 50% E Keppra for I.V. Infusion 500 mg (UCB Japan Co., Ltd.)	Change Change Change Change	Levetiracetam	Drugs with a revised indication and a new dosage for the treatment of partial seizure in patients with epilepsy (including secondary generalized seizure).
3-1	Mar. 20, 2015	20	J Zoloft Tablets 25 mg J Zoloft Tablets 50 mg J Zoloft Tablets 100 mg J Zoloft OD Tablets 25 mg J Zoloft OD Tablets 50 mg J Zoloft OD Tablets 100 mg (Pfizer Japan Inc.)	Change Change Change Change Change Change	Sertraline hydrochloride	Drugs with a new additional indication for the treatment of posttraumatic stress disorder.
3-1	Mar. 26, 2015	21	ABILIFY Prolonged Release Aqueous Suspension for IM Injection 300 mg ABILIFY Prolonged Release Aqueous Suspension for IM Injection 400 mg ABILIFY Prolonged Release Aqueous Suspension for IM Injection 300 mg Syringe ABILIFY Prolonged Release Aqueous Suspension for IM Injection 400 mg Syringe (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval	Aripiprazole hydrate	Drugs with a new route of administration indicated for the treatment of schizophrenia.
3-2	Jun. 20, 2014	22	Fentos Tape 1 mg Fentos Tape 2 mg Fentos Tape 4 mg Fentos Tape 6 mg Fentos Tape 8 mg (Hisamitsu Pharmaceutical Co., Inc.)	Change Change Change Change Change	Fentanyl citrate	Drugs with a new 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	Sep. 19, 2014	23	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 for the treatment of choroidal neovascularization in patients with pathologic myopia.
3-2	Sep. 26, 2014	24	Glanatec Ophthalmic Solution 0.4% (Kowa Company, Ltd.)	Approval	Ripasudil hydrochloride hydrate	A drug with a new active ingredient indicated for the treatment of glaucoma or ocular hypertension in patients who have not sufficiently responded to other therapeutic drugs for glaucoma or who are unable to use them.
3-2	Nov. 18, 2014	25	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 diabetic macular edema.
3-2	Dec. 26, 2014	26	Nopicor Capsules 2.5 μg (Toray Medical Co., Ltd.)	Approval	Nalfurafine hydrochloride	A drug with a new active ingredient indicated for the improvement of pruritus in patients with chronic liver diseases (for use only when conventional therapies are not sufficiently effective).

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-2	Mar. 26, 2015	27	Onetram Tablets 100 mg (Nippon Shinyaku Co., Ltd.)	Approval	Tramadol hydrochloride	A drug in a new dosage form indicated for analgesia in patients with cancers-associated pain or chronic pain, which cannot be managed by treatments with non-opioid analgesics.
4	May 23, 2014	28	Vancomycin Hydrochloride for Intravenous Drip Infusion 0.5 g (Shionogi & Co., Ltd.)	Change	Vancomycin hydrochloride	A drug with new additional indications for the treatment of: (1) sepsis, infective endocarditis, secondary infection of trauma, burn or surgical wounds, osteomyelitis, arthritis, peritonitis and purulent meningitis caused by vancomycin-sensitive methicillin-resistant coagulase-negative *Staphylococcus* (MRCNS); or (2) febrile neutropenia which is suspected of MRSA or MRCNS infection. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Jul. 4, 2014	29	Clenafin Topical Solution 10% for Nail (Kaken Pharmaceutical Co., Ltd.)	Approval	Efinaconazole	A drug with a new active ingredient indicated for the treatment of tinea unguium caused by dermatophyte (*trichophyton*).
4	Jul. 4, 2014	30	Deltyba Tablets 50 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval	Delamanid	A drug with a new active ingredient indicated for the treatment of multidrug-resistant pulmonary tuberculosis caused by delamanid-sensitive *Mycobacterium tuberculosis*. [Orphan drug]
4	Jul. 4, 2014	31	Anaemetro Intravenous Infusion 500 mg (Pfizer Japan Inc.)	Approval	Metronidazole	A drug with a new route of administration indicated for the treatment of different kinds of anaerobic bacterial infections, infectious enteritis, and amebic dysentery.
4	Jul. 4, 2014	32	Daklinza Tablets 60 mg (Bristol-Myers K.K.) Sunvepra Capsules 100 mg (Bristol-Myers K.K.)	Approval Approval	Daclatasvir hydrochloride Asunaprevir	Drugs with new active ingredients indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1) who are untreated and ineligible for, or are intolerant to therapy including interferon; or who did not respond to therapy including interferon. [Priority review]
4	Sep. 19, 2014	33	Telavic 250 mg Tablet (Mitsubishi Tanabe Pharma Corporation)	Change	Telaprevir	A drug with a new additional indication for the improvement of viremia in serogroup 2 (genotype III [2a] or IV [2b]) chronic hepatitis C in patients who did not respond to, or in whom the symptom relapsed with, interferon monotherapy or interferon-ribavirin combination therapy. [Priority review]
4	Sep. 26, 2014	34	Vfend Tablets 50 mg Vfend Tablets 200 mg Vfend for Intravenous Use 200 mg Vfend Dry Syrup 2800 mg (Pfizer Japan Inc.)	Change Change Change Approval	Voriconazole	Drugs with new additional pediatric dosages, and a drug with a new additional pediatric dosage in an additional dosage form of dry syrup indicated for the treatment of severe or refractory fungus infection.
4	Sep. 26, 2014	35	Vanihep Capsules 150 mg (MSD K.K.)	Approval	Vaniprevir	A drug with a new active ingredient indicated for the improvement of viremia in the following patients with serogroup 1 (genotype I [1a] or II [1b]) chronic hepatitis C: Patients with high levels of blood HCV RNA who are treatment-naive, or Patients who are non-responders or relapsed to therapy including interferon. [Priority review]
4	Nov. 18, 2014	36	Valtrex Tablets 500 Valtrex Granules 50% (GlaxoSmithKline K.K.)	Change Change	Valaciclovir hydrochloride	Drugs with a new additional indication and revised indications with a new dosage for prevention of herpes simplex virus infection in adult or pediatric haematopoietic stem cell transplant patients, for treatment of herpes simplex /herpes zoster, and for prevention of recurrent genital herpes in pediatric patients.
4	Dec. 18, 2014	37	Cancidas for Intravenous Drip Infusion 50 mg Cancidas for Intravenous Drip Infusion 70 mg (MSD K.K.)	Change Change	Caspofungin acetate	Drugs with a new additional pediatric dosage indicated for the treatment of febrile neutropenia with suspected fungal infection, esophageal candidiasis, invasive candidiasis, and aspergillosis caused by *Candida* or *Aspergillus*.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Dec. 26, 2014	38	Rozex Gel 0.75% (Galderma S.A.)	Approval	Metronidazole	A drug with a new route of administration indicated for disinfection/deodorisation of odorous fungating tumours.
4	Mar. 20, 2015	39	Pentcillin for Injection 1 g Pentcillin for Injection 2 g Pentcillin Intravenous Injection 1 g Bag Pentcillin Intravenous Injection 2 g Bag (Toyama Chemical Co., Ltd.)	Approval Approval Approval Approval	Piperacillin sodium	Drugs with a new dosage indicated for the treatment of sepsis, acute bronchitis, pneumonia, lung abscess, thoracic empyema, secondary infection of chronic respiratory disease, cystitis, pyelonephritis, cholecystitis, choledochitis, bartholinitis, intrauterine infection, uterine adnexitis, parametritis, and purulent meningitis.
4	Mar. 20, 2015	40	Daklinza Tablets 60 mg (Bristol-Myers K.K.) Sunvepra Capsules 100 mg (Bristol-Myers K.K.)	Change Change	Daclatasvir hydrochloride Asunaprevir	Drugs with a revised indication for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1). [Priority review]
4	Mar. 26, 2015	41	Duac Combination Gel (GlaxoSmithKline K.K.)	Approval	Clindamycin phosphate hydrate/ Benzoyl peroxide	A new combination drug with a new active ingredient indicated for the treatment of acne vulgaris.
4	Mar. 26, 2015	42	Sovaldi Tablets 400 mg (Gilead Sciences, Inc.)	Approval	Sofosbuvir	A drug with a new active ingredient indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 2 (genotype 2) . [Priority review]
4	Mar. 26, 2015	43	Copegus Tablets 200 mg (Chugai Pharmaceutical Co., Ltd.)	Change	Ribavirin	A drug with a new additional indication and a new dosage for the improvement of viremia with the concomitant use of sofosbuvir in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 2 (genotype 2) . [Expedited review]
4	Mar. 26, 2015	44	Aldreb for Injection 150 mg (GlaxoSmithKline K.K.)	Approval	Colistin sodium methanesulfonate	A drug with a new route of administration indicated for the treatment of infections caused by colistin-sensitive *Escherichia coli, Citrobacter, Klebsiella, Enterobacter, Pseudomonas aeruginosa,* and *Acinetobacter* (limited to the strains resistant to other antimicrobial drugs). [Orphan drug]
5	Jun. 20, 2014	45	Mirena 52 mg (Bayer Yakuhin, Ltd.)	Change	Levonorgestrel	A drug with a new additional indication for the treatment of hypermenorrhea. [Public knowledge-based application after PAFSC's preliminary assessment]
5	Jul. 4, 2014	46	Pareplus for IV. Infusion (Ajinomoto Pharmaceutical Co., Ltd.)	Approval	N/A for this combination drug	A combination prescription drug with similar formulations indicated for the supplementation of amino acids, electrolyte, hydrosoluble vitamins, and water. It is used in patients with mild hypoproteinemia or in a mild malnutrition state due to insufficient oral intake or used in perioperative patients.
5	Sep. 26, 2014	47	Lutinus Vaginal Tablet 100 mg (Ferring Pharmaceuticals Co.,Ltd.)	Approval	Progesterone	A drug with a new route of administration indicated for luteal support as part of assisted reproductive technology for infertile women.
5	Nov. 18, 2014	48	Mirena 52 mg (Bayer Yakuhin, Ltd.)	Change	Levonorgestrel	A drug with a new additional indication for the treatment of dysmenorrhoea. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Jul. 4, 2014	49	Anoro Ellipta 7 doses Anoro Ellipta 30 doses (GlaxoSmithKline K.K.)	Approval Approval	(1) Umeclidinium bromide/ (2) Vilanterol trifenatate	New combination drugs with a new active ingredient 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	Jul. 4, 2014	50	Rapalimus Tablets 1 mg (Nobelpharma Co., Ltd.)	Approval	Sirolimus	A drug with a new active ingredient indicated for the treatment of lymphangioleiomyomatosis. [Orphan drug]
6-1	Jul. 4, 2014	51	kenketu Glovenin-I for I.V. Injection 2500 mg kenketu Glovenin-I for I.V. Injection 500 mg kenketu Glovenin-I for I.V. Injection 5000 mg (Nihon Pharmaceutical Co., Ltd.)	Change Change Change	Freeze-dried polyethylene glycol treated human normal immunoglobulin	Drugs with new additional indications for the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis (for use when steroid drugs are not sufficiently effective). [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Aug. 29, 2014	52	Solu-Medrol for Intravenous Use 40 mg Solu-Medrol for Intravenous Use 125 mg Solu-Medrol for Intravenous Use 500 mg Solu-Medrol for Intravenous Use 1000 mg (Pfizer Japan Inc.)	Change Change Change Change	Methylprednisolone sodium succinate	Drugs with new additional indications and a new dosage for the treatment of the following treatment-resistant rheumatic diseases: systemic vasculitis (including microscopic polyangiitis, Wegener's granulomatosis, polyarteritis nodosa, Churg-Strauss syndrome, aortitis syndrome), systemic lupus erythematosus, polymyositis, dermatomyositis, scleroderma, mixed connective tissue disease, and refractory rheumatic disease. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Sep. 26, 2014	53	Calonal Tab. 500 (Showa Yakuhin Kako Co., Ltd.)	Approval	Acetaminophen	A drug in an additional dosage form. Note: the product was submitted for an approval application as a drug with a new additional indication for the treatment of osteoarthrosis and with an expanded dosage of acetaminophen in an additional dosage form. The new additional indication and the expanded dosage were approved on January 21, 2011, whereas approval of the additional dosage form had been under review.
6-1	Nov. 18, 2014	54	Spiriva 2.5 µg Respimat 60 puffs (Nippon Boehringer Ingelheim Co., Ltd.)	Change	Tiotropium bromide hydrate	A drug with a new additional indication for the relief of symptoms secondary to airway obstructive disorders in bronchial asthma (for use only in patients with the severe persistent type).
6-1	Dec. 26, 2014	55	Allergen Extract for Subcutaneous Injection-HDM "TORII"100,000 JAU/mL Allergen Extract for Subcutaneous Injection-HDM "TORII"10,000 JAU/mL (Torii Pharmaceutical Co., Ltd.)	Approval Approval	*Dermatophagoides farinae* extract 10,000 AU/mL, *Dermatophagoides pteronyssinus* extract 10,000 AU/mL	Drugs with new active ingredients indicated for the allergen immunotherapy for house dust mite antigen-induced allergic rhinitis and bronchial asthma.
6-1	Dec. 26, 2014	56	Cosentyx for S.C. Injection 150 mg Syringe Cosentyx for S.C. Injection 150 mg (Novartis Pharma K.K.)	Approval Approval	Secukinumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of plaque psoriasis and psoriatic arthritis in patients who have not responded sufficiently to conventional therapies.
6-1	Dec. 26, 2014	57	Allergen Extract for Scratch Test - HDM "TORII" 100,000 JAU/mL (Torii Pharmaceutical Co., Ltd.)	Approval	*Dermatophagoides farinae* extract 10,000 AU/mL, *Dermatophagoides pteronyssinus* extract 10,000 AU/mL	A drug with new active ingredients indicated for the identification of allergen in patients with allergic diseases.
6-1	Mar. 20, 2015	58	Dopram Injectable 400 mg (Kissei Pharmaceutical Co., Ltd.)	Change	Doxapram hydrochloride hydrate	A drug with a new additional indication and a new dosage for the treatment of primary apnoea (apnea of prematurity) in immature or low birth weight infants who have not responded sufficiently to conventional therapies.
6-1	Mar. 26, 2015	59	Eklira 400 µg Genuair 30 doses Eklira 400 µg Genuair 60 doses (Kyorin Pharmaceutical Co., Ltd.)	Approval Approval	Aclidinium bromide	Drugs with a new active ingredient indicated for the relief of symptoms secondary to airway obstructive disorder in chronic obstructive pulmonary disease (chronic bronchitis, emphysema).
6-1	Mar. 26, 2015	60	Actair 100 IR Sublingual Tablets-HDM Actair 300 IR Sublingual Tablets-HDM (Shionogi & Co., Ltd.)	Approval Approval	*Dermatophagoides farinae* extract bulk powder, *Dermatophagoides pteronyssinus* extract bulk powder	Drugs with new active ingredients indicated for the allergen immunotherapy for house dust mite antigen-induced allergic rhinitis.
6-1	Mar. 26, 2015	61	Encruse 62.5 µg Ellipta 7 doses Encruse 62.5 µg Ellipta 30 doses (GlaxoSmithKline K.K.)	Approval Approval	Umeclidinium bromide	Other drugs with a new dosage indicated for the relief of symptoms secondary to airway obstructive disorder in chronic obstructive pulmonary disease (chronic bronchitis, emphysema).

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	May 23, 2014	62	Januvia Tablets 12.5 mg Januvia Tablets 25 mg Januvia Tablets 50 mg Januvia Tablets 100 mg (MSD K.K.) Glactiv Tablets 12.5 mg Glactiv Tablets 25 mg Glactiv Tablets 50 mg Glactiv Tablets 100 mg (Ono Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change Change	Sitagliptin phosphate hydrate	Drugs with a new indication for the treatment of type 2 diabetes mellitus.
6-2	May 23, 2014	63	Nesina Tablets 6.25 mg Nesina Tablets 12.5 mg Nesina Tablets 25 mg (Takeda Pharmaceutical Company Limited)	Change Change Change	Alogliptin benzoate	Drugs with a new indication for the treatment of type 2 diabetes mellitus.
6-2	May 23, 2014	64	Aredia for I.V. Infusion 15 mg Aredia for I.V. Infusion 30 mg (Novartis Pharma K.K.)	Change Change	Pamidronate disodium hydrate	Drugs with a new additional indication and a new dosage for the treatment of osteogenesis imperfecta. [Public knowledge-based application after PAFSC's preliminary assessment]
6-2	Jul. 4, 2014	65	Canaglu Tablets 100 mg (Mitsubishi Tanabe Pharma Corporation)	Approval	Canagliflozin hydrate	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Jul. 4, 2014	66	Vpriv for Intravenous Injection 400 U (Shire Japan KK)	Approval	Velaglucerase alfa (genetical recombination)	A drug with a new active ingredient indicated for the improvement of various symptoms of Gaucher disease (anemia, thrombocytopenia, hepatosplenomegaly, and bone disease). [Orphan drug]
6-2	Jul. 4, 2014	67	Nicystagon Capsules 50 mg Nicystagon Capsules 150 mg (Mylan Seiyaku Ltd.)	Approval Approval	Cysteamine bitartrate	Drugs with a new active ingredient indicated for the treatment of nephropathic cystinosis. [Orphan drug]
6-2	Aug. 29, 2014	68	Victoza Subcutaneous Injection 18 mg (Novo Nordisk Pharma Ltd.)	Change	Liraglutide (genetical recombination)	A drug with a new indication for the treatment of type 2 diabetes mellitus.
6-2	Aug. 29, 2014	69	Metgluco Tablets 250 mg Metgluco Tablets 500 mg (Sumitomo Dainippon Pharma Co., Ltd.)	Change Change	Metformin hydrochloride	Drugs with a new dosage indicated for the treatment of type 2 diabetes mellitus (for pediatric use).
6-2	Nov. 18, 2014	70	Surepost Tablets 0.25 mg Surepost Tablets 0.5 mg (Sumitomo Dainippon Pharma Co., Ltd.)	Change Change	Repaglinide	Drugs with a revised indication for the treatment of type 2 diabetes mellitus.
6-2	Dec. 26, 2014	71	Orfadin Capsules 2 mg Orfadin Capsules 5 mg Orfadin Capsules 10 mg (Astellas Pharma Inc.)	Approval Approval Approval	Nitisinone	Drugs with a new active ingredient indicated for the treatment of type I hypertyrosinemia.
6-2	Dec. 26, 2014	72	Jardiance Tablets 25 mg Jardiance Tablets 10 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval	Empagliflozin	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Dec. 26, 2014	73	Vimizim Intravenous Infusion 5 mg (BioMarin Pharmaceutical Japan K.K.)	Approval	Elosulfase alfa (genetical recombination)	A drug with a new active ingredient indicated for the treatment of mucopolysaccharidosis type IVA. [Orphan drug]
6-2	Mar. 26, 2015	74	Zafatek Tablets 50 mg Zafatek Tablets 100 mg (Takeda Pharmaceutical Company Limited)	Approval Approval	Trelagliptin succinate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Mar. 26, 2015	75	Cerdelga Capsule 100 mg (Genzyme Japan K.K)	Approval	Eliglustat tartrate	A drug with a new active ingredient indicated for the improvement of various symptoms of Gaucher disease (anemia, thrombocytopenia, hepatosplenomegaly, and bone disease). [Orphan drug]
In vivo diagnostics	Dec. 26, 2014	76	Patch Test Panel (S) (Sato Pharmaceutical Co., Ltd.)	Approval	N/A for this drug used for patch tests	A drug indicated for use in patch tests to identify allergens in patients with allergic dermatitis.
In vivo diagnostics	Mar. 26, 2015	77	Gadovist IV Inj. 1.0 mol/L 7.5 mL Gadovist IV Inj. 1.0 mol/L Syringe 5 mL Gadovist IV Inj. 1.0 mol/L Syringe 7.5 mL Gadovist IV Inj. 1.0 mol/L Syringe 10 mL (Bayer Yakuhin, Ltd.)	Approval Approval Approval Approval	Gadobutrol	Drugs with a new active ingredient indicated for visibility of brain/spinal cord and trunk/extremities in magnetic resonance computer tomographic imaging as a contrast agent.
Oncology drugs	May 23, 2014	78	Imunomax-γ for Injection 50 Imunomax-γ for Injection 100 (Shionogi & Co., Ltd.)	Change Change	Interferon gamma-1a (genetical recombination)	Drugs with new additional indications and a new dosage for the treatment of mycosis fungoides and Sézary syndrome. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	May 23, 2014	79	Ranmark Subcutaneous Injection 120 mg (Daiichi Sankyo Company, Limited)	Change	Denosumab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of giant cell tumor of bone. [Orphan drug]
Oncology drugs	Jun. 20, 2014	80	Nexavar Tablets 200 mg (Bayer Yakuhin, Ltd.)	Change	Sorafenib tosilate	A drug with a new additional indication for the treatment of unresectable differentiated thyroid carcinoma. [Orphan drug]
Oncology drugs	Jul. 4, 2014	81	Zytiga Tablets 250 mg (Janssen Pharmaceutical K.K.)	Approval	Abiraterone acetate	A drug with a new active ingredient indicated for the treatment of castration-resistant prostate cancer. [Priority review]
Oncology drugs	Jul. 4, 2014	82	Jevtana 60 mg I.V. Infusion (Sanofi K.K.)	Approval	Cabazitaxel acetonate	A drug with a new active ingredient indicated for the treatment of prostate cancer. [Priority review]
Oncology drugs	Jul. 4, 2014	83	Jakavi Tablets 5 mg (Novartis Pharma K.K.)	Approval	Ruxolitinib phosphate	A drug with a new active ingredient indicated for the treatment of myelofibrosis. [Orphan drug]
Oncology drugs	Jul. 4, 2014	84	Alecensa Capsule 20 mg Alecensa Capsule 40 mg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval	Alectinib hydrochloride	Drugs with a new active ingredient indicated for the treatment of unresectable advanced/relapsed ALK fusion gene-positive non-small-cell lung cancer. [Orphan drug]
Oncology drugs	Jul. 4, 2014	85	Opdivo Intravenous Infusion 20 mg Opdivo Intravenous Infusion 100 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval	Nivolumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable malignant melanoma. [Orphan drug]
Oncology drugs	Sep. 26, 2014	86	G-Lasta Subcutaneous Injection 3.6 mg (Kyowa Hakko Kirin Co., Ltd.)	Approval	Pegfilgrastim (genetical recombination)	A drug with a new active ingredient indicated for decreasing the incidence of cancer chemotherapy-induced febrile neutropenia.
Oncology drugs	Sep. 26, 2014	87	Agrylin Capsules 0.5 mg (Shire Japan KK)	Approval	Anagrelide hydrochloride hydrate	A drug with a new active ingredient indicated for the treatment of essential thrombocythemia. [Orphan drug]
Oncology drugs	Sep. 26, 2014	88	MabCampath Intravenous infusion 30 mg (Sanofi K.K.)	Approval	Alemtuzumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of relapsed or refractory chronic lymphocytic leukemia. [Orphan drug]
Oncology drugs	Sep. 26, 2014	89	Bosulif Tablets 100 mg (Pfizer Japan Inc.)	Approval	Bosutinib hydrate	A drug with a new active ingredient indicated for the treatment of chronic myelogenous leukemia with resistance or intolerance to prior drug therapies. [Orphan drug]
Oncology drugs	Sep. 26, 2014	90	Zanosar for Intravenous Injection 1 g (Nobelpharma Co., Ltd.)	Approval	Streptozocin	A drug with a new active ingredient indicated for the treatment of neuroendocrine tumors of the pancreas and gastrointestinal tract. [Orphan drug]
Oncology drugs	Dec. 18, 2014	91	Nesp Injection 5 μg Plastic Syringe 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 Change	Darbepoetin alfa (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of anemia due to myelodysplastic syndrome. [Orphan drug]
Oncology drugs	Dec. 18, 2014	92	Abraxane I.V. Infusion 100 mg (Taiho Pharmaceutical Co., Ltd.)	Change	Paclitaxel	A drug with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer. [Priority review]
Oncology drugs	Dec. 18, 2014	93	Poteligeo Injection 20 mg (Kyowa Hakko Kirin Co., Ltd.)	Change	Mogamulizumab (genetical recombination)	A drug with a revised indication and a new dosage for the treatment of CCR4-positive adult T-cell leukemia/lymphoma. [Expedited review]
Oncology drugs	Dec. 18, 2014	94	Adriacin Injection 10 Adriacin Injection 50 (Kyowa Hakko Kirin Co., Ltd.)	Change Change	Doxorubicin hydrochloride	Drugs with a revised indication and a new dosage for the relief of symptoms of malignant lymphoma. [Expedited review]
Oncology drugs	Dec. 18, 2014	95	Doxorubicin Hydrochloride for Injection 10 mg "NK" Doxorubicin Hydrochloride for Injection 50 mg "NK" (Nippon Kayaku Co., Ltd.)	Change Change	Doxorubicin hydrochloride	Drugs with a revised indication and a new dosage for the relief of symptoms of malignant lymphoma. [Expedited review]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Dec. 18, 2014	96	Cylocide Injection 20 mg Cylocide Injection 40 mg Cylocide Injection 60 mg Cylocide Injection 100 mg Cylocide Injection 200 mg (Nippon Shinyaku Co., Ltd.)	Change Change Change Change Change	Cytarabine	Drugs with a new route of administration indicated for the treatment of acute leukemia (including acute erythroid leukemia and blast crisis of chronic myelogenous leukemia). [Expedited review]
Oncology drugs	Dec. 18, 2014	97	Cymerin 50 mg Injection Cymerin 100 mg Injection (Mitsubishi Tanabe Pharma Corporation)	Change Change	Ranimustine	Drugs with a new dosage indicated for the treatment of malignant lymphoma. [Expedited review]
Oncology drugs	Dec. 26, 2014	98	Zelboraf Tablet 240 mg (Chugai Pharmaceutical Co., Ltd.)	Approval	Vemurafenib	A drug with a new active ingredient indicated for the treatment of unresectable malignant melanoma with BRAF mutation. [Orphan drug]
Oncology drugs	Mar. 20, 2015	99	Lonsurf Combination Tablet T15 Lonsurf Combination Tablet T20 (Taiho Pharmaceutical Co., Ltd.)	Change Change	(1) Trifluridine (2) Tipiracil hydrochloride	Drugs with a revised indication for the treatment of unresectable advanced or recurrent colorectal cancer. [Expedited review]
Oncology drugs	Mar. 20, 2015	100	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 advanced or recurrent gastric cancer. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 26, 2015	101	Lenvima Capsule 4 mg Lenvima Capsule 10 mg (Eisai Co., Ltd.)	Approval Approval	Lenvatinib mesilate	Drugs with a new active ingredient indicated for the treatment of unresectable thyroid cancer. [Orphan drug]
Oncology drugs	Mar. 26, 2015	102	Pomalyst Capsules 1 mg Pomalyst Capsules 2 mg Pomalyst Capsules 3 mg Pomalyst Capsules 4 mg (Celgene K.K.)	Approval Approval Approval Approval	Pomalidomide	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Mar. 26, 2015	103	Cyramza Injection 100 mg Cyramza Injection 500 mg (Eli Lilly Japan K.K.)	Approval Approval	Ramucirumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable advanced or recurrent gastric cancer. [Priority review]
HIV/AIDS drugs	Nov. 18, 2014	104	Complera Combination Tablets (Janssen Pharmaceutical K.K.)	Approval	Rilpivirine hydrochloride, Emtricitabine, Tenofovir disoproxil fumarate	A new combination drug indicated for the treatment of HIV-1 infection. [Orphan drug]
HIV/AIDS drugs	Mar. 16, 2015	105	Triumeq Combination Tablets (ViiV Healthcare K.K.)	Approval	Dolutegravir sodium, Abacavir sulfate, Lamivudine	A new combination drug indicated for the treatment of HIV infection. [Orphan drug]
Vaccines	Jun. 20, 2014	106	Prevenar 13 Suspension Liquid for Injection (Pfizer Japan Inc.)	Change	Pneumococcal 13-valent conjugate vaccine adsorbed (mutated diphtheria CRM_{197} conjugate)	A drug with a new additional indication and a new dosage for the prophylaxis of pneumococcal disease. (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) in the elderly.
Vaccines	Jul. 4, 2014	107	Menactra Intramuscular Injection (Sanofi K.K.)	Approval	Meningococcal quadrivalent vaccine (diphtheria toxoid conjugate)	A drug with a new active ingredient indicated for the prophylaxis of invasive meningococcal disease. (serotypes A, C, Y, and W-135).
Vaccines	Jul. 4, 2014	108	Squarekids Subcutaneous Injection Syringe (Kitasato Daiichi Sankyo Vaccine Co., Ltd.)	Approval	Adsorbed diphtheria-purified pertussis-tetanus-inactivated polio (salk vaccine) combined vaccine	A new combination drug indicated for the prevention of pertussis, diphtheria, tetanus, and acute poliomyelitis.
Vaccines	Mar. 26, 2015	109	Cell Culture-derived Influenza Emulsion HA Vaccine (prototype) for Intramuscular Injection "Kaketsuken" (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Cell culture-derived influenza emulsion HA vaccines (prototype)	A drug with a new active ingredient indicated for the prevention of pandemic influenza. [Orphan drug]
Vaccines	Mar. 26, 2015	110	Synflorix Aqueous Suspension for Intramuscular Injection (Japan Vaccine Co., Ltd.)	Approval	Pneumococcal 10-valent conjugate vaccine adsorbed (Non-Typeable *Haemophilus influenzae* (NTHi) protein D, diphtheria or tetanus toxoid conjugates)	A drug with a new active ingredient indicated for the prophylaxis of pneumonia and pneumococcal invasive disease. (serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F)

