THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2012

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I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

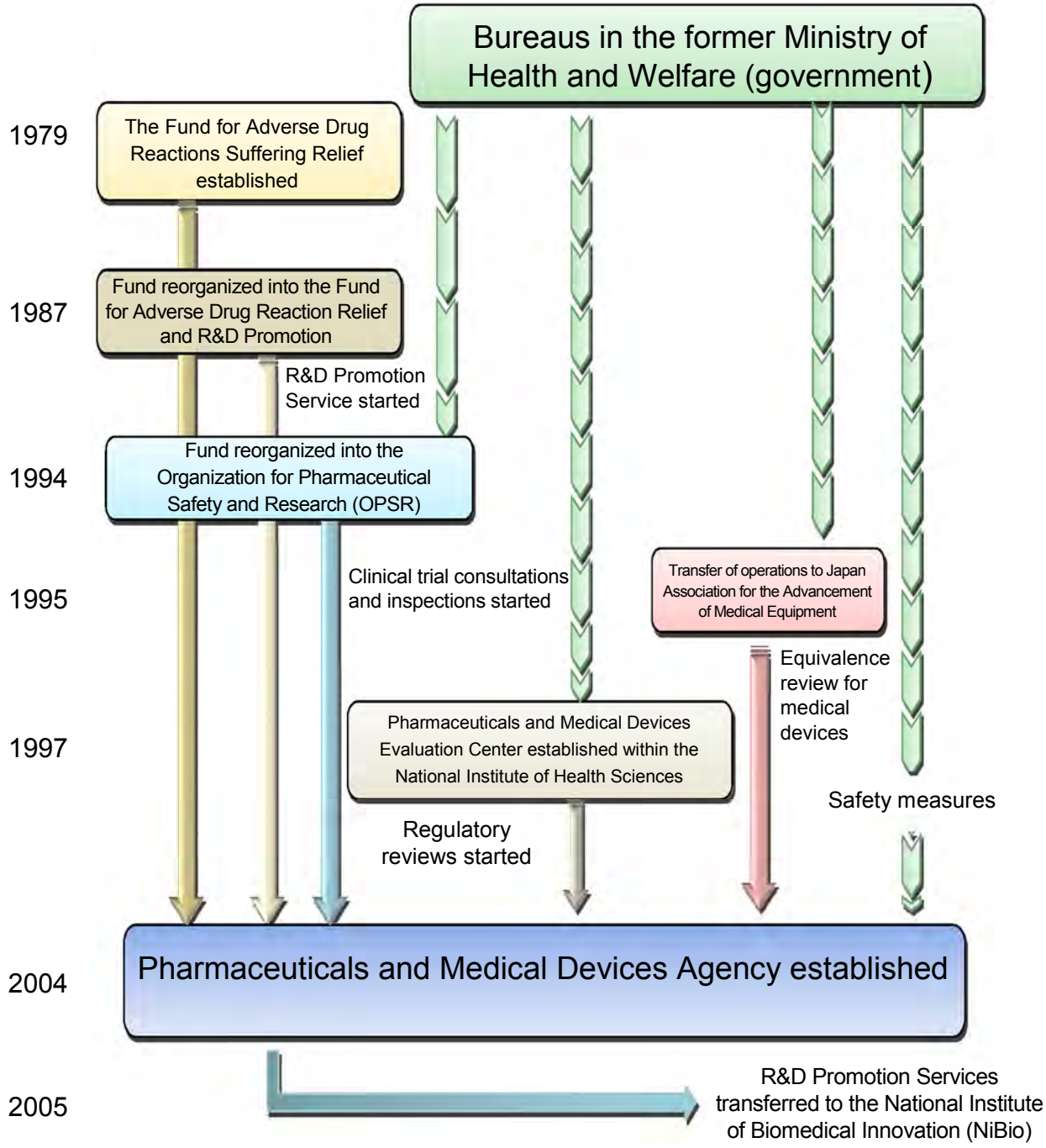
PART 1 History and Objective of PMDA

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

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

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

History of PMDA



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 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 (Act No. 2 of 2008) (Specified Relief Service).
- PMDA is also commissioned by the government and pharmaceutical companies to provide healthcare allowances and nursing care expenses to SMON patients (Service for Healthcare Allowances). In addition, PMDA works under the commission of the Yu-ai Welfare Foundation to make payments for healthcare expenses for HIV-positive and AIDS patients (Service for Healthcare Allowances).

2.2. Reviews

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

2.3. Safety Measures

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

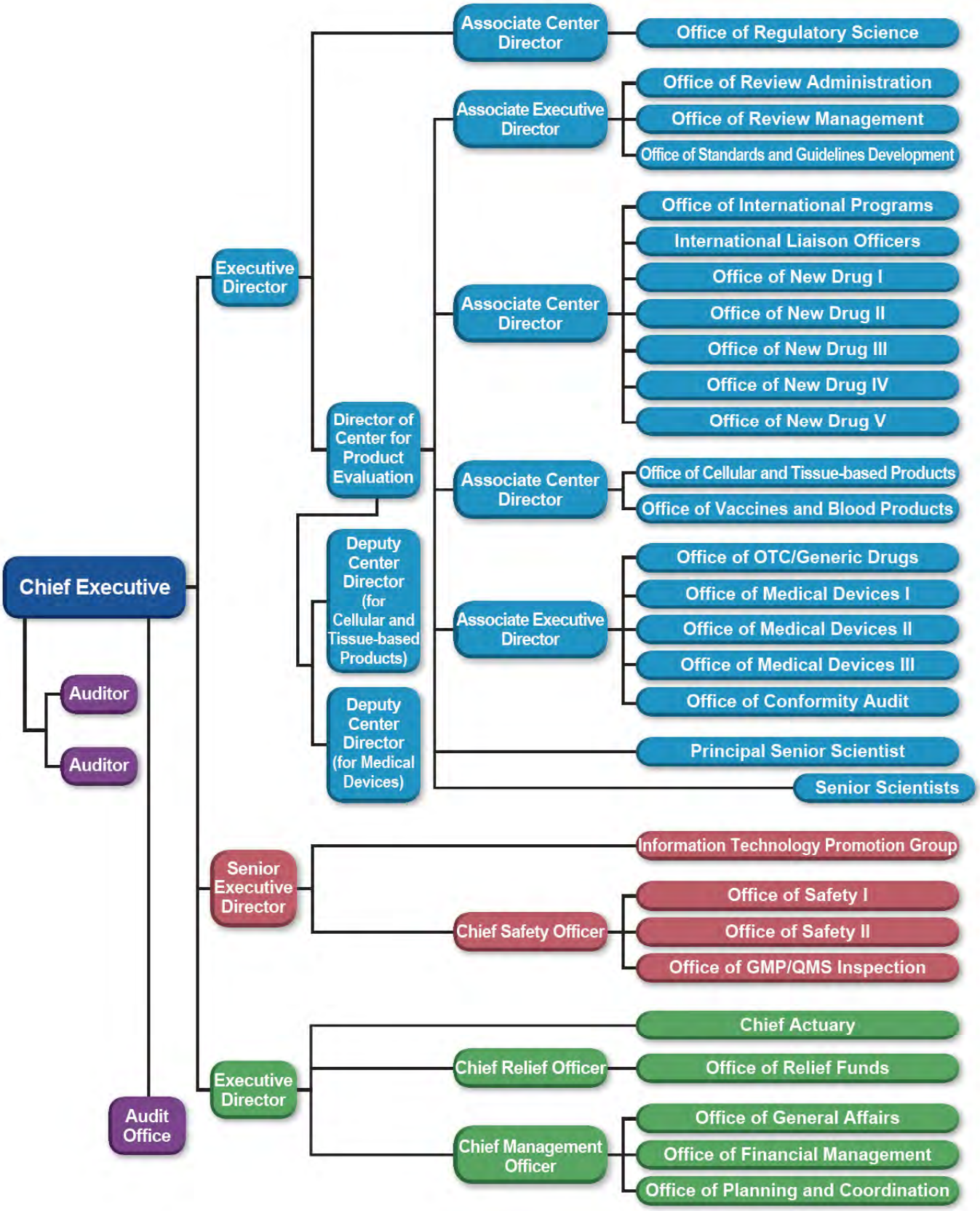
(i) Centrally collecting and organizing information on the post-marketing safety of drugs and medical devices from a broad range of sources, such as reports from companies, information from medical institutions, information from foreign regulatory agencies, and reports presented at academic conferences,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

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

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

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

[Structure of PMDA (as of March 31, 2013)]



II. OPERATING PERFORMANCE FOR FY 2012

PART 1 Development of Fiscal Year 2012 Plan

1.1. Development and Implementation of Fiscal Year 2012 Plan

- PMDA is required to develop the Mid-term Plan in accordance with the Mid-term Targets designated by the Minister of Health, Labour and Welfare, and to obtain the Minister's approval for the plan (effective period of the Second Mid-term Targets: April 2009 to March 2014). In order to achieve the Mid-term Plan, PMDA is required to develop a plan on its management of operations for each fiscal year (fiscal year plan), submit these plans to the Minister, and announce these plans to the public.
- Also for FY 2012, the fiscal year plan was developed at the end of FY 2011 based on the Second Mid-term Targets and Mid-term Plan, the results of the evaluation on operating performance for FY 2011 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 2011

- It is stipulated that each ministry in charge of an incorporated administrative agency should establish an "Evaluation Committee for Incorporated Administrative Agencies" to conduct administrative processing relating to the agencies under its control. (Article 12 of the Act on General Rules for Incorporated Administrative Agencies [Act No. 103 of 1999])
- On August 31, 2012, PMDA received the "Results of the Evaluation on Operating Performance for FY 2011" 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 the following two evaluation items for its reviews and related services: "cost control efforts" and "expeditious operation and improvement of the system (drugs)" and "A" ratings for 16 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 2011" was released on the PMDA website, and was also reported at the Advisory Council Meeting held on November 2, 2012.

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 2010 Performance	FY 2011 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 goal-oriented 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 from 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 if applicable				
Part 6	Use of surplus funds				
Part 7	Other operational matters specified by a ministerial ordinance of the competent ministry				
	(1) Personnel matters	18	Personnel matters and establishment of security	A	A
	(2) Ensuring security				

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

- The results of the evaluation conducted by the Evaluation Committee for Incorporated Administrative Agencies of MHLW was reviewed by the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of MIC, which submitted its conclusions as of January 21, 2013, highlighting the following issues concerning the evaluation results for PMDA:

Opinion from the Commission of MIC on the results of the evaluation for FY 2011

- For approval application reviews of medical devices, the goal of the total review time including the applicant's time being shortened sequentially from FY 2009 was set up in the Mid-term Plan to resolve device lags.

  As the opinion for fiscal year 2009, the Commission pointed out to the Committee of MHLW as follows: "In the case of non-achievement of targets, PMDA should analyze the factors leading to the non-achievement and clearly present improvement measures, and then PMDA's efforts should be strictly evaluated."

  However, the actual applicant's time in review time for improved medical devices (with clinical data) was 7.2 months versus 6 months in the FY 2011 plan, and similarly, the actual applicant's time in review time for generic medical devices was 2.3 months versus 1 month in the FY 2011 plan, showing lower levels than those in the plan; but the factors leading to the non-achievement are not analyzed and improvement measures are not clearly presented in the operating performance report, and the Committee of MHLW has not mentioned this matter.

  In future evaluations, the Committee of MHLW should assess the achievement of targets for not only the total review time but also the applicant's time and the regulatory review time. When the actual levels are below the planned levels, the MHLW Committee should strictly evaluate PMDA's efforts based on the results of factor analysis conducted and improvement measures proposed by PMDA.

1.3. Trends in Review of System/Organization of Incorporated Administrative Agencies

- The "Basic Policy for Review of System/Organization of Incorporated Administrative Agencies" was adopted by the Cabinet on January 20, 2012. However, in the "Basic Policy for Budgeting for FY 2013 adopted by the Cabinet on January 24, 2013", it was decided that work on the items determined before the policy for FY 2013 would be suspended for the meantime and that budgets for FY 2013 should be organized based on the existing system/organization and the reform of system/organization of incorporated administrative agencies should continuously be the subject of consideration.

* Basic Policy for Review of System/Organization of Incorporated Administrative Agencies (adopted by the Cabinet on January 20, 2012) [excerpt]

- The necessary measures to implement this reform shall be taken toward the shift to the new system and organization in April 2014.
  [Pharmaceuticals and Medical Devices Agency (PMDA)]
  - ○ PMDA shall be an agency established based on a specific governing law.
  - ○ Reviews of drugs, etc. performed by PMDA are related to the life and safety of Japanese citizens and the competent minister is immediately responsible for the review results. For these reasons, the government's regulatory powers shall be appropriately placed and the involvement of the government shall be enhanced. In addition, taking into account these characteristics of the activities, the governance of PMDA shall be stricter compared to that of other similar agencies from the viewpoint of securing its neutrality/impartiality.
  - ○ The specific way of the system will be discussed to respond to the following issues pointed out in the results of budget screening, the "New Growth Strategies" (adopted by the Cabinet on June 18,

2010) and other government policies: strategic securing of human resources to resolve drug lags and device lags, drastic reform of the governance of PMDA, including the position of personnel seconded from the central government, proactive disclosure of information to secure transparency and accountability, introduction of a thorough agency evaluation system based on external viewpoints, and minimization of national burden.

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

2.1. Efficient and Flexible Management of Operations

2.1.(1) Operation through target management

- In managing operations, PMDA clarifies the objectives and responsibilities of operations for each department, and strives to identify and resolve problems through managing its operational progress on a daily basis.
- In conjunction with the development of PMDA's annual plan for FY 2012, each office and division formulated their operating plans for the duties and responsibilities. PMDA has operated through management of the targets set in the operating plans.
- In order to enhance the overall performance of PMDA by using the plan-do-check-act (PDCA) cycle, in November 2012, PMDA executives conducted hearings with office directors about the status of operations up to half way through the fiscal year as an opportunity for the executives to comprehend the current situations and challenges at respective offices.

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

- PMDA intends to reinforce its function of policy 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, consecutively from FY 2011, PMDA has been establishing opportunities for the Chief Executive to directly comprehend the operational progress and provide necessary instructions, and has also been reinforcing internal communication and coordination on its overall operations.

  Specifically, PMDA has regularly (once a week in principle) held "Board of Directors meetings", attended by the Chief Executive, executives and office directors. In addition, to reinforce communication and coordination with the Pharmaceutical and Food Safety Bureau (PFSB), MHLW, a luncheon meeting was held between the Chief Executive and the Head of the PFSB for discussion of the latest issues and topics.
- "Meetings of the Headquarters of Information Systems Management" (headed by the Chief Executive) established with the aim of further reinforcing the structure of PMDA's information system management were held. At the meetings, the "Optimization Plan for Operations and Systems" was revised in accordance with the actual status of PMDA's operations. In addition, several meetings of the "Committee on Investment in Information Systems," which is the subcommittee of the Headquarters, were held to assess the necessity, cost-effectiveness, technical difficulties, etc., of the new system development and the modification of existing operational systems from a comprehensive viewpoint, and then select systematic and efficient investment options (three meetings were held during FY 2012).
- In order to maintain sound financial performance and adequate operations, the "Financial Management Committee," headed by the Chief Executive, has been holding regular meetings (12 meetings in FY 2012), during which reports were made on the monthly filing status and monthly cash flow analysis regarding review-related user fees by division, and the declared amount of contributions.
- In March 2013, a "Meeting to Hear from Employees" was held, and policies to deal with opinions,

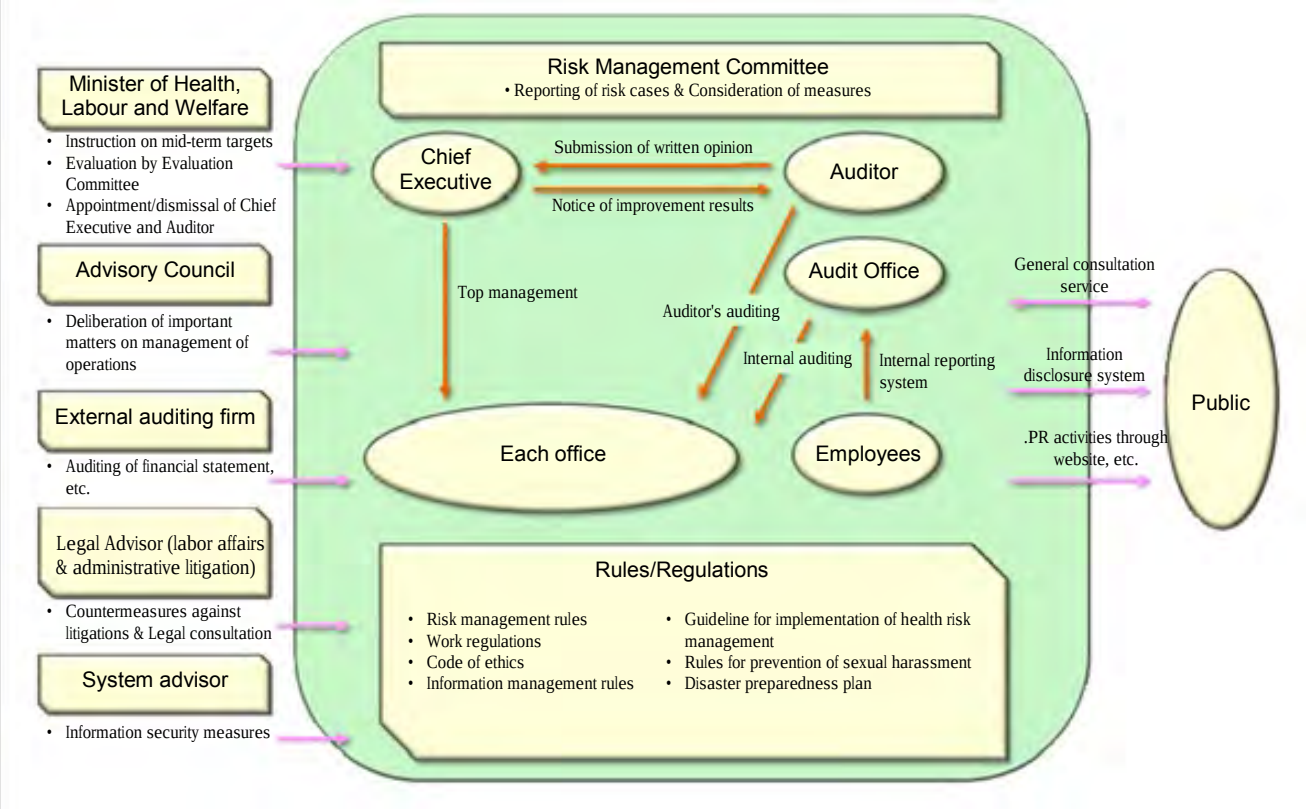
requests, etc. from employees of each department/division were examined.

- PMDA convened two opinion exchange sessions on new drugs (July 2012 and January 2013) and two opinion exchange sessions on drug safety (July 2012 and January 2013) with the pharmaceutical industry.

  Also, regarding medical devices and in vitro diagnostics, PMDA helped the MHLW to hold the regular opinion exchange forum on regulatory affairs for medical devices (July 2012) and to manage and hold the Action Program Review Committee's meetings (July and December 2012).

- 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.

Risk Management System at PMDA



Note: 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 respond to 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 subject to clinical trials)

- To systematically promote PR activities as a whole during the effective period of the Second Mid-term Targets in consideration of the needs of the public and international perspectives, PMDA developed the "PMDA Public Relations Strategic Plan" (July 11, 2008) as a basic policy for its overall PR activities. The Agency is striving to proactively provide information in line with the strategic plan.
- Based on the "PMDA International Strategic Plan" developed in 2009 as a basic policy for its overall international activities, and the "PMDA International Vision" developed in 2011 that provides a concrete goal to be attained, PMDA are conducting proactive international activities such as reinforcing collaborations with Western and Asian countries, participating and contributing to international harmonization, and providing information to foreign countries. In addition, PMDA established the International Strategy Meeting for the purpose of increasing PMDA's presence in the international community with the effort of its executives and staff. In the Meeting, international topics are reported and discussed, including the progress status of the international vision roadmap and its position for discussions to be made in main international conferences.
- In FY 2012, PMDA started four designated research projects taking into account the results of examinations at the Regulatory Science Research Evaluation Committee, etc., based on the "Basic Concept on Regulatory Science in PMDA" (developed in October 2011) from the viewpoint of proactively promoting regulatory science research and making use of its outcomes for PMDA's operations.
- To reinforce the system for the offices of biologics, PMDA reorganized the offices of biologics to the Office of Cellular and Tissue-based Products and the Office of Vaccines and Blood Products, and also established the Liaison Meeting on Cellular and Tissue-based Products. (October 2012)

2.1.(3) Advisory Council meetings

- To create opportunities for exchange of opinions between knowledgeable persons of diverse fields, PMDA holds meetings of the "Advisory Council" (chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University), which are open to the public. The Council consists of academic experts, healthcare professionals, representatives from relevant industries, consumer representatives, and representatives of people who have suffered from adverse health effects caused by drugs, etc. By seeking opinions on operations and the management system, the Council serves to secure fairness and transparency of PMDA's operations, in addition to contributing to streamlining the efficiency of its operations. Under the "Advisory Council", the "Committee on Relief Services" (chaired by Hideaki Mizoguchi, Professor Emeritus, Tokyo Women's Medical University) and the "Committee on Review and Safety Operations" (chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University) were also formed to discuss specialized operational issues. The dates of the meetings and specific agenda for FY 2012 are as follows.

[Advisory Council] (FY 2012)

Agenda for the 1st Meeting (June 21, 2012)

(1) Annual Report FY 2011
(2) Financial Report FY 2011
(3) Improvement/reinforcement of the review system responding to medical innovation
(4) Trial implementation of adverse drug reaction reporting by patients
(5) Report on the 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 2, 2012)

(1) Selection of the Chairperson and appointment of the Acting Chairperson
(2) Status of the Science Board and the Subcommittees meetings
(3) Recent main efforts
(4) Results of the evaluation of operating performance for FY 2011 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(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 3rd Meeting (March 18, 2013)

(1) Fiscal year 2013 plan (draft)
(2) Budget for FY 2013 (draft)
(3) Extension of interim measures for restrictions on employment of personnel from the private sector
(4) Recent main efforts
(5) Status of PMDA's responses to opinions given by members at the Advisory Council meetings for the past one year
(6) Employment status of personnel from the private sector
(7) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(8) Others

[Committee on Relief Services] (FY 2012)

Agenda for the 1st Meeting (June 20, 2012)

(1) Annual Report FY 2011
(2) Fiscal year 2012 plan
(3) Others

Agenda for the 2nd Meeting (December 12, 2012)

(1) Selection of the Chairperson and Acting Chairperson
(2) Results of the evaluation of operating performance for FY 2011 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(3) Operating performance by the end of October 2012
(4) Rate of contributions for the adverse drug reaction fund for FY 2013 and later
(5) Others

[Committee on Review and Safety Operations] (FY 2012)

Agenda for the 1st Meeting (June 21, 2012)

(1) Annual Report FY 2011
(2) Financial Report FY 2011
(3) Improvement/reinforcement of the review system responding to medical innovation
(4) Trial implementation of adverse drug reaction reporting by patients
(5) Report on the 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 26, 2012)

(1) Selection of the Chairperson and appointment of the Acting Chairperson
(2) Operating performance by the end of October 2012 and issues to be addressed hereafter
(3) Results of the evaluation of operating performance for FY 2011 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(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 meeting minutes and materials were publicly released on the PMDA website.
  Note: Information on the Advisory Council is available at:
  http://www.pmda.go.jp/guide/hyogikaikankei.html

2.1.(4) Holding of Science Board meetings

- The Science Board was established in May 2012 as an external body to deliberate scientific aspects of drugs and medical devices reviews in order to ensure more appropriate responses to the products using advanced science and technologies as well as to advance regulatory science, and reinforce collaborations and communications with academia and medical professionals in line with the future promotion of health care innovation. Members are external experts in areas including medicine, dentistry, pharmacy and industry, and the board consists of "Science Board (parent committee)" and its subsidiary organizations, "Pharmaceuticals Subcommittee," "Medical Devices Subcommittee," "Bio-products Subcommittee," and "Cellular and Tissue-based Products Subcommittee." Materials relating to individual products may be used for discussion, and therefore meetings are closed to the public. The number of meetings and members in FY 2012 (as of March 31, 2013) were as follows:

  1) The Science Board (parent committee), consisting of 17 members, had three meetings.
  2) The Pharmaceuticals Subcommittee, consisting of 13 members, had three meetings (jointly with the Bio-products Subcommittee).
  3) The Medical Devices Subcommittee, consisting of 17 members, had three meetings.
  4) The Bio-products Subcommittee, consisting of 11 members, had three meetings (jointly with the Pharmaceuticals Subcommittee).
  5) The Cellular and Tissue-based Products Subcommittee, consisting of 14 members, had four meetings.

- The meeting minutes and materials were publicly released on the PMDA website.
  Operations relating to the Science Board: http://www.pmda.go.jp/guide/kagakuiinkaikankei.html

2.1.(5) Approaches for an efficient operation system

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

  PMDA has continuously invited commissioned external experts to seek their professional opinions relating to scientifically significant matters at Expert Discussions on reviews and safety measures. (1,165 external experts are commissioned as of March 31, 2013)
- 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. (118 external experts are commissioned as of March 31, 2013)
- The list of the commissioned external experts is available on the PMDA website.
- Based on the need to secure impartiality and transparency of judgment given by external experts, PMDA developed the "Rules for Convening Expert Discussions etc. by the Pharmaceuticals and Medical Devices Agency" (December 25, 2008) as rules for conflict of interest. The establishment of these rules enables PMDA to ensure the transparency by releasing review reports and information on conflict of interest of commissioned external experts, and also allows outside parties to check the decision making process. Reports on cash contributions and contract money received by external experts are made 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 in order to handle operations that require legal and tax expertise. In addition, the Agency 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 person with an academic background as the special adviser to the Chief Executive, to seek strategic and operational advice on issues in particular areas.
- PMDA has continued to appoint a person who has advanced professional expertise regarding information systems and knowledge of pharmaceutical affairs as an information system advisor, in order to ensure consistency and coordination of operations relating to the Agency's information systems.

2.1.(6) Standardization of operating procedures

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

2.1.(7) Development of databases

- In FY 2012, meetings of the "Committee on Investment in Information Systems," etc., were held to discuss the status of each information system, upgrading of the shared LAN system that serves as the common infrastructure system, and improvements in the security of the e-mail system, thereby

taking effective measures.

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

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

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

- Based on the "Plan for the Development of e-Government" (decided at the Liaison Meeting of the Chief Information Officers [CIO] of the Ministries and Agencies held on July 17, 2003) and the "Measures for the Realization of Optimal Operations/Systems at Incorporated Administrative Agencies" (decided at the Liaison Meeting of the CIOs of the Ministries and Agencies held on June 29, 2005), PMDA developed and publicized the Optimization Plan for Operations and Systems on March 28, 2008. PMDA publicized the 3rd revised version of the Optimization Plan in June 2012 and carried out tasks for building appropriate systems for PMDA operations based on this Plan.

  In FY 2012, PMDA decided to design and develop a review integration system, build information systems and upgrade existing systems for safety measure operations and the relief services, and optimize the system for management division's operations. For that purpose, the Agency created requirement definitions and conducted research and reviews to reinforce the information management and IT control of PMDA as a whole. It is planned that the system upgrade, etc. will be carried out in line with the deliverables.

2.2. Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general and administrative expense

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

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

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

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

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

- In FY 2012, in order to pursue more efficient operations within the annual budget, PMDA promoted general competitive bidding based on the Plan for the Review of Optional Contracts, etc., which was developed in April 2010. As with the previous year, PMDA conducted procurement activities through general competitive bidding for leasing of personal computers and purchase of office furniture resulting from the increase of employees, as well as purchase of expendables such as copy paper, thereby reducing procurement costs.

  Consequently, PMDA successfully reduced general and administrative expenses by 8.6% of its budget size which was subject to more efficient budget control, even excluding the unused budget amounts due to non-achievement of the target number of new employees.

2.2.(2) Cost control of operating expenses

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

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

  2) Operating expenses incurred starting in FY 2009, FY 2010, FY 2011, and FY 2012 with efforts to speed up medical device application reviews based on the "Action Program to Accelerate Reviews of Medical Devices"

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

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

appropriately operating within the allocated budget.

- In FY 2012, PMDA promoted general competitive bidding in relation to operating expenses, as with the case of general and administrative expenses, based on the "Plan for the Review of Optional Contracts, etc." In the meantime, PMDA steadily managed the operations and strived to reduce costs while securing necessary operations, taking account of the trends for income as user fees and contributions, which are the financial sources of operations.

  Consequently, PMDA successfully reduced operating expenses by 10.2% of its budget size which was subject to more efficient budget control, even excluding the unused budget amounts due to non-achievement of the target number of new employees.

2.2.(3) Competitive bidding

- PMDA promoted bidding for all contracts based on the "Plan for the Review of Optional Contracts, etc."

	FY 2011	FY 2012	Change
General competitive bidding (including competitive request for proposals and invitation to bids)	115 bids (81.6%) 4,892 million yen (76.0%)	123 bids (82.6%) 2,748 million yen (62.9%)	8 bids (1.0%) -2,144 million yen (13.1%)
Non-competitive optional contracts	26 bids (18.4%) 1,546 million yen (24.0%)	26 bids (17.5%) 1,622 million yen (37.1%)	±0 bids (-0.9%) 76 million yen (13.1%)
Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	10 bids (7.1%) 94 million yen (1.5%)	10 bids (6.7%) 51 million yen (1.2%)	±0 bids (-0.4%) -43 million yen (-0.3%)
Total	141 bids 6,438 million yen	149 bids 4,369 million yen	8 bids -2,069 million yen

2.2.(4) Contract Review Committee meetings

- Based on "Inspection/Review of the Contract Status of Incorporated Administrative Agencies" (adopted by the Cabinet on November 17, 2009), PMDA established the "Contract Review Committee" in the Agency. The Committee consists of external knowledgeable experts as well as internal auditors. In the Committee meeting, PMDA underwent a pre-inspection of procurement cases, etc., for which conclusion of a contract is planned in FY 2012, regarding the appropriateness of contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 5 meetings in FY 2012 and disclosed the summary of review on the website.

2.2.(5) Collection and management of contributions

- Contributions from marketing authorization holders of the industry enable PMDA to secure 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 marketing authorization holders of approved drugs, contributions to the relief fund for infections acquired through biological products ("infection contributions") are declared and made by marketing authorization holders of approved biological products, and contributions to safety measures are declared and made by marketing

authorization holders 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 2012, the collection rates achieved for ADR contributions, infection contributions, and safety measure contributions were 100%, 100%, and 99.8%, respectively.

FY 2012 Contribution Collection Results

Category		Number of parties obligated to make contributions	Number of parties who made contributions	Collection Rate	Contribution amount (Million yen)
ADR contributions	MAHs of drugs	688	688	100%	4,548
	MAHs of pharmacy-compounded drugs	6,186	6,186	100%	6
	Total	6,874	6,874	100%	4,554
Infection contributions	MAHs of approved biological products	92	92	100%	866
Post-marketing safety measures contributions	MAHs of drugs	596	596	100%	1,034
	MAHs of medical devices	2,177	2,163	99.4%	219
	MAHs of drugs/ medical devices	211	211	100%	1,515
	MAHs of pharmacy-compounded drugs	6,186	6,186	100%	6
	Total	9,170	9,156	99.8%	2,774

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.

- 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 marketing authorization holders of pharmacy-compounded drugs.

  2) PMDA continued to make requests for entities to declare and make contributions to safety measures through industry associations and lectures, as well as through advertisements on websites and relevant trade journals. PMDA also created and distributed a "handbook on the procedure for declaring and making contributions" in order to make the procedure known to all the parties obligated to make contributions. Also, written requests for making contributions were sent to all contributors who have not yet made contributions, with the exception of marketing authorization holders of pharmacy-compounded drugs.

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

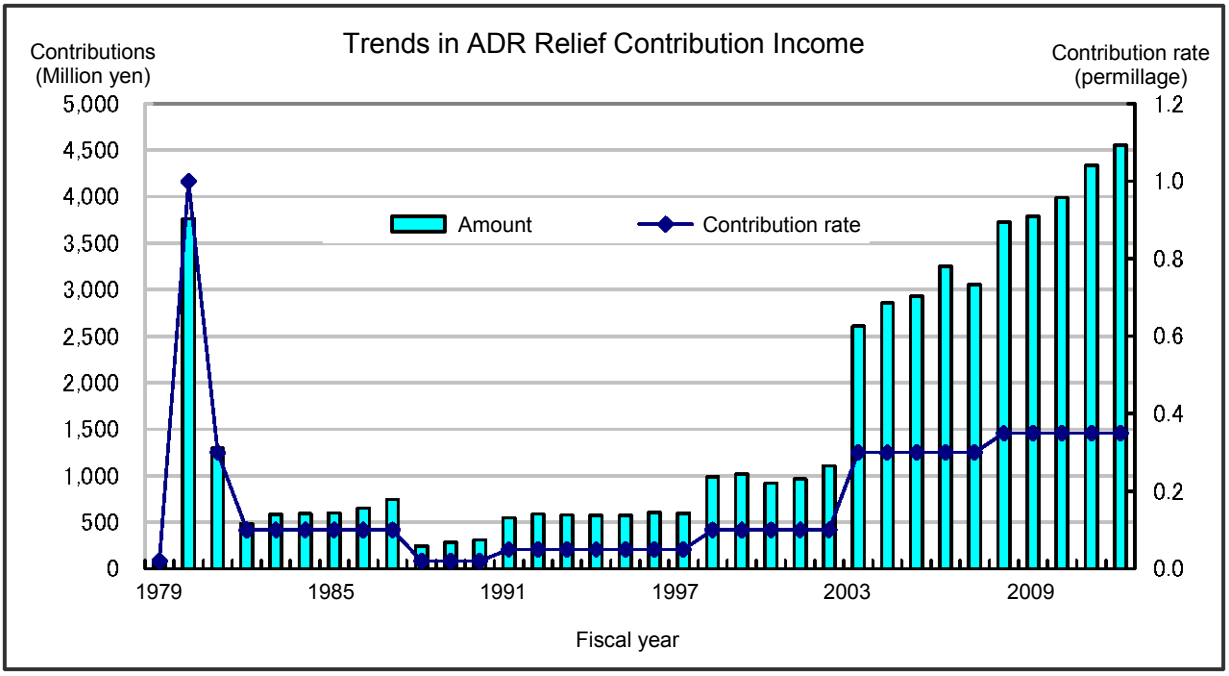
a. ADR contributions

- To fund the relief service for adverse drug reactions, PMDA has collected ADR contributions from marketing authorization holders of approved drugs. In FY 2012, the contribution rate applied to such marketing authorization holders was set at 0.35/1000 and the collected amount was 4,554 million yen.