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Blood products	Jun. 20, 2014	111	Feiba NF for Injection 500 Feiba NF for Injection 1000 (Baxter Limited)	Change Change	Anti-inhibitor coagulant complex	Drugs with a revised indication and a new dosage for inhibition of bleeding tendency by promoting the blood coagulation in the plasma in patients with inhibitors to blood coagulation factor VIII or factor IX.
Blood products	Jul. 4, 2014	112	Byclot Combination Intravenous Injection (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Freeze-dried activated human blood coagulation factor VII concentrate containing factor X	A new combination drug with a new active ingredient indicated for prevention of bleeding in patients who have inhibitors against blood coagulation factor VIII or IX. [Orphan drug]
Blood products	Jul. 4, 2014	113	Alprolix Intravenous 250 Alprolix Intravenous 500 Alprolix Intravenous 1000 Alprolix Intravenous 2000 Alprolix Intravenous 3000 (Biogen Idec Japan Ltd.)	Approval Approval Approval Approval Approval	Eftrenonacog alfa (genetical recombination)	Drugs with a new active ingredient indicated for inhibition of bleeding tendency in patients with blood coagulation factor IX deficiency.
Blood products	Dec. 26, 2014	114	Rixubis Intravenous 250 Rixubis Intravenous 500 Rixubis Intravenous 1000 Rixubis Intravenous 2000 Rixubis Intravenous 3000 (Baxter Limited)	Approval Approval Approval Approval Approval	Nonacog gamma (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with blood coagulation factor IX deficiency.
Blood products	Dec. 26, 2014	115	Eloctate Intravenous 250 Eloctate Intravenous 500 Eloctate Intravenous 750 Eloctate Intravenous 1000 Eloctate Intravenous 1500 Eloctate Intravenous 2000 Eloctate Intravenous 3000 (Biogen Idec Japan Ltd.)	Approval Approval Approval Approval Approval Approval Approval	Efraloctocog alfa (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Blood products	Feb. 2, 2015	116	Venoglobulin IH 5% I.V. 2.5 g/50 mL (Japan Blood Products Organization)	Change	Polyethylene glycol treated human normal immunoglobulin	A drug with a new indication and a new dosage for the prevention of acute otitis media, acute bronchitis, or pneumonia caused by *Pneumococcus or Haemophilus influenzae* in patients associated with a decrease in serum IgG2 levels. (for use only in patients who have not responded sufficiently to prevention by vaccination and other appropriate treatments, and have repeated the relapse of these diseases).
Blood products	Mar. 26, 2015	117	NovoThirteen i.v.injection 2500 (Novo Nordisk Pharma Ltd.)	Approval	Catridecacog (genetical recombination)	A drug with a new active ingredient indicated for the control of bleeding tendency in patients with congenital blood coagulation factor XIII A-subunit deficiency. [Orphan drug]
Bio-CMC	Jul. 4, 2014	118	(1) Infliximab BS for I.V. Infusion 100 mg "NK" (Nippon Kayaku Co., Ltd.) (2) Infliximab BS for I.V. Infusion 100 mg "CTH" (Celltrion Inc.)	Approval Approval	Infliximab (genetical recombination) [infliximab biosimilar 1]	Follow-on biologics indicated for the treatment of rheumatoid arthritis in patients who have not responded sufficiently to conventional treatments (including prevention of structural joint damage), the treatment and maintenance therapy of Crohn's disease (for use only in patients in an active phase of moderate to severe Crohn's disease or with external fistula who have not responded sufficiently to conventional treatments), or the treatment of moderate to severe ulcerative colitis (for use only in patients who have not responded sufficiently to conventional treatments).
Bio-CMC	Dec. 26, 2014	119	Insulin Glargine BS Inj. Cartridges [Lilly] Insulin Glargine BS Inj. MirioPen [Lilly] (Eli Lilly Japan K.K.)	Approval Approval	Insulin glargine (genetical recombination) [Insulin glargine biosimilar 1]	Follow-on biologics indicated for the treatment of diabetes mellitus where insulin therapy is indicated.

Table 2. Products Approved in FY 2014: 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	Mar. 10, 2015 Total review time: 126 days Regulatory review time: 80 days	– No clinical study results	1	Hoya CTR (Hoya Corporation)	Change	Medical products 4 Ophthalmic intracapsular ring	An intracapsular ring inserted into a lens capsule is used when surgical difficulty can be expected in a cataract surgery because of the risks associated with completion of the surgery due to a weakness or rupture of Zinn's Zonule. An application for partial changes of approval application for medical device to mainly add the insertion method using an injector in the usage instructions. (A partial change during the reexamination period)
3-1	Apr. 7, 2014 Total review time: 255 days Regulatory review time: 110 days	Nov. 21, 2013 Global clinical trial and foreign clinical study results	2	Promus Premier Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system consisting of a drug-eluting stent coated with everolimus to inhibit neointimal proliferation and a delivery catheter. The delivery catheter was improved by adding a link at the proximal end of a stent to produce axial strength to be superior to the original product. Clinical studies were conducted to confirm the efficacy and safety of this product in the treatment of symptomatic ischemic diseases.
3-1	May 20, 2014 Total review time: 110 days Regulatory review time: 76 days	Dec. 21, 2012 Domestic clinical study results	3	XIENCE Xpedition Drug Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A coronary stent consisting of a drug-eluting stent used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion (a lesion length of 32 mm or less) with a reference vessel diameter of 2.25-3.75 mm and a delivery catheter used to implant a stent to the coronary stenosis site. This application for partial changes of approval application for medical device to add a stent size of 2.25mm diameter and change a drug release profile determination method. The added stent is identical to the company's approved product "XIENCE PRIME SV Drug-Eluting Stent (22500BZX00070000, hereinafter referred to as XIENCE PRIME SV). The stent delivery system is identical to that of the product of 2.5 mm diameter except for the balloon size. Results from clinical studies on "XIENCE PRIME SV" were submitted to confirm the efficacy and safety of this product in the treatment of symptomatic ischemic diseases.
3-1	Jun. 12, 2014 Total review time: 43 days Regulatory review time: 41 days	- No clinical study results	4	XIENCE PRIME SV Drug-Eluting Stent System (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A coronary stent used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion (a lesion length of 22 mm or less) with a reference vessel diameter of 2.25-2.5 mm. This application for a partial change of approval application for medical device to modify inconsistent information provided in the raw material or component field. (A partial change during the reexamination period)
3-1	Jul. 25, 2014 Total review time: 91 days Regulatory review time: 48 days	- No clinical study results	5	Zilver Flex Vascular Stent for SFA (Cook Japan Inc.)	Change	Instrument & apparatus 7 Stent for blood vessel	A vascular stent to be used in patients with symptomatic vascular diseases of the above-the-knee femoropopliteal artery with reference vessel diameter of 4-7 mm. This product is used for the treatment for acute or impending occlusion caused by failure of intervention therapy or for dissection, etc. after the maximum number of "Zilver PTX Drug-Eluting Peripheral Stent" implantations. This application for a partial change of approval application for medical device to add a manufacturing site. (A partial change during the reexamination period)
3-1	Sep. 25, 2014 Total review time: 360 days Regulatory review time: 218 days	Nov. 7, 2012 Domestic clinical study results	6	SMART CONTROL Stent (Johnson & Johnson K.K.)	Change	Instrument & apparatus 7 Stent for iliac artery	A self-expanding nickel-titanium alloy stent inserted into the site of lesion in the iliac artery and/or the superficial femoral artery to expand/maintain a vascular lumen. This application for a partial change to add an elective therapy for symptomatic vascular diseases to indications for the superficial femoral artery. A clinical study was conducted to evaluate the safety and efficacy of this product in elective patients. (A partial change during the reexamination period)
3-1	Sep. 25, 2014 Total review time: 360 days Regulatory review time: 218 days	Nov. 7, 2012 Domestic clinical study results	7	SMART Stent (Johnson & Johnson K.K.)	Change	Instrument & apparatus 7 Stent for blood vessel	A self-expanding nickel-titanium alloy stent inserted into the site of lesion in the superficial femoral artery to expand/maintain a vascular lumen. This application to add an indication of elective therapy for symptomatic vascular diseases. A clinical study was conducted to evaluate the safety and efficacy of this product in elective patients. (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
3-1	Jan. 14, 2015 Total review time: 404 days Regulatory review time: 178 days	May 22, 2015 Domestic and global clinical study results	8	Misago (Terumo Corporation)	Change	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nickel-titanium alloy stent and a delivery system to deliver the stent to the site of lesion, used for the treatment of symptomatic artery disease by dilatation of artery and maintenance of the lumen with target vessel diameter of 4-7 mm and target lesion of 40-150 mm in the superficial femoral artery region, and for the treatment of acute or impending occlusion associated with unsuccessful intervention treatment in the lesion. An application for a partial change to add palliative treatment for symptomatic vascular disease to the indications of this product. Clinical studies were conducted to evaluate efficacy and safety of this product for palliative cases.
3-2	May 29, 2014 Total review time: 358 days Regulatory review time: 172 days	Jun. 12, 2012 Foreign clinical study results	9	AMPLATZER Vascular Plug 4 (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	This device is used to occlude blood vessels, and reduce, block, or modify blood flow, by transdermally inserting and placing it in arteries/veins, except blood vessels within the heart and the skull. It was changed to a form with two conical blocks, and improved its components to reduce the profile of the whole plug (the diameter in its closed state) so that the device can be advanced through an imaging catheter, maintaining the same barrier area to blood flow as that of the approved product "AMPLATZER Vascular Plug (approval No.: 22400BZX00361000) (hereinafter referred to as AVP). Results from domestic clinical studies using AVP were submitted as clinical data of this product because several non-clinical studies including design verification and animal studies had shown that the same efficiency of this product is secured as that of AVP.
3-2	Nov. 7, 2014 Total review time: 728 days Regulatory review time: 281 days	- Foreign clinical study results	10	COOK Zenith Dissection Endovascular System (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	A stent graft system used for the treatment of acute complicated Stanford type B aortic dissection, consisting of a stent graft that is placed to close the primary entry tear, a bare stent that enlarges compressed or narrowed intravascular lumen due to aortic dissection, and a delivery system that delivers/places them in the lesions. Results from clinical studies were submitted to evaluate efficacy and safety on this product for patients with acute complicated Stanford type B aortic dissection.
3-2	Nov. 14, 2014 Total review time: 135 days Regulatory review time: 81 days	- No clinical study results	11	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 protrusion and/or dropout of embolic coils into/from the parent artery during coil embolization. An application for partial changes to add VRD that improves conformability and visibility of the vascular wall, and a delivery system that improves the operability. This product is an orphan medical device. (A partial change during the reexamination period)
3-2	Dec. 24, 2014 Total review time: 398 days Regulatory review time: 146 days	Oct. 26, 2001 Clinical evaluation report	12	BIOPATCH Protective Disk with CHG (Johnson & Johnson K.K.)	Approval	Medical products 4 Protective patch for puncture site	A sterilized disk pad with a slit, which consists of a layer of polyurethane foam impregnated with chlorhexidine gluconate antimicrobial constituent and a covering layer of foam. This product protects the insertion site of various percutaneous devices by covering the site and absorbing the fluids like wound exudate. In patients who are inserted with central venous or arterial catheters, this product also reduces the incidence of catheter-related bloodstream infections and local infections. Clinical evaluation report summarizing the clinical results on this product was submitted to evaluate the reduction of catheter-related bloodstream infections and safety of this product.
3-2	Mar. 24, 2015 Total review time: 361 days Regulatory review time: 240 days	Jun. 16, 2014 Domestic and foreign clinical study results	13	Sapien XT (Edwards Lifesciences Limited)	Change	Instrument & apparatus 7 Transcatheter bovine pericardial valve	A prosthetic heart valve system is used for transcatheter valve implantation for patients with symptomatic severe aortic valve stenosis and for whom surgical aortic valve replacement cannot be performed due to the risks of complications. An application for a partial change of approval application to add the 20 mm- and 29 mm-diameter valves as the variation in size. A clinical study was conducted to confirm the equivalence in efficacy and safety between the new sizes and approved existing sizes. (A partial change during the reexamination period)
3-2	Mar. 25, 2015 Total review time: 357 days Regulatory review time: 198 days	Jan. 17, 2014 Domestic and foreign clinical study results	14	CoreValve (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Transcatheter porcine pericardial valve	A self-expanding biological percutaneous aortic valve (porcine pericardial valve) system is used for transcatheter valve implantation in the native aortic valve for patients with symptomatic severe aortic stenosis attributed to sclerosis and degeneration of the cusp of the native aortic valve, for whom surgery cannot be performed. A clinical study was conducted to evaluate the efficacy and safety of this product and to confirm the compatibility to the domestic medical environment.

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	May 30, 2014 Total review time: 287 days Regulatory review time: 144 days	- Clinical evaluation report	15	Entovis MRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to be used by connecting it to electrodes placed within the heart. 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	May 30, 2014 Total review time: 287 days Regulatory review time: 144 days	- Clinical evaluation report	16	Safio S (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. 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. 5, 2014 Total review time: 108 days Regulatory review time: 106 days	- Clinical evaluation report	17	Etrinsa 8-T ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to be used by connecting it to electrodes placed within the heart. 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	Jun. 5, 2014 Total review time: 108 days Regulatory review time: 106 days	- Clinical evaluation report	18	Etrinsa 6 ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to be used by connecting it to electrodes placed within the heart. 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	Jun. 30, 2014 Total review time: 271 days Regulatory review time: 95 days	- No clinical study results	19	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 the need for cardiac transplantation is indicated, showing 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 a heart transplant. An application for a partial change to alter the alarm setting when the automatic restart function of a blood pump (automatic return mechanism) works. (A partial change during the reexamination period) [Orphan device]
4	Jul. 31, 2014 Total review time: 265 days Regulatory review time: 177 days	- No clinical study results	20	Solia JT (Biotronik Japan, Inc.)	Change	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. An application for a partial change to add a new lead size of 45 cm in length. (A partial change during the reexamination period)
4	Aug. 5, 2014 Total review time: 89 days Regulatory review time: 73 days	- Clinical evaluation report	21	Iforia 7 ICD ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	An implantable defibrillator connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report summarizing clinical data on this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Aug. 5, 2014 Total review time: 60 days Regulatory review time: 51 days	- Clinical evaluation report	22	Linox Smart Pro S (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A catheter electrode connected with an implantable defibrillator. The patients implanted with the device can conditionally undergo an MRI scan. This application for a partial change of approval application to change conditions of MRI compatibility. A clinical evaluation report summarizing clinical data on this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Aug. 5, 2014 Total review time: 60 days Regulatory review time: 51 days	- Clinical evaluation report	23	Linox Smart Pro SD (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A catheter electrode connected with an implantable defibrillator. The patients implanted with the device can conditionally undergo an MRI scan. This application for a partial change of approval application to change conditions of MRI compatibility. A clinical evaluation report summarizing clinical data on this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Aug. 5, 2014 Total review time: 60 days Regulatory review time: 51 days	- Clinical evaluation report	24	Linox Smart Pro S DX (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A catheter electrode connected with an implantable defibrillator. The patients implanted with the device can conditionally undergo an MRI scan. This application for a partial change of approval application to change conditions of MRI compatibility. A clinical evaluation report summarizing clinical data on this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)