(Million yen)

Fiscal year	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
MAHs of drugs [Number of MAHs]	3,722 [752]	3,783 [742]	3,984 [716]	4,330 [713]	4,548 [688]
MAHs of pharmacy-compounded drugs [Number of MAHs]	8 [8,015]	8 [7,598]	7 [7,082]	7 [6,694]	6 [6,186]
Total amount	3,730	3,790	3,991	4,337	4,554
Contribution rate	0.35/1000	0.35/1000	0.35/1000	0.35/1000	0.35/1000

- 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

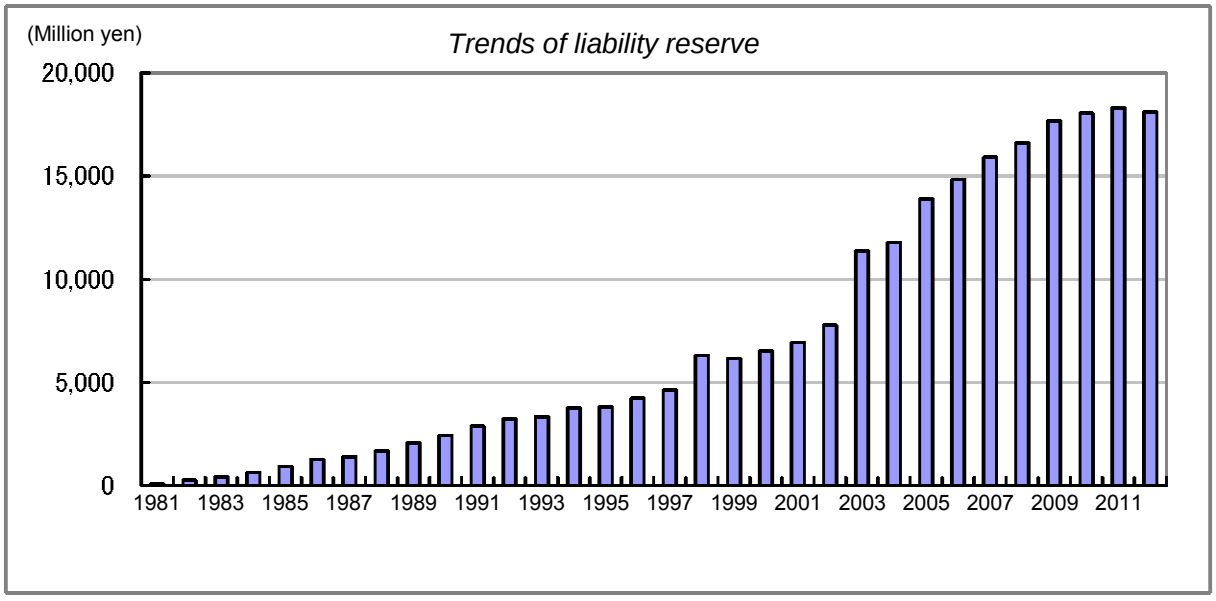
- To fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from marketing authorization holders of approved biological products. In FY 2012, the contribution rate applied to such marketing authorization holders was set at 1/1000 and the collected amount was 866 million yen.

(Million yen)

Fiscal year	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
MAHs of approved biological products [Number of MAHs]	620 [96]	631 [97]	693 [93]	785 [92]	866 [92]
Contribution rate	1/1000	1/1000	1/1000	1/1000	1/1000

c. Liability reserve

- 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 2012 was 18,129 million yen.



(ii) Collected contributions for post-marketing safety measures

- To fund services for improvements in the quality, efficacy, and safety of drugs, etc., PMDA has collected contributions to safety measures from marketing authorization holders of drugs and medical devices. In FY 2012, the contribution rate applied to such marketing authorization holders 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 2,774 million yen.

(Million yen)

Fiscal year	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
MAHs of drugs/ medical devices [Number of MAHs]	1,284 [3,053]	2,354 [3,019]	2,530 [2,922]	2,596 [2,974]	2,768 [2,970]
MAHs of pharmacy-compounded drugs [Number of MAHs]	8 [8,013]	8 [7,594]	7 [7,082]	7 [6,694]	6 [6,186]
Total amount	1,292	2,362	2,537	2,603	2,774
Contribution rate	0.11/1000	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)

2.2.(6) Reduction in personnel expenses, etc.

- The personnel expenses for FY 2012 were reduced by approximately 13.1% (in comparison with personnel expense per person for FY 2005), such as by steadily putting in place the remuneration system that was introduced in April 2007, taking into account the reform of the remuneration structure of national government employees.
- PMDA compared the remuneration system for its staff for FY 2011 with that of national government employees in order to facilitate the public's understanding of its remuneration levels, and released the results on its website.

(thousand yen)

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

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

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

- PMDA steadily carried out the measures stipulated in the plan, "Reinforcement of the efforts to reduce unnecessary expenditures" (March 31, 2011). The plan was first developed in FY 2009 and then revised in FY 2011, taking into account the efforts made in FY 2010.
- Details of cost-cutting in these measures were thoroughly informed to all staff members so that they would make self-starting and proactive efforts to achieve "Cost-cutting targets toward reduction of unnecessary expenditures in PMDA", which was developed at the end of FY 2010. Consequently, some results were achieved. The major results for FY 2012 were a 15% reduction in the duration of overtime work, a 88% reduction in the number of taxi tickets used (a 89% reduction in terms of the monetary amount) and a 27% reduction in utility costs compared to the first year of the efforts (FY 2009).

  * Regarding the utility costs, the electricity cost was increased by 2.46 yen per kwh in April 2012, and if the rise is reflected in the calculation, the cost will be reduced by 32%.

2.3. Improvement of Services to the Public

2.3.(1) General consultation service

- Based on the General Consultation Guidelines that specify how to handle inquiries directed to PMDA and how to make use of comments and opinions to improve 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 operations.
- Among the 2,107 inquiries that PMDA received in FY 2012, 740 or approximately 30% of the total inquiries received were those relating to applications and consultations for drugs and medical devices.

	Inquiry/ consultation	Complaint	Opinion/ request	Others	Total
FY 2012	1,918 (681)	6 (3)	183 (56)	0 (0)	2,107 (740)

Note 1:Numbers in parentheses indicate the cases related to consultations and applications for approval of drugs and 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 and medical devices, separately from this general consultation service.

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

- In addition to responding to consultations and complaints from general consumers, PMDA also handles complaints from relevant companies regarding product reviews and product safety operations.
- In FY 2004, PMDA established a system where, if an applicant files claims of dissatisfaction, etc., regarding product reviews and product safety operations, the responsible office director (the Director of the Center for Product Evaluation or Chief Safety Officer, if claims of dissatisfaction have been filed more than once) is to directly conduct an investigation and respond to the applicant within 15 working days. PMDA continues to operate the system in FY 2012.
- In addition, PMDA developed a consultation manual to handle complaints from relevant companies. From among the complaints received, PMDA is reviewing those that would be helpful in improving its operations.

2.3.(3) Improvement in the PMDA website

- PMDA has prepared and posted on its website the "Annual Report for FY 2011," which discloses the Agency's operating performance for FY 2011.
- In addition, materials and minutes of the Advisory Council meetings and other meetings were also posted on the website smoothly to release the details of the meetings.
- "What's New" and "Topics" links on the top page and existing web content were updated smoothly in accordance with requests made by relevant offices.

2.3.(4) Proactive PR activities

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

  In FY 2012, PMDA created leaflets to introduce PMDA to the general public and distributed them at events in various locations. In addition, PMDA notified patient groups of distribution of leaflets, etc., and provided them to groups that requested.

  For the occasion of "Drug and Health Week," PMDA conducted PR activities by distributing brochures/leaflets on PMDA's services, brochures on relief systems, give-away goods, etc., in cooperation with pharmaceutical associations in 10 prefectures.

  In addition, PMDA's operations were introduced 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., in Japan and overseas (22 times in Japan and 6 times overseas).

2.3.(5) Disclosure request for agency documents

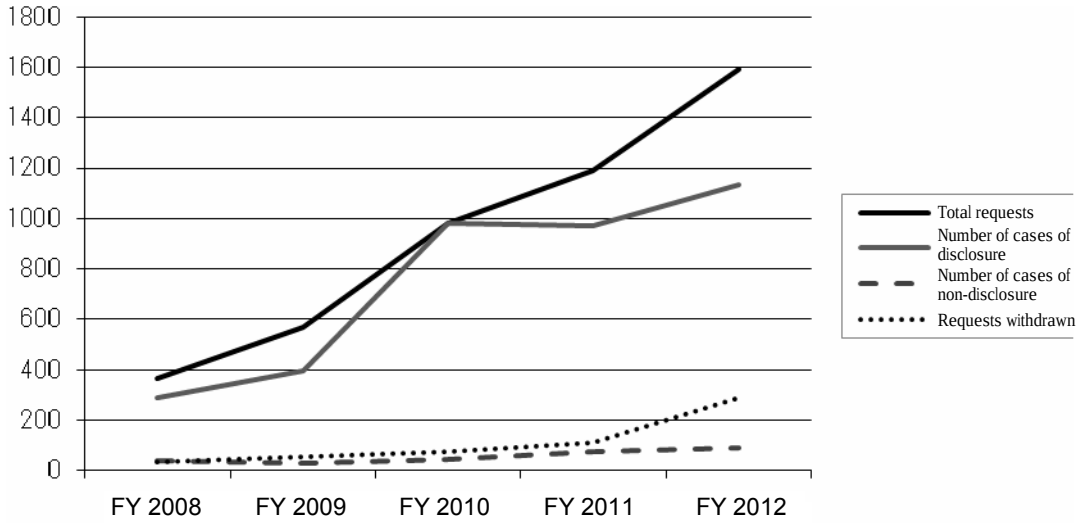
- The status of requests for disclosure of the documents based on the "Act on Access to Information Held by Incorporated Administrative Agencies" is shown below (for the past five years). In FY 2012, the number of requests increased by 33.6% compared to the previous fiscal year. PMDA appropriately processed them in accordance with the relevant laws and regulations.

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

	Total requests	Requests withdrawn	Decisions*					Objections	Carry-over into FY 2013 **
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer about existence/ non-existence of the document		
FY 2008	367	36	14	276	7	29	5	1	0
FY 2009	568	54	27	371	1	31	0	0	0
FY 2010	983	74	150	833	4	40	1	1	0
FY 2011	1192	112	138	831	1	74	0	1	0
FY 2012	1593	287	147	988	0	81	10	5	291

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

** *"Carry-over into FY 2013" 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 about the existence/non-existence of the document.

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

(Unit: Case)

Operational category/FY	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	Examples
Product application review	315	479	902	1046	1410	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post marketing Safety	52	89	78	139	176	ADR reports, etc
Others	0	0	3	7	7	
Total	367	568	983	1192	1593	

Note: The numbers include requests that were withdrawn or were decided not to be disclosed, those for non-existing documents and those for refusals to answer about the existence/non-existence of the document.

2.3.(6) Disclosure request 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	Carry-over into FY 2013
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer about existence/ non-existence of the document		
FY 2008	5	0	0	3	2	0	0	0	0
FY 2009	1	0	0	0	1	0	0	0	0
FY 2010	3	0	0	1	0	1	0	0	0
FY 2011	1	0	0	2	0	0	0	0	0
FY 2012	3	1	0	2	0	0	0	0	0

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 2012, PMDA conducted internal audits on the management status of documents, cash and cash equivalents, goods, information systems, and the status of compliance with rules restricting the work assignment of personnel from the private sector.

2.3.(8) Report on the financial standing

- From the perspective of ensuring the transparency of expenditures, PMDA disclosed its financial standing for FY 2011, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2012 on its website.

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

- Following the inspection/review of optional contracts, etc., PMDA released a report entitled "Follow-up on contract status of FY 2011" on the website in August 2012.

2.4. Personnel Issues

2.4.(1) Personnel evaluation system

- According to the Mid-term Targets, PMDA is required to conduct proper personnel evaluation taking individual performance of employees into consideration. Moreover, in the Second Mid-term Plan, PMDA intends to manage a personnel evaluation system in which the results of the evaluation and the attainment of individual goals are properly reflected in remuneration, pay raises, and promotions, to enhance the morale of employees.
- To this end, PMDA appropriately reflected the results of personnel evaluation during the period from April 2011 to March 2012 in pay raises, etc., as of July 2012. 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.
- The PMDA's personnel evaluation system was introduced and put into effect in April 2007 ahead of the implementation of such a system by the government. As several years have passed since the introduction, PMDA began to review the system in 2011 to make the system better, and continued the review in FY 2012.

2.4.(2) Systematic implementation of staff training

- In the operations for reviews, post-marketing safety measures, and relief service conducted by PMDA, an extremely high level of expertise is required. In addition, rapid strides are constantly being made in the advancement of technology for developing drugs and medical devices.
- Under such circumstances, it is necessary for PMDA to provide more effective capacity building activities to enhance the level of expertise of its staff. Therefore, in FY 2007, PMDA reorganized the existing training courses into two training courses: the "General Training Course" and the "Specialized Training Course." In FY 2012, these structured training courses were continuously provided for employees.

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

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

1) General Training Course

(i) New recruit training conducted between April and May 2012. The major subjects are as follows:
- Operations of each office, related systems/procedures
- Human skills (e.g., business etiquette, communications, motivation)
- Document management, reduction of unnecessary expenditures, etc.

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

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

(iv) In order to improve English communication skills of employees, PMDA enhanced its English training by providing two types of programs: practical business English program and intermediate-level English program. The participants were assigned to either of the programs according to their English proficiency. In addition, a TOEIC examination was conducted as part of efforts to improve the language skills of employees.

(v) E-Learning-based IT literacy training to promote further utilization of electronic documents

(vi) Three training program sessions by inviting lecturers from organizations of adverse drug reaction sufferers and organizations of patients, etc.

(vii) On-site training programs, such as visits to drug or medical device manufacturing facilities (5 facilities) and IRB of medical institutions (including hands-on training, workshops, etc.)

2) Specialized Training Course

(i) Dispatch of a total of 75 employees (60 in Japan, 15 overseas) to universities in Japan and overseas as well as foreign regulatory authorities as dispatch training

(ii) Special training programs mainly addressing technical issues which are provided by experts, etc., invited as lecturers from regulatory authorities, corporations, and universities in Japan or overseas (32 sessions), training programs on laws and regulations including the Pharmaceutical Affairs Act to learn the regulatory system, etc. (1 session), and training programs on clinical study design to learn biostatistics (10 sessions). PMDA also conducted special training programs featuring product development programs at companies and design and management of medical devices.

(iii) Training on case studies and medical writing related to product application reviews mainly for new recruits

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

(v) Medical device training programs were provided with observation of surgery for medical devices such as pacemakers, biological heart valves, and catheters for placing transvascular stents, etc. Product hands-on training using orthopedic medical devices was also provided. For the acquisition of basic knowledge about medical devices, class II ME (Biomedical Engineering) technical training was also given (21 employees).

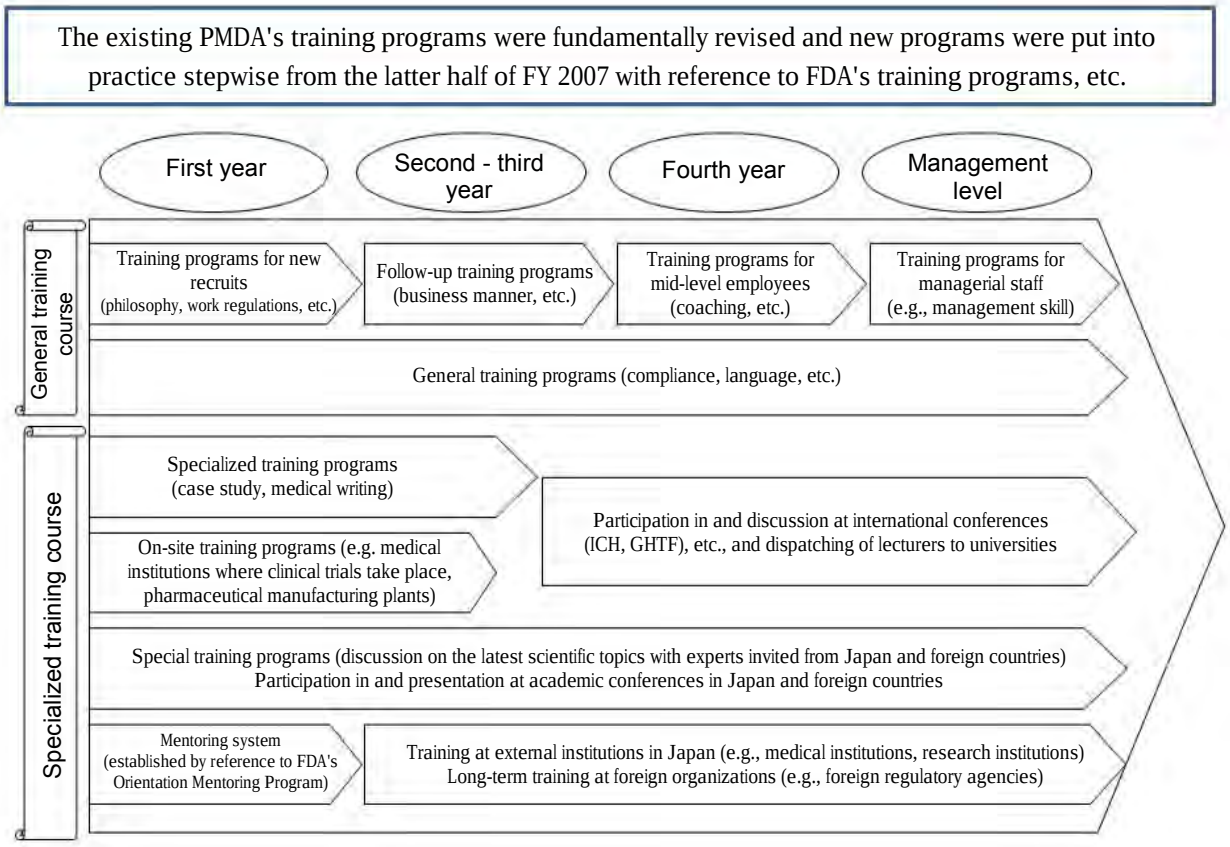
(vi) Five employees were dispatched to one medical institution for practical training with pharmacists conducted at hospitals to learn the clinical practice.