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4	Sep. 9, 2014 Total review time: 187 days Regulatory review time: 126 days	- Clinical evaluation report	25	Sentus ProMRI OTW BP (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A pacemaker lead connected with an implantable pulse generator and implanted in the coronary vein. The patients implanted with the device can conditionally undergo an MRI scan. A clinical evaluation report summarizing clinical data on this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Sep. 9, 2014 Total review time: 102 days Regulatory review time: 31 days	Jul. 26, 2013 No clinical study results	26	Arctic Front Advance Cryoablation Catheter (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 51 Cardiovascular ablation catheter	A flexible over-the-wire balloon catheter inserted into a blood vessel using a conventional minimally invasive procedure. It is used in cryoablation of cardiac tissue. This application for partial changes of approval application to remove a leak detection wire traveling in an outer lumen, and to add a manufacturing site. (A partial change during the reexamination period)
4	Sep. 17, 2014 Total review time: 265 days Regulatory review time: 158 days	Apr. 27, 2010 Foreign clinical study results	27	Alair Bronchial Thermoplasty System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 51 Bronchial thermoplasty catheter system	A catheter system used to apply high frequency energization to the bronchial wall to reduce asthmatic symptoms in patients aged 18 or older with severe asthma whose asthmatic symptoms are not well controlled with high-dose inhaled steroids and long-acting beta2-agonists. Foreign clinical studies were conducted to demonstrate its relieving effect on asthmatic symptoms.
4	Sep. 25, 2014 Total review time: 209 days Regulatory review time: 154 days	- Foreign clinical study results	28	Evera MRI ICD Series (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	An implantable defibrillator intended for the treatment of ventricular tachycardia, etc. The patients implanted with the device can conditionally undergo an MRI scan. This is a new application for the product with which an MRI scan can be conditionally conducted, based on the company's own approved products. In order to evaluate the safety of this product in MRI scans, results of clinical studies using the original product were submitted, in which the extrapolability in the evaluation was explained. (The original product is in a reexamination period)
4	Sep. 25, 2014 Total review time: 209 days Regulatory review time: 142 days	- Foreign clinical study results	29	Sprint Quattro MRI Screw-In Lead (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable catheter electrode connected with an implantable defibrillator and a defibrillator with biventricular pacing. The patients implanted with the device can conditionally undergo an MRI scan. This is a new application for the product with which an MRI scan can be conditionally conducted, based on the company's own approved products. In order to evaluate the safety of this product in MRI scans, results of clinical studies using the original product were submitted, in which the extrapolability in the evaluation was explained. (The original product is in a reexamination period)
4	Sep. 25, 2014 Total review time: 209 days Regulatory review time: 142 days	- Foreign clinical study results	30	Sprint Quattro MRI Screw-In Lead S (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An implantable catheter electrode connected with an implantable defibrillator and a defibrillator with biventricular pacing. The patients implanted with the device can conditionally undergo an MRI scan. This is a new application for the product with which an MRI scan can be conditionally conducted, based on the company's own approved products. In order to evaluate the safety of this product in MRI scans, results of clinical studies using the original product were submitted, in which the extrapolability in the evaluation was explained. (The original product is in a reexamination period)
4	Sep. 25, 2014 Total review time: 87 days Regulatory review time: 44 days	Dec. 10, 2010 No clinical study results	31	Medtronic CryoConsole (Medtronic Japan Co., Ltd.)	Change	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 cryoablation catheters. This application for a partial change of approval application for medical device to add a manufacturing site. The application falls under "expedited review of changes of manufacturing site" stated in "Acceleration of the Procedure for Changing or Adding Manufacturing Site of Medical Devices and In-vitro Diagnostics" (PFSB/ELD Notification No. 0330004, PFSB/CND Notification No. 0330012 dated on March 30, 2007). (A partial change during the reexamination period)
4	Oct. 9, 2014 Total review time: 164 days Regulatory review time: 95 days	Oct. 13, 2014 Foreign clinical study results	32	CapSureFIX Novus Lead (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	The device is an implantable pacing lead used by connecting it to an implantable cardiac pacemaker or defibrillator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for requirements for imaging. The application is for a partial change to conditionally allow MRI scan with this device. Data on foreign clinical study results related to this product were 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	2014/10/20 Total review time: 343 days Regulatory review time: 86 days	Oct. 13, 2014 Foreign clinical study results	33	CapSureFIX Novus MRI Lead (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker leads	The device is an endocardial implantable pacemaker lead used by connecting it to pulse generators including an implantable cardiac pacemaker or defibrillator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. Data on foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 14, 2014 Total review time: 162 days Regulatory review time: 95 days	- Foreign clinical study results	34	Medtronic Advisa MRI (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to add a single-chamber type which conditionally allows MRI scan to the existing dual-chamber type. Data on foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 17, 2014 Total review time: 130 days Regulatory review time: 83 days	- Clinical evaluation report	35	Iperia 7 ICD DF-1 ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	The device is an implantable cardiac defibrillator used by connecting it to electrodes placed in the heart. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. This product was developed based on the approved product "Ilesto 7 ICD Pro" (Approval No.: 22500BZX00292000). The major improvements from the approved product include the addition of conditions for the strength of static magnetic field used in MRI and an additional function for detecting ventricular tachycardia. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 17, 2014 Total review time: 105 days Regulatory review time: 80 days	- Clinical evaluation report	36	Itrevia 7 CRT-D ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	The device is an implantable biventricular pacing pulse generator with defibrillator function used by connecting it to electrodes placed in the heart. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. This product was developed based on the approved product "Ilesto 7 CRT-D Pro" (Approval No.: 22500BZX00293000). The major improvement from the approved product is an additional function of ventricular tachycardia detection. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 17, 2014 Total review time: 41 days Regulatory review time: 40 days	- Clinical evaluation report	37	Linox Smart Pro S (Biotronik Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead used by connecting it to an implantable defibrillator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to add the condition for the strength of static magnetic field used in MRI scans. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Nov. 17, 2014 Total review time: 41 days Regulatory review time: 40 days	- Clinical evaluation report	38	Linox Smart Pro SD (Biotronik Japan, Inc)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead used by connecting it to an implantable defibrillator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to add the condition for the strength of static magnetic field used in MRI scans. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)

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4	Nov. 17, 2014 Total review time: 41 days Regulatory review time: 40 days	- Clinical evaluation report	39	Linox Smart Pro S DX (Biotronik Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead used by connecting it to an implantable defibrillator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to add the condition for the strength of static magnetic field used in MRI scans. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (A partial change during the reexamination period)
4	Nov. 20, 2014 Total review time: 168 days Regulatory review time: 105 days	- No clinical study results	40	Nuance MRI RF (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker to regulate the heart rhythm by cardiac stimulation for a long term. Patients implanted with the device can undergo an MRI scan under specific conditions. The application is for a partial change to add concomitant medical devices to perform MRI scan. (A partial change during the reexamination period)
4	Nov. 20, 2014 Total review time: 168 days Regulatory review time: 105 days	- No clinical study results	41	Accent MRI RF (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker to regulate the heart rhythm by cardiac stimulation for a long term. Patients implanted with the device can undergo an MRI scan under specific conditions. The application is for a partial change to add concomitant medical devices to perform MRI scan. (A partial change during the reexamination period)
4	Nov. 20, 2014 Total review time: 168 days Regulatory review time: 105 days	- Clinical evaluation report	42	IsoFlex Optim J (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead. The patient implanted with the device except for the 46 cm straight lead can undergo an MRI scan under specific conditions. The application is for a partial change to conditionally allow MRI scan with this device. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Nov. 20, 2014 Total review time: 168 days Regulatory review time: 105 days	- Clinical evaluation report	43	IsoFlex Optim (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead. The patient implanted with the device except for the 46 cm straight lead can undergo an MRI scan under specific conditions. The application is for a partial change to conditionally allow MRI scan with this device. A clinical evaluation report summarizing foreign clinical study results related to this product was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Dec. 22, 2014 Total review time: 115 days Regulatory review time: 59 days	- No clinical study results	44	Ingenio MRI (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker to regulate the heart rhythm by cardiac stimulation for a long term in order to perform the treatment of bradycardia. The application is for a partial change to change the materials of the header part. (A partial change during the reexamination period)
4	Jan. 19, 2015 Total review time: 109 days Regulatory review time: 62 days	- No clinical study results	45	Jarvik 2000 Implantable Ventricular Assist Device (Century Medical, Inc.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	The device is an axial-flow implantable ventricular assist device system used to improve the blood circulation until heart transplant. The device is used for severe cardiac failure patients who is are qualified to receive heart transplant, shown continuous decompensation in spite of drug therapy or circulation assist techniques, such as an external ventricular assist system and considered difficult to survival without heart transplant. The application is for partial changes to mainly change the battery cell incorporated into the portable battery. (A partial change during the reexamination period)
4	Jan. 21, 2015 Total review time: 125 days Regulatory review time: 55 days	Jun. 29, 2012 No clinical study results	46	LifeVest Wearable Cardioverter Defibrillator (ZOLL Lifecor Corporation)	Change	Instrument & apparatus 12 Wearable defibrillator	The device is a wearable cardioverter defibrillator intended for the following patients: Patients for whom indication for an implantable cardiac defibrillator (ICD) is unconfirmed despite having a high risk of sudden cardiac death due to ventricular tachycardia or ventricular fibrillation; Patients in whom an ICD cannot be implanted immediately due to their medical conditions although ICD is indicated. This wearable cardioverter defibrillator is used in the period until the propriety of indication of ICD is determined or the implantation is performed. The application is for a partial change to add an attaching method of velocro to electrocardiogram electrodes without an adhesive to the existing direct adhesive method. (A partial change during the reexamination period)

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4	Feb. 3, 2015 Total review time: 418 days Regulatory review time: 174 days	- Clinical evaluation report	47	Beflex lead (Sorin CRM SAS)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	The device is an endocardial implantable pacemaker lead used by connecting it to an implantable cardiac pacemaker. The application is for a partial change to allow MRI scan only when the patient's condition is suitable for the requirements for imaging. A clinical evaluation report was submitted to confirm the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Feb. 3, 2015 Total review time: 417 days Regulatory review time: 173 days	- Clinical evaluation report	48	Kora 100 (Sorin CRM SAS)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker used by connecting it to electrodes placed in the heart. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. A clinical evaluation report was submitted to confirm the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Mar. 4, 2015 Total review time: 132 days Regulatory review time: 87 days	- Clinical evaluation report	49	Itrevia 7 CRT-D QP ProMRI (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	The device is an implantable biventricular pacing pulse generator with a defibrillator function implanted in the chest or abdomen for the treatment of ventricular tachycardia, etc. by ventricular sensing, pacing and defibrillation. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. A clinical evaluation report was submitted to confirm the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Mar. 4, 2015 Total review time: 132 days Regulatory review time: 87 days	- Clinical evaluation report	50	Sentus ProMRI OTW QP (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is a pacemaker lead with four electrodes at its tip used by placing it in the coronary vein and connecting it to an implantable pulse generator. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. A clinical evaluation report was submitted to confirm the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Mar. 23, 2015 Total review time: 101 days Regulatory review time: 84 days	- No clinical evaluation report	51	Linox Smart Pro DF4 SD (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead used for conducting ventricular sensing and pacing, antitachycardia pacing, and defibrillation by connecting it to an implantable defibrillator, etc. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to change the condition allowed an MRI scan when the device is connected to a specific implantable defibrillator. (A partial change during the reexamination period)
4	Mar. 23, 2015 Total review time: 101 days Regulatory review time: 84 days	- No clinical evaluation report	52	Protego Pro S (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead used for conducting ventricular sensing and pacing, antitachycardia pacing, and defibrillation by connecting it to an implantable defibrillator, etc. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change to change the condition allowed an MRI scan when the device is connected to a specific implantable defibrillator. (A partial change during the reexamination period)
4	Mar. 23, 2015 Total review time: 101 days Regulatory review time: 84 days	- No clinical study results	53	Iforia 7 ICD ProMRI (Biotronik Japan, Inc.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	The device is an implantable defibrillator used by connecting it to electrodes placed in the heart. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change of approval application to add a model having a different header. (A partial change during the reexamination period)
4	Mar. 23, 2015 Total review time: 101 days Regulatory review time: 84 days	- No clinical study results	54	Solia S (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Endocardial implantable pacemaker leads	The device is an endocardial implantable pacemaker lead used by connecting it to an implantable defibrillator, etc. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change of approval application to change the condition allowed an MRI scan when the device is connected to a specific implantable defibrillator. (A partial change during the reexamination period)

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4	Mar. 26, 2015 Total review time: 125 days Regulatory review time: 97 days	- Foreign clinical study results	55	Sprint Quattro Screw-In Lead S (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable catheter electrode used by connecting it to an implantable defibrillator and a defibrillator with biventricular pacing. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change for some components with which an MRI scan can be conditionally conducted. In order to evaluate the safety of this product in MRI scans, the results of clinical studies using the original product were submitted, in which the extrapolability in the evaluation was explained. (The original product is in a reexamination period)
4	Mar. 26, 2015 Total review time: 125 days Regulatory review time: 97 days	- Foreign clinical study results	56	Sprint Quattro Screw-In Lead (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable catheter electrode used by connecting it to an implantable defibrillator and a defibrillator with biventricular pacing. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. The application is for a partial change for some components with which an MRI scan can be conditionally conducted. In order to evaluate the safety of this product in MRI scans, the results of clinical studies using the original product were submitted, in which the extrapolability in the evaluation was explained. (The original product is in a reexamination period)
5	Sep. 30, 2014 Total review time: 305 days Regulatory review time: 202 days	Apr. 18, 2014 No clinical study results	57	InterStim II Neurostimulator for Sacral Neuromodulation (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Implantable stimulator for bladder and bowel control	An implantable nerve stimulation system consisting of an electric stimulator and leads to be used in sacral nerve stimulation therapy for fecal incontinence. This application for a partial change of approval application to change a testing stimulator to a new type. A testing stimulator control is changed from a constant voltage control to a constant current control, while an implantable electric stimulator remains to be controlled by a constant voltage. (A partial change during the reexamination period)
6-1	Jun. 5, 2014 Total review time: 160 days Regulatory review time: 40 days	Jul. 20, 2006 Clinical evaluation report	58	Aequalis Reversed Shoulder Prosthesis (Tornier S.A.S.)	Change	Medical products 4 Total shoulder prosthesis	A reversed shoulder prosthesis system used in patients with shoulder rotator cuff dysfunction. This application for partial changes to add new components (eccentric or other type of inserts and glenoid sphere, small-diameter and HA-coated base plate, conversion adaptor for anatomical type) and to add usage (fixation of glenoid component with specific bone graft: BIO-RSA). A clinical evaluation report was submitted to demonstrate that this device is equivalent to the approved product and that there is no new unacceptable risk while option for the product is extended by the added components and the usage.
6-1	Sep. 25, 2014 Total review time: 118 days Regulatory review time: 79 days	Oct. 11, 2012 No clinical study results	59	Trabecular Metal Reverse Shoulder System (Zimmer K.K.)	Change	Medical products 4 Total shoulder prosthesis	A reversed shoulder prosthesis system used in patients with shoulder rotator cuff dysfunction including arthropathy with tendon rupture and massive rotator cuff tears. This application for a partial change of approval application to add a new component with a changed base plate (extended post length and off-set model), which is intended to improve suitability to patients' bone shapes. Based on the results of non-clinical studies, it was judged that new additional clinical evaluation is not required, because it is difficult to assume that a new clinical risk is actualized by the difference from the approved product. (A partial change during the reexamination period)
6-1	Oct. 9, 2014 Total review time: 197 days Regulatory review time: 90 days	Aug. 18, 2011 Clinical evaluation report	60	Lima Reverse Shoulder System (Lima Japan K.K.)	Approval	Medical products 4 Total shoulder prosthesis	A shoulder prosthesis having the concept of a reversed shoulder prosthesis system in which the anatomical structure is reversed. It is used for cases of rotator cuff dysfunction such as a massive rotator cuff tears or rotator cuff tear arthropathy. When it is difficult to be combined with a reversed shape, it can be combined with an anatomical shape in humerus or total shoulder joint replacement. A clinical evaluation report was submitted to confirm that the efficacy and safety of this device are equivalent to the existing approved devices based on overseas usage histories and publications of this device and similar devices.
8	Jul. 3, 2014 Total review time: 415 days Regulatory review time: 200 days	- Domestic and foreign clinical study results	61	Radioactive Pharmaceutical Synthesizer NEPTIS Plug-01 (Eli Lilly Japan K.K.)	Approval	Instrument & apparatus 10 Radiopharmaceutical synthesizer	A radioactive pharmaceutical synthesizer used for the semi-automated preparation of a radioisotope labeled compound, florbetapir (18F) injection by remote control system indicated for the visualization of beta-amyloid plaque in the brain in patients with cognitive impairment who are suspected of having Alzheimer's disease. Results from non-clinical studies, and domestic and foreign clinical studies were submitted as evaluation data on the efficacy and safety of this product and florbetapir (18F) injection.

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
8	Nov. 7, 2014 Total review time: 322 days Regulatory review time: 180 days	Oct. 18, 2012 Foreign clinical study results	62	MR-Guided Focused Ultrasound Surgery System ExAblate 2000 (GE Healthcare Japan Corporation)	Change	Instrument & apparatus 12 Ultrasound hyperthermia system	The device is a focused ultrosonic surgery system intended for heating and necrotizing target tissues by focusing ultrasound generated using an external transducer on internal targets. The application is for partial changes to (1) add a new indication, "relief of pain due to painful metastatic bone cancer" and (2) make an improvement intended to enhance operability in a previously approved indication, "improvement of symptoms of symptomatic uterine myoma." For (1), results of clinical study conducted to evaluate the efficacy and safety of this device in the new additional indication were submitted. For (2), results of non-clinical study conducted to evaluate efficiency of the additional capability, etc. in previously approved indication were submitted.
8	Dec. 12, 2014 Total review time: 73 days Regulatory review time: 19 days	Jan. 21, 2010 No clinical study results	63	Magnetic Navigation System Niobe (Medix Japan, Inc.)	Change	Instrument & apparatus 51 Cardiac Mapping System Workstation	The device is a guiding system that navigates an exclusive catheter for this system to a target region in the diagnosis of arrhythmia and intervention procedures. This device is used in combination with cardiovascular fluoroscopic X-ray diagnosing apparatus, and consists of a magnetic positioner, a control cabinet, a user interface, a ceiling-suspended monitor and a catheter advancement system. The application is for partial changes to add an image control support device, and to change the monitor size and emergency switch. (A partial change during the reexamination period)
8	Mar. 25, 2015 Total review time: 266 days Regulatory review time: 174 days	Apr. 8, 2011 Foreign clinical study results	64	NovoTTF-100A System (NovoCure Ltd.)	Approval	Instrument & apparatus 12 Alternating electric field tumor treatment system	The medical device is a non-invasive device that delivers alternating electric fields -referred to as Tumor Treating Fields (TTfield) - that inhibit cancer cell replication and cause cancer cell death. TTFields are delivered to the tumor in the brain through insulated transducer arrays (INE transducer array) that are placed on the scalp. A clinical trial was conducted to compare the efficacy and safety of the device to chemotherapy in patients with recurrent glioblastoma multiforme after receiving all possible surgery and radiation therapy options. [Priority review]
Specified partial change	May 1, 2014 Total review time: 76 days Regulatory review time: 32 days	- No clinical study results	65	Kawasumi Najuta Thoracic Stent Graft System (Kawasumi Laboratories, Incorporated)	Change	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft used for the treatment of thoracic aortic aneurysm. This application for a partial change of approval application for medical device to add a PFOA-free raw material to a raw material of graft “polytetrafluoroethylene.” The application was submitted as a "specified partial change” based on “Acceleration of Procedure for Specified Change for Medical Devices” (PFSB/ELD/OMDE Notification No.1110001 dated on November 10, 2008).
Specified partial change	Jul. 25, 2014 Total review time: 121 days Regulatory review time: 36 days	Jan. 4, 2008 No clinical study results	66	NaviStar RMT ThermoCool (Johnson & Johnson K.K.)	Change	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter for the radiofrequency catheter ablation and for the electrophysiological study; it is used to treat symptomatic drug refractory paroxysmal and persistent atrial fibrillation, atrial flutter and ventricular tachycardia which is not treated effectively in other ways. This device is manipulated with a magnetic navigation system. It also has an irrigation system that flows with saline from an irrigation hole at the tip of the electrode. This application for a partial change of approval application for medical device to change a raw material of the hub (polycarbonate). The application was submitted as a "specified partial change" based on “Acceleration of Procedure for Specified Change for Medical Devices” (PFSB/ELD/OMDE Notification No.1110001 dated on November 10, 2008). (A partial change during the reexamination period)
Specified partial change	Aug. 29, 2014 Total review time: 80 days Regulatory review time: 80 days	- No clinical study results	67	Matsudaito (Sanyo Chemical Industries, Ltd.)	Change	Medical products 4 Non-absorbable topical hemostatic material for central circulatory system	A non-absorbable topical hemostatic material consisting of sealant liquid (main body) filled in a syringe and accessory sheets and spatula. This application for a partial change of approval application for medical device to add a manufacturer of a raw material of sealant liquid, fluorine-containing diisocyanate. The application was submitted as a "specified partial change" based on “Acceleration of Procedure for Specified Change for Medical Devices” (PFSB/ELD/OMDE Notification No.1110001 dated on November 10, 2008). (A partial change during the reexamination period)

Table 3. Products Approved in FY 2014: 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. 3, 2014 Total review time: 83 days Regulatory review time: 58 days	- Domestic clinical study results	1	Alcon Acrysof IQ Restor +2.5D Single-Piece (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal posterior chamber lens to be inserted as a substitute for a crystalline lens to correct near and/or far vision in patients with aphakia. The raw materials, basic form and principle of the multifocal mechanism are identical to those of the company's approved product, "Alcon Acrysof IQ Restor Single-Piece" (Approval No.: 22000BZX00970000). However, the diameter of apodized diffraction region, diffraction region number and central refractive region are different from the existing approved product. Domestic clinical study results were submitted to evaluate the efficacy and safety of the multifocal mechanism.
1	Jun. 30, 2014 Total review time: 349 days Regulatory review time: 178 days	Mar. 8, 2012 Clinical evaluation report	2	Advanced Femtosecond Laser (AMO Japan K.K.)	Change	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An ophthalmic laser corneal surgical instrument to create lamellar cut/resection of the cornea by irradiating a focused ultrashort pulsed laser beam (wavelength 1053 nm, few hundred femtosecond) on corneal tissue. It is used for creation of a corneal flap in LASIK (laser in-situ keratomileusis) and for corneal resection in keratoplasty. An application for partial changes to mainly add arcuate incisions in the cornea (penetrating incision or intrastromal incision) in ophthalmic surgery to the intended use. A clinical evaluation report was submitted to confirm the safety of intrastromal incision in actual clinical practice because an intrastromal incision cannot be performed with a diamond knife.
1	Aug. 25, 2014 Total review time: 299 days Regulatory review time: 66 days	Oct. 18, 2010 Foreign clinical study results	3	LenSx Laser System (Alcon Japan Ltd.)	Approval	Instrument & apparatus 31 Ophthalmic pulsed laser surgical instrument	An ophthalmic pulsed laser surgical instrument used for incision of anterior lens capsule, split of crystalline lens and corneal incision in cataract surgery. It consists of main body of the laser oscillator and patient interface that sucks and fixes the affected patient's eye. Although in conventional cataract surgery, incision of the anterior lens capsule, split of crystalline lens and corneal incision are performed using a cystotome, ultrasonic shock wave generated by cataract surgery instrument and ophthalmic knife, respectively, this device enables these procedures to be performed consecutively or in arbitrary combinations of each function using a femtosecond laser having a maximum energy of 15 microjoules. A foreign clinical study was conducted to confirm that this product has no particular problems by comparing this method to existing methods in cataract surgery.
2	Jun. 11, 2014 Total review time: 168 days Regulatory review time: 76 days	Jun. 30, 2004 Domestic clinical study result and clinical evaluation report	4	Straumann Implant (SLActive) BL (Straumann Japan K.K.)	Approval	Medical products 4 Dental implant body	Pure titanium dental implant body having the roughened surface by sandblasting and acid etching. This product is a bone level type of the company's approved product "Straumann Implant (SLActive) TL" (Approval No.: 22600BZX00016000), which accelerates osteointegration and enables earlier loading by providing the product sealed into a vial filled with normal saline to keep the hydrophilic nature of titanium until just before use. 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.
2	Jan. 23, 2015 Total review time: 1488 days Regulatory review time: 319 days	Dec. 14, 2011 Clinical evaluation report	5	Tapered Screw-Vent X (Zimmer K.K.)	Approval	Medical products 4 Intraosseous dental implant	An implant fixture partially or wholly implanted in the jawbone, which supports for the upper structure. In order to confirm the bone fixation performance of the new structure with a porous structure on the surface, a clinical evaluation report created from clinical results in published literatures on this product was submitted to evaluate the clinical performance in addition to the normal performance evaluation test.
3-1	Jul. 25, 2014 Total review time: 512 days Regulatory review time: 183 days	- Domestic clinical study results	6	MOMO Coronary Stent System (Japan Stent Technology Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A coronary stent consisting of a stent to be inserted and placed at the site of a lesion to maintain the patency of the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion in percutaneous coronary stent placement. This stent is made of a cobalt-chromium alloy and the surface is coated with a diamond-like carbon to reduce in-stent restenosis. A domestic clinical study was conducted to verify the efficacy and safety of this product in patients with symptomatic ischemic heart disease who have a new stenosis or restenosis of a coronary lesion (lesion length is 26 mm or less) with a reference vascular diameter ranging from 3.0 mm to 4.0 mm.

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	Aug. 29, 2014 Total review time: 336 days Regulatory review time: 118 days	Jan. 11, 2013 Clinical evaluation report	7	TransForm Occlusion Balloon Catheter (Stryker Japan K.K.)	Approval	Instrument & apparatus 51 Intravascular catheter for embolization of the central circulation system	An intravascular catheter for embolization of the central circulation system used for temporary interruption of blood flow in percutaneous intravascular surgery or for prevention of a coil mass from protruding into and/or prolapsing into the parent artery as an adjunct of coil embolization for cerebral aneurysms. A clinical evaluation report was submitted to confirm the efficacy and safety of balloon-assisted coil embolization using this device.
3-1	Oct. 30, 2014 Total review time: 269 days Regulatory review time: 195 days	Feb. 17, 2012 Foreign clinical study results	8	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 zotarolimus-eluting stent to be inserted and placed at the site of a lesion to maintain the patency of the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. An application for a partial change to add a 4.0-mm diameter stent. Foreign clinical study results were submitted to evaluate the efficacy and safety of a stent having a diameter of 4.0 mm.
3-1	Nov. 17, 2014 Total review time: 836 days Regulatory review time: 250 days	- Domestic clinical study results	9	Vival Coronary Stent (Goodman Co., LTD.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a stent to be placed at the narrowed or blocked segment of coronary artery to maintain the patency of the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion and dilate the stent. The raw materials were changed from those of the "Duraflex Coronary Stent" (Approval No.: 21500BZY00516000) to reduce the thickness of the stent, and the delivery catheter was also changed. A domestic clinical study was conducted to evaluate the efficacy and safety of this product in patients with symptomatic ischemic heart diseases who have a new stenosis or restenosis lesion in a coronary artery (a lesion length of 25 mm or less).
3-1	Nov. 28, 2014 Total review time: 246 days Regulatory review time: 164 days	Nov. 21, 2013 Global clinical trial and foreign clinical study results	10	Promus Premier LV Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a everolimus-eluting stent with diameter of 4.0 mm to be inserted and placed at the site of a lesion to maintain the patency of the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. The product having a diameter of 2.25 - 3.5 mm was previously approved in Japan as "Promus Premier Stent System" (Approval No.: 22600BZX00181000). A clinical study was conducted to evaluate the efficacy and safety of the stent with a 4.0 mm diameter.
3-1	Jan. 19, 2015 Total review time: 528 days Regulatory review time: 220 days	Jan. 21, 2005 Clinical evaluation report	11	Outback Re-entry Catheter (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Vascular recanalization catheter	A catheter consisting of a cannula, an outer shaft, a lure assembly and a handle. It assists recanalization back into the true lumen with a guidewire advanced via the subintimal space during percutaneous angioplasty to treat chronic total occlusion in the region of the femoropopliteal artery. A clinical evaluation report has been created based on the reports that were collected from an adverse-event database with clinical results and published literatures. The clinical report was submitted to confirm the performance and safety of this product to be used for the lesions with chronic total occlusion.
3-1	Feb. 12, 2015 Total review time: 240 days Regulatory review time: 116 days	Oct. 26, 2011 Foreign clinical study results	12	ASSURANT COBALT Stent (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Stent for iliac artery	A balloon expandable stent and the delivery system used to maintain the patency of the vessel lumen of de novo and restenotic symptomatic lesions in the common iliac artery and external iliac artery. A clinical study was conducted to evaluate the efficacy and safety of this product in clinical use.
3-2	May 19, 2014 Total review time: 220 days Regulatory review time: 92 days	Scepter C：Sep. 29, 2011, Scepter XC：Jan. 13, 2012 Clinical evaluation report	13	Scepter C (Terumo Corporation)	Change	Instrument & apparatus 51 Intravascular catheter for embolization of the central circulation system	A balloon catheter used for temporary interruption of blood flow in percutaneous intravascular surgery or for prevention of a coil clot protruding into and/or dropping out from the parent artery as an adjunct of coil embolization for cerebral aneurysms. A clinical evaluation report was submitted to confirm the efficacy and safety of balloon-assisted coil embolization using this device.

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	Aug. 1, 2014 Total review time: 458 days Regulatory review time: 265 days	Feb. 14, 2013 Foreign clinical study results	14	AORFIX AAA Stent Graft System (Medico's Hirata Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft system consisting of a stent graft and delivery system used for intravascular treatment of abdominal aortic aneurysms and aortic aneurysms extended from the abdominal aorta to the iliac artery. For the indication of infrarenal aortic aneurysm, although an existing approved stent graft for abdominal aortic aneurysms is limited to treat patients with an aortic neck angle not greater than 60 degrees, this product enable to treat patients with the angles of up to 90 degrees. A foreign clinical study was conducted to evaluate the efficacy and safety of this product in case groups where the aortic neck angles are ranging from 60 degrees to 90 degrees.
3-2	Nov. 20, 2014 Total review time: 262 days Regulatory review time: 181 days	- Domestic clinical study results	15	Steering Microcatheter (Akita Sumitomo Bakelite Co., Ltd.)	Approval	Instrument & apparatus 51 Central circulation system Microcatheter	An intravascular microcatheter for the central circulation system (except for the cardiac and cerebral [intracranial] vessels) used for selective angiography, drug infusion and embolization. The direction of the catheter tip can be controlled by rotating a dial and thereby the catheter can be inserted selectively into the bent vessels without a guidewire. The results of a domestic clinical study was submitted to confirm the efficacy and safety of this product that enables directional operation of the catheter tip by the dial.
3-2	Jan. 23, 2015 Total review time: 490 days Regulatory review time: 100 days	Apr. 9, 2013 Foreign clinical study results	16	Gore Acuseal Vascular Graft (W.L. GORE & Associates, Co., Ltd.)	Approval	Instrument & apparatus 7 Artificial blood vessel using heparin of the non-central circulation system	An artificial triple-layered blood vessel used for vascular access. The lumen is coated with heparin. A clinical study was conducted to evaluate the efficacy and safety of this product in patients requiring hemodialysis.
4	Aug. 8, 2014 Total review time: 294 days Regulatory review time: 197 days	Oct. 28, 2010 Foreign clinical study results	17	ccNexfin Hemodynamic Monitor (Edwards Lifescience Limited)	Approval	Instrument & apparatus 21 Monitor of arterial blood pressure and cardiac output	The device is an apparatus for continuously monitoring hemodynamic parameters including systolic/diastolic blood pressures (BP), heart rate (HR), stroke volume (SV), cardiac output (CO) and systemic vascular resistance (SVR). The hemodynamic parameters are calculated from arterial blood pressure waveform at the fingertips measured non-invasively and continuously by using the volume-clamp method. Non-clinical study and foreign clinical study results were submitted as the evaluation data on the efficacy and safety of this product.
4	Aug. 19, 2014 Total review time: 560 days Regulatory review time: 252 days	Jun. 30, 2010 Foreign clinical study results	18	TVC Imaging System (Nipro Corporation)	Approval	Instrument & apparatus 12 Cardiovascular ultrasonic diagnostic imaging instrument	The device is a device to visualize the form and characteristics of the vascular lumen and wall in the central circulation system and to provide the image data for diagnosis. This device has a function to detect a lipid core plaque using near-infrared light and to provide image data combined with an ultrasonogram. However, the image detected by this function is not intended to diagnose. A clinical study was conducted to evaluate that the device can detect a lipid core plaque using near-infrared light.
4	Aug. 19, 2014 Total review time: 512 days Regulatory review time: 159 days	Jun. 30, 2010 Foreign clinical study results	19	TVC Insight Catheter (Nipro Corporation)	Approval	Instrument & apparatus 51 Central circulation system intravascular ultrasound catheter	The device is a catheter equipped with a transducer for sending and receiving ultrasound on the tip to visualize the form and characteristics of the vascular lumen and wall in the central circulation system. This device is also equipped with an optical mirror and an optical fiber that irradiate and collect near-infrared light to detect a lipid core plaque and to provide image data combined with an ultrasonogram. However, the image detected by near-infrared light is not intended to diagnose. A clinical study was conducted to evaluate that the device can detect a lipid core plaque using near-infrared light.
4	Nov. 26, 2014 Total review time: 299 days Regulatory review time: 115 days	- Foreign clinical study results and clinical evaluation report	20	Vercise DBS System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 12 Electrical brain stimulation device for tremor	The device is an electrical brain stimulation device used to reduce tremors that do not sufficiently respond to drug therapy and symptoms of movement disorder associated with Parkinson's disease by providing an electrical stimulus unilaterally or bilaterally to the deep brain (thalamus, subthalamic nucleus or internal globus pallidus). This device consists of an implantable pulse generator and lead, an external trial stimulator to evaluate presence or absence of effect by test stimulation, and a remote controller to control stimulation parameter. Foreign clinical study results to evaluate the efficacy and safety in patients with Parkinson's disease and a clinical evaluation report summarizing foreign clinical studies and published papers to evaluate the efficacy and safety in patients with tremors 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
4	Dec. 22, 2014 Total review time: 361 days Regulatory review time: 268 days	Jan. 30, 2014 Foreign clinical study results	21	Navvus Catheter (ACIST Medical Systems, Inc.)	Approval	Instrument & apparatus 51 Central circulation system transducer-tipped catheter	The device is a catheter with a pressure sensor at the distal tip. It is used for invasive measuring of intravascular pressure in the central and non-central circulation systems excluding the cerebral blood vessel and carotid artery, and also used for evaluation of hemodynamics. The catheter type was adopted to enhance the operability by comparing with a conventional wire type of a similar medical device. The data on results of clinical study to compare the measurement accuracy with that of a previously approved product "SJM PressureWire Certus" (Approval No.: 22300BZX00247000) was submitted.
5	Jul. 9, 2014 Total review time: 575 days Regulatory review time: 159 days	Jan. 28, 1993 Clinical evaluation report	22	EHL Autolith (AMCO Inc.)	Approval	Instrument & apparatus 12 Intracorporeal electrohydraulic shock wave lithotriptor	An intracorporeal electrohydraulic shock wave lithotriptor used to crush calculuses in the kidney and bladder (urinary calculus) and bileduct stone using an electrohydraulic shock wave. A clinical evaluation report was submitted to evaluate the efficacy and safety of this product in patients with bile duct stone.
5	Sep. 10, 2014 Total review time: 376 days Regulatory review time: 84 days	Mar. 29, 2011 Clinical evaluation report	23	Cook Evolution Duodenal Stent System (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Gastroduodenal stent	A stent system to place a stent by endoscopically inserting a delivery system to maintain patency in gastroduodenal obstruction and duodenal stenosis associated with malignant tumors in patients for whom alleviative gastrectomy is considered difficult to be performed or other treatments is unlikely to have an effect. A clinical evaluation report was submitted to confirm the efficacy and safety of treatment using this stent in patients with malignant gastric outlet obstruction.
6-2	May 7, 2014 Total review time: 303 days Regulatory review time: 116 days	May 31, 2007 Clinical evaluation report	24	VEPTR II System (Johnson & Johnson K.K.)	Approval	Medical products 4 Internal fixation system	An internal fixation system made of titanium alloy and titanium which corrects thoracic deformity while allowing further growth of thorax by implanting an expandable-metallic rod which is extendable along body axial direction in the thorax of the patients with thoracic insufficiency syndrome. Based on the approved product "VEPTR system (Approved No.: 22000BZX01655000)", and major difference from the approved product is that the usability and compatibility of this device with the patient's thorax were enhanced by adding variations on the components or improving the components. A clinical evaluation was conducted with the literatures on this product and the approved product, overseas safety information and clinical evaluation report based on a use-results survey of the approved product to confirm that efficacy and safety of this device equivalent to or greater than that of the approved product were also maintained by the differences.
6-2	May 26, 2014 Total review time: 124 days Regulatory review time: 91 days	Apr. 11, 2013 Domestic clinical study results	25	HEALICOIL RG Suture Anchor (Smith & Nephew Endoscopy KK)	Approval	Medical products 4 Absorbable ligament fixation	A suture anchor used to fix soft tissues of the tendons and ligaments to the bones of the shoulder, elbow, groin (gluteal tendons), knee and foot/ankle. It consists of an absorbable anchor that adopts the hollow coil configuration of the approved product "HEALICOIL Suture Anchor" (Approval No.: 22500BZX00193000), sutures and an inserter. The point of improvement is that a glycolic acid/L-lactic copolymer and a mixture of calcium sulfate and beta-tricalcium phosphate which are new bioabsorbable materials, were adopted as raw materials. The results of a domestic clinical study on arthroscopic labrum repair in shoulder for traumatic shoulder instability using "Osteoraptor OS Anchor" (Approval No.: 22600BZX00228000) made of the same raw materials as this product were submitted to confirm the efficacy and safety of the new bioabsorbable materials.
6-2	May 26, 2014 Total review time: 180 days Regulatory review time: 119 days	May 18, 2012 Domestic clinical study results	26	PICO Wound Therapy System (Smith & Nephew Wound Management KK)	Approval	Medical products 4 Single-use negative pressure wound therapy system	A negative pressure wound therapy system to promote wound healing by providing a locally managed negative-pressure for patients with a refractory wound who have not responded to or are considered to be unlikely to respond to existing treatment. This device consists of a negative pressure maintenance unit, dressing and a tube to connect the unit and the dressing. Exudate is retained in the dressing applied to wound area and transpired through the backing film. The point of improvement from the approved product "RENASYS Wound Therapy System" (Approval No: 22400BZX00276000) is a downsizing and weight lightening of the main body of the device which allows the device to be used for outpatient. A clinical study on inpatients and outpatients was conducted to evaluate if the performance of this device was equivalent to that of approved product, and to confirm any defects or adverse events specific to this 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	May 26, 2014 Total review time: 124 days Regulatory review time: 103 days	Jan. 27, 2011 Domestic clinical study results	27	Osteoraptor OS Anchor (Smith & Nephew Endoscopy KK)	Approval	Medical products 4 Absorbable ligament fixation	A suture anchor used to fix the soft tissues of tendons and ligaments to the bone in the shoulder, elbow, wrist/hand, groin, knee and foot/ankle. It consists of an absorbable anchor, sutures and an inserter. The point of improvement is that a glycolic acid/L-lactic acid copolymer and a mixture of calcium sulfate and beta-tricalcium phosphate which are new bioabsorbable materials, were adopted as raw materials for the anchor. The results of a domestic clinical study on arthroscopic labrum repair in shoulder for traumatic shoulder instability using this device were submitted to confirm the efficacy and safety of the new bioabsorbable materials.
6-2	Jun. 23, 2014 Total review time: 1242 days Regulatory review time: 281 days	Apr. 30, 1998 Foreign clinical study results	28	OASIS Extracellular Matrix (Cook Japan Inc.)	Approval	Medical products 4 Collagen-based artificial skin	Collagen-based artificial skin for control and treatment of full and partial thickness wounds. Porcine small-intestinal submucosa is used as a raw material. Viral clearance study results were submitted to evaluate the virus safety of this product. In addition, foreign post-marketing clinical study results were submitted to evaluate the efficacy and safety in clinical use for patients with venous ulceration and pressure ulcers (decubitus ulcers).
6-2	Dec. 3, 2014 Total review time: 244 days Regulatory review time: 85 days	Mar. 18, 1998 Clinical evaluation report	29	Orthofix HA Coating Pin (Orthofix S. r. l.)	Approval	Medical products 4 Internal fixation pin	A stainless steel pin used with external fixators. No products such as pins coated with hydroxyapatite to enhance the fixation have been approved in Japan. Therefore, in addition to the results of a tensile strength test, a clinical evaluation report summarizing overseas published papers was submitted to evaluate the efficacy and safety of fixation with this product.
6-2	Feb. 6, 2015 Total review time: 267 days Regulatory review time: 196 days	- Foreign clinical study results	30	Duolith SD1 (Storz Medical AG)	Approval	Instrument & apparatus 12 Extracorporeal shock wave pain therapy system	An extracorporeal shock wave pain therapy system designed to enable adjustment of output by the conventional electromagnetic induction-type extracorporeal shock wave lithotripter to the low power output. It is used for pain relief in patients with refractory plantar aponeurositis. A clinical study was conducted to evaluate the efficacy and safety of this product in patients with refractory plantar aponeurositis.
8	Mar. 26, 2015 Total review time: 209 days Regulatory review time: 150 days	- Clinical evaluation report	31	Leksell Gamma Knife C (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	The device is a gamma knife used for non-incisional surgery by gamma ray irradiation in patients with brain diseases including cerebral vascular disorder or brain tumor, and brain functional disorder. The application is for a partial change to add the indication for trigeminal neuralgia for which pain control is difficult by drug therapy. A clinical evaluation report summarizing domestic and overseas published papers was submitted to evaluate the efficacy and safety of gamma knife treatment for trigeminal neuralgia with difficult pain control by drug therapy.
8	Mar. 26, 2015 Total review time: 209 days Regulatory review time: 150 days	- Clinical evaluation report	32	Leksell Gamma Knife 4C (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	The device is a gamma knife used for non-incisional surgery by gamma ray irradiation in patients with brain diseases including cerebral vascular disorder or brain tumor, and brain functional disorder. The application is for a partial change to add the indication for trigeminal neuralgia for which pain control is difficult by drug therapy. A clinical evaluation report summarizing domestic and overseas published papers was submitted to evaluate the efficacy and safety of gamma knife treatment for trigeminal neuralgia with difficult pain control by drug therapy.
8	Mar. 26, 2015 Total review time: 209 days Regulatory review time: 150 days	- Clinical evaluation report	33	Leksell Gamma Knife Model-C (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	The device is a gamma knife used for non-incisional surgery by gamma ray irradiation in patients with brain diseases including cerebral vascular disorder or brain tumor, and brain functional disorder. The application is for a partial change to add the indication for trigeminal neuralgia for which pain control is difficult by drug therapy. A clinical evaluation report summarizing domestic and overseas published papers was submitted to evaluate the efficacy and safety of gamma knife treatment for trigeminal neuralgia with difficult pain control by drug 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
8	Mar. 26, 2015 Total review time: 209 days Regulatory review time: 150 days	May. 24, 2012 Clinical evaluation report	34	Leksell Gamma Knife Perfexion (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	The device is a gamma knife used for non-incisional surgery by gamma ray irradiation in patients with brain diseases including cerebral vascular disorder or brain tumor, and brain functional disorder. The application is for a partial change to add the indication for trigeminal neuralgia for which pain control is difficult by drug therapy. A clinical evaluation report summarizing domestic and overseas published papers was submitted to evaluate the efficacy and safety of gamma knife treatment in trigeminal neuralgia with difficult pain control by drug therapy.
8	Mar. 26, 2015 Total review time: 209 days Regulatory review time: 150 days	- Clinical evaluation report	35	Leksell Gamma Knife (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	The device is a gamma knife used for non-incisional surgery by gamma ray irradiation in patients with brain diseases including cerebral vascular disorder or brain tumor, and brain functional disorder. The application is for a partial change to add the indication for trigeminal neuralgia for which pain control is difficult by drug therapy. A clinical evaluation report summarizing domestic and overseas published papers was submitted to evaluate the efficacy and safety of gamma knife treatment for trigeminal neuralgia with difficult pain control by drug therapy.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs etc., Directed by MHLW in FY 2014

○ Post-marketing safety measures implemented by MHLW in FY 2014

	Drugs	Medical devices
Directions for revision to precautions in package insert	102	2
Information published in the Pharmaceuticals and Medical Devices Safety Information	30	1

** Note: Including the issuance of notifications on self-check for medical devices, etc.*

○ Revision of PRECAUTIONS for Drugs Directed by MHLW in FY 2014

Date	Drug name
Apr. 17, 2014	01. Paliperidone palmitate
Apr. 23, 2014	01. Pentamidine isetionate
Jun 4, 2014	01. Azilsartan Azilsartan/Amlodipine besilate Irbesartan tablets Irbesartan/Amlodipine besilate Olmesartan medoxomil Olmesartan medoxomil/Azelnidipine Candesartan cilexetil tablets Valsartan tablets Valsartan/Amlodipine besilate Valsartan/Cilnidipine 02. Alacepril Imidapril hydrochloride tablets Enalapril maleate tablets Captopril Quinapril hydrochloride Cilazapril hydrate Temocapril hydrochloride Delapril hydrochloride Trandolapril Benazepril hydrochloride Perindopril erbumine Lisinopril hydrate 03. Irbesartan/Trichlormethiazide 04. Candesartan cilexetil/Amlodipine besilate Candesartan cilexetil/Hydrochlorothiazide Valsartan/Hydrochlorothiazide Losartan potassium/Hydrochlorothiazide 05. Telmisartan Telmisartan/Amlodipine besilate 06. Telmisartan/Hydrochlorothiazide 07. Losartan potassium Losartan potassium 08. Rosuvastatin calcium 09. Imidafenacin 10. Nartograstim (genetical recombination) 11. Filgrastim (genetical recombination) (biosimilar 1) Filgrastim (genetical recombination) (biosimilar 2) Filgrastim (genetical recombination) (biosimilar 3) Lenograstim (genetical recombination)
Jul 9, 2014	01. Paroxetine hydrochloride hydrate 02. Teriparatide (genetical recombination)

Date	Drug name
	03. Loratadine 04. Inchinkoto 05. Amphotericin B [non-liposome preparation (injectable dosage form)] 06. Simeprevir sodium 07. Ibuprofen/Pseudoephedrine hydrochloride/Chlorpheniramine maleate/Dihydrocodeine phosphate/Caffeine anhydrous (OTC drugs) Ibuprofen/Pseudoephedrine hydrochloride/L-Carbocisteine/d-Chlorpheniramine maleate/Dihydrocodeine phosphate/Caffeine anhydrous (OTC drugs) 08. Inchinkoto (OTC drugs)
Aug. 6, 2014	01. Pramipexole hydrochloride hydrate 02. Tolvaptan 03. Carvedilol 04. Infliximab (genetical recombination) Infliximab (genetical recombination) (biosimilar 1) 05. Sugammadex sodium 06. Carboplatin 07. Doxycycline hydrochloride hydrate 08. Lansoprazole/Amoxicillin hydrate/Metronidazole Rabeprazole sodium/Amoxicillin hydrate/Metronidazole 09. Linezolid 10. Metronidazole (oral dosage form)
Sep. 16, 2014	01. Pregabalin 02. Imatinib mesilate
Oct. 21, 2014	01. Teneligliptin hydrobromide hydrate 02. Enzalutamide 03. Vancomycin hydrochloride (for oral use) 04. Vancomycin hydrochloride (for injection)
Oct. 21, 2014	01. Acetaminophen (oral dosage form, injectable dosage form, suppository)
Oct. 24, 2014	01. Simeprevir sodium
Nov. 20, 2014	01. Galantamine hydrobromide
Dec. 22, 2014	01. Cabazitaxel acetonate
Jan. 9, 2015	01. Levetiracetam 02. Ipragliflozin L-proline Empagliflozin Canagliflozin hydrate Dapagliflozin propylene glycolate hydrate Luseogliflozin hydrate Tofogliflozin hydrate 03. Tofogliflozin hydrate 04. Linagliptin 05. Amoxicillin hydrate

Date	Drug name
	Amoxicillin hydrate/ Potassium clavulanate Lansoprazole/Amoxicillin hydrate/Clarithromycin Lansoprazole/Amoxicillin hydrate/Metronidazole Rabeprazole sodium/Amoxicillin hydrate/Clarithromycin Rabeprazole Sodium/amoxicillin hydrate/Metronidazole 06. Simeprevir sodium 07. Freeze-dried live attenuated mumps virus vaccine
Feb. 2, 2015	01. Abiraterone acetate
Feb. 4. 2015	01. Lamotrigine
Feb. 17, 2015	01. Memantine hydrochloride 02. Apixaban 03. Montelukast sodium 04. Telaprevir
Mar. 24, 2015	01. Rebamipide (Ophthalmic solution) 02. Triamcinolone acetonide (Injectable dosage form for Intramuscular/Intradermal/ Intra-articular) 03. Sitagliptin phosphate hydrate 04. Cyclophosphamide hydrate 05. Pazopanib hydrochloride 06. Panitumumab (genetical recombination)

**Note: Detailed information is available at the PMDA's web page.*

Table 5. Revision of PRECAUTIONS for Medical Devices Directed by MHLW in FY 2014

Date	Title
Jul 28, 2014	Revision of the Precautions in the package insert of Drug-eluting coronary stent or Drug-coated balloon dilatation catheter for coronary angioplasty
Dec. 9, 2014	Revision of the Precautions in the package insert of the Small-intestinal capsule endoscope

**Note: Detailed information is available at the PMDA's web page.*

Table 6. FY 2014 Pharmaceuticals and Medical Devices Safety Information (No.312-321)