(vii) Dispatch of one employee to an accounting training course provided by the Accounting

Center, Ministry of Finance to improve administrative processing skills. Also, 2 employees attended a grade 2 or 3 bookkeeping course. Logical thinking training and labor management training were conducted for administrative staff members who are on the main career tracks.

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

Training and Human Resource Development



2.4.(3) Appropriate personnel allocation

- To maintain the expertise of the staff members and operational continuity, PMDA aims to conduct appropriate personnel allocation. To achieve this target, PMDA conducted personnel allocation taking the knowledge and work experience of staff members into consideration. PMDA conducts mid-and-long-term rotation of personnel with the exception of cases such as health-related issues and special reasons related to operations.
- Also in FY 2012, personnel change and career progression were implemented in line with the basic policies for the PMDA Career Paths that were developed in March 2011.
- For technical employees, a high-level position among specialists was considered, and the position of "Principal Senior Scientist" was set up on April 1, 2012.
- To improve and strengthen operations of the Center for Product Evaluation, the Director of the Center for Product Evaluation, which the executive director responsible for product reviews, etc., had been concurrently serving as, was newly employed and made full time on June 1, 2012. In addition, to strengthen the system for approval application reviews and collaborate with academia, new posts for deputy directors of the Center for Product Evaluation were set up each for the area

of cellular and tissue-based products and the area of medical devices, and one person each was employed on June 1, 2012.

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 fairness of PMDA, in order to conduct its operation of reviews and post-marketing safety measures promptly and accurately.
- In the Second Mid-term Plan, in accordance with the recommendations of the Council for Science and Technology Policy, the Action Program to Accelerate Reviews of Medical Devices, and the proposals by the Committee for Investigation of Drug-induced Hepatitis Cases, the target number of regular employees at the end of the period (at the end of FY 2013) is set to be 751. PMDA is required to recruit capable people 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 3 times in FY 2012 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2012 *(as of April 1, 2013)*

1)	Technical employees (3 public recruitments)	
	Number of applicants	519
	Number of employments	42
	Number of prospective employees	2
2)	Administrative employees (2 public recruitments)	
	Number of applicants	206
	Number of employments	10

FY 2012 Recruitment Activities

- PMDA information sessions
  - February: Two sessions in Tokyo and one session each in Osaka, Sendai, and Fukuoka (total: 290 participants)
  - May to June: Two sessions in Tokyo and one session in Osaka (total: 178 participants)
  - September: Two sessions in Tokyo and one session in Osaka (total: 94 participants)
- Activities performed in collaboration with directors/employees
  - Lectures on and explanation of the services at universities, etc., by directors/ employees
  - Students' visits to the university's young alumni working at PMDA
- 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
  - Website presenting job offers for new graduates in 2014 ("NIKKEI NAVI 2014," "My NAVI 2014," "RIKUNABI 2014")
  - Total number of distributed direct mails: 117,656
- Recruitment advertising via academic journals
  - "Japan Medical Journal," "Proceedings of Lectures at the Annual Meetings of the Japanese Federation of Statistical Science Associations," and "Computational Statistics Seminar Textbook"

Numbers of Executives and Regular Employees

	April 1, 2009	April 1, 2010	April 1, 2011	April 1, 2012	April 1, 2013	At the end of the effective period for the Second Mid-term Plan (end of FY 2013)
Total	521	605	648	678	708	751
Review Department	350	389	415	438	460	
Safety Department	82	123	133	136	140	
Relief Department	32	34	34	33	33	

Note 1:The "Total" includes 6 executives (including one part-time auditor).

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

Note 3:The Safety Department consists of the Chief Safety Officer, Offices of Safety I and II, and Office of GMP/QMS Inspection (formerly Office of Compliance and Standards).

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.
- Meanwhile, restrictions were placed on re-employment at profit-making companies for 2 years after resignation from PMDA. However, making use of the knowledge and experience gained through PMDA's operations in companies will contribute to the improvement of the efficacy and safety of drugs and medical devices. Also, persons with work experience in the regulatory authority, when joining in companies, are expected to contribute to corporate compliance; and therefore the work regulations on re-employment at profit-making companies began to be reviewed in June 2012 to improve the fluidity of human resources.
- 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.

- For specially appointed experts accepted from universities, research institutes, etc., with the implementation of "Initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products," a handbook which briefly summarizes services and ethics in PMDA was made and distributed, and training sessions were provided to all specially appointed experts.

2.5. Ensuring Security

2.5.(1) Entry/exit access control

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

  In May 2010, in order to reinforce security, PMDA set up non-stop floors at which elevators do not stop unless the user (PMDA executives and employees, etc.) has the appropriate ID card.
- In order to ensure further strict access control, PMDA has also prescribed rules on 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 2012 plan, PMDA strived to maintain and improve the security of information in the 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	56	653
Within PMDA		1,063

Note: The numbers of registered companies and issued certificates as of the end of March 2013

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

3.1. Relief Services for Adverse Health Effects

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

3.1.(1) Expansion and reconsideration of the provision of information

(i) Online disclosure of cases of payment of benefits

- PMDA has promptly posted its decision on approval/rejection of adverse reaction relief benefits on its website with due consideration to protecting personal information. Since February 2010, PMDA has posted approved/rejected cases on its website every month, following the decision.
  In December 2012, PMDA started to provide the information through its email service called "PMDA medi-navi" together with posting information on the website.
  Information on cases of approval/rejection is available at:
  http://www.pmda.go.jp/kenkouhigai/help/information2.html
- Based on relevant information obtained from claims submitted for relief benefits, PMDA calls users' attention to the cases of health damage which have repeatedly occurred although precautions have already been provided in package inserts. The information was described in the "PMDA Request for Proper Use of Drugs" posted on the Medical Product Information web page and also provided through "PMDA medi-navi" to further promote the proper use of drug products.
- To make the "Information on decision on payment/non-payment of adverse reaction relief benefits" web page and the "Medical Product Information" web page, which provides information on package inserts, adverse drug reactions/medical device malfunctions, recalls, application reviews, etc., accessible to each other, banners have been placed on the top page of both websites.
- For the purpose of improving safety measures for drugs, such as understanding the trend in occurrence of adverse drug reactions, PMDA started to collect reports on adverse drug reactions from patients via the Internet on March 26, 2012, on a trial basis. A new link was set up to enable access from the web page of the "Patient's Report for Adverse Drug Reactions" to the web page of "Relief System for Adverse Health Effects."
- From the viewpoint of making the administration of the system more transparent, PMDA released the operating performance until the end of October FY 2012 on its website.
- At the meeting of the Committee on Relief Services held on December 12, 2012, PMDA reported on the efforts of medical institutions to promote the use of the Relief System for Sufferers from Adverse Drug Reactions and release the report on the website.

(ii) Improvement of brochures, etc.

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

a) For the general public, a catch-phrase "for You Just in Case" was created for use in leaflets, etc. The catch phrase is used to promote PR to remind of the Relief System in case any health damage occurs, thereby increasing familiarity to the system.

The brochure for healthcare professionals was updated and its catch-phrase was modified to "Know it better than anyone and pass along." The information on deision on approval/rejection and voices of users of the system are included to enrich the contents.

In addition, an electronic file (PDF format) of the same brochure was posted on the website to improve the convenience for users.

b) PMDA has improved the instructions for doctors to fill in the drug administrations and diagnoses on certificates of prescription and medical certificates more easily. In FY 2012, the instructions for certificates of prescription to patients with blood cell disorders were newly created. In addition, the instructions for medical certificates of patients with respiratory disorders were also created as the “other disorders” category among the instructions for medical certificates for claiming disability pensions/pensions for raising handicapped children.

These revised instructions were posted on the website.

c) PMDA made efforts to improve the convenience for users by publicizing the fact that claim forms can be downloaded from its website.

Claim forms are available at: http://search.pmda.go.jp/fukusayo_dl/

d) The guidance for claims and the checklists for claimants were revised to reduce the claimants’ burden. The revised guidance and checklists intelligibly indicate how to fill in the required information for the claiming and which documents should be enclosed with claim forms, and additionally, a checklist for medical institutions was newly created and enclosed with claim documents. These materials were also posted on the website.

3.1.(2) Proactive PR activities

PMDA utilized an external consultant to implement efficient publicity, and implemented the following items.

Activities newly conducted in FY 2012

(i) To develop new PR activities through TV broadcasting, a symposium for the general public for the purpose of disseminating the system was held at Chiyoda Broadcasting Hall on November 18, 2012 (Sun) and aired at "TV Symposium" in NHK E-tele on March 16, 2013 (Sat).
(The keynote lecture was made by Dr. Mizoguchi, Professor Emeritus of Tokyo Women’s Medical University and Chairperson of the Committee on Relief Services, and also Ms.Yuasa, a committee member, Dr. Amagai, a deputy director of Keio University Hospital, and Ms. Miho Takagi, a TV personality were invited for a panel discussion (Coordinator: Ms. Naoko Hisada, a freelance announcer)

(ii) Presentation materials for training workshops were posted on the iPad application "Medical Board Pro".
(October 1, 2012 to March 31, 2013)

(iii) To promote the understanding of the name and details of the Relief System for Sufferers from Adverse Drug Reactions, the below mediums were used.

- Placed search advertising to lead people to the specially created web page
  (Late November 2012 to Late January 2013)
- In-train advertisement (February 18, 2013 to March 17, 2013)

Activities conducted on-site

(i) Dispatch of lecturers to training workshops for employees in medical institutions

In January 2012, the MHLW issued an administrative notice* to prefectural governments and healthcare-related organizations, to request them to utilize PR materials on the Relief System in their training sessions for safety management of medical services and informed that PMDA is willing to send materials explaining the relief system and dispatch lecturers. After the issuance of the notice, PMDA staff members visited healthcare-related organizations to request for cooperation to implement training sessions for the Relief System.

In response to requests from medical institutions based on the above approach, PMDA has dispatched its staff members as lecturers to 35 medical institutions, etc., and sent the materials to 31 medical institutions since April 2012.

* Administrative notice "Training Materials for Healthcare Professionals on Safe Use of Drugs Which Are Available for Pharmaceuticals Safety Management Supervisors" dated January 30, 2012 issued by the Office of Medical Safety Promotion at General Affairs Division, Health Policy Bureau, MHLW and the Office of Drug Induced Damages at the General Affairs Division, Pharmaceutical and Food Safety Bureau, MHLW

(ii) Academic conferences

PMDA conducted the following publicity activities at academic conferences:

- Poster presentations
  - Academic general meeting of the Japan Society for Health Care Management, Annual meeting of the Pharmaceutical Society of Japan
- Distribution of booklets and brochures
  - Annual Meeting of the Japanese Society of Internal Medicine
  - Annual Meeting of the Japanese Respiratory Society
  - Annual Meeting of the Japanese Association for Infectious Diseases: A total of 26 academic conferences including the above.

(iii) Training workshops

PMDA staff explained the Relief System at various workshops.

- Josai University Faculty of Pharmaceutical Sciences
- Training course for the Medical Care Section of the Tokyo Metropolitan Society of Health System Pharmacists
- Administrative/academic lecture meetings of Japan Kampo Medicines Manufacturers Association
- The University of Tokyo, Graduate School of Medicine, Department of Health Care Safety Management
- MR Education & Accreditation Center of Japan "Accreditation Renewal Workshop for Educational Training Supervisors": A total of 12 organizations including the above.

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

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

- 6 government bodies, 1 public health center, 1 medical safety support center
- 3 medical/dental associations, 2 pharmacists' associations, 1 nursing association
- 9 other organizations

(v) Others

At the 14th Forum on Eradication of Drug-induced Sufferings (sponsored by the Japan Confederation of Drug-induced Sufferers Organizations), PMDA opened a consultation desk for the Relief Systems and distributed leaflets.

Activities conducted continuously

(i) The original character "Doctor Q" was continuously used from FY 2011. Also, a period from September to November, 2012 covering the "Drug and Health Week (October 17 to 23)" was set

up as an intensive publicity period, during which a nationwide publicity campaign for the Relief Systems was carried out.

- Newspaper advertisement (Asahi, Mainichi, and Yomiuri)
- On-screen advertisement at hospitals/ pharmacies
- Square banner on the Qlife medicine search website
- Advertisement in professional magazines, etc. (medical journals, medical newspapers)
- Distribution and request for displaying the posters, etc. (at pharmacies, drug stores)
- Advertisement in free magazines, website, etc.
- Creation of a special web page

(ii) In order to find out the level of people's awareness of the Relief System for Sufferers from Adverse Drug Reactions and provide more effective publicity activities, PMDA conducted the awareness survey on the Relief System for the general public and healthcare professionals.
Survey period: March 19 - March 21, 2013

(iii) 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.

- Enclosed the brochures in the Journal of the Japan Medical Associations (about 171,000 copies) and the Journal of Japan Pharmaceutical Association (about 102,000 copies).
- Posted the on-line brochures (PDF format) on PMDA's website.
- Distributed the brochures to universities/colleges (colleges of pharmacy, faculties of pharmaceutical sciences), clinical training hospitals, university hospitals, and nursing training schools.
  i) Colleges of pharmacy, faculties of pharmaceutical sciences: 14,000 copies
  ii) Clinical training hospitals, university hospitals: 11,000 copies
  iii) Nursing schools, nurses training schools: 58,000 copies
- PMDA requested the MR Education & Accreditation Center of Japan to distribute the brochureat the MR educational trainings conducted by the Center.

(iv) In March 2012, PMDA posted the latest version of the presentation slide entitled "What is the Relief System for Sufferers from Adverse Drug Reactions?" on its website to accelerate the use of the slide in lectures, training sessions, etc. at universities and hospitals.

(v) PMDA posted downloadable poster and medicine envelops on which the advertisement of the Relief Systems is pre-designed for pharmacies to use.

(vi) PMDA distributed the DVD introducing the Relief Systems upon request.

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

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

(ix) PMDA requested the Japanese Red Cross Society Blood Center to distribute the leaflet on the Relief System for Sufferers from Adverse Drug Reactions and the Relief System for Infections Acquired through Biological Products to medical institutions to which the Blood Center delivers blood products.

(x) PMDA placed the advertisement using the same design as the leaflet on the Relief System for Sufferers from Adverse Drug Reactions in programs and abstract journals of academic conferences of the All Japan Hospital Association, Japan Municipal Hospital Association and Japanese Society of National Medical Services.

(xi) PMDA placed the information on the Relief Systems in "medication record book" published by the Japan Pharmaceutical Association.

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

(xiii) PMDA placed an article titled "Summary of Payment/Non-payment of Adverse Drug Reaction Relief Benefits and Drugs with Many Cases of Improper Use" in the "Pharmaceuticals and Medical

Devices Safety Information No. 296 (November 2012)" issued by the MHLW.

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

(xv) PMDA placed the website address for the Relief Systems in the education material "Let's Learn About Drug-Induced Sufferings", which was distributed to junior high schools nationwide by MHLW.

Symposium held on November 18, 2012

Newspaper advertisement using the original character "Doctor Q"

Brochure for healthcare professionals

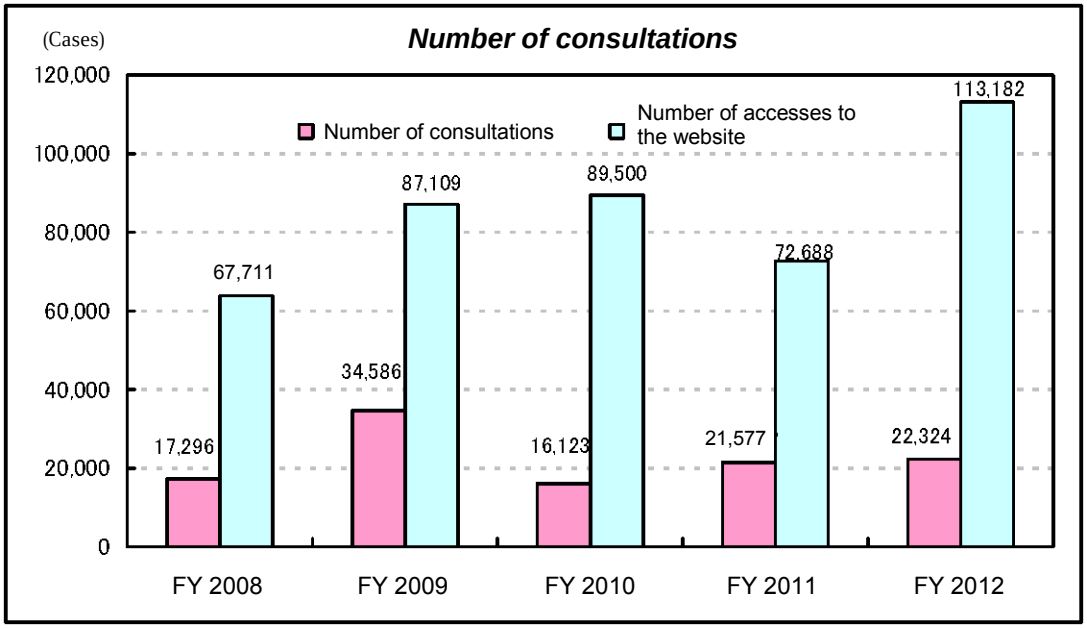
On-screen advertisement at hospital/pharmacy

3.1.(3) Efficient management of the consultation service

- In FY 2012, the number of consultations at the Relief System Consultation Service was 22,324, with a ratio of 103% compared with the previous fiscal year (21,577 consultations).
- In FY 2012, the number of accesses to the website was 113,182, with a ratio of 158% compared with the previous fiscal year (72,688 accesses).
- The number of accesses to the feature page of the Relief System was 29,375.
- PMDA tried to keep the people who seek consultation informed of the fact that the request form, etc. can be downloaded from its website.