Date	No.	Table of Contents
Apr. 30, 2014	312	1. Use of Topical Ketoprofen (dermatologic preparation) during Pregnancy 2. Important Safety Information [1] Ketoprofen (tapes) [2] Paclitaxel (excluding paclitaxel protein-bound particles for injectable suspension) [3] Levetiracetam 3. Revision of Precautions (No. 255) Ketoprofen (injectable dosage form, suppository) (and 7 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
May 27, 2014	313	1. Fatal cases with XEPLION® Aqueous Suspension for IM injection 2. Important Safety Information [1] Paliperidone Palmitate 3. Revision of Precautions (No. 256) Pentamidine Isetionate 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jul 29, 2014	314	1. Revision of Report Form in Drugs and Medical Devices Safety Information Reporting System 2. Revision of Precautions (No. 257) Azilsartan (and 7 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance
Aug. 26, 2014	315	1. Safety Measures for New Drugs during the Early Post-marketing Phase 2. Important Safety Information [1] Inchinkoto [2] Simeprevir Sodium [3] Teriparatide (Genetical Recombination) [4] Loratadine 3. Revision of Precautions (No. 258) Paroxetine Hydrochloride Hydrate (and 3 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Sep. 30, 2014	316	1. Project of Japan Drug Information Institute in Pregnancy 2. Effects of Angiotensin II Receptor Blockers and Angiotensin Converting Enzyme Inhibitors on Pregnant Women and Foetuses 3. Revision of Precautions (No. 259) Paroxetine Hydrochloride Hydrate (and 9 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 28, 2014	317	1. Guidelines for Use of Mobile Phones and Other Devices in Hospitals 2. Change in the Submission Place for Reports in the Safety Information Reporting System 3. Important Safety Information [1] Imatinib Mesilate [2] Pregabalin 4. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
Nov. 25, 2014	318	List of errata for MHLW Pharmaceuticals and Medical Devices Safety Information No. 318 1. Simeprevir Sodium and Hyperbilirubinaemia 2. Surveillance on Access to, Dissemination, and Utilization of Drug Safety Information in Medical Institutions and Pharmacies 3. Adverse Reactions to Influenza Vaccine in the 2013 Season 4. Important Safety Information [1] Enzalutamide [2] Teneligliptin Hydrobromide Hydrate [3] Vancomycin Hydrochloride (for Injection) [4] Simeprevir Sodium 5. Revision of Precautions (No. 260) Acetaminophen (and 1 other) 6. List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 24, 2014	319	1. Summary of Relief System for Sufferers from Adverse Drug Reactions and Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs 2. Revision of Precautions (No. 261) Galantamine Hydrobromide 3. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) Handling of Fire during Long-term Oxygen Therapy
Jan, 29, 2015	320	1. Cabazitaxel Acetonate and Severe Febrile Neutropenia 2. Use of Capsule Endoscopy for Small Intestine Screening in Pediatrics and Geriatrics 3. Important Safety Information [1] Cabazitaxel Acetonate [2] Sodium-Glucose Co-Transporter 2 Inhibitors [3] Freeze-Dried Live Attenuated Mumps Virus Vaccine [4] Levetiracetam 4. Revision of Precautions (No. 262) Linagliptin (and 2 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Mar. 30, 2015	321	1. Lamotrigine and Serious Skin Disorders 2. Abiraterone Acetate and Hypokalaemia 3. The MIHARI Project 4. Important Safety Information [1] Abiraterone Acetate [2] Lamotrigine [3] Apixaban [4] Memantine Hydrochloride 5. Revision of Precautions (No. 263) Montelukast Sodium (and 1 other) 6. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) The Drug and Medical Devices Safety Information Reporting System - Reporting via e-Gov was closed

**Note: Detailed information is available at the PMDA's web page.*

Table 7. FY 2014 PMDA Medical Safety Information

No.	Month and year published	Title
44	May 2014	Medication Errors in Prescription Orders
45	August 2014	Precautions in Handling of Indwelling Venous Needles

**Note: Detailed information is available at the PMDA's 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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145, 1960)

[On and after November 25, 2014]

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics. (Yen)

Classification					User fees		
					Review	Inspection	Total
Assessment for manufacturing license of drugs							
New license				On-site		152,300 Article 31, Paragraph 1, Item 1 (a)	152,300
				Document		114,700 Article 31, Paragraph 1, Item 1 (b)	114,700
Change/addition of classification				On-site		100,200 Article 31, Paragraph 1, Item 2 (a)	100,200
				Document		56,900 Article 31, Paragraph 1, Item 2 (b)	56,900
Renewal of existing license				On-site		100,200 Article 31, Paragraph 1, Item 3 (a)	100,200
				Document		56,900 Article 31, Paragraph 1, Item 3 (b)	56,900
Assessment for foreign manufacturers' accreditation of drugs							
New accreditation				On-site		137,100 + overseas travel expenses Article 31, Paragraph 2, Item 1 (a)	137,100 + overseas travel expenses
				Document		59,700 Article 31, Paragraph 2, Item 1 (b)	59,700
Change/addition of classification				On-site		66,400 + overseas travel expenses Article 31, Paragraph 2, Item 2 (a)	66,400 + overseas travel expenses
				Document		40,900 Article 31, Paragraph 2, Item 2 (b)	40,900
Renewal of existing accreditation				On-site		66,400 + overseas travel expenses Article 31, Paragraph 2, Item 3 (a)	66,400 + overseas travel expenses
				Document		40,900 Article 31, Paragraph 2, Item 3 (b)	40,900
Review for approval of drugs (new approval)							
New drugs (No. 1) (non-orphan drugs)				First application products	23,788,100 Article 32, Paragraph 1, Item 1 (a)-(1)	6,747,000 + overseas travel expenses Article 32, Paragraph 2, Item 1 (a) and Paragraph 3	30,535,100 + overseas travel expenses
				Line extension products	2,464,000 Article 32, Paragraph 1, Item 1 (a)-(3)	1,686,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (c) and Paragraph 3	4,150,600 + overseas travel expenses
New drugs (No. 1) (orphan drugs)				First application products	19,934,100 Article 32, Paragraph 1, Item 1 (a)-(2)	3,379,900 + overseas travel expenses Article 32, Paragraph 2, Item 1 (b) and Paragraph 3	23,314,000 + overseas travel expenses
				Line extension products	2,061,500 Article 32, Paragraph 1, Item 1 (a)-(4)	841,500 + overseas travel expenses Article 32, Paragraph 2, Item 1 (d) and Paragraph 3	2,903,000 + overseas travel expenses
New drugs (No. 2)(non-orphan drugs)				First application products	11,353,100 Article 32, Paragraph 1, Item 1 (a)-(5)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (e) and Paragraph 3	13,886,700 + overseas travel expenses
				Line extension products	1,174,300 Article 32, Paragraph 1, Item 1 (a)-(7)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (g) and Paragraph 3	1,807,900 + overseas travel expenses
New drugs (No. 2) (orphan drugs)				First application products	9,345,700 Article 32, Paragraph 1, Item 1 (a)-(6)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 1 (f) and Paragraph 3	10,613,400 + overseas travel expenses
				Line extension products	1,004,100 Article 32, Paragraph 1, Item 1 (a)-(8)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 1 (h) and Paragraph 3	1,323,100 + overseas travel expenses
Generic prescription drugs			with inspections		618,200 Article 32, Paragraph 1, Item 1 (a)-(9)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	948,400 + overseas travel expenses
			without inspection		618,200 Article 32, Paragraph 1, Item 1 (a)-(9)		618,200
BTC/OTC drugs	Switch to OTC status, etc.	First application products	with inspections		1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	1,621,800 + overseas travel expenses
			without inspection		1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)		1,291,600
		Line extension products	with inspections		1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	1,621,800 + overseas travel expenses
			without inspection		1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)		1,291,600
	Others		with inspections		110,300 Article 32, Paragraph 1, Item 1 (a)-(11)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	440,500 + overseas travel expenses
			without inspection		110,300 Article 32, Paragraph 1, Item 1 (a)-(11)		110,300
See "List of user fees for reviews etc. of medical devices" for in vitro diagnostics.							

[Until November 24, 2014]

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. (Yen)

Classification				User fees		
				Review	Inspection	Total
Assessment for manufacturing license of drugs						
New license			On-site		152,300 Article 16, Paragraph 1, Item 1 (a)	152,300
			Document		114,700 Article 16, Paragraph 1, Item 1 (b)	114,700
Change/addition of classification			On-site		100,200 Article 16, Paragraph 1,Item 2 (a)	100,200
			Document		56,900 Article 16, Paragraph 1,Item 2 (b)	56,900
Renewal of existing license			On-site		100,200 Article 16, Paragraph 1, Item 3 (a)	100,200
			Document		56,900 Article 16, Paragraph 1, Item 3 (b)	56,900
Assessment for foreign manufacturers' accreditation of drugs						
New accreditation			On-site		137,100 + travel expenses Article 16, Paragraph 2, Item 1 (a)	137,100 + travel expenses
			Document		59,700 Article 16, Paragraph 2, Item 1 (b)	59,700
Change/addition of classification			On-site		66,400 + travel expenses Article 16, Paragraph 2, Item 2 (a)	66,400 + travel expenses
			Document		40,900 Article 16, Paragraph 2,, Item 2 (b)	40,900
Renewal of existing accreditation			On-site		66,400 + travel expenses Article 16, Paragraph 2, Item 3 (a)	66,400 + travel expenses
			Document		40,900 Article 16, Paragraph 2, Item 3 (b)	40,900
Review for approval of drugs (new approval)						
New drugs (No. 1) (non-orphan drugs)			First application products	23,788,100 Article 17, Paragraph 1, Item 1 (a)-(1)	6,747,000 Article 17, Paragraph 2, Item 1 (a)	30,535,100
			Line extension products	2,464,000 Article 17, Paragraph 1, Item 1 (a)-(3)	1,686,600 Article 17,Paragraph 2, Item 1 (c)	4,150,600
New drugs (No. 1) (orphan drugs)			First application products	19,934,100 Article 17, Paragraph 1, Item 1 (a)-(2)	3,379,900 Article 17, Paragraph 2, Item 1 (b)	23,314,000
			Line extension products	2,061,500 Article 17, Paragraph 1, Item 1 (a)-(4)	841,500 Article 17, Paragraph 2, Item 1 (d)	2,903,000
New drugs (No. 2) (non-orphan drugs)			First application products	11,353,100 Article 17, Paragraph 1, Item 1 (a)-(5)	2,533,600 Article 17, Paragraph 2, Item 1 (e)	13,886,700
			Line extension products	1,174,300 Article 17, Paragraph 1, Item 1 (a)-(6)	633,600 Article 17, Paragraph 2, Item 1 (f)	1,807,900
New drugs (No. 2) (orphan drugs)			First application products	9,345,700 Article 17, Paragraph 1, Item 1 (a)-(7)	1,267,700 Article 17,Paragraph 2, Item 1 (g)	10,613,400
			Line extension products	1,004,100 Article 17, Paragraph 1, Item 1 (a)-(8)	319,000 Article 17,Paragraph 2, Item 1 (h)	1,323,100
Generic prescription drugs (with inspections)				412,100 Article 17, Paragraph 1, Item 1 (a)-(9)	220,100 Article 17,Paragraph 2, Item 1 (i)	632,200
OTC drugs	Switch to OTC status, etc.	First application products		1,291,600 Article 17, Paragraph 1, Item 1 (a)-(10)		1,291,600
		Line extension products		1,291,600 Article 17, Paragraph 1, Item 1 (a)-(10)		1,291,600
	Others			110,300 Article 17, Paragraph 1, Item 1 (a)-(11)		110,300
In vitro diagnostics (without approval standards)				584,100 Article 17, Paragraph 1, Item 1 (a)-(14)		584,100
In vitro diagnostics (with approval standards)			Basic	282,900 Article 17, Paragraph 1, Item 1 (a)-(13)		282,900
			Addition of series	60,300 Article 17, Paragraph 1, Item 1 (a)-(12)		60,300

[On and after November 25, 2014]

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics. (Yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of drugs (new approval)					
Quasi-drugs		New active ingredients	2,981,100 Article 32, Paragraph 1, Item 1 (b)-(1)		2,981,100
		New dosage, etc.	246,600 Article 32, Paragraph 1, Item 1 (b)-(2)		246,600
		Others	63,500 Article 32, Paragraph 1, Item 1 (b)-(3)		63,500
Pest control agents		New active ingredients	4,987,900 Article 32, Paragraph 1, Item 1 (a)-(12) and (b)-(4)		4,987,900
		New dosage, etc.	392,200 Article 32, Paragraph 1, Item 1 (a)-(13) and (b)-(5)		392,200
		Others	95,500 Article 32, Paragraph 1, Item 1 (a)-(14) and (b)-(6)		95,500
Cosmetics			63,500 Article 32, Paragraph 1, Item 1 (c)		63,500
New application for change or replacement of brand name			35,600 Article 32, Paragraph 1, Item 1 (d)		35,600
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 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
		Line extension products	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
	Others		205,100 Article 32, Paragraph 1, Item 2 (a)-(3)	124,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	329,300 + overseas travel expenses
New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300 Article 32, Paragraph 1, Item 2 (a)-(4)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	9,702,000 + overseas travel expenses
		Line extension products	875,600 Article 32, Paragraph 1, Item 2 (a)-(5)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	1,194,600 + overseas travel expenses
	Others		132,700 Article 32, Paragraph 1, Item 2 (a)-(6)	112,900 + overseas travel expenses Article 32, Paragraph 2, Item 2 (f) and Paragraph 3	245,600 + overseas travel expenses
New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
		Line extension products	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
	Others		205,100 Article 32, Paragraph 1, Item 2 (a)-(3)	124,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	329,300 + overseas travel expenses
New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300 Article 32, Paragraph 1, Item 2 (a)-(4)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	9,702,000 + overseas travel expenses
		Line extension products	875,600 Article 32, Paragraph 1, Item 2 (a)-(5)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	1,194,600 + overseas travel expenses
	Others		132,700 Article 32, Paragraph 1, Item 2 (a)-(6)	112,900 + overseas travel expenses Article 32, Paragraph 2, Item 2 (f) and Paragraph 3	245,600 + overseas travel expenses
Generic prescription drugs	Changes in indications, etc.	First application products	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
		Line extension products	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
	Changes based on guidelines, etc.		53,400 Article 32, Paragraph 1, Item 2 (a)-(7)		53,400
	Others		307,700 Article 32, Paragraph 1, Item 2 (a)-(8)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	493,900 + overseas travel expenses

[Until November 24, 2014]

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. (Yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of drugs (new approval)					
Quasi-drugs/cosmetics			63,500 Article 17, Paragraph 1, Item 1 (b) (c)		63,500
New application for change or replacement of brand name			35,600 Article 17, Paragraph 1, Item 1 (e)		35,600
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 Article 17, Paragraph 1, Item 2 (a)-(1)	2,533,600 Article 17, Paragraph 2, Item 2 (a)	12,724,100
		Line extension products	1,057,400 Article 17, Paragraph 1, Item 2 (a)-(2)	633,600 Article 17, Paragraph 2, Item 2 (b)	1,691,000
	Others		205,100 Article 17, Paragraph 1, Item 2 (a)-(3)	124,200 Article 17, Paragraph 2, Item 2 (c)	329,300
New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300 Article 17, Paragraph 1, Item 2 (a)-(4)	1,267,700 Article 17,Paragraph 2, Item 2 (d)	9,702,000
		Line extension products	875,600 Article 17, Paragraph 1, Item 2 (a)-(5)	319,000 Article 17,Paragraph 2, Item 2 (e)	1,194,600
	Others		132,700 Article 17, Paragraph 1, Item 2 (a)-(6)	112,900 Article 17,Paragraph 2, Item 2 (f)	245,600
New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products	10,190,500 Article 17, Paragraph 1, Item 2 (a)-(1)	2,533,600 Article 17, Paragraph 2, Item 2 (a)	12,724,100
		Line extension products	1,057,400 Article 17, Paragraph 1, Item 2 (a)-(2)	633,600 Article 17, Paragraph 2, Item 2 (b)	1,691,000
	Others		205,100 Article 17, Paragraph 1, Item 2 (a)-(3)	124,200 Article 17, Paragraph 2, Item 2 (c)	329,300
New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300 Article 17, Paragraph 1, Item 2 (a)-(4)	1,267,700 Article 17,Paragraph 2, Item 2 (d)	9,702,000
		Line extension products	875,600 Article 17, Paragraph 1, Item 2 (a)-(5)	319,000 Article 17,Paragraph 2, Item 2 (e)	1,194,600
	Others		132,700 Article 17, Paragraph 1, Item 2 (a)-(6)	112,900 Article 17,Paragraph 2, Item 2 (f)	245,600
Generic prescription drugs (with inspections)	Changes in indications, etc.	First application products	10,190,500 Article 17, Paragraph 1, Item 2 (a)-(1)	2,533,600 Article 17, Paragraph 2, Item 2 (a)	12,724,100
		Line extension products	1,057,400 Article 17, Paragraph 1, Item 2 (a)-(2)	633,600 Article 17, Paragraph 2, Item 2 (b)	1,691,000
	Changes based on guidelines, etc.		35,600 Article 17, Paragraph 1, Item 2 (a)-(7)		35,600
	Others		205,100 Article 17, Paragraph 1, Item 2 (a)-(3)	124,200 Article 17, Paragraph 2, Item 2 (c)	329,300

[On and after November 25, 2014]

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification					User fees		
					Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)							
BTC/OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	with inspections	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	10,376,700 + overseas travel expenses
				without inspection	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)		10,190,500
			Line extension products	with inspections	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	1,243,600 + overseas travel expenses
				without inspection	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)		1,057,400
	Changes based on guidelines, etc.			with inspections	35,600 Article 32, Paragraph 1, Item 2 (a)-(10)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	221,800 + overseas travel expenses
				without inspection	35,600 Article 32, Paragraph 1, Item 2 (a)-(10)		35,600
	Others			with inspections	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	242,600 + overseas travel expenses
				without inspection	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)		56,400
See "List of user fees for reviews etc. of medical devices" for in vitro diagnostics.							
Quasi-drugs/cosmetics					35,600 Article 32, Paragraph 1, Item 2 (b)-(1) and (c)		35,600
Pest control agents					48,400 Article 32, Paragraph 1, Item 2 (a)-(1) and (b)-(2)		48,400
GMP inspection of drugs							
Approval, partial change and manufacture for export	New drugs			Domestic		760,900 Article 32, Paragraph 5, Item 1 (b)-(1)	760,900
				Overseas		960,200 + overseas travel expenses Article 32, Paragraph 5, Item 1 (b)-(2) and Paragraph 7	960,200 + overseas travel expenses
	Biological drugs/Radiopharmaceuticals, etc.			Domestic		685,100 Article 32, Paragraph 5, Item 1 (a)-(1)	685,100
				Overseas		868,600 + overseas travel expenses Article 32, Paragraph 5, Item 1 (a)-(2) and Paragraph 7	868,600 + overseas travel expenses
	Sterile drugs/Sterile quasi-drugs			Domestic		522,600 Article 32, Paragraph 5, Item 1 (c)-(1)	522,600
				Overseas		658,300 + overseas travel expenses Article 32, Paragraph 5, Item 1 (c)-(2) and Paragraph 7	658,300 + overseas travel expenses
	Other Drugs/quasi-drugs			Domestic		379,500 Article 32, Paragraph 5, Item 1 (d)-(1)	379,500
				Overseas		478,000 + overseas travel expenses Article 32, Paragraph 5, Item 1 (d)-(2) and Paragraph 7	478,000 + overseas travel expenses
	Packaging, labeling, storage, external testing, etc.			Domestic		65,600 Article 32, Paragraph 5, Item 2 (a) and Paragraph 6, Item 1 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 32, Paragraph 5, Item 2 (b) and Paragraph 6, Item 1 (b) and Paragraph 7	87,200 + overseas travel expenses
Renewal of approval/ Renewal of manufacture for export	Biological drugs/ Radiopharmaceuticals, etc.	Basic		Domestic		448,500 Article 32, Paragraph 5, Item 3 (a)-(1)	448,500
				Overseas		570,100 + overseas travel expenses Article 32, Paragraph 5, Item 3 (a)-(2) and Paragraph 7	570,100 + overseas travel expenses
		Addition of products		Domestic		31,400 Article 32, Paragraph 5, Item 3 (a)-(1)	31,400
				Overseas		31,400 Article 32, Paragraph 5, Item 3 (a)-(2)	31,400
	Sterile drugs/Sterile quasi-drugs	Basic		Domestic		390,900 Article 32, Paragraph 5, Item 3 (b)-(1)	390,900
				Overseas		493,800 + overseas travel expenses Article 32, Paragraph 5, Item 3 (b)-(2) and Paragraph 7	493,800 + overseas travel expenses
		Addition of products		Domestic		12,800 Article 32, Paragraph 5, Item 3 (b)-(1)	12,800
				Overseas		12,800 Article 32, Paragraph 5, Item 3 (b)-(2)	12,800

[Until November 24, 2014]

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.