Fiscal Year	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	Compared with FY2011
Number of consultations	17,296	34,586	16,123	21,577	22,324	103%
Number of accesses to the website	67,711	87,109	89,500	72,688	113,182	158%

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



Relief system consultation service
- ♦ Toll-free number: 0120-149-931
  (office hours: Monday - Friday [except public holidays and New Year's holidays] 9:00 - 17:00)
- ♦ e-mail for relief system consultation: kyufu@pmda.go.jp

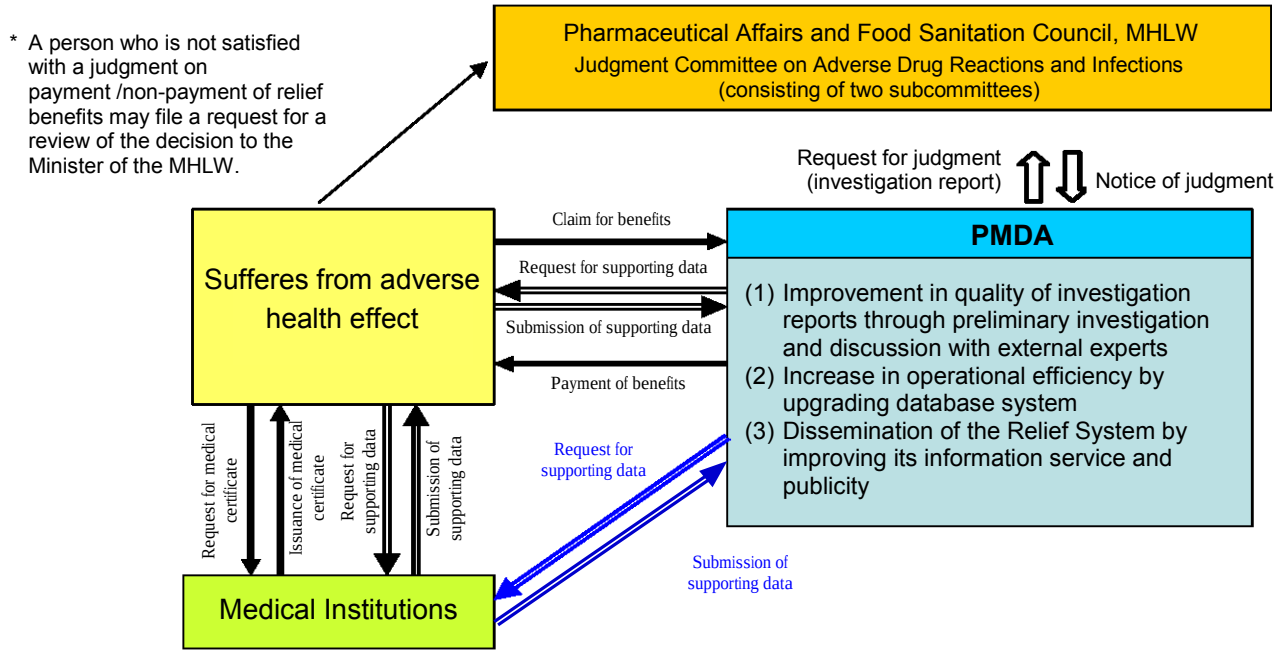
3.1.(4) Integrated management of information through databases

- Based on the Optimization Plan for Operations and Systems, the payment system and integration/analysis system have been upgraded to mutually link the both systems in an effort toward optimization of the system for Relief Services for Adverse Health Effects.

3.1.(5) Prompt 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: (i) Fact-finding investigations of the claimed event, (ii) Preparation of a summary chart showing case narratives over time, and (iii) Preparation of investigation reports, etc.

Flow of Adverse Health Effect Relief Services



- In accordance with the Second Mid-term Plan, PMDA plans to exercise judgment on approval/rejection of claims within 6 months for 60% or more of the total number of judged cases in each fiscal year. In FY 2012, PMDA planned to have the number of claims judged within 6 months at 55% or more, while ensuring that 70% or more of claims are judged within 8 months of the standard administrative processing time and then made an effort to expedite the operations.

  In FY 2012, the number of claims was markedly increased from 1,075 in FY 2011 to 1,280, and the number of claims judged was also increased from 1,103 in FY 2011 to 1,216. The number of claims judged within 8 months was 923, which was much higher than 809 in FY 2011 and accounts for 75.9% of the total judged cases; the annual target was achieved. The number of claims judged within 6 months was increased from 534 in FY2011 to 553, but the achievement rate of claims judged within 6 months was 45.5% of the total judged cases (see the note below).

Note: If the meeting of the second Judgment Committee on Adverse Drug Reactions and Infections, Pharmaceutical Affairs and Food Sanitation Council in May 2012 had been held as scheduled, the number of claims judged within 8 months would have been 944, with an achievement rate of 77.6%, and the number of claims judged within 6 months would have been 576, with an achievement rate of 47.4%.

(i) Relief Service for Adverse Drug Reactions

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

a. Performance of Relief Service for Adverse Drug Reactions

The performance for FY 2012 is shown below.

Fiscal -Year			FY 2008	FY 2009	FY 2010	FY 2011	FY 2012 *4
Number of claims			926	1,052	1,018	1,075	1,280
Number of judged cases			919	990	1,021	1,103	1,216
	Approved		782	861	897	959	997
	Rejected		136	127	122	143	215
	Withdrawal		1	2	2	1	4
	Within 8 months	Number of cases	683	733	765	809	923 (944)
		Achievement rate *1	74.3%	74.0%	74.9%	73.3%	75.9% (77.6%)
	Within 6 months	Number of cases	355	360	434	534	553 (576)
		Achievement rate *2	38.6%	36.4%	42.5%	48.4%	45.5% (47.4%)
Cases in progress *3			684	746	743	715	779
Median processing time (months)			6.5	6.8	6.4	6.1	6.2

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

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

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

**4 Values in parentheses are data given that the meeting of the second Judgment Committee on Adverse Drug Reactions and Infections, Pharmaceutical Affairs and Food Sanitation Council in May 2012 was held as scheduled.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2012 by type of benefit are shown below.

Fiscal Year		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of claims		926	1,052	1,018	1,075	1,280
Types of benefit	Medical expenses	769	902	854	909	1,101
	Medical allowances	824	943	911	964	1,168
	Disability pensions	79	71	74	77	83
	Pensions for raising handicapped children	7	11	4	4	1
	Bereaved family pensions	26	36	46	47	46
	Lump-sum benefits for bereaved families	49	50	54	63	53
	Funeral expenses	78	83	100	107	98

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 2012 by type of benefit are shown below.

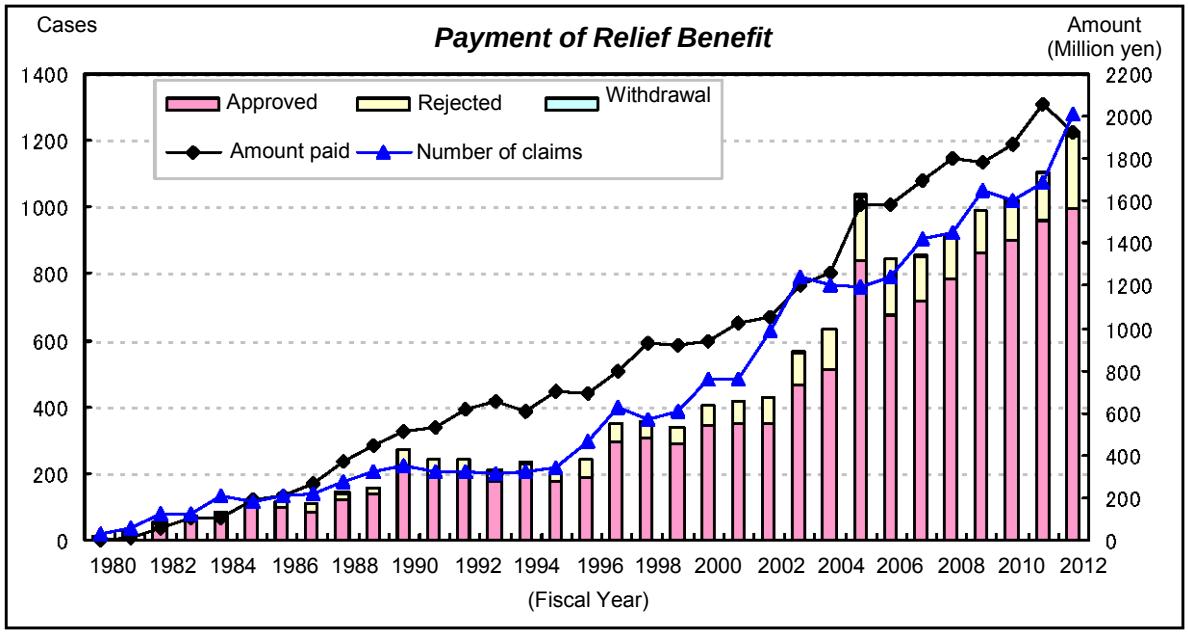
(Unit: thousand yen)

Types	FY 2008		FY 2009		FY 2010	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	659	75,339	763	86,666	803	87,475
Medical allowances	711	62,055	813	70,963	837	71,142
Disability pensions	27	747,362	26	804,251	38	853,854
Pensions for raising handicapped children	7	40,127	7	50,804	5	44,210
Bereaved family pensions	22	523,455	18	545,843	31	583,501
Lump-sum benefits for bereaved families	47	335,977	30	215,342	29	214,081
Funeral expenses	72	14,391	46	9,914	63	12,927
Total	1,545	1,798,706	1,703	1,783,783	1,806	1,867,190

Types	FY 2011		FY 2012	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	836	93,284	892	97,905
Medical allowances	895	75,198	947	75,326
Disability pensions	28	881,885	28	861,595
Pensions for raising handicapped children	6	49,606	0	43,744
Bereaved family pensions	35	614,318	32	602,068
Lump-sum benefits for bereaved families	47	328,093	32	227,696
Funeral expenses	80	16,006	62	12,438
Total	1,927	2,058,389	1,993	1,920,771

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

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



(ii) Relief Service for Infections Acquired through Biological Products

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

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

a. Performance of relief for infections

The performance for FY 2012 is shown below.

Fiscal Year		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of claims		13	6	6	9	4
Number of judged cases		11	10	7	7	6
	Approved	6	8	6	3	4
	Rejected	5	2	1	4	2
	Withdrawal	0	0	0	0	0
Cases in progress *1		7	3	2	4	2
Achievement rate *2		100.0%	100.0%	85.7%	100.0%	100.0%
Median processing time (months)		5.2	5.4	6.9	4.4	4.7

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

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

b. Number of claims by type of benefit

The numbers of claims filed in FY 2012 by type of benefit are shown below.

Fiscal Year		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of claims		13	6	6	9	4
Types of benefits	Medical expenses	11	5	5	6	2
	Medical allowances	13	6	5	8	4
	Disability pensions	0	0	1	0	0
	Pensions for raising handicapped children	0	0	0	1	0
	Bereaved family pensions	0	0	0	0	0
	Lump-sum benefits for bereaved families	1	0	1	0	0
	Funeral expenses	1	0	1	0	0

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 2012 by type of benefit are shown below.

(Unit: thousand yen)

Types	FY 2008		FY 2009		FY 2010		FY 2011		FY 2012	
	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	204	6	375	5	425	3	213	2	83
Medical allowances	6	386	8	567	5	384	3	282	4	282
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,378	–	2,378	–	2,378	–	2,370	–	2,362
Lump-sum benefits for bereaved families	1	7,135	–	–	1	7,160	–	–	–	–
Funeral expenses	1	199	–	–	1	193	–	–	–	–
Total	13	10,302	14	3,320	12	10,540	6	2,865	6	2,726

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 appropriate communication of information through collaboration between operational divisions

- To enhance collaboration with the other divisions at PMDA, information on claims and decisions on payment/non-payment of 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 "PMDA Request for Proper Use of Drugs" posted on the Medical Product Information web page, explaining points for safe use of drugs, etc. in an easy-to-understand way that allows healthcare professionals to readily use the information, in order to further promote the proper use of drug products.

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

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

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

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

(i) Investigative Research for Improvements in Quality of Life of Sufferers of Serious and Rare Adverse Health Effects Caused by Drug Products:
As part of health and welfare services, PMDA established an Investigative Research Team for Improvements in the Quality of Life (QOL) of Sufferers from Serious and Rare Adverse Health Effects Caused by Drug Products in April 2006, and the team initiated investigative research to obtain information for examining the ideal way to provide necessary services and measures for improving the QOL of sufferers from serious and rare adverse health effects, who have not necessarily been supported sufficiently by general measures for disabled people. This research project was carried out, taking into account the results (March 2006) of a survey on the actual state of adverse health effects stemming from adverse drug reactions that was conducted in FY 2005.

In FY 2012, PMDA summarized the operating performance for FY 2011, and conducted research in 85 subjects, including sufferers from serious adverse health effects similar to Reye's syndrome who were newly added in FY 2012, taking into account discussions at the Committee on Relief Services.

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 (85 volunteers in FY 2012).

Research 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 (Departmentof Ophthalmology)
Chieko Matsunaga Associate professor, School of Health and Welfare, International University of Health and Welfare

(ii) Consultation Services to Address Mental Issues, etc.
The survey on the actual state of adverse health effects stemming from adverse drug reactions, which was conducted in FY 2005, showed the necessity of care for persons with deep mental trauma due to adverse health effects such as diseases, disabilities, etc. caused by adverse drug reactions, as well as the importance of consultation support for persons with remarkable restrictions in daily living due to such adverse health effects. Therefore, PMDA held many discussions with organizations of adverse drug reaction sufferers, etc. regarding the conduct of

support services for persons who have received benefits under the Relief Systems, and consequently, Consultation Services to Address Mental Issues, etc. were initiated in January 2010.

Consultation services by experts who are qualified for welfare were conducted, for the purpose of providing advice, etc. on mental care and on the use of welfare services to persons suffering from adverse health effects caused by adverse drug reactions or infections acquired through biological products, and their families. In FY 2012, 38 consultations were performed.

(iii) Distribution of the Benefit Recipient Card

For beneficiaries of adverse reaction relief benefits, in January 2010, PMDA started a service in which a handy, credit-card size certificate is issued upon request. The card shows specific information such as the name of the drug(s) that is considered or suspected to have caused the adverse reaction to the card holder. In FY 2012, the card was issued to 432 persons. In addition, the explanatory text on the distribution of the benefit recipient card was revised taking into account the discussion at the Committee on Relief Services.

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

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

In FY 2012, PMDA summarized the operating performance for FY 2011, and conducted research in 177 subjects.

Contents of the Research

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 (177 volunteers in FY 2012).

Research Team

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

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

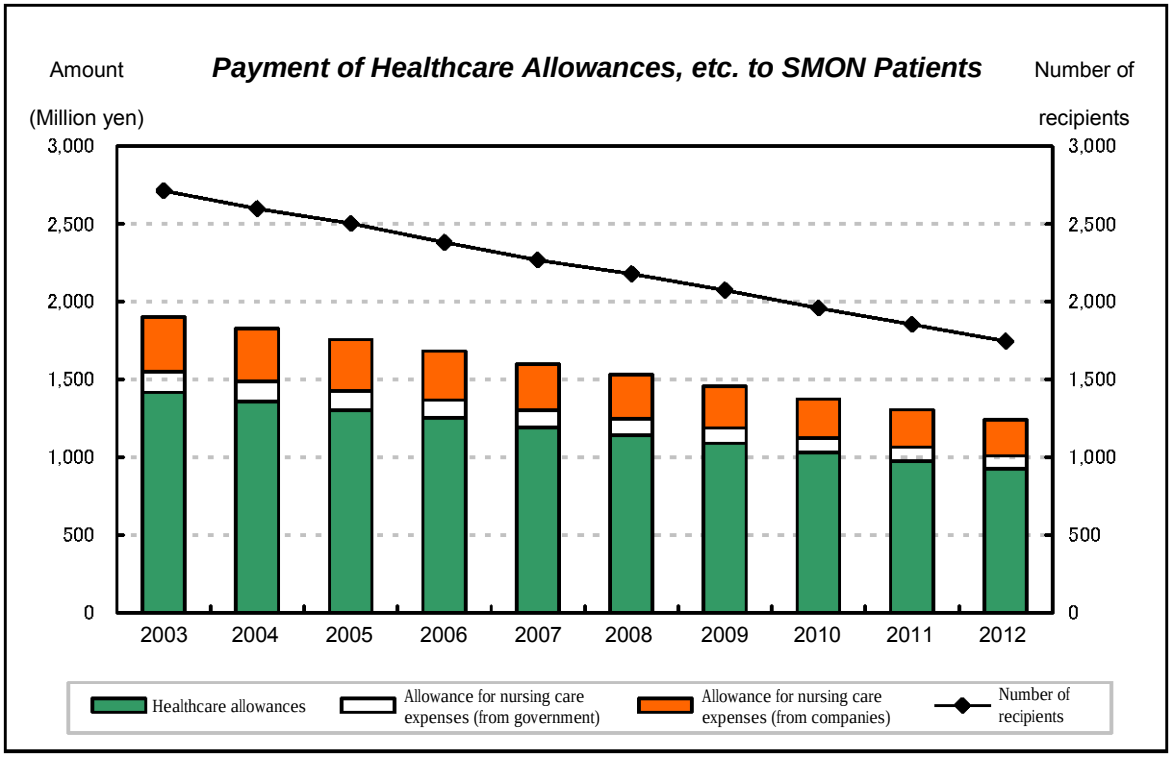
- PMDA appropriately provided healthcare allowances, etc. to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

(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 2012, the number of patients receiving such allowances was 1,748, and the total amount paid was 1,241 million yen.