(Yen)

Classification					User fees		
					Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)							
OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products		10,190,500 Article 17, Paragraph 1, Item 2 (a)-(1)		10,190,500
			Line extension products		1,057,400 Article 17, Paragraph 1, Item 2 (a)-(2)		1,057,400
	Changes based on guidelines, etc.				35,600 Article 17, Paragraph 1, Item 2 (a)-(7)		35,600
	Others				56,400 Article 17, Paragraph 1, Item 2 (a)-(8)		56,400
In vitro diagnostics (without approval standards)					295,800 Article 17, Paragraph 1, Item 2 (a)-(11)		295,800
In vitro diagnostics (with approval standards)			Basic		143,500 Article 17, Paragraph 1, Item 2 (a)-(10)		143,500
			Addition of series		31,900 Article 17, Paragraph 1, Item 2 (a)-(9)		31,900
Quasi-drugs/cosmetics					35,600 Article 17, Paragraph 1, Item 2 (b) and (c)		35,600
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) and Paragraph 5, Item 1 (a)	65,600
				Overseas		87,200 + travel expenses Article 17, Paragraph 4, Item 2 (b) and 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

[On and after November 25, 2014]

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics. (Yen)

Classification				User fees		
				Review	Inspection	Total
GMP inspection of drugs						
Renewal of approval/ Renewal of manufacture for export	Other Drugs/quasi-drugs	Basic	Domestic		346,100 Article 32, Paragraph 5, Item 3 (c)-(1)	346,100
			Overseas		421,100 + overseas travel expenses Article 32, Paragraph 5, Item 3 (c)-(2) and Paragraph 7	421,100 + overseas travel expenses
		Addition of products	Domestic		9,900 Article 32, Paragraph 5, Item 3 (c)-(1)	9,900
			Overseas		9,900 Article 32, Paragraph 5, Item 3 (c)-(2)	9,900
	Packaging, labeling, storage, external testing, etc.	Basic	Domestic		265,900 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	265,900
			Overseas		347,800 + overseas travel expenses Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b) and Paragraph 7	347,800 + overseas travel expenses
		Addition of products	Domestic		6,900 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	6,900
			Overseas		6,900 Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b)	6,900
GLP inspection of drugs						
GLP		Domestic			2,121,400 Article 32, Paragraph 4, Item 1 (a) and Paragraph 10, Item 2 (a)-(1)	2,121,400
		Overseas			2,347,900 + overseas travel expenses Article 32, Paragraph 4, Item 1 (b) and Paragraph 10, Item 2 (a)-(2) and Paragraph 11	2,347,900 + overseas travel expenses
GCP inspection of drugs						
New GCP		First application products	Domestic		2,801,000 Article 32, Paragraph 4, Item 2 (a)-(1) and (b)-(1)	2,801,000
			Overseas		3,098,000 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(2) and (b)-(2)	3,098,000 + overseas travel expenses
		Line extension products	Domestic		741,400 Article 32, Paragraph 4, Item 2 (a)-(3) and (b)-(3)	741,400
			Overseas		773,300 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(4) and (b)-(4)	773,300 + overseas travel expenses
GCP inspection of generic drugs			Domestic		663,600 Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	663,600
			Overseas		977,400 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	977,400 + overseas travel expenses
GCP inspection of BTC /OTC drugs			Domestic		663,600 Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	663,600
			Overseas		977,400 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	977,400 + overseas travel expenses
Re-examination of drugs						
Re-examination		First application products		806,600 Article 32, Paragraph 9, Item 1	2,750,100 + overseas travel expenses Article 32, Paragraph 10, Item 1 (a) and Paragraph 11	3,556,700 + overseas travel expenses
		Line extension products		271,500 Article 32, Paragraph 9, Item 2	917,600 + overseas travel expenses Article 32, Paragraph 10, Item 1 (b) and Paragraph 11	1,189,100 + overseas travel expenses
GPSP		First application products	Domestic		2,256,000 Article 32, Paragraph 10, Item 2 (b)-(1)	2,256,000
			Overseas		2,478,500 + overseas travel expenses Article 32, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	2,478,500 + overseas travel expenses
		Line extension products	Domestic		774,100 Article 32, Paragraph 10, Item 2 (b)-(3)	774,100
			Overseas		794,400 + overseas travel expenses Article 32, Paragraph 10, Item 2 (b)-(4) and Paragraph 11	794,400 + overseas travel expenses

[Until November 24, 2014]

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. (Yen)

Classification				User fees		
				Review	Inspection	Total
GMP inspection of drugs						
Renewal of the above	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) and Paragraph 5, Item 2 (a)	265,900
			Overseas		347,800 ＋travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	347,800 ＋travel expenses
		Addition of products	Domestic		6,900 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,900
			Overseas		6,900 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,900
GLP inspection of drugs						
GLP		Domestic			2,121,400 Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	2,121,400
		Overseas			2,347,900 ＋travel expenses Article 17, Paragraph 3, Item 1 (b) and 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

8-2. List of user fees for reviews etc. of medical devices under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145, 1960)

[On and after November 25, 2014]

List of user fees for reviews etc. of medical devices and in vitro diagnostics under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification	User fees		
	Review	Inspection	Total
Review for approval of medical devices and in vitro diagnostics (new approval)			
New medical devices (Class IV)	10,881,700 Article 33, Paragraph 1, Item 1 (a)-(1)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	11,736,000 + overseas travel expenses
New medical devices (Class II/III)	7,766,200 Article 33, Paragraph 1, Item 1 (a)-(3)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	8,620,500 + overseas travel expenses
Improved medical devices with clinical data (Class IV)	6,213,000 Article 33, Paragraph 1, Item 1 (a)-(2)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	6,896,500 + overseas travel expenses
Improved medical devices with clinical data (Class II/III)	3,721,200 Article 33, Paragraph 1, Item 1 (a)-(4)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	4,404,700 + overseas travel expenses
Improved medical devices without clinical data, without approval standards (Class IV)	2,355,400 Article 33, Paragraph 1, Item 1 (a)-(7)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	2,425,900 + overseas travel expenses
Generic medical devices without clinical data, without approval standards (Class IV)	1,767,700 Article 33, Paragraph 1, Item 1 (a)-(8)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	1,838,200 + overseas travel expenses
Improved/generic medical devices without clinical data, without approval standards (Class II/III)	1,409,900 Article 33, Paragraph 1, Item 1 (a)-(9)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	1,480,400 + overseas travel expenses
Generic medical devices with approval standards (Class IV)	429,200 Article 33, Paragraph 1, Item 1 (a)-(5)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	499,700 + overseas travel expenses
Generic medical devices with approval standards (Class II/III)	344,100 Article 33, Paragraph 1, Item 1 (a)-(6)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	414,600 + overseas travel expenses

[Until November 24, 2014]

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 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		152,300 Article 16, Paragraph 1, Item 1 (a)	152,300
		Document		114,700 Article 16, Paragraph 1, Item 1 (b)	114,700
Change/addition of classification		On-site		100,200 Article 16, Paragraph 1, Item 2 (a)	100,200
		Document		56,900 Article 16, Paragraph 1, Item 2 (b)	56,900
Renewal of existing license		On-site		100,200 Article 16, Paragraph 1, Item 3 (a)	100,200
		Document		56,900 Article 16, Paragraph 1, Item 3 (b)	56,900
Assessment for foreign manufacturers accreditation of medical devices					
New accreditation		On-site		137,100 + travel expenses Article 16, Paragraph 2, Item 1 (a)	137,100 + travel expenses
		Document		59,700 Article 16, Paragraph 2, Item 1 (b)	59,700
Change/addition of classification		On-site		66,400 + travel expenses Article 16, Paragraph 2, Item 2 (a)	66,400 + travel expenses
		Document		40,900 Article 16, Paragraph 2, Item 2 (b)	40,900
Renewal of existing accreditation		On-site		66,400 + travel expenses Article 16, Paragraph 2, Item 3 (a)	66,400 + travel expenses
		Document		40,900 Article 16, Paragraph 2, Item 3 (b)	40,900
Review for approval of medical devices (new approval)					
Medical devices (with clinical data)	Class IV	New medical devices	8,705,500 Article 17, Paragraph 1, Item 1 (d)-(1)	683,500 Article 17, Paragraph 2, Item 1 (j)	9,389,000
		Improved medical devices	6,213,000 Article 17, Paragraph 1, Item 1 (d)-(2)	683,500 Article 17, Paragraph 2, Item 1 (j)	6,896,500
	Class III	New medical devices	6,213,000 Article 17, Paragraph 1, Item 1 (d)-(3)	683,500 Article 17, Paragraph 2, Item 1 (j)	6,896,500
		Improved medical devices	3,721,200 Article 17, Paragraph 1, Item 1 (d)-(4)	683,500 Article 17, Paragraph 2, Item 1 (j)	4,404,700
	Class II	New medical devices	6,213,000 Article 17, Paragraph 1, Item 1 (d)-(3)	683,500 Article 17, Paragraph 2, Item 1 (j)	6,896,500
		Improved medical devices	3,721,200 Article 17, Paragraph 1, Item 1 (d)-(4)	683,500 Article 17, Paragraph 2, Item 1 (j)	4,404,700
Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	2,355,400 Article 17, Paragraph 1, Item 1 (d)-(7)	70,500 Article 17, Paragraph 2, Item 1 (l)	2,425,900
		Generic medical devices	1,767,700 Article 17, Paragraph 1, Item 1 (d)-(8)	70,500 Article 17, Paragraph 2, Item 1 (l)	1,838,200
	Class III	Improved medical devices	1,409,900 Article 17, Paragraph 1, Item 1 (d)-(9)	70,500 Article 17, Paragraph 2, Item 1 (l)	1,480,400
		Generic medical devices	1,409,900 Article 17, Paragraph 1, Item 1 (d)-(9)	70,500 Article 17, Paragraph 2, Item 1 (l)	1,480,400
	Class II	Improved medical devices	1,409,900 Article 17, Paragraph 1, Item 1 (d)-(9)	70,500 Article 17, Paragraph 2, Item 1 (l)	1,480,400
		Generic medical devices	1,409,900 Article 17, Paragraph 1, Item 1 (d)-(9)	70,500 Article 17, Paragraph 2, Item 1 (l)	1,480,400
Medical devices (with approval standards, without clinical data)	Class IV		429,200 Article 17, Paragraph 1, Item 1 (d)-(5)	70,500 Article 17, Paragraph 2, Item 1 (k)	499,700
	Class III		344,100 Article 17, Paragraph 1, Item 1 (d)-(6)	70,500 Article 17, Paragraph 2, Item 1 (k)	414,600
	Class II		344,100 Article 17, Paragraph 1, Item 1 (d)-(6)	70,500 Article 17, Paragraph 2, Item 1 (k)	414,600

[On and after November 25, 2014]

List of user fees for reviews etc. of medical devices and in vitro diagnostics under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics. (Yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of medical devices and in vitro diagnostics (new approval)					
In vitro diagnostics	New products		2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
	Out of scope of approval standards		2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
	Nonconformity with approval standards	With clinical data	2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
		Without clinical data	996,900 Article 33, Paragraph 1, Item 1 (b)-(4)		996,900
	Conformity with approval standards	Without clinical data	362,000 Article 33, Paragraph 1, Item 1 (b)-(3)		362,000
	Addition of series		60,300 Article 33, Paragraph 1, Item 1 (b)-(1)		60,300
Change of brand name			35,600 Article 33, Paragraph 1, Item 1 (c)		35,600
Review for approval of medical devices and in vitro diagnostics (approval of partial changes to approved matters)					
New medical devices (Class IV)			5,446,600 Article 33, Paragraph 1, Item 2 (a)-(1)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 2 (a) and Paragraph 3	6,300,900 + overseas travel expenses
New medical devices (Class II/III)			3,887,300 Article 33, Paragraph 1, Item 2 (a)-(3)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 2 (a) and Paragraph 3	4,741,600 + overseas travel expenses
Improved medical devices with clinical data (Class IV)			3,109,900 Article 33, Paragraph 1, Item 2 (a)-(2)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 2 (b) and Paragraph 3	3,793,400 + overseas travel expenses
Improved medical devices with clinical data (Class II/III)			1,872,400 Article 33, Paragraph 1, Item 2 (a)-(4)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 2 (b) and Paragraph 3	2,555,900 + overseas travel expenses
Improved medical devices without clinical data, without approval standards (Class IV)			1,181,200 Article 33, Paragraph 1, Item 2 (a)-(7)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	1,219,400 + overseas travel expenses
Generic medical devices without clinical data, without approval standards (Class IV)			884,200 Article 33, Paragraph 1, Item 2 (a)-(8)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	922,400 + overseas travel expenses
Improved/generic medical devices without clinical data, without approval standards (Class II/III)			709,500 Article 33, Paragraph 1, Item 2 (a)-(9)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	747,700 + overseas travel expenses
Generic medical devices with approval standards (Class IV)			217,600 Article 33, Paragraph 1, Item 2 (a)-(5)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	255,800 + overseas travel expenses
Generic medical devices with approval standards (Class II/III)			173,600 Article 33, Paragraph 1, Item 2 (a)-(6)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	211,800 + overseas travel expenses
Others (medical devices)			143,500 Article 33, Paragraph 1, Item 2 (a)-(10)	38,200 + overseas travel expenses Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	181,700 + overseas travel expenses
Review for approval of medical devices and in vitro diagnostics (approval of partial changes to approved matters)					
In vitro diagnostics	Out of scope of approval standards	With clinical data	998,300 Article 33, Paragraph 1, Item 2 (b)-(2)		998,300
		Without clinical data	503,600 Article 33, Paragraph 1, Item 2 (b)-(3)		503,600
	Nonconformity with approval standards	With clinical data	998,300 Article 33, Paragraph 1, Item 2 (b)-(2)		998,300
		Without clinical data	503,600 Article 33, Paragraph 1, Item 2 (b)-(3)		503,600
	Conformity with approval standards	Without clinical data	206,200 Article 33, Paragraph 1, Item 2 (b)-(4)		206,200
	Addition of series		31,900 Article 33, Paragraph 1, Item 2 (b)-(1)		31,900
Others (in vitro diagnostics)			143,500 Article 33, Paragraph 1, Item 2 (b)-(5)		143,500

[Until November 24, 2014]

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 on Fees related to the Pharmaceutical Affairs Act. (Yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of drugs (new approval)					
In vitro diagnostics (without approval standards)			584,100 Article 17, Paragraph 1, Item 1 (a)-(14)		584,100
In vitro diagnostics (with approval standards)		Basic	282,900 Article 17, Paragraph 1, Item 1 (a)-(13)		282,900
		Addition of series	60,300 Article 17, Paragraph 1, Item 1 (a)-(12)		60,300
Change of brand name			35,600 Article 17, Paragraph 1, Item 1 (e)		35,600
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 Article 17, Paragraph 1, Item 2 (d)-(1)	683,500 Article 17, Paragraph 2, Item 2 (g)	5,041,000
		Improved medical devices	3,109,900 Article 17, Paragraph 1, Item 2 (d)-(2)	683,500 Article 17, Paragraph 2, Item 2 (g)	3,793,400
	Class III	New medical devices	3,109,900 Article 17, Paragraph 1, Item 2 (d)-(3)	683,500 Article 17, Paragraph 2, Item 2 (g)	3,793,400
		Improved medical devices	1,872,400 Article 17, Paragraph 1, Item 2 (d)-(4)	683,500 Article 17, Paragraph 2, Item 2 (g)	2,555,900
	Class II	New medical devices	3,109,900 Article 17, Paragraph 1, Item 2 (d)-(3)	683,500 Article 17, Paragraph 2, Item 2 (g)	3,793,400
		Improved medical devices	1,872,400 Article 17, Paragraph 1, Item 2 (d)-(4)	683,500 Article 17, Paragraph 2, Item 2 (g)	2,555,900
Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	1,181,200 Article 17, Paragraph 1, Item 2 (d)-(7)	38,200 Article 17, Paragraph 2, Item 2 (i)	1,219,400
		Generic medical devices	884,200 Article 17, Paragraph 1, Item 2 (d)-(8)	38,200 Article 17, Paragraph 2, Item 2 (i)	922,400
	Class III	Improved medical devices	709,500 Article 17, Paragraph 1, Item 2 (d)-(9)	38,200 Article 17, Paragraph 2, Item 2 (i)	747,700
		Generic medical devices	709,500 Article 17, Paragraph 1, Item 2 (d)-(9)	38,200 Article 17, Paragraph 2, Item 2 (i)	747,700
	Class II	Improved medical devices	709,500 Article 17, Paragraph 1, Item 2 (d)-(9)	38,200 Article 17, Paragraph 2, Item 2 (i)	747,700
		Generic medical devices	709,500 Article 17, Paragraph 1, Item 2 (d)-(9)	38,200 Article 17, Paragraph 2, Item 2 (i)	747,700
Medical devices (with approval standards, without clinical data)	Class IV		217,600 Article 17, Paragraph 1, Item 2 (d)-(5)	38,200 Article 17, Paragraph 2, Item 2 (h)	255,800
	Class III		173,600 Article 17, Paragraph 1, Item 2 (d)-(6)	38,200 Article 17, Paragraph 2, Item 2 (h)	211,800
	Class II		173,600 Article 17, Paragraph 1, Item 2 (d)-(6)	38,200 Article 17, Paragraph 2, Item 2 (h)	211,800
Review for approval of drugs (approval for partial changes to approved matters)					
In vitro diagnostics (without approval standards)			295,800 Article 17, Paragraph 1, Item 2 (a)-(11)		295,800
In vitro diagnostics (with approval standards)		Basic	143,500 Article 17, Paragraph 1, Item 2 (a)-(10)		143,500
		Addition of series	31,900 Article 17, Paragraph 1, Item 2 (a)-(9)		31,900

[On and after November 25, 2014]

List of user fees for reviews etc. of medical devices and in vitro diagnostics under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
QMS inspection of medical devices and in vitro diagnostics					
Issuance fee for certification of conformity with approval standards				50,400 Article 33, Paragraph 5, Item 1 (a) and Item 2 (a) and Item 3 (a)	50,400
Fee paid by MAH	New	New medical devices		386,600 Article 33, Paragraph 5, Item 1 (a)-(2)	386,600
		Class IV		374,500 Article 33, Paragraph 5, Item 1 (a)-(3)	374,500
		Biological products		398,500 Article 33, Paragraph 5, Item 1 (a)-(1)	398,500
		Others		374,500 Article 33, Paragraph 5, Item 1 (a)-(4)	374,500
		In vitro diagnostics		272,900 Article 33, Paragraph 5, Item 1 (a)-(5)	272,900
	Partial change	Class IV		134,000 Article 33, Paragraph 5, Item 2 (a)-(2)	134,000
		Biological products		145,600 Article 33, Paragraph 5, Item 2 (a)-(1)	145,600
		Others		127,800 Article 33, Paragraph 5, Item 2 (a)-(3)	127,800
		In vitro diagnostics		93,200 Article 33, Paragraph 5, Item 2 (a)-(4)	93,200
	Renewal	Class IV		167,600 Article 33, Paragraph 5, Item 3 (a)-(2)	167,600
		Biological products		176,900 Article 33, Paragraph 5, Item 3 (a)-(1)	176,900
		Others		149,200 Article 33, Paragraph 5, Item 3 (a)-(3)	149,200
		In vitro diagnostics		129,700 Article 33, Paragraph 5, Item 3 (a)-(4)	129,700
New	Design			86,100 Article 33, Paragraph 5, Item 1 (b)-(1) and Paragraph 9, Item 1 (a)	86,100
	Sterilization			91,200 Article 33, Paragraph 5, Item 1 (b)-(3) and Paragraph 9, Item 1 (c)	91,200
	Assembly			104,100 Article 33, Paragraph 5, Item 1 (b)-(2) and Paragraph 9, Item 1 (b)	104,100
	Others			90,500 Article 33, Paragraph 5, Item 1 (b)-(4) and Paragraph 9, Item 1 (d)	90,500
	Unregistered			87,500 Article 33, Paragraph 5, Item 1 (b)-(5) and Paragraph 9, Item 1 (e) and Paragraph 10, Item 1	87,500
Partial change	Design			64,400 Article 33, Paragraph 5, Item 2 (b)-(1)	64,400
	Sterilization			75,900 Article 33, Paragraph 5, Item 2 (b)-(3)	75,900
	Assembly			87,700 Article 33, Paragraph 5, Item 2 (b)-(2)	87,700
	Others			75,800 Article 33, Paragraph 5, Item 2 (b)-(4)	75,800
	Unregistered			75,900 Article 33, Paragraph 5, Item 2 (b)-(3)	75,900
Renewal	Design			68,800 Article 33, Paragraph 5, Item 3 (b)-(1) and Paragraph 9, Item 2 (a)	68,800
	Sterilization			80,100 Article 33, Paragraph 5, Item 3 (b)-(3) and Paragraph 9, Item 2 (c)	80,100

[Until November 24, 2014]

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 on Fees related to the Pharmaceutical Affairs Act.

(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) and Paragraph 5, Item 1 (a)	65,600
				Overseas		87,200 + travel expenses Article 17, Paragraph 4, Item 2 (b) and 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) and Paragraph 5, Item 2 (a)	265,900
				Overseas		347,800 + travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	347,800 + travel expenses
		Addition of products		Domestic		6,900 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,900
				Overseas		6,900 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,900

[On and after November 25, 2014]

List of user fees for reviews etc. of medical devices and in vitro diagnostics under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
QMS inspection of medical devices and in vitro diagnostics					
Renewal	Assembly			97,400 Article 33, Paragraph 5, Item 3 (b)-(2) and Paragraph 9, Item 2 (b)	97,400
Renewal	Others			79,600 Article 33, Paragraph 5, Item 3 (b)-(4) and Paragraph 9, Item 2 (d)	79,600
Renewal	Unregistered			76,100 Article 33, Paragraph 5, Item 3 (b)-(5) and Paragraph 9, Item 2 (e) and Paragraph 10, Item 2	76,100
Options	Micro machine			47,500 Article 33, Paragraph 6, Item 1	47,500
Options	Nano materials			47,500 Article 33, Paragraph 6, Item 2	47,500
Options	Others			47,500 Article 33, Paragraph 6, Item 3	47,500
Travel expenses for on-site inspection (per day)		Domestic		212,400 Article 33, Paragraph 7, Item 1 and Paragraph 11	212,400
		Overseas		179,500 ＋overseas travel expenses Article 33, Paragraph 7, Item 2 (a) and (b)	179,500 ＋overseas travel expenses
Re-issue/renewal of compliance certification				11,000 Article 33, Paragraph 15	11,000
GLP inspection of medical devices and in vitro diagnostics					
GLP		Domestic		2,121,400 Article 33, Paragraph 4, Item 1 (a) and Paragraph 13, Item 2 (a)-(1)	2,121,400
GLP		Overseas		2,347,900 + overseas travel expenses Article 33, Paragraph 4, Item 1 (b) and Paragraph 13, Item 2 (a)-(2) and Paragraph 14	2,347,900 + overseas travel expenses
GCP inspection of medical devices					
GCP		Domestic		653,400 Article 33, Paragraph 4, Item 2 (a)	653,400
GCP		Overseas		944,700 + overseas travel expenses Article 33, Paragraph 4, Item 2 (b)	944,700 + overseas travel expenses
Use-results surveys of medical devices and in vitro diagnostics					
Target medical devices and in vitro diagnostics			502,600 Article 33, Paragraph 12, Item 1 (a) and Item 2	642,400 + overseas travel expenses Article 33, Paragraph 13, Item 1 and Paragraph 14	1,145,000 + overseas travel expenses
Child items with multiple brand names of the target medical device			35,600 Article 33, Paragraph 12, Item 1 (b)		35,600
GPSP		Domestic		628,200 Article 33, Paragraph 13, Item 2 (b)-(1)	628,200
GPSP		Overseas		976,100 + overseas travel expenses Article 33, Paragraph 13, Item 2 (b)-(2) and Paragraph 14	976,100 + overseas travel expenses

[Until November 24, 2014]

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 on Fees related to the Pharmaceutical Affairs Act.