Fiscal Year		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of recipients		2,180	2,075	1,960	1,855	1,748
Amount paid (thousand yen)		1,531,745	1,457,724	1,375,622	1,306,329	1,241,368
Break down	Healthcare allowances	1,140,517	1,089,491	1,031,376	975,567	924,669
	Allowance for nursing care expenses (from companies)	284,981	268,749	250,946	241,890	233,050
	Allowance for nursing care expenses (from government)	106,247	99,485	93,300	88,872	83,650

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.



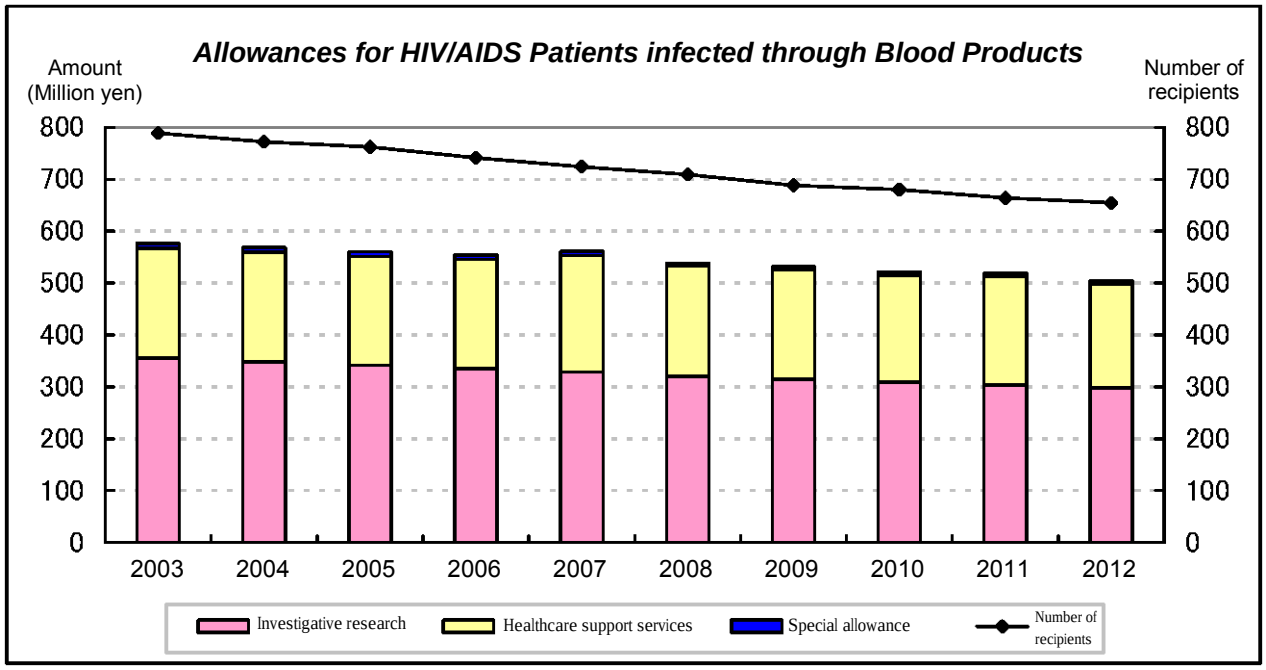
(ii) HIV-related services (commissioned payment of healthcare allowances)

- 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 2012, 540 HIV-positive patients received allowances relating to the investigative research, 112 AIDS patients received allowances relating to the healthcare support service and 3 AIDS patients received special allowances. The total number of patients receiving allowances relating to the 3 services was 655, and the total amount paid was 503 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 2008		FY 2009		FY 2010	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	586	320,122	566	313,676	562	309,355
Healthcare support services	121	211,800	120	210,600	116	206,100
Special allowance	2	6,300	2	6,300	2	6,300
Total	709	538,222	688	530,576	680	521,755

Fiscal Year	FY 2011		FY 2012	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	547	302,763	540	297,790
Healthcare support services	115	210,000	112	199,500
Special allowance	2	6,276	3	6,362
Total	664	519,039	655	503,652



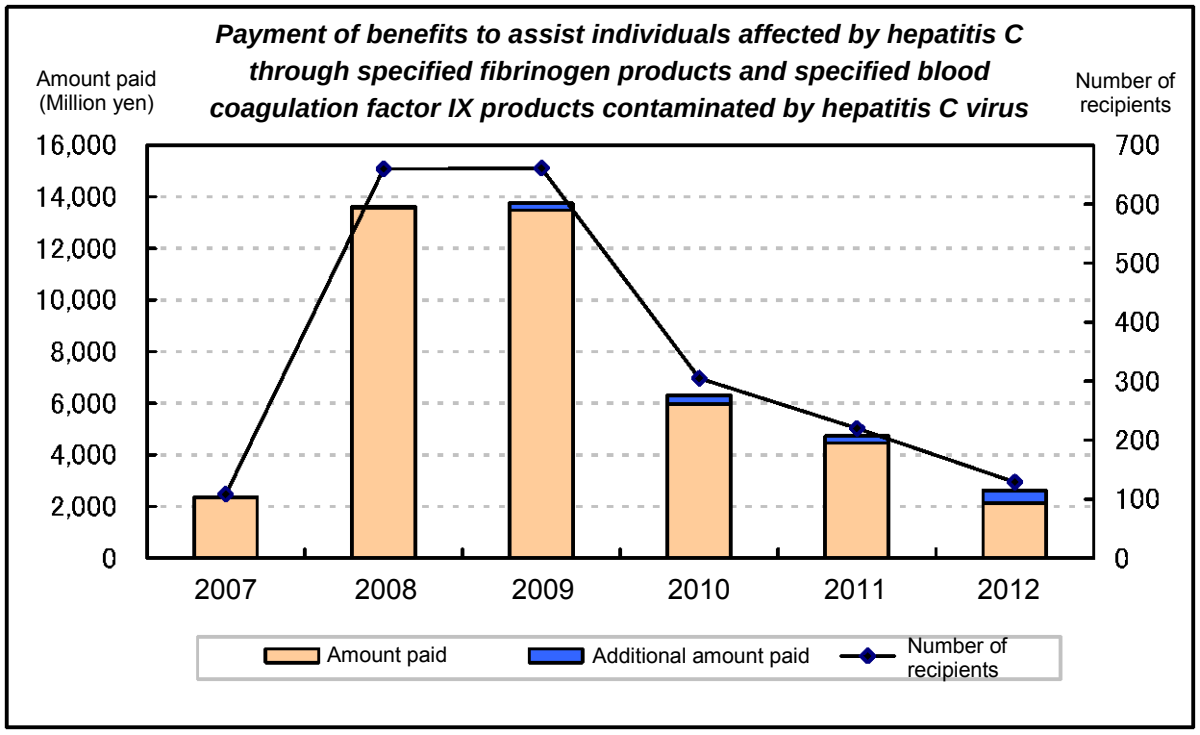
3.1.(9) Appropriate provision of the payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus

- 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 129, with 2,624 million yen as the total amount paid in FY 2012.

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

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

	FY 2011	FY 2012
Number of recipients	220	129
(Of which: number of recipients of additional payment)	(20)	(28)
Amount paid (thousand yen)	4,732,000	2624,000
(Of which: amount of additional payment)	(268,000)	(488,000)
Number of consultations (cases)	674	982



3.2. Reviews and Related Services and Safety Measures Services

In order to enable the public to safely use drugs and medical devices that meet international standards, through reviews and related services and post-marketing safety measures, PMDA is required to provide more effective drugs and medical devices to clinical practice faster and with greater safety, while ensuring that drugs and medical devices are used properly, preventing health hazards, and responding appropriately and promptly if any hazard occurs. To this end, PMDA has taken the following operations to reinforce the systems for consultations/reviews and post-marketing safety measures, and to organically link the operations, thereby achieving the Mid-term Targets and FY 2012 plan.

In FY 2012, to deal with products using advanced science and technologies in a more focused manner, the Science Board consisting of external experts in the areas of medicine, dentistry, pharmacy, industry, etc. was established, and also the Office of Review Innovation was established with the aim of improving the quality of PMDA's operations ranging from reviews/consultations to post-marketing safety measures.

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

New drugs

- Various measures were implemented with the aim of increasing the number of reviewers and improving the quality of reviews, based on the 5-year Strategy for Medical Innovation (Medical Innovation Conference on June 6, 2012), successor to the 5-year Strategy for Creating Innovative Drugs and Medical Devices (dated April 26, 2007).

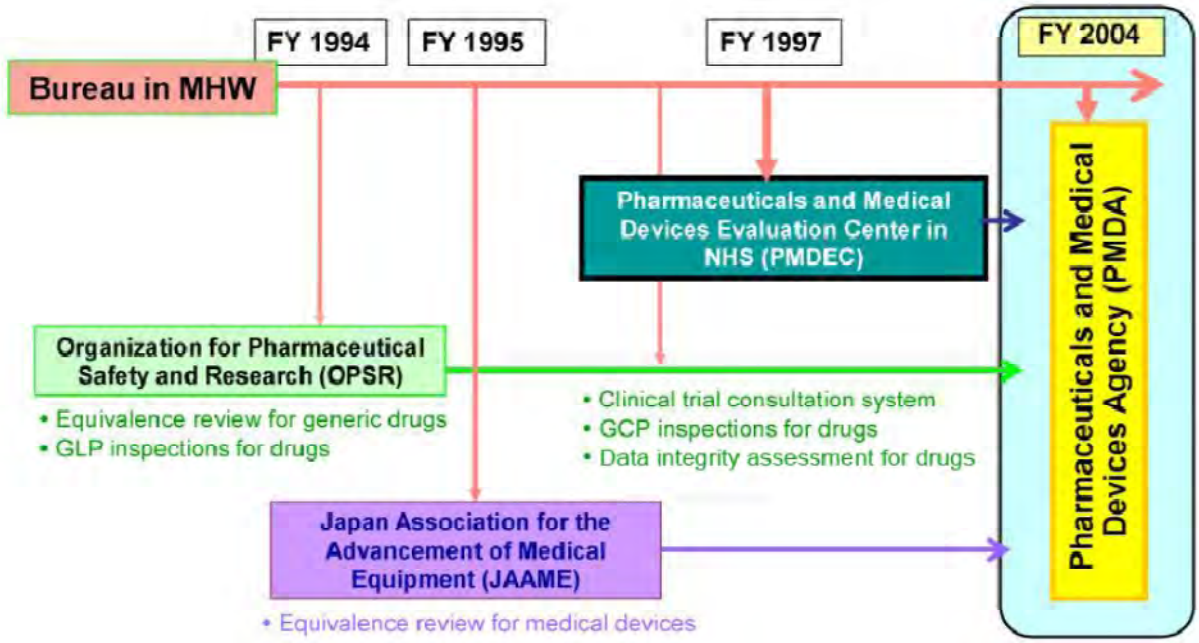
(i) Appropriate and prompt reviews

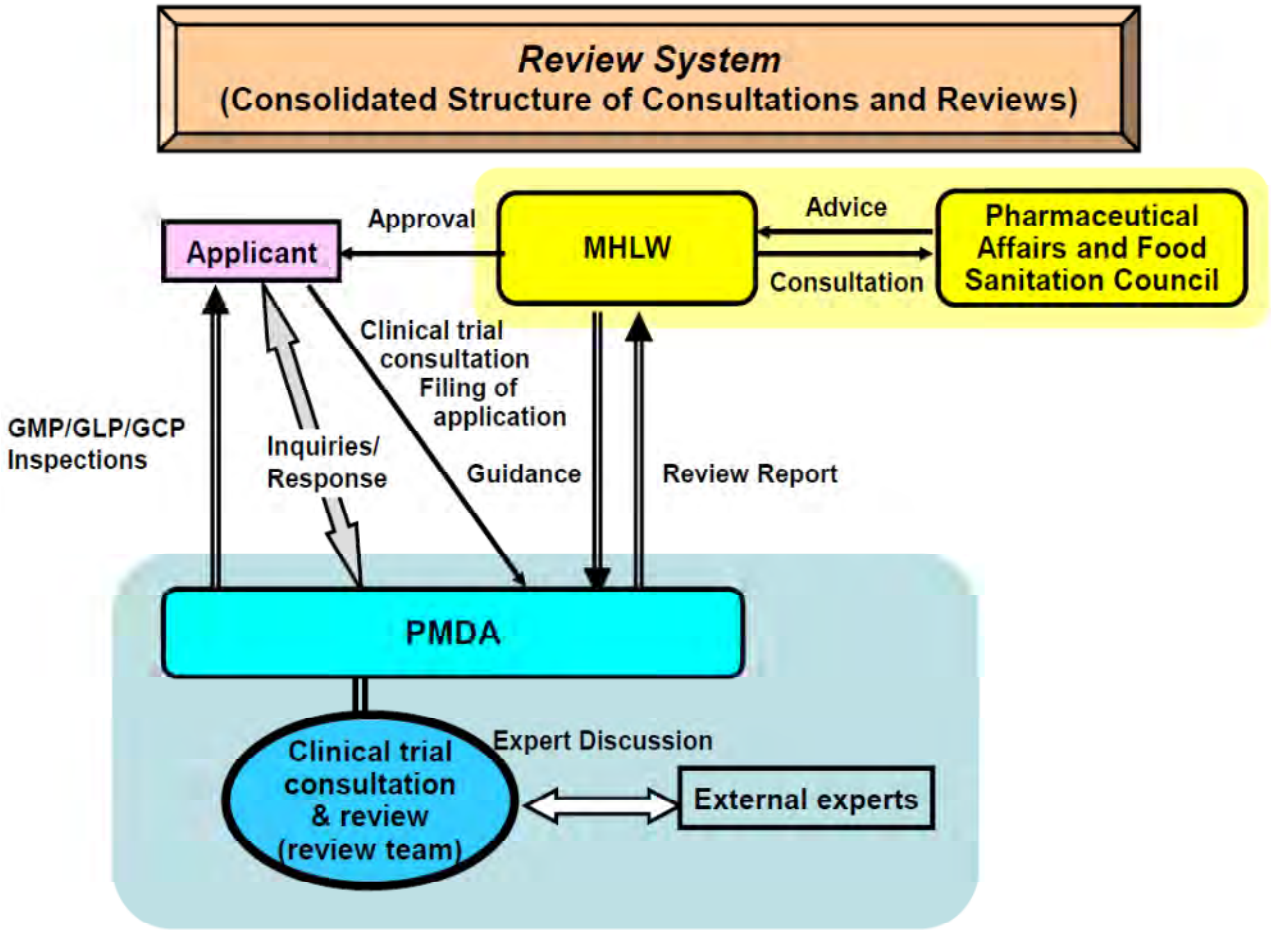
a. Structure for clinical trial consultations and reviews

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

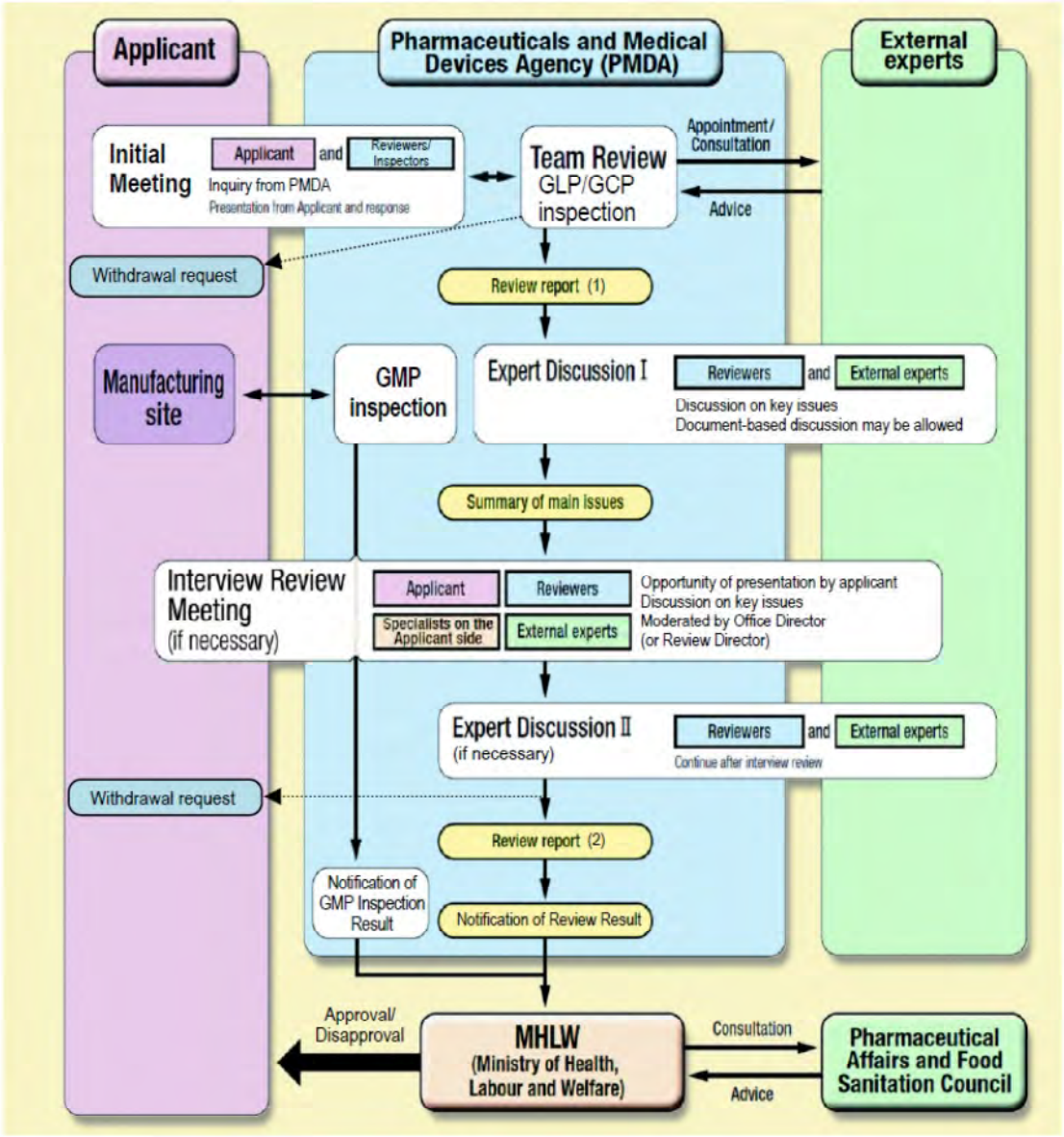
  1) In order to ensure the consistency and efficiency, the roles of three review-related agencies were examined thoroughly, and integrated into one agency as "incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency."
  2) Substantial increase in the number of staff including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