(Yen)

Classification			User fees		
			Review	Inspection	Total
GLP inspection of medical devices					
GLP		Domestic		2,121,400 Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	2,121,400
GLP		Overseas		2,347,900 ＋travel expenses Article 17, Paragraph 3, Item 1 (b) and 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
GCP		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 the 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
GPSP		Overseas		976,100 ＋travel expenses Article 17, Paragraph 9, Item 2 (b)-(6)	976,100 ＋travel expenses

8-3. List of user fees for reviews etc. of cellular and tissue-based products based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (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 Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of cellular and tissue-based products					
	New license	On-site		152,300	152,300
				Article 34, Paragraph 1, Item 1 (a)	
		Document		114,700	114,700
				Article 34, Paragraph 1, Item 1 (b)	
	Renewal of existing license	On-site		100,200	100,200
				Article 34, Paragraph 1, Item 2 (a)	
		Document		56,900	56,900
				Article 34, Paragraph 1, Item 2 (b)	
	Change/addition of classification	On-site		100,200	100,200
				Article 34, Paragraph 1, Item 3 (a)	
		Document		56,900	56,900
				Article 34, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers accreditation of cellular and tissue-based products					
	New accreditation	On-site		137,100 + overseas travel expenses	137,100 + overseas travel expenses
				Article 34, Paragraph 2, Item 1 (a)	
		Document		59,700	59,700
				Article 34, Paragraph 2, Item 1 (b)	
	Renewal of existing license	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 34, Paragraph 2, Item 2 (a)	
		Document		40,900	40,900
				Article 34, Paragraph 2, Item 2 (b)	
	Change/addition of classification	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 34, Paragraph 2, Item 3 (a)	
		Document		40,900	40,900
				Article 34, Paragraph 2, Item 3 (b)	
Review for approval of cellular and tissue-based products (new approval)					
	New cellular and tissue-based products		10,881,700	854,300 + overseas travel expenses	11,736,000 + overseas travel expenses
			Article 35, Paragraph 1, Item 1 (a)	Article 35, Paragraph 2, Item 1 and Paragraph 3	
	Cellular and tissue-based products in case of new application for approval after the time-limited conditional approval		5,446,600	854,300 + overseas travel expenses	6,300,900 + overseas travel expenses
			Article 35, Paragraph 1, Item 1 (b)	Article 35, Paragraph 2, Item 1 and Paragraph 3	
	Application for change of brand name		35,600		35,600
			Article 35, Paragraph 1, Item 1 (c)		
Review for approval of cellular and tissue-based products (approval of partial changes to approved matters)					
	Cellular and tissue-based products (change of indications, etc.)		5,446,600	854,300 + overseas travel expenses	6,300,900 + overseas travel expenses
			Article 35, Paragraph 1, Item 2 (a)	Article 35, Paragraph 2, Item 2 (a) and Paragraph 3	
	Cellular and tissue-based products (other changes)		1,181,300	38,200 + overseas travel expenses	1,219,500 + overseas travel expenses
			Article 35, Paragraph 1, Item 2 (b)	Article 35, Paragraph 2, Item 2 (b) and Paragraph 3	

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification					User fees		
					Review	Inspection	Total
GCTP inspection of cellular and tissue-based products							
	Approval/partial change	Manufacturing sites other than those conducting only packaging, labelling, or storage		Domestic		760,900 Article 35, Paragraph 5, Item 1 (a)	760,900
				Overseas		960,200 + overseas travel expenses Article 35, Paragraph 5, Item 1 (b) and Paragraph 7	960,200 + overseas travel expenses
		Packaging, labelling, or storage		Domestic		65,600 Article 35, Paragraph 5, Item 2 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 35, Paragraph 5, Item 2 (b) and Paragraph 7	87,200 + overseas travel expenses
		Testing institutions		Domestic		65,600 Article 35, Paragraph 6, Item 1 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 35, Paragraph 6, Item 1 (b) and Paragraph 7	87,200 + overseas travel expenses
	Renewal	Manufacturing sites other than those conducting only packaging, labelling, or storage	Basic	Domestic		448,500 Article 35, Paragraph 5, Item 3 (a)-(1)	448,500
				Overseas		570,100 + overseas travel expenses Article 35, Paragraph 5, Item 3 (a)-(2) and Paragraph 7	570,100 + overseas travel expenses
			Addition of products	Domestic		31,400 Article 35, Paragraph 5, Item 3 (a)-(1)	31,400
				Overseas		31,400 Article 35, Paragraph 5, Item 3 (a)-(2)	31,400
		Packaging, labelling, or storage	Basic	Domestic		265,900 Article 35, Paragraph 5, Item 3 (b)-(1)	265,900
				Overseas		347,800 + overseas travel expenses Article 35, Paragraph 5, Item 3 (b)-(2) and Paragraph 7	347,800 + overseas travel expenses
			Addition of products	Domestic		6,900 Article 35, Paragraph 5, Item 3 (b)-(1)	6,900
				Overseas		6,900 Article 35, Paragraph 5, Item 3 (b)-(2)	6,900
		Testing institutions	Basic	Domestic		265,900 Article 35, Paragraph 6, Item 2 (a)	265,900
				Overseas		347,800 + overseas travel expenses Article 35, Paragraph 6, Item 2 (b) and Paragraph 7	347,800 + overseas travel expenses
			Addition of products	Domestic		6,900 Article 35, Paragraph 6, Item 2 (a)	6,900
				Overseas		6,900 Article 35, Paragraph 6, Item 2 (b)	6,900
GLP inspection of cellular and tissue-based products							
	GLP			Domestic		2,121,400 Article 35, Paragraph 4, Item 1 (a) and Paragraph 10, Item 2 (a)-(1)	2,121,400
				Overseas		2,347,900 + overseas travel expenses Article 35, Paragraph 4, Item 1 (b) and Paragraph 10, Item 2 (a)-(2) and Paragraph 11	2,347,900 + overseas travel expenses
GCP inspection of cellular and tissue-based products							
	GCP			Domestic		653,400 Article 35, Paragraph 4, Item 2 (a)	653,400
				Overseas		944,700 + overseas travel expenses Article 35, Paragraph 4, Item 2 (b)	944,700 + overseas travel expenses
GPSP inspection of cellular and tissue-based products							
	GPSP			Domestic		628,500 Article 35, Paragraph 4, Item 3 (a)	628,500
				Overseas		976,100 + overseas travel expenses Article 35, Paragraph 4, Item 3 (b)	976,100 + overseas travel expenses
Re-examination of cellular and tissue-based products							
	Cellular and tissue-based products				504,400 Article 35, Paragraph 9	642,400 + overseas travel expenses Article 35, Paragraph 10, Item 1 and Paragraph 11	1,146,800 + overseas travel expenses
	GPSP			Domestic		628,500 Article 35, Paragraph 10, Item 2 (b)-(1)	628,500
				Overseas		976,100 + overseas travel expenses Article 35, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	976,100 + overseas travel expenses

8-4. List of user fees for PMDA's investigation based on the Act on Securing Safety of Regenerative Medicine (Act No. 85, 2013)

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Safety of Regenerative Medicine (Cabinet Order No. 278).

(Yen)

Classification			Inspection	Total
Investigation into license for manufacturing specified cellular products				
	New license	On-site	144,000	144,000
			Article 8, Paragraph 1, Item 1	
		Document	98,200	98,200
			Article 8, Paragraph 1, Item 2	
	Renewal of license	On-site	97,100	97,100
			Article 8, Paragraph 2, Item 1	
		Document	48,600	48,600
			Article 8, Paragraph 2, Item 2	
Investigation into accreditation for manufacturing specified cellular products				
	New accreditation	On-site	120,500 + overseas travel expenses	120,500 + overseas travel expenses
			Article 8, Paragraph 3, Item 1	
		Document	54,200	54,200
			Article 8, Paragraph 3, Item 2	
	Renewal of accreditation	On-site	56,500 + overseas travel expenses	56,500 + overseas travel expenses
			Article 8, Paragraph 4, Item 1	
		Document	37,100	37,100
			Article 8, Paragraph 4, Item 2	

8-5. 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

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(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 post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	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/GPSP compliance for drugs	per consultation	2,957,700	
	(Deleted)			
	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	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	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	
	(Transferred to the classification of R&D strategy)			
	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	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	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 institutions 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	

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices		Preparatory interview of consultations for medical devices	per consultation	29,400	Payment by the date of consultation application after arrangement of the consultation date
		Pre-development consultation for medical devices	per consultation	294,100	
		Pre-development consultation for medical devices (after the preparatory interview)	per consultation	264,700	
		Pre-development consultation for medical devices (additional consultation)	per consultation	147,000	
		Consultation on necessity of clinical trials for medical devices	per consultation	980,300	
		Consultation on necessity of clinical trials for medical devices (after the preparatory interview)	per consultation	950,600	
		Consultation on necessity of clinical trials for medical devices (additional consultation)	per consultation	490,200	
		Consultation on necessity of clinical trials for medical devices (ascertained with reference to clinical literature, etc.)	per consultation	1,960,900	
		Consultation on necessity of clinical trials for medical devices (ascertained with reference to clinical literature, etc.) (after the preparatory interview)	per consultation	1,931,500	
		Consultation on necessity of clinical trials for medical devices (ascertained with reference to clinical literature, etc.) (additional consultation)	per consultation	980,300	
	Consultation on protocol for medical devices	Safety (1 test)	per consultation	98,000	
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	
		Exploratory clinical trial	per consultation	1,076,200	
		Exploratory clinical trial (after the preparatory interview)	per consultation	1,046,800	
		Exploratory clinical trial (additional consultation)	per consultation	539,100	
		Clinical trial	per consultation	2,353,100	
		Clinical trial (after the preparatory interview)	per consultation	2,323,700	
		Clinical trial (additional consultation)	per consultation	1,176,500	
	(Deleted)				
	Consultation on data sufficiency/category of application for medical devices		per consultation	134,800	
	(Deleted)				
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices		per consultation	399,700	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (after the preparatory interview)		per consultation	370,300	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (additional consultation)		per consultation	197,900	

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees		Timing of payment
Consultations				
Medical devices				
	Pre-development consultation for medical devices	per consultation	139,100	Payment by the date of consultation application after arrangement of the consultation date
	Clinical evaluation consultation for medical devices	per consultation	1,055,900	
	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	
	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	
	Additional consultation for medical devices	per consultation	1,162,400	
	Consultation on GLP/GCP compliance for medical devices	per consultation	795,000	

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Assessment consultation for medical devices	Safety (1 test)	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (unevaluated protocol)	per consultation	147,000	
		Safety (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (unevaluated protocol)	per consultation	293,800	
		Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (unevaluated protocol)	per consultation	441,200	
		Safety (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Safety (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (unevaluated protocol)	per consultation	588,200	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (unevaluated protocol)	per consultation	441,200	
		Performance (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Performance (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees		Timing of payment
Consultations				
Medical devices	Prior assessment consultation for medical devices (quality)	per consultation	3,067,600	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for medical devices (non-clinical)	per consultation	3,067,600	

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Assessment consultation for medical devices	Exploratory clinical trial	per consultation	980,300	Payment by the date of consultation application after arrangement of the consultation date
		Exploratory clinical trial (after the preparatory interview)	per consultation	950,900	
		Exploratory clinical trial (unevaluated protocol)	per consultation	1,519,700	
		Exploratory clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	1,488,100	
		Exploratory clinical trial (additional consultation)	per consultation	490,200	
		Clinical trial	per consultation	1,470,700	
		Clinical trial (after the preparatory interview)	per consultation	1,441,300	
		Clinical trial (unevaluated protocol)	per consultation	2,647,200	
		Clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	2,617,700	
		Clinical trial (additional consultation)	per consultation	733,000	
	(Transferred to the classification of R&D strategy)				
	Consultation on GCP/GLP/GPSP for medical devices		per consultation	196,000	
	Consultation on GCP/GLP/GPSP for medical devices (after the preparatory interview)		per consultation	166,600	
	Consultation on GCP/GLP/GPSP for medical devices (additional consultation)		per consultation	98,000	
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics		per consultation	29,400	
	Pre-development consultation for in vitro diagnostics		per consultation	196,000	
	Pre-development consultation for in vitro diagnostics (after the preparatory interview)		per consultation	166,600	
	Pre-development consultation for in vitro diagnostics (additional consultation)		per consultation	98,000	
	Pre-development consultation for companion diagnostics		per consultation	293,800	
	Pre-development consultation for companion diagnostics (after the preparatory interview)		per consultation	264,400	
	Pre-development consultation for companion diagnostics (additional consultation)		per consultation	147,000	
	Consultation on protocol for in vitro diagnostics	Quality	per consultation	98,000	
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	490,200	
		Clinical performance study (after the preparatory interview)	per consultation	458,700	
		Clinical performance study (additional consultation)	per consultation	245,100	
		Clinical evaluation study for companion diagnostics	per consultation	733,000	
		Clinical evaluation study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
		Clinical evaluation study for companion diagnostics (additional consultation)	per consultation	367,600	
	(Deleted)				
	Application procedure consultation for in vitro diagnostics		per consultation	78,300	
	(Deleted)				

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees		Timing of payment
Consultations				
Medical devices	Prior assessment consultation for medical devices (clinical)	per consultation	4,619,100	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately)	per consultation	87,400	
In vitro diagnostics	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 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	

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Quality	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (unevaluated protocol)	per consultation	147,000	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (other than quality) (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (other than quality) (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (unevaluated protocol)	per consultation	441,200	
		Performance (other than quality) (3 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (unevaluated protocol)	per consultation	293,800	
		Correlation (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	293,800	
		Clinical performance study (after the preparatory interview)	per consultation	264,400	
		Clinical performance study (unevaluated protocol)	per consultation	539,100	
		Clinical performance study (unevaluated protocol) (after the preparatory interview)	per consultation	509,700	
		Clinical performance study (additional consultation)	per consultation	147,000	
		Clinical evaluation study for companion diagnostics	per consultation	441,200	
		Clinical evaluation study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical evaluation study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical evaluation study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical evaluation study for companion diagnostics (additional consultation)	per consultation	220,600	
Cellular and tissue-based products	Procedural consultation for cellular and tissue-based products		per consultation	134,800	
	Pre-development consultation for cellular and tissue-based products		per consultation	299,800	
	Pre-development consultation for cellular and tissue-based products (additional consultation)		per consultation	149,900	
	Non-clinical consultation for cellular and tissue-based products (effectiveness)		per consultation	899,500	
	Non-clinical consultation for cellular and tissue-based products (effectiveness) (additional consultation)		per consultation	449,700	
	Non-clinical consultation for cellular and tissue-based products (safety)		per consultation	946,200	
	Non-clinical consultation for cellular and tissue-based products (safety) (additional consultation)		per consultation	473,200	
	Quality consultation for cellular and tissue-based products		per consultation	946,200	
	Quality consultation for cellular and tissue-based products (additional consultation)		per consultation	473,200	
	Consultation before therapeutic exploratory study for cellular and tissue-based products		per consultation	1,098,500	
	Consultation before therapeutic exploratory study for cellular and tissue-based products (additional consultation)		per consultation	549,700	
	Consultation after therapeutic exploratory study for cellular and tissue-based products		per consultation	1,098,500	
	Consultation after therapeutic exploratory study for cellular and tissue-based products (additional consultation)		per consultation	549,700	

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees		Timing of payment
Consultations				
In vitro diagnostics	Quality consultation for in vitro diagnostics	per consultation	355,400	Payment by the date of consultation application after arrangement of the consultation date
	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	
	Consultation on conformity with standards for in vitro diagnostics	per consultation	455,400	
	Prior assessment consultation for in vitro diagnostics (clinical)	per consultation	4,619,100	
	Clinical evaluation consultation for in vitro diagnostics	per consultation	694,700	

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees		Timing of payment
Consultations				
Cellular and tissue-based products	Prior assessment consultation for cellular and tissue-based products (safety, quality, effectiveness)	per consultation	2,398,600	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for cellular and tissue-based products (therapeutic exploratory study)	per consultation	1,098,500	
	Prior assessment consultation for cellular and tissue-based products (confirmatory clinical study)	per consultation	2,398,600	
	Pre-application consultation for cellular and tissue-based products	per consultation	2,398,600	
	Pre-application consultation for cellular and tissue-based products (additional consultation)	per consultation	1,199,300	
	Consultation on protocols of clinical trials for cellular and tissue-based products after the time-limited conditional approval (with protocol)	per consultation	1,098,500	
	Consultation on protocols of clinical trials for cellular and tissue-based products after the time-limited conditional approval (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of clinical trials for cellular and tissue-based products after the time-limited conditional approval (only for investigation)	per consultation	824,500	
	Consultation on protocols of clinical trials for cellular and tissue-based products after the time-limited conditional approval (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of clinical trials for cellular and tissue-based products after the time-limited conditional approval (with protocol)	per consultation	1,098,500	
	Consultation at completion of clinical trials for cellular and tissue-based products after the time-limited conditional approval (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of clinical trials for cellular and tissue-based products after the time-limited conditional approval (only for investigation)	per consultation	824,500	
	Consultation at completion of clinical trials for cellular and tissue-based products after the time-limited conditional approval (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on protocols of post-marketing clinical trials for cellular and tissue-based products (with protocol)	per consultation	1,098,500	
	Consultation on protocols of post-marketing clinical trials for cellular and tissue-based products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of post-marketing clinical trials for cellular and tissue-based products (only for investigation)	per consultation	824,500	
	Consultation on protocols of post-marketing clinical trials for cellular and tissue-based products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of post-marketing clinical trials for cellular and tissue-based products (with protocol)	per consultation	1,098,500	
	Consultation at completion of post-marketing clinical trials for cellular and tissue-based products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of post-marketing clinical trials for cellular and tissue-based products (only for investigation)	per consultation	824,500	
	Consultation at completion of post-marketing clinical trials for cellular and tissue-based products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on GLP/GCP (including GCTP) compliance for cellular and tissue-based products	per consultation	399,700	
	Consultation on GLP/GCP (including GCTP) compliance for cellular and tissue-based products (additional consultation)	per consultation	197,900	
	Pre-interview for cellular and tissue-based products (with recording)	per consultation	94,500	
	Post-consultation for cellular and tissue-based products (with recording)	per consultation	94,500	
	(Deleted)			
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately)	per consultation	154,100	
	Consultation on quality and safety for cellular and tissue-based products	per consultation	1,541,600	
	Consultation on quality and safety of cellular and tissue-based products (universities/research institutions and venture companies meeting the requirements specified separately)	per consultation	154,100	
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately)	per consultation	87,400	
	Consultation on R&D strategy for cellular and tissue-based products	per consultation	874,000	
	Consultation on R&D strategy for cellular and tissue-based products (universities/research institutions and venture companies meeting the requirements specified separately)	per consultation	87,400	
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600	

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

	User fees		Timing of payment
Consultations			
			Payment by the date of consultation application after arrangement of the consultation date
Consultation on preparation of documents for gene therapy products	per consultation	229,900	
(Transferred from the "Drugs" classification)			
(Transferred from the "Medical Devices" classification)			

[On and after November 25, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Simple consultations	Generic drugs		per consultation	21,600	Payment by the date of consultation application after arrangement of the consultation date
	OTC drugs		per consultation	21,600	
	Quasi-drugs (including pest control agents)		per consultation	21,600	
	Medical devices or in vitro diagnostics		per consultation	39,400	
	Preparation of new drug applications		per consultation	21,600	
	Cellular and tissue-based products		per consultation	21,600	
	GCP/GLP/GPSP for drugs		per consultation	19,400	
	GCP/GLP/GPSP for medical devices		per consultation	19,400	
	GCP/GLP/GPSP for cellular and tissue-based products		per consultation	19,400	
	GMP/QMS inspection		per consultation	25,400	
	GCTP inspection		per consultation	25,400	
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	
GLP inspection of test facilities					
(Deleted)					Request to PMDA after advanced payment
All test items	Basic fee	With animal-rearing facility	per facility	1,299,600	
		Without animal-rearing facility	per facility	799,500	
	Additional fee for target tests	General toxicity studies	per study	399,700	
		Reproduction toxicity studies	per study	199,800	
		Safety pharmacology core battery (only for drugs)	per study	199,800	
		Hemocompatibility studies (only for medical devices)	per study	199,800	
		In vitro studies	per study	199,800	
		Other studies (dependence, TK, pathology, and other studies)	per study	199,800	
	Additional fee for target classification	Drugs	per facility	199,800	
		Medical devices	per facility	199,800	
		Cellular and tissue-based products	per facility	199,800	
	(Deleted)				
(Deleted)					
Additional compliance accreditation			per facility	959,300	
Additional inspection			per inspection from the second inspection onwards	396,500	
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 (without on-site inspection)			per product of one facility	15,500	
Certification of drug products			per product	15,500	
Other certifications (including GMP/QMS certification)			per matter of one product	8,700	
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

* 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 the following specified amount or more from the government, to proceed with the research on the seed-stage resource
  For the consultation on R&D strategy for drugs or consultation on quality and safety for cellular and tissue-based products, 90 million yen
  For the consultation on R&D strategy for medical devices or consultation on R&D strategy for cellular and tissue-based products, 50 million yen
- Having not received research expenses from a pharmaceutical company, medical device company, etc. 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

[Until November 24, 2014]

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Simple consultations	Generic drugs		per consultation	21,600	Payment by the date of consultation application after arrangement of the consultation date
	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	
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	
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 exp	
Limited test items			per facility	1,023,600	
Additional compliance accreditation			per facility	959,300	
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 (without on-site inspection)			per product of one facility	15,500	
Certification of drug products			per product	15,500	
Other certifications (including GMP/QMS certification)			per matter of one product	8,700	
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

* 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

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) mplement 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 (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.

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.

Attachment 1

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	Commissioned 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	Commissioned 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	Commissioned 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.

Rules of Calculation of the Running Expenses Grant for Accounts for Reviews, etc.

The rules of calculation of the running expenses grant in the target mid-term period (FY 2014 - FY 2018) are as follows.

1. FY 2014

Expenses required for implementation of services are individually estimated and calculated.

2. In or after FY 2015

The following calculation formula is used:

Running expenses grant	=	Service division personnel expenses	+	Expenses	+	Special factor	-	Self-generated income

○ Service division personnel expenses = Basic salaries, etc. (A) + Termination benefits (S)

A: Personnel expenses including basic salaries, various benefits, and contribution to mutual aid association (excluding termination benefits) which are calculated by using the following formula:

$A = [\{P1 \times \alpha \times \beta\} + \{P2 \times \beta\} + P3]$

A: Basic salaries, etc. for the said fiscal year
P1: Those influenced by salary raises and salary revisions among basic salaries in the preceding fiscal year
P2: Those influenced by salary revisions among basic salaries in the preceding fiscal year
P3: Those not influenced by salary raises and salary revisions among basic salaries in the preceding fiscal year
α: Salary raise resource rate in view of running status, etc.
β: Salary revision rate in view of running status, etc.

S: Amount of termination benefits for the said fiscal year corresponding to persons expected to terminate in the said fiscal year and persons expected to terminate in the preceding fiscal year or before

○ Expenses = ((General administrative expenses (B) × γ1 × δ) + (Operating expenses (R) × γ2 × δ))

B: Non-personnel expenses related to the management division in the preceding fiscal year
R: Non-personnel expenses related to services in the preceding fiscal year
γ1: Efficiency coefficient (general administrative expenses)
γ2: Efficiency coefficient (operating expenses)
δ: Consumer price index

○ Special factor = A measure required in association with law/regulation revision, etc. or a demand for fund occurring due to a reason unpredictable at present which is determined in the process of budget-making for every fiscal year.

○ Self-generated income = The estimated mount of an income that may occur from clerical works/projects implemented with the running expenses grant as the financial resource

[Notes]

1. For α, β, δ, γ1, and γ2, concrete discrete values are determined for the said fiscal year in the process of budget-making for the year in view of the followings:
   δ (consumer price index): The actual value in the preceding fiscal year is used.
2. Budgets for the overall mid-term plan were estimated,
   [1] assuming that the increase rate is 0 for α, β, and δ.
   [2] assuming that γ1 (efficiency coefficient) is ▲3.75% in FY 2015, ▲3.90% in FY 2016, ▲4.05% in FY 2017, and ▲4.23% in FY 2018.
   [3] assuming that γ2 (efficiency coefficient) is ▲1.25% in FY 2015, ▲1.27% in FY 2016, ▲1.28% in FY 2017, and ▲1.30% in FY 2018.

Budgets

Attachment 1

Budgets for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount of money								
			Review account						
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Total	Specified relief account	Commission and loan account	Commissioned payment account	Total
Income									
Administrative subsidies			532	749	1,281				1,281
Governmental subsidies	177	142	269	304	574				892
Contributions	3,878	91		2,911	2,911	4,927			11,807
User fees			11,012		11,012				11,012
Commissioned operations			185		185		1,197	646	2,028
Management income	403	78							481
Miscellaneous income	1	0	28	7	36	0	2	1	40
Total	4,459	311	12,027	3,972	15,999	4,928	1,198	647	27,541
Expenditure									
Operating expenses	3,049	307	11,540	5,041	16,581	8,105	1,191	642	29,876
Personnel expenses	241	27	4,960	1,189	6,149	18	37	19	6,490
Administrative expenses	2,808	281	6,581	3,852	10,433	8,087	1,154	623	23,385
General administrative expenses	126	19	1,752	371	2,123	3	7	5	2,284
Personnel expenses	67		617	134	752				819
Non-personnel expenses	59	19	1,135	237	1,371	3	7	5	1,465
Total	3,174	327	13,293	5,412	18,704	8,108	1,198	647	32,159

As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Income and Expenditure Plan for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount									
	Adverse drug reactions relief account	Infection relief account	Review account				Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Adjusted	Total				
Ordinary expenses	4,716	440	13,734	5,079	△ 5	18,808	8,108	1,199	648	33,919
Relief benefits	2,107	31								2,138
Operating expenses for health and welfare	37	124								161
Operating expenses for reviews			4,885			4,885				4,885
Operating expenses for safety measures				2,770		2,770				2,770
Specified relief benefits							8,064			8,064
Benefits (healthcare allowances, etc.)								1,133		1,133
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									349	349
Provision for liability reserve	1,521	111								1,632
Other administrative expenses	923	154	7,061	1,917		8,978	41	57	38	10,190
Personnel expenses	227	25	4,497	1,092		5,589	17	34	18	5,910
Depreciation expenses	27	3	816	505		1,321	0	1	0	1,352
Retirement benefit expenses	6	1	197	47		244	0	1	0	253
Provision for accrued bonuses	7	1	278	41		319	1	2	1	331
Other expenses	655	124	1,272	232		1,504	23	19	18	2,344
General administrative expenses	126	20	1,782	388	△ 5	2,166	3	7	5	2,327
Personnel expenses	64		521	123		644				708
Depreciation expenses	0		73	12		85				85
Retirement benefit expenses	2		24	4		28				30
Provision for accrued bonuses	1		36	8		43				45
Other expenses	59	20	1,129	241	△ 5	1,366	3	7	5	1,460
Financial expenses	0		6	3		8				8
Miscellaneous losses	1	1		1		1		2	1	6
Ordinary income	4,432	309	12,023	4,027	△ 5	16,045	8,108	1,198	647	30,740
Governmental subsidies	177	142	269	304		574				892
Administrative subsidies			532	674		1,206				1,206
Other governmental grants							42			42
Contributions	3,878	91		2,911		2,911				6,879
User fees			11,012			11,012				11,012
Gain on reversal of specified relief fund deposit received							8,066			8,066
Commissioned operations			185			185		1,197	646	2,028
Reversal of asset offset subsidies			17	119		137	0			137
Reversal of asset offset administrative subsidies			0	17		17				17
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	378	77								455
Miscellaneous income			7	0	△ 5	3		2	1	5
Ordinary net income (△ net loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179
Current net income before tax (△ net loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179
Current net income (△ net loss)	△ 284	△ 131	△ 1,711	△ 628		△ 2,339	0	△ 1	△ 1	△ 3,179
Reversal of appropriated surplus	-	-	0	0		0	-	-	-	0
Current gross income (△ gross loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179

[Note]
As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Cash Flow Plan

Attachment 3

Cash Flow Plan for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount									
	Adverse drug reactions relief account	Infection relief account	Review account				Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Adjusted	Total				
Cash Outflows										
Cash outflows from operating activities	3,203	363	15,456	5,260	▲ 6	20,710	8,109	1,215	655	34,254
Relief benefits	2,109	30								2,139
Operating expenses for health and welfare	37	124								161
Operating expenses for reviews			7,938			7,938				7,938
Operating expenses for safety measures				3,537		3,537				3,537
Administrative expenses	673	126					24	20	18	862
Specified relief benefits							8,064			8,064
Benefits (healthcare allowances, etc.)								1,135		1,135
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									349	349
General administrative expenses	59	20	1,450	319		1,768	3	7	5	1,863
Personnel expenses	298	26	5,326	1,265		6,590	18	36	19	6,986
Repayment money	1	1		1		1		2	1	6
Other cash outflow from operating activities	25	37	743	139	▲ 6	876	0	15	7	960
Cash outflow from investing activities	4,000	300	5	802		807			0	5,107
Amount carried forward to next fiscal year	1,919	217	8,259	936		9,195	1,743	39	131	13,245
Total	9,122	880	23,720	6,998	▲ 6	30,713	9,852	1,253	786	52,606
Cash Inflows										
Cash inflows from operating activities	4,465	311	12,200	3,981	▲ 6	16,176	4,934	1,201	647	27,734
Contributions	3,878	91		2,911		2,911	4,934			11,813
Administrative subsidies			532	749		1,281				1,281
Governmental subsidies	177	142	269	304		574				892
User fees			11,177			11,177				11,177
Commissioned operations			150			150		1,199	646	1,995
Amount of interests received	403	78								481
Miscellaneous incomes			66	16		82		2	1	85
Other incomes	8	0	6		▲ 6	0	0	0	0	9
Cash inflows from investing activities	2,904	302								3,206
Amount brought forward from preceding fiscal year	1,753	267	11,520	3,017		14,537	4,918	53	138	21,666
Total	9,122	880	23,720	6,998	▲ 6	30,713	9,852	1,253	786	52,606

[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	Commissioned 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 2014

Budgets

Attachment 1

Budgets for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount of money								
	Adverse drug reactions relief account	Infection relief account	Review account			Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Total				
Income									
Administrative subsidies			532	749	1,281				1,281
Governmental subsidies	177	142	269	304	574				892
Contributions	3,878	91		2,911	2,911	4,927			11,807
User fees			11,012		11,012				11,012
Commissioned operations			185		185		1,197	646	2,028
Management income	403	78							481
Miscellaneous income	1	0	28	7	36	0	2	1	40
Total	4,459	311	12,027	3,972	15,999	4,928	1,198	647	27,541
Expenditure									
Operating expenses	3,049	307	11,540	5,041	16,581	8,105	1,191	642	29,876
Personnel expenses	241	27	4,960	1,189	6,149	18	37	19	6,490
Administrative expenses	2,808	281	6,581	3,852	10,433	8,087	1,154	623	23,385
General administrative expenses	126	19	1,752	371	2,123	3	7	5	2,284
Personnel expenses	67		617	134	752				819
Non-personnel expenses	59	19	1,135	237	1,371	3	7	5	1,465
Total	3,174	327	13,293	5,412	18,704	8,108	1,198	647	32,159

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									
	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	Adjusted	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 2014

Income and Expenditure Plan　　Attachment 2

Income and Expenditure Plan for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount									
	Adverse drug reactions relief account	Infection relief account	Review account				Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Adjusted	Total				
Ordinary expenses	4,716	440	13,734	5,079	△ 5	18,808	8,108	1,199	648	33,919
Relief benefits	2,107	31								2,138
Operating expenses for health and welfare	37	124								161
Operating expenses for reviews			4,885			4,885				4,885
Operating expenses for safety measures				2,770		2,770				2,770
Specified relief benefits							8,064			8,064
Benefits (healthcare allowances, etc.)								1,133		1,133
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									349	349
Provision for liability reserve	1,521	111								1,632
Other administrative expenses	923	154	7,061	1,917		8,978	41	57	38	10,190
Personnel expenses	227	25	4,497	1,092		5,589	17	34	18	5,910
Depreciation expenses	27	3	816	505		1,321	0	1	0	1,352
Retirement benefit expenses	6	1	197	47		244	0	1	0	253
Provision for accrued bonuses	7	1	278	41		319	1	2	1	331
Other expenses	655	124	1,272	232		1,504	23	19	18	2,344
General administrative expenses	126	20	1,782	388	△ 5	2,166	3	7	5	2,327
Personnel expenses	64		521	123		644				708
Depreciation expenses	0		73	12		85				85
Retirement benefit expenses	2		24	4		28				30
Provision for accrued bonuses	1		36	8		43				45
Other expenses	59	20	1,129	241	△ 5	1,366	3	7	5	1,460
Financial expenses	0		6	3		8				8
Miscellaneous losses	1	1		1		1		2	1	6
Ordinary income	4,432	309	12,023	4,027	△ 5	16,045	8,108	1,198	647	30,740
Governmental subsidies	177	142	269	304		574				892
Administrative subsidies			532	674		1,206				1,206
Other governmental grants							42			42
Contributions	3,878	91		2,911		2,911				6,879
User fees			11,012			11,012				11,012
Gain on reversal of specified relief fund deposit received							8,066			8,066
Commissioned operations			185			185		1,197	646	2,028
Reversal of asset offset subsidies			17	119		137	0			137
Reversal of asset offset administrative subsidies			0	17		17				17
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	378	77								455
Miscellaneous income			7	0	△ 5	3		2	1	5
Ordinary net income (△ net loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179
Current net income before tax (△ net loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179
Current net income (△ net loss)	△ 284	△ 131	△ 1,711	△ 628		△ 2,339	0	△ 1	△ 1	△ 3,179
Reversal of appropriated surplus	-	-	0	0		0	-	-	-	0
Current gross income (△ gross loss)	△ 284	△ 131	△ 1,711	△ 1,052		△ 2,763	0	△ 1	△ 1	△ 3,179

[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 3

Cash Flow Plan for Fiscal Year Plan (FY 2013)

(Unit: million yen)

Classification	Amount									
	Adverse drug reactions relief account	Infection relief account	Review account				Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Adjusted	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.

Plan for FY 2014

Cash Flow Plan

Attachment 3

Cash Flow Plan for Fiscal Year Plan (FY 2014)

(Unit: million yen)

Classification	Amount									
	Adverse drug reactions relief account	Infection relief account	Review account				Specified relief account	Commission and loan account	Commissioned payment account	Total
			Review segment	Safety segment	Adjusted	Total				
Cash Outflows										
Cash outflows from operating activities	3,203	363	15,456	5,260	▲ 6	20,710	8,109	1,215	655	34,254
Relief benefits	2,109	30								2,139
Operating expenses for health and welfare	37	124								161
Operating expenses for reviews			7,938			7,938				7,938
Operating expenses for safety measures				3,537		3,537				3,537
Administrative expenses	673	126					24	20	18	862
Specified relief benefits							8,064			8,064
Benefits (healthcare allowances, etc.)								1,135		1,135
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									349	349
General administrative expenses	59	20	1,450	319		1,768	3	7	5	1,863
Personnel expenses	298	26	5,326	1,265		6,590	18	36	19	6,986
Repayment money	1	1		1		1		2	1	6
Other cash outflow from operating activities	25	37	743	139	▲ 6	876	0	15	7	960
Cash outflow from investing activities	4,000	300	5	802		807			0	5,107
Amount carried forward to next fiscal year	1,919	217	8,259	936		9,195	1,743	39	131	13,245
Total	9,122	880	23,720	6,998	▲ 6	30,713	9,852	1,253	786	52,606
Cash Inflows										
Cash inflows from operating activities	4,465	311	12,200	3,981	▲ 6	16,176	4,934	1,201	647	27,734
Contributions	3,878	91		2,911		2,911	4,934			11,813
Administrative subsidies			532	749		1,281				1,281
Governmental subsidies	177	142	269	304		574				892
User fees			11,177			11,177				11,177
Commissioned operations			150			150		1,199	646	1,995
Amount of interests received	403	78								481
Miscellaneous incomes			66	16		82		2	1	85
Other incomes	8	0	6		▲ 6	0	0	0	0	9
Cash inflows from investing activities	2,904	302								3,206
Amount brought forward from preceding fiscal year	1,753	267	11,520	3,017		14,537	4,918	53	138	21,666
Total	9,122	880	23,720	6,998	▲ 6	30,713	9,852	1,253	786	52,606

[Note]
As each count was obtained by rounding off in principle, some fractions are not consistent with the total.

Basic Implementation Policy for the Third Mid-term Plan

The Executive Board Decision
November 25, 2014

1. Goals for PMDA to attain by the end of the third mid-term period

In order to meet the public expectations at a higher level in ever-changing business environment, PMDA, as the one and only organization that performs three regulatory operations (review, safety, and relief services) in Japan, aims for the goals described below by the end of the effective period of the mid-term plan, in accordance with the Third Mid-term Plan based on the universally applicable "PMDA Philosophy."

PMDA aims to:

○ Provide fast and high-quality review, safety measures, and relief services for adverse health effects, using the latest scientific knowledge in accordance with the concept of regulatory science;

○ Collaborate with regulatory authorities of other countries and take the lead to promote international harmonization;

○ Contribute to improvement of medical standards in terms of ensuring the efficacy, safety, and quality of medical products and assuring their reliability, in collaboration with academia, etc.;

○ Act and communicate in a way that will earn trust of stakeholders including the general public; and

○ Enhance the standardization, efficiency, and advancement of operations and thereby reduce workload of applicants, persons receiving consultation, and employees of PMDA, while creating a comfortable work environment attracting highly qualified and competent employees and allowing them to pursue long-term careers with PMDA.

2. Basic strategic perspective and policy for implementing the Third Mid-term Plan

○ In order to ensure high-quality and reliable operations, PMDA will:

- Respond to reform of the systems appropriately;
- Improve quality of reviews and enhance transparency of review results;
- Deepen the possessed scientific knowledge and sophisticate the efficiency and efficacy of data analysis; and
- Reinforce the consultation for practical application of promising seed-stage resources in academia and companies.

○ In order to play its expected roles and to increase its presence, PMDA will:

- Enhance its contribution to the international harmonization of regulations and standards and strengthen commitment particularly to Asian countries;
- Strengthen the training function for transferring knowledge and technique/methods of conformity audit and quality control, etc., to stakeholders; and
- Reinforce provision of information about the operations and achievements of PMDA in a clear and transparent manner.

○ In order to make full use of limited resources, PMDA will:

- Promote prioritization/rationalization of operations and systematic implementation while accommodating any situational change in a flexible manner;
- Increase the productivity of individual employees and thereby enhance the performance of PMDA as a whole;
- Work on development or modification of IT systems and cost reduction in order to standardize and streamline operations; and
- Establish appropriate systems for personnel management and training in order to be able to secure competent personnel and to train them.

Balance Sheet (corporate basis)

(As of March 31, 2015)

(Unit: yen)

Account item	Amount		Account item	Amount	
Assets			Liabilities		
I Current assets			I Current liabilities		
Cash and deposits		22,920,110,097	Administrative subsidy obligations		99,576,603
Securities		3,998,995,734	Deposit subsidy, etc.		135,403,253
Expenses for work-in-process reviews, etc.		1,593,413,594	Accrued benefits		364,967,830
Prepaid expenses		196,088	Accounts payable		3,053,474,842
Accounts due		579,366,425	Advances received		8,175,749,053
Accrued income		47,265,702	Deposits received		142,436,978
Other current assets		330,508	Lease obligations		34,738,052
			Allowance		
Total of current assets		29,139,678,148	Accrued bonuses	466,079,064	466,079,064
			Total of current liabilities		12,472,425,675
II Fixed assets			II Fixed liabilities		
Tangible fixed assets			Per contra liabilities for property acquisition		
Tools, equipment and fixtures	2,299,275,215		Administrative subsidies for assets as per contra	80,969,437	
Cumulative total of depreciation	△ 881,691,491	1,417,583,724	Governmental subsidies, etc. for assets as per contra	562,494,697	
Total of tangible fixed assets		1,417,583,724	Amount of received goods for assets as per contra	149,088	643,613,222
			Deposits of specific relief funds		
Intangible fixed assets			Long-term deposit subsidy, etc.	191,853,874	
Software		5,393,401,398	Deposit contribution	4,590,836,642	4,782,690,516
Software in progress		374,392,800	Long-term lease obligations		62,092,673
Telephone subscription right		286,000	Allowances		
Total of intangible fixed assets		5,768,080,198	Allowances for retirement benefits	1,799,941,872	1,799,941,872
			Liability reserve		20,141,170,146
Investments and other assets			Total of fixed liabilities		27,429,508,429
Investment securities		32,738,175,557	Total of liabilities		39,901,934,104
Rental deposit		8,714,160	Net assets		
Total of investments and other assets		32,746,889,717	I Capital funds		
			Government investment		1,179,844,924
Total of fixed assets		39,932,553,639	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 (△)		△ 658,940,661
			Loss on retirement or sale of fixed assets that are not recorded as expenses (△)		△ 98,706,116
			Total of capital surplus		△ 752,976,137
			III Retained earnings		28,743,428,896
			Total of net assets		29,170,297,683
Total of assets		69,072,231,787	Total of liabilities and net assets		69,072,231,787

Profit and Loss Statement (Corporate basis)

(From April 1, 2014 to March 31, 2015)

(Unit: yen)

Account item	Amount		
Ordinary expenses			
Adverse drug reaction relief benefits		2,113,286,412	
Infection relief benefits		3,238,831	
Operating expenses for health and welfare		127,425,120	
Operating expenses for reviews		3,177,760,590	
Operating expenses for safety measures		1,623,621,196	
Specific relief benefits		2,100,000,000	
Benefits for healthcare allowances, etc.		1,082,991,904	
Benefits for special allowances, etc.		203,589,600	
Investigative research		288,735,800	
Provision of liability reserves		1,184,206,725	
Other operating expenses			
Personnel expenses	5,460,506,177		
Depreciation expenses	1,467,542,893		
Retirement benefit expenses	230,704,790		
Provision for accrued bonuses	304,476,585		
Estate rental fees	1,337,347,239		
Other expenses	525,872,566	9,326,450,250	
General administrative expenses			
Personnel expenses	672,935,124		
Depreciation expenses	175,019,127		
Retirement benefit expenses	26,040,487		
Provision for accrued bonuses	44,513,639		
Estate rental fees	252,667,211		
Other expenses	975,879,140	2,147,054,728	
Financial expenses			
Interest paid		6,088,775	
Miscellaneous losses		2,521,600	
Total of ordinary expenses			23,386,971,531
Ordinary revenues			
Administrative subsidies		1,148,620,621	
Reversal of provision for deposits of specific relief funds			
Revenues from contributions		2,100,000,000	
User fees		10,066,401,757	
Contributions		6,927,565,700	
Revenue from governmental subsidies		656,914,254	
Commissioned operations for government		69,801,190	
Commissioned operations for others		1,754,282,390	
Return of administrative subsidies for assets as per contra		10,793,944	
Return of subsidies, etc. for assets as per contra		142,231,240	
Return of amount of received goods for assets as per contra		36,220	
Return of liability reserves		992,748	
Financial revenue			
Interest on securities	442,297,876	442,297,876	
Miscellaneous gains		19,231,856	
Total of ordinary revenues			23,339,169,796
Ordinary losses			△ 47,801,735
Extraordinary losses			
Loss on retirement of fixed assets		4	
Provision of liability reserves		1,015,346,126	1,015,346,130
Current net losses			△ 1,063,147,865
Reversal of reserve carried forward from the previous Mid-term target period			1,342,439,372
Current gross losses			279,291,507

Cash Flow Statement (Corporate basis)

(From April 1, 2014 to March 31, 2015)

(Unit: yen)

Account item	Amount of money
I. Cash flow from operating activities	
Expenditure for adverse drug reaction relief benefits	△ 2,133,497,485
Expenditure for infection relief benefits	△ 3,239,431
Expenditure for operating expenses for health and welfare	△ 125,732,946
Expenditure for operating expenses for reviews	△ 3,690,835,106
Expenditure for operating expenses for safety measures	△ 1,502,421,842
Expenditure for specific relief benefits	△ 2,100,000,000
Expenditure for benefits for healthcare allowances, etc.	△ 1,023,778,114
Expenditure for benefits for special allowances, etc.	△ 204,041,200
Expenditure for expenses for investigative research	△ 290,070,300
Expenditure for personnel expenses	△ 6,511,475,627
Expenditure for money refunded for settlement of subsidies, etc.	△ 198,590,916
Other operating expenditures	△ 3,339,468,314
Income from administrative subsidies	1,280,986,000
Income from governmental subsidies	1,022,658,750
Income from contributions	7,798,259,700
Income from user fees	10,957,671,841
Income from commissioned operations for government	69,801,190
Income from commissioned operations for others	1,704,647,540
Other incomes	145,842,809
Subtotal	1,856,716,549
Interest paid	△ 6,088,775
Interest received	469,647,837
Payment to national treasury	△ 865,144,900
Cash flow from operating activities	1,455,130,711
II. Cash flow from investing activities	
Expenditure for acquisition of investment securities	△ 4,298,111,000
Income from redemption of investment securities at maturity	3,200,000,000
Expenditure for acquisition of tangible fixed assets	△ 709,930,562
Expenditure for acquisition of intangible fixed assets	△ 2,069,340,184
Expenditure for payment of lease deposits	△ 4,043,520
Cash flow from investing activities	△ 3,881,425,266
III. Cash flow from financing activities	
Expenditure for repayment of finance lease obligations	△ 106,005,102
Cash flow from financing activities	△ 106,005,102
IV. Increase in funds	△ 2,532,299,657
V. Beginning-of-term balance of funds	25,452,409,754
VI. End-of-term balance of funds	22,920,110,097

Government Service Implementation Cost Statement (Corporate basis)

(From April 1, 2014 to March 31, 2015)

(Unit: yen)

Account item	Amount of money		
I. Operating expenses			
(1) Expenses in the profit and loss statement			
Adverse drug reaction relief benefits	2,113,286,412		
Infection relief benefits	3,238,831		
Operating expenses for health and welfare services	127,425,120		
Operating expenses for reviews	3,177,760,590		
Operating expenses for safety measures	1,623,621,196		
Specific relief benefits	2,100,000,000		
Benefits for healthcare allowances, etc.	1,082,991,904		
Benefits for special allowances, etc.	203,589,600		
Expenses for investigative research	288,735,800		
Provision of liability reserves	1,184,206,725		
Other operating expenses	9,326,450,250		
General administrative expenses	2,147,054,728		
Financial expenses	6,088,775		
Miscellaneous losses	2,521,600		
Loss on retirement of fixed assets	4		
Provision of liability reserves	1,015,346,126	24,402,317,661	
(2) (Exemption) Self-generated income, etc.			
Income from contributions	△ 9,027,565,700		
Income from user fees	△ 10,066,401,757		
Income from commissioned operations for government	△ 69,801,190		
Income from commissioned operations for others	△ 1,754,282,390		
Return of liability reserves	△ 992,748		
Financial revenue	△ 442,297,876		
Miscellaneous gains	△ 19,231,856	△ 21,380,573,517	
Total of operating expenses			3,021,744,144
II. Amount equivalent to depreciation that are not recorded as expenses			14,024,581
III. Estimated amount of non-allowance bonuses			17,906,148
IV. Estimated increased amount of non-allowance retirement benefits			104,462,099
V. Opportunity costs			
Opportunity costs of investments by the government or local governments, etc.			1,716,841
VI. Government service implementation costs			3,159,853,813

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 recorded 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 0.400% with reference to the yield rate at the end of March 2015 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	22,920,110,097	22,920,110,097	0
B. Securities and investment securities	36,737,171,291	38,005,700,000	1,268,528,709
C. Accounts payable	(3,053,474,842)	(3,053,474,842)	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	36,737,171,291	38,005,700,000	1,268,528,709
Bonds with current prices not exceeding balance sheet amount	0	0	0
Total	36,737,171,291	38,005,700,000	1,268,528,709

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	1,000,000,000	3,200,000,000	7,200,000,000	0
Government-guaranteed bonds	0	4,600,000,000	12,300,000,000	0
Local government bonds	2,500,000,000	0	0	0
Corporate bonds	0	2,000,000,000	0	0
FILP agency bonds	500,000,000	3,300,000,000	0	0
Bonds issued by agency under a special act		0	0	0
Total	4,000,000,000	13,100,000,000	19,500,000,000	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: 70,024,512 yen

(3) Estimated amount of non-allowance retirement benefits

Estimated amount of retirement benefits to be covered by the administrative subsidies: 64,381,558 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.

(6) The amount of 1,015,346,126 yen of provision shortfall due to miscalculation of liability reserves in previous fiscal years was calculated as an extraordinary loss.

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: 22,920,110,097 yen

End-of-term balance of funds: 22,920,110,097 yen

4. Notes for government service implementation cost statements

The estimated increased amount of non-allowance retirement benefits includes 66,505,100 yen for executives and regular employees temporally transferred 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, 2015
[1] Retirement benefit obligations	1,575,538,051
[2] Unrecognized actuarial difference	224,403,821
[3] Allowance for retirement benefits ([1] + [2])	1,799,941,872

(3) Items related to retirement benefits expenses

(Unit: yen)

Classification	April 1, 2014 - March 31, 2015
[1] Service expenses	250,206,648
[2] Interest expenses	15,972,635
[3] Amortization expenses for actuarial difference	△9,434,006
[4] Retirement benefits expenses ([1] + [2] + [3])	256,745,277

(Note) As burdens of retirement benefits expenses for workers temporally transferred from other institution, [1] 4,327,183 yen for service expenses and [2] 323,678 yen for interest expenses were allocated.

(4) Items related to the basis for calculation of retirement benefit obligations, etc.

Classification	As of March 31, 2015
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

There are no corresponding events.

IV. Important Subsequent Events

There are no corresponding events.

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