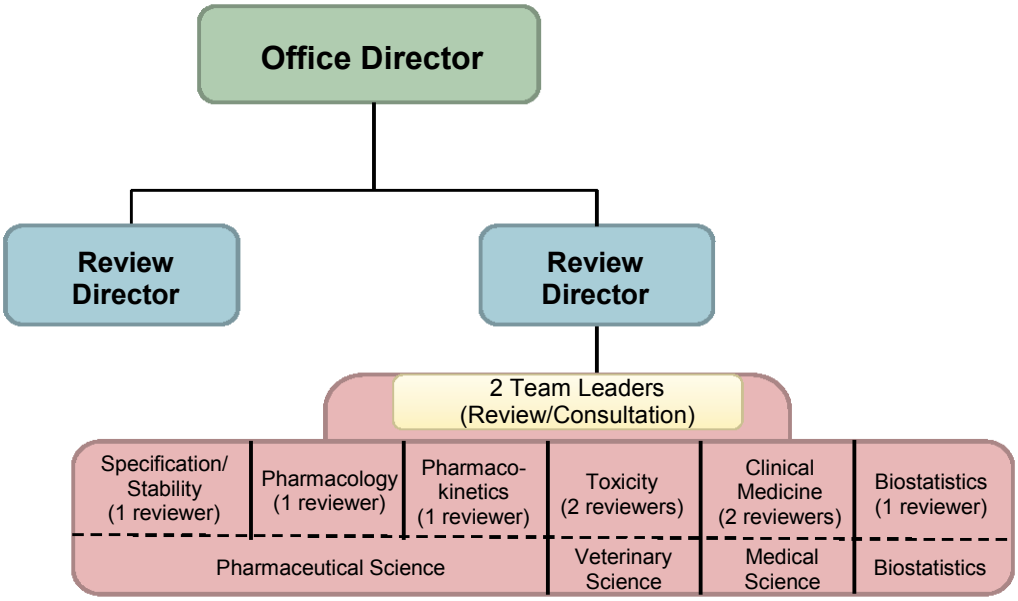


Review Performance for FY 2012 (drugs)

(1) Number of Expert Discussions conducted: 221 (of which, 163 through document-based discussions, 58 through meetings)
(2) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 78
Applications reported to the Drug Committees (under PAFSC): 54

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

Organization Chart for Reviews of New Drugs



- In order to enhance the review system, PMDA increased the number of reviewers allocated to the categories where many new drug applications were filed and the review process for them was likely to be prolonged.
- Reviews of new drug applications are assigned to the responsible offices and teams according to the therapeutic categories for review. 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
		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, antithrombotics, anti-Alzheimer's drugs
		Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs
		Radiopharmaceuticals	Radiopharmaceuticals
		In vivo diagnostics	Contrast media
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, vermifuge, antifungal drugs, antiviral drugs (excluding AIDS drugs)
		Category 6-1	Respiratory tract drugs, anti-allergy drugs (excluding dermatologic drugs), sensory organ drugs for inflammatory diseases
		AIDS drugs	Anti-HIV drugs
Office of New Drug V		Oncology drugs	Antineoplastic drugs
Until Sep. 2012 *	Office of Biologics I	Blood products	Globulin, blood coagulation factor products
		Bio-CMC	Quality of biologics (including gene therapy products)
	Office of Biologics II	Biological products	Vaccines, antitoxic serum
		Cellular and tissue-based products	Cell therapy products
From Oct. 2012 *	Office of Cellular and Tissue-based Products	Cellular and tissue-based products	Cellular and tissue-based products
		Gene therapy products	Gene therapy products, Cartagena
		Bio-CMC	Quality of biologics, biosimilars
		Biological devices (quality)	Biological devices (quality)
	Office of Vaccines and Blood Products	Vaccines	Vaccines, antitoxic serum, etc.
		Blood products	Blood products

* *As of October 1, 2012, review categories were changed in association with the set-up of the Office of Cellular and Tissue-based Products and the Office of Vaccines and Blood Products.*

- PMDA conducted clinical trial consultations for new drugs based on the team-reviewed guidance plan drafted by 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 2012, 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 ensured that the Progress Management Committee for Reviews and Related Services hold meetings once every 3 months so that the Chief Executive and other executives of PMDA could accurately grasp the progress of reviews

and related services and support improvement. The Committee thus monitored operational progress, and particularly for new drugs, comprehensively considered relevant information and approaches for solving operational challenges.

- 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 2012. In the meetings, opinions for the advancement of the system were exchanged, information on the overall review status for new drugs and associated issues were shared, measures addressing challenges and future approaches were examined, and the detailed review status of new drugs and other products under review were informed. (11 meetings were held in FY 2012).

  At the Review Segment Committee for Progress Management, the Director of the Center for Product Evaluation and Associate Center Director continuously provided necessary guidance, taking into account reports from office directors of review divisions. In addition, efforts to share the results of discussion on issues and improvement measures for products with a trouble within review segments were newly started at the end of the FY 2012.

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

c. Standardization of review

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

d. Consultations and reviews based on medical care needs

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

  * A total of 1,378 PMDA staff members participated in 414 academic conferences and seminars held in Japan.

- In order to encourage pharmaceutical companies to develop drugs and indications that have been approved in Europe and the U.S. but not approved or available for off-label use 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 the activities have been continued. PMDA continuously supports this Committee, and deals with clinical trial consultations and reviews based on the results of the investigations.

- To respond to issues of unapproved drugs and off-label use drugs of high medical need, PMDA created a simple database (MS Excel) of products such as drugs with a new active ingredient approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) between April 2009 and December 2012, and examined 246 products in terms of equivalence with already-approved drugs in Japan and development status in Japan.

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. Close links between consultations and reviews are maintained and teams are flexibly organized as necessary.

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, etc.

  Already-approved drugs that have been specified by the Minister of Health, Labour and Welfare are re-evaluated for their efficacy and safety, in the light of the current standards of medical/ pharmaceutical sciences, based on the data submitted by marketing authorization holders. In addition, re-evaluations for quality are conducted to ensure that the dissolution of drugs in solid oral dosage forms meets the quality requirements, based on the data submitted by marketing authorization holders. 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 2012, 50 products underwent re-examination, no product underwent re-evaluation for drug efficacy, and no product underwent re-evaluation for quality.

Number of Re-examinations/Re-evaluations Conducted

		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Products that underwent re-examination		235	164	115	81	50
Re-evaluation	Products that underwent re-evaluation for drug efficacy	0	0	0	0	0
	Products that underwent re-evaluation for quality	89	12	53	0	0

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

g. Promotion of digitization in reviews

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

- This new application/review system enables the PMDA staff to manage progress through the entire process from acceptance of applications for marketing approval and manufacturer's license and notifications, etc. on drugs, quasi-drugs, cosmetics and medical devices, until those approvals or licenses come into effect. In addition, PMDA uses this system for operations related to registration and licensing, such as entry of the information included in product application forms (product application management software), acceptance of the product applications, data exchange among review/inspection authorities, recording of review memorandums, preparation of

Marketing Approval Documents and management of the registration list.

- The status of upgrading, etc. of review systems in FY 2012 is shown below.

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

- Toward the realization of the Optimization Plan for Operations and Systems, the status of response to requests from PMDA users of the current review system was reviewed, the systems were integrated, and information necessary to sort out elements for integrated data management was compiled. In addition, requirement definitions and hearings from external professionals on design for the system to be implemented from the second half of the FY 2011 to FY 2013 were conducted.

2) Improvement of the Web application platform for medical devices (function added)

- The Web application platform for medical devices was upgraded to improve the convenience for applicants.

3) Upgrading of the eCTD viewer system

- To enable searches for contents of Electronic Common Technical Document (eCTD) in a cross-sectional manner, a method of linking PRO-Search and the new eCTD viewer was created. In addition, the new eCTD viewer was upgraded to improve the browsing/display speed.

4) Conversion of final decision documents for regulatory approval for drugs etc. and clinical trial notifications into electronic media

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

5) IT literacy training

- In order to utilize electronic documents more efficiently, IT literacy training (Microsoft Office) was carried out for a total of 46 members through e-learning in which trainees learn at the personal computer on their own desk.

h. Improvement of environment for eCTD

- To allow external expert advisors to access application documents, PMDA created an access environment for the eCTD with a higher level of security and has started to operate it. The increased accessibility enabled faster presentation of eCTD to external experts. It also reduced the risk of information leakage.

i. Development of the Japanese Pharmacopoeia

- In FY 2012, the Japanese Pharmacopoeia Draft Committee held a total of 74 meetings, and posted information on the PMDA website to seek public comments regarding 161 official monographs (53 new articles, 108 amendments, 1 deletion), 11 general tests (3 new tests, 8 amendments), 9 ultraviolet-visible reference spectra, 12 infrared reference spectra, amendments to other General Notices, and partial revision of the General Rules for Preparations as a draft of Supplement 2 to the 16th edition of the Japanese Pharmacopoeia (JP) (scheduled to be published as a Ministerial Announcement in March 2014).

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

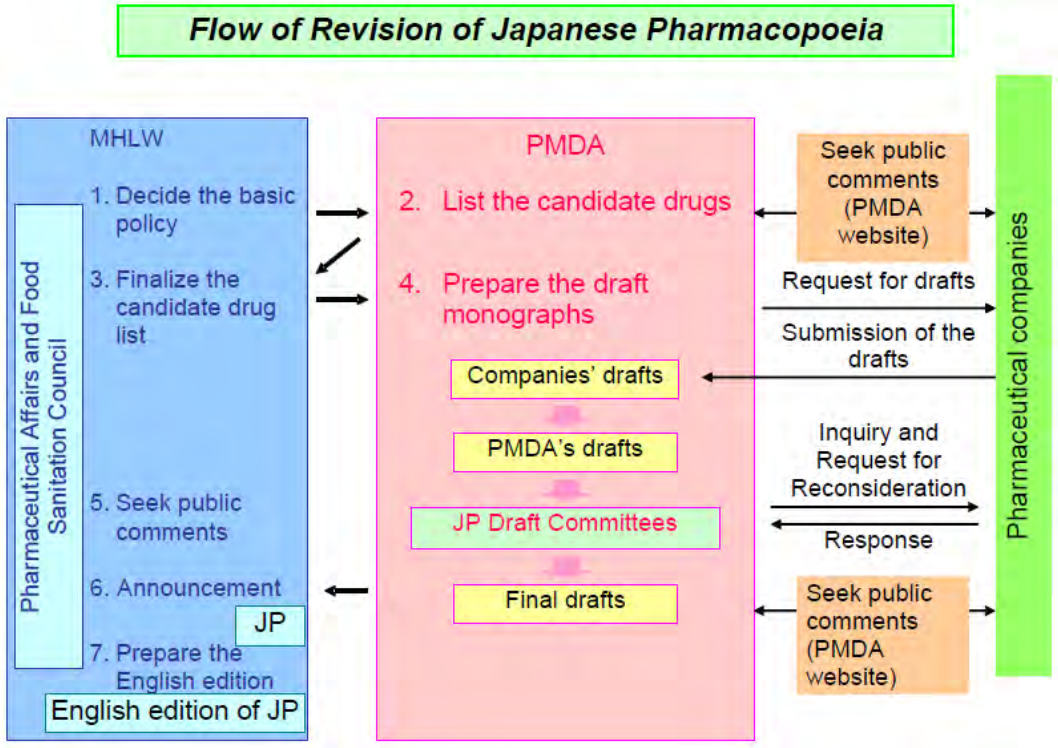
Month and year reported	2005 Sep.	2007 Mar.	2008 Nov.	2009 Mar.	2009 Aug.	2010 Aug.	2012 Mar.	2013 Jan.
New monographs	102	90	1	106	–	106	77	0
Amendments	276	171	1	122	2	330	176	1

Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for General Notices, General Rules for Preparations, General Rules for Crude Drugs, General Tests, Processes, and Apparatus, and General Information. PMDA usually provides those drafts to MHLW 6 months before the publication. In FY 2012, PMDA reported the draft of partial revision (scheduled to be published as a Ministerial Announcement in May to June 2013) to MHLW in January 2013.

Ministerial Announcement on the Japanese Pharmacopoeia (JP) by MHLW

	15th edition	1st supplement to the 15th edition	Partial revision	2nd supplement to the 15th edition	Partial revision	16th edition	1st supplement to the 16th edition
Month and year announced	2006 Mar.	2007 Sep.	2009 Mar.	2009 Sep.	2010 Jul.	2011 Mar.	2012 Sep.
New monographs	102	90	1	106	0	106	77
Amendments	272	171	1	122	2	330	176
Deleted monographs	8	6	0	1	0	15	4
Total number of monographs	1,483	1,567	1,568	1,673	1,673	1,764	1,837

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



(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 2012, the request forms were separately received for consultations to be conducted in the first half of the year and those in the second half of the year. Consultations provided are broken down by review category, as follows.

  Review category (hereinafter referred to as "Category") 1, 1 product (1 consultation item; same hereafter); Category 6-2, 2 products (7); Category 2, 3 products (11)

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

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

- To consistently monitor the safety of drugs from the clinical trial stage to the post-marketing stage, risk managers, who were placed in 9 review teams in FY 2010, were increased and placed in 12 review teams in FY 2011. In FY 2012, the number of risk managers was increased by one to have 13 risk managers for 12 review teams. Safety evaluation of new drugs by review teams, preparation of the reports on cancellation of conditions for approval in relation to post-marketing surveillance, and sharing of submitted risk management plans for drugs among risk managers, were performed.
- Regarding all submitted risk management plans for drugs, information was shared among risk managers. In addition, discussions were carried out toward a steady implementation of risk management plans for drugs. A Q&A collection was created and released, and examples of described cases were compiled.

(iii) Approaches to solve the drug lag

- The targets for total review time (from application date to approval date; same hereinafter) for drug applications submitted on or after April 1, 2004, the regulatory review time (including the review time at the MHLW; same hereinafter), and the applicant's time were set up. Both the regulatory authorities and applicants have been making efforts toward the achievement of the targets.
- New drug applications (for drugs that are clearly different from approved drugs in terms of active ingredients, contents, administration, dosage, indications, efficacy, etc.; same hereinafter) submitted to MHLW were reviewed by PMDA review teams consisting of experts in pharmaceutical science, veterinary medicine, medicine, biostatistics, etc.
- With regard to reviews of new drugs, in order to ensure consistency among the review teams and carry out review work promptly and appropriately, 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 2012 is shown below:

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

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

Median Review Time for New Drugs (Priority Review Products)

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	15.4 (19.1)	11.9 (24.5)	9.2 (12.6)	6.5 (9.2)	6.1 (9.0)
Regulatory review time [months]	7.3 (8.3)	3.6 (6.7)	4.9 (6.8)	4.2 (5.5)	3.8 (4.7)
Applicant's time [months]	6.8 (11.4)	6.4 (15.9)	3.4 (7.6)	2.0 (4.7)	1.5 (5.7)
Number of approved applications	24	15	20	50	53

Note 1:Products covered were those for which applications were filed in or after FY 2004. The number of applications is expressed on an active ingredient basis. See Products Approved in FY 2012 in the Supplementary Information for details.

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

Note 3:For FY 2010 or thereafter, products submitted for public knowledge-based applications, as recommended by the Study Group on Unapproved and Off-label Drugs of High Medical Need, are included as priority review products.

Reference Information: Review Time of New Drug Applications Excluding Those of Unapproved Drugs Submitted based on Public Knowledge (FY 2010 or thereafter)

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

- Reviews of applications for orphan drugs and other drugs that are regarded as having particularly high medical need (i.e., drugs for serious diseases with distinctly superior efficacy or safety to existing drugs or therapies) were conducted on a priority basis as priority review products, and 53 applications were approved in FY 2012 in this category (including 28 public knowledge-based applications as recommended by the Study Group on Unapproved and Off-label Drugs of High Medical Need).

- In FY 2012, 5 applications requesting priority reviews were submitted for drugs regarded as having particularly high medical need. Of the 5 applications submitted, 5 were judged to be "eligible" for priority review, and 0 was "not eligible," and 0 was currently under consideration as of the end of FY 2012.
- The median total review time for priority review products in FY 2012 was 6.1 months, the median regulatory review time was 3.8 months, and the median applicant's time was 1.5 months, all showing achievement of the target.

  Among approved applications in FY 2012, priority review products accounted for 40%, showing a higher percentage than for FY 2011 (38%).

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

Median Review Time for New Drugs (Standard Review Products)

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	22.0 (27.6)	19.2 (24.8)	14.7 (22.7)	11.5 (15.7)	10.3 (11.9)
Regulatory review time [months]	11.3 (18.5)	10.5 (15.3)	7.6 (10.9)	6.3 (8.2)	5.7 (7.1)
Applicant's time [months]	7.4 (14.1)	6.7 (10.7)	6.4 (12.2)	5.1 (9.6)	4.2 (6.0)
Number of approved applications	53	92	92	80	81

Note 1:Products covered were those for which applications were filed in or after FY 2004. The number of applications is expressed on an active ingredient basis. See Products Approved in FY 2012 in the Supplementary Information for details.

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

- In FY 2012, the median total review time for standard review products was 10.3 months, showing a reduction compared to 11.5 months in FY 2011. The median regulatory review time was 5.7 months, showing a reduction of 0.6 months compared to 6.3 months in FY 2011. The median applicant's time was 4.2 months, showing a reduction of 0.9 months compared to 5.1 months in FY 2011.
- PMDA reviewed the submitted product applications in the order of acceptance, giving full consideration to the target review time.

  Meanwhile, the target for applicant's time could not be achieved, but toward its improvement, PMDA asked companies of new drugs to provide cooperation and to proactively utilize clinical trial

consultations before filing applications, through periodic exchanges of opinions between the industry and PMDA.

- The number of applications under review at the end of FY 2012 was 113 (including 10 applications for orphan drugs; 4 public knowledge-based applications for unapproved drugs; 4 applications for priority review products excluding orphan drugs and public knowledge-based applications for unapproved drugs).

Review Status of New Drugs by Fiscal Year of Application

New drugs (Filed in)	Applications	Approved	Not approved	Withdrawal	Under review
On or before Mar. 31, 2004	140	108	0	29 (1)	3 [-1]
FY 2004	87	78	0	9	0
FY 2005	57	50	0	7	0
FY 2006	102	93 (1)	0	9	0 [-1]
FY 2007	92	78	0	14	0
FY 2008	81	76	0	4	1
FY 2009	106	87	1	18	0
FY 2010	116	104 (3)	0	11	1 [-3]
FY 2011	130 (7)	125 (98)	0	2 (2)	3 [-100]
FY 2012	139	32 (32)	0	2 (2)	105 [105]
Total	1,050	831 (134)	1	105 (5)	113 [1]

Note 1:Values in parentheses indicate those processed in FY 2012 (included in values on their left).
Note 2:Values in brackets indicate difference from the status reported in FY 2011.

Number of Applications Processed and Time Spent by Review Process

	Review process	1. From receipt of applications to initial meeting	2. From initial meeting to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2012	Number of processed applications	52	48	102	134
	Median total review time	67.5 days	168.5 days	28.0 days	38.5 days

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

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- In FY 2012, there were no requests for designation for priority consultations of drugs that are considered to have particularly high medical necessity. PMDA conducted one consultation for a designated ingredient.

b. Acceleration of the procedure for clinical trial consultations

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

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

Number of Consultations Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	315	370	390	447	387
Withdrawals	23	23	44	30	20
Total (conducted and withdrawn consultations)	338	393	434	477	407

Number of Prior Assessment Consultations for Drugs Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	–	33	30	33	19
Withdrawals	–	0	0	0	0
Total (conducted and withdrawn consultations)	–	33	30	33	19

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	–	1	1	1	0
Withdrawals	–	0	0	0	0
Total (conducted and withdrawn consultations)	–	1	1	1	0

Number of Consultations on Drug Product Eligibility for Priority Review Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	–	–	–	2	7
Withdrawals	–	–	–	0	0
Total (conducted and withdrawn consultations)	–	–	–	2	7

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 2012, PMDA conducted a total of 407 consultations (including 20 withdrawals).
- To cope with all the requests for clinical trial consultations (excluding prior assessment consultations, consultations on pharmacogenomics/biomarkers, and consultations on drug product eligibility for priority review) as a general rule, the date is arranged according to requests for schedule arrangement received, and when the consultation schedule cannot be fixed for a desired month, the date is arranged within one month before or after that month. In FY 2012, PMDA provided a total of 381 consultations (including 20 withdrawals), basically responding to all of the consultations requested.
- PMDA aimed to complete the process from consultation to finalization of meeting records within 30 business days for 80% of all consultations conducted. In FY 2012, the process was completed within 30 business days for 338 (93.9%) out of 360 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 2012

Review category	Actual results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs, etc.)	7	3	0	2	5	4	3	3	2	0	5	3	37
Category 6-2 (Hormone drugs)	3	2	8	1	2	0	1	4	3	1	0	1	26
Category 2 (Cardiovascular drugs)	3	5	3	17	3	2	2	3	4	5	6	3	56
Category 5 (Drugs for the urogenital system, etc.)	1	3	1	1	0	0	1	1	3	1	1	1	14
Radiopharmaceuticals	0	0	0	1	1	0	0	0	0	0	0	1	3
In vivo diagnostics	1	0	0	1	0	0	0	0	0	0	0	0	2
Category 3-1 (Central nervous system drugs, etc.)	1	0	2	3	5	2	7	5	2	6	3	1	37
Category 3-2 (Anesthetic drugs, etc.)	3	2	2	0	1	1	2	2	6	0	3	1	23
Category 4 (Antibacterial agents, etc.)	2	1	4	4	3	4	0	2	3	1	3	3	30
Category 6-1 (Respiratory tract drugs, etc.)	4	2	3	4	2	3	4	5	5	1	5	2	40
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Oncology drugs	10	6	2	5	2	3	2	9	7	2	9	4	61
Bio-CMC (Note 7)	2	0	3	0	1	3	1	1	2	1	1	3	18
Gene therapy products	–	–	–	–	–	–	0	0	0	0	0	1	1
Blood products	3	0	5	1	0	0	0	3	0	0	3	1	16
Biological products (Note 8)	1	3	0	3	2	0	2	2	1	1	1	4	20
Cellular and tissue-based products (Note 9)	0	0	0	0	0	2	0	0	0	0	0	0	2
[Re-listed] Prior assessment	0	0	7	10	0	0	0	1	0	0	1	0	19
[Re-listed] Drug product eligibility for priority review	1	0	0	0	0	2	0	1	1	0	2	0	7
Pharmacogenomics/biomarkers	0	0	0	0	0	0	0	0	0	0	0	0	0
GLP/GCP compliance	0	0	0	0	0	0	0	1	0	0	0	0	1
Total	41	27	33	43	27	24	25	41	38	19	40	29	387
Withdrawals	3	1	2	0	3	1	2	0	3	3	0	2	20
Grand Total	44	28	35	43	30	25	27	41	41	22	40	31	407

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

Note 2:Including consultations on preparation of documents for gene therapy products.

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 compliance were all conducted by the Office of Conformity Audit, regardless of category.

Note 7: Consultation on preparation of documents for gene therapy products have been handled in the Category of gene therapy products since the organizational change made on October 1, 2012.

Note 8: The consultations for the category of vaccines were counted after the organizational change made on October 1, 2012.

Note 9: The consultations for the category of cellular and tissue-based products were counted after the organizational change made on October 1, 2012.

(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 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, 2013, the number of commissioned experts is 1,165 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2012 was 221 (of which, 163 through document-based discussions; 58 through meetings).

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

b. Support for the development of national guidelines

- PMDA assisted the development of guidelines by study groups for evaluation of regenerative medicine and vaccines.

  PMDA provided cooperation for the creation and release of the '"Guidance on the Evaluation of Quality of Antibody Drugs" and the questions & answers (Q&A) for the guidance. (PFSB/ELD Notification No. 1214-1 and Administrative Notice of the Evaluation and Licensing Division, PFSB, MHLW, dated December 14, 2012)

- PMDA worked with MHLW to develop the following guidelines issued as the notifications (PFSB Notifications No. 0907-2, -3, -4, -5, and -6, dated September 7, 2012) based on the report of the research project supported by the FY 2012 Health and Labour Sciences Research Grants (multidisciplinary research project on regulatory science for drugs, medical devices, etc.) which is titled "Multidisciplinary Research on Quality and Safety Assurance of Products Derived from Human Stem Cells and Related Elements to Contribute to the Acceleration of Actual Utilization of Regenerative Medicine," and led by Dr. Takao Hayakawa, the principal researcher. PMDA posted the guidelines on its website and gave lectures at academic conferences, etc., to disseminate the contents.

  - Guideline on Quality and Safety Assurance of Drug Product, etc. Derived from Human (Autologous) Somatic Stem Cells

  - Guideline on Quality and Safety Assurance of Drug Product, etc. Derived from Human (Allogeneic) Somatic Stem Cells

  - Guideline on Quality and Safety Assurance of Drug Product, etc. Derived from Human (Autologous) iPS(-like) Cells

- Guideline on Quality and Safety Assurance of Drug Product, etc. Derived from Human (Allogeneic) iPS(-like) Cells
- Guideline on Quality and Safety Assurance of Drug Product, etc. Derived from Human ES Cells

- PMDA participated in the examination in a research project supported by the Health and Labour Sciences Research Grants (Health and Labour Sciences Special Research Project), which is titled "Research on Methods for Evaluating Quality and Efficacy of Vaccines, etc. Against Emerging Infections" and led by Dr. Teruhide Yamaguchi, the principal researcher. PMDA provided cooperation for studies of methods for developing vaccines for travelers.

- In addition, PMDA participated in the examination by a research project supported by Health and Labour Sciences Research Grants (multidisciplinary research project on regulatory science for drugs, medical devices, etc.), which is titled "Study for Development of Guidance in Relation to Guidelines for Practical Application of Next-generation Influenza Vaccines" and led by Dr. Koichi Yamanishi, the principal researcher. PMDA provided cooperation for studies of methods for developing nasal inactivated influenza vaccines.

- The team of the global clinical trial project, one of the PMDA's cross-sectional projects, provided cooperation for drafting the "Basic Principles on Global Clinical Trials (Reference Cases)" (PFSB/ELD Administrative Notice dated September 5, 2012), and the nanomedicine initiative project team provided cooperation for drafting the "Reflection Paper on the Development of Block Copolymer Micelles Products" (public comments solicitated by MHLW between February 1 and March 31, 2013).

- The teams of the microdose clinical trial project and the nano drug project examined the handling procedures of clinical trial notifications for development of relevant drugs, and submitted a proposal to the Evaluation and Licensing Division, PFSB, MHLW. As a result, the notifications including the proposed procedures were issued (PFSB/ELD Notifications No. 1228-15 and 19, dated December 28, 2012).

- Centering on PMDA's companion diagnostics project team, PMDA organized basic principles on companion diagnostics and related drugs, and cooperated for drafting the notification of "Points to Consider on Application for Approval of Companion Diagnostics and Related Drugs." The draft notification is currently being revised at MHLW and is scheduled to be issued.

- In addition to the above, more than 20 notifications, etc. were issued in FY 2012 with the cooperation of relevant review teams or offices in PMDA.

- From the viewpoint of proactively promoting regulatory science research and making use of its achievements in PMDA's operations, PMDA started to work on four designated research projects in FY 2012, taking into account the results of examinations at the Regulatory Science Research Evaluation Committee, etc., based on the "Basic Concept on Regulatory Science in PMDA" (developed in October 2011). PMDA published a paper discussing the current situation of regulatory science research at PMDA in *Therapeutic Innovation & Regulatory Science*, an international scientific journal (January 2013) to promote international understanding of regulatory science.

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

- PMDA conducts preliminary reviews of gene therapy products prior to the initiation of clinical trials as to whether the quality and safety of the products conform to the guidelines.

Number of Applications for Preliminary Reviews and Number of Completed Reviews

	FY 2008		FY 2009		FY 2010		FY 2011		FY 2012	
	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases
Cellular and tissue-based products	1	0	2	2	0	1	1	1	–	–
Gene therapy products	1	0	0	2	1	1	1	0	2	2

Note: The preliminary reviews of cellular and tissue-based drugs and medical devices were abolished in July 2011.

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

Review under the Cartagena Act (Median Regulatory Review Time)

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
No. of preliminary reviews for Type 1 Use	0	0	0	0	0
Median review time	–	- months	- months	- months	- months
No. of preliminary reviews for Type 2 Use	24	11	13	15	21
Median review time	–	2.5 months	2.5 months	2.0 months	1.2 months

Note 1:"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.

Note 2:Because the targets for review time were set up beginning in FY 2009, no previous data were available.

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

- PMDA started to offer Pharmaceutical Affairs Consultations on R&D Strategy in July 2011 to provide guidance and advice concerning studies and clinical trials that are necessary at the initial stage of product development in order to allow innovative pharmaceuticals and medical devices to be developed in Japan. The service is mainly intended to support universities, research institutions, and venture companies that have promising seed-stage resources. In addition to having briefing sessions in Osaka, Tokyo, Sendai, etc. so far, PMDA held individual orientations, and seminars at universities, etc., on its consultation service. Consequently, the number of consultations conducted has been increasing. The figures as of March 31, 2013 are shown in the table below.

Number of Pharmaceutical Affairs Consultations on R&D Strategy
(cumulative total from July 1, 2011 to March 31, 2013)

Individual orientations	Drugs (excluding CTP*)	Medical devices (excluding CTP*)	CTP	Total	%
Universities	68	82	14	164	39%
Companies/Ventures	43	162	4	209	50%
Research institutions/Others	17	26	4	47	11%
Total	128	270	22	420	
%	30%	64%	5%		100%

Pre-consultation meetings	Drugs (excluding CTP*)	Medical devices (excluding CTP*)	CTP	Total	%
Universities	104	51	31	186	46%
Companies/Ventures	24	66	50	140	34%
Research institutions/Others	32	15	34	81	20%
Total	160	132	115	407	
%	39%	32%	28%		100%

Consultations	Drugs (excluding CTP*)	Medical devices (excluding CTP*)	CTP	Total	%
Universities	30	4	5 (8)	39 (42)	55% (53%)
Companies/Ventures	3	3	8 (10)	14 (16)	20% (20%)
Research institutions/Others	12	1	5 (8)	18 (21)	25% (27%)
Total	45	8	18 (26)	71 (79)	
%	63% (57%)	11% (10%)	25% (33%)		100% (100%)

**CTP: cellular and tissue-based products*

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

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

- PMDA did not hold consultation meetings on pharmaceutical regulatory affairs for the Super Special Consortia for development of advanced medicine in FY 2012. However, PMDA maintained its structure for cooperation for related issues.

  Clinical trial consultations, etc. concerning topics addressed by the Super Special Consortia were conducted as follows: 1 clinical trial consultation for medical devices, and 4 pharmaceutical affairs consultations on R&D strategy (2 consultations on drug strategy and 2 consultations on medical device strategy). PMDA promptly dealt with all of the consultations. There were no cases for clinical trial consultations for drugs.

Over-the-counter drugs and generic drugs

- To promote self-medication and wide use of generic drugs, PMDA conducted presentation sessions in various symposia intended for the general public, and in international conferences, and various briefing sessions on filing of applications. PMDA posted the materials used for those sessions on its website.

(i) Appropriate and prompt reviews

a. Consultations and reviews based on medical care needs

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

  * A total of 1,378 PMDA staff members participated in 414 academic conferences and seminars held in Japan.

b. Efforts toward Introduction of Risk Management Plans for Generic Drugs

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

c. Promotion of digitization in reviews

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

d. Development of the Japanese Pharmacopoeia

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

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

- PMDA supported the MHLW's process of the revision of Japanese Standards of Quasi-drug Ingredients, by helping MHLW to hold a total of 6 meetings of the "Review Committee on Japanese Standards of Quasi-drug Ingredients" in FY 2012. Based on the results of deliberation at the review committee, the PFSB Notification was issued on March 29, 2013, regarding the partial revision of the "Japanese Standards of Quasi-drug Ingredients 2006."

f. Enhancement of the review system for Chinese herbal medicine products and crude drug products

- In Expert Discussions on Chinese herbal medicine products and western herbs, discussion was made on how individual products should be evaluated, and opinions from experts regarding desirable review practices were sought. Taking into account these opinions, PMDA has been considering the enhancement and strengthening of the review system. PMDA's other efforts to improve the expertise of reviewers include opinion exchange on reviews of Chinese herbal medicine and crude drug products with the Division of Pharmacognosy, Phytochemistry and Narcotics at the National Institute of Health Sciences (NIHS).

(ii) Approaches to shorten review times

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

In addition to periodically collecting data on the achievement level of the target review time and informing the reviewers of these levels, meetings of the Progress Management Committee for Reviews and Related Services were held to monitor and examine operational progress. (4 meetings were held in FY 2012).

- The approval statuses of generic drugs, OTC drugs and quasi-drugs in FY 2012 are as follows:

Median Regulatory Review Time for Approved Generic Drugs, etc.

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Generic drugs	1,980	3,271	2,633	3,091	3,421
Of which: Number of approved applications filed in or after April 2004	1,960	3,245	2,590	3,046	3,388
Median review time (for the applications filed in or after April 2004)	5.3 months	7.5 months	6.9 months	6.5 months	5.9 months
OTC drugs	1,821	2,171	1,008	1,031	881
Of which: Number of approved applications filed in or after April 2004	1,807	2,166	1,007	1,029	881
Median review time (for the applications filed in or after April 2004)	3.5 months	4.6 months	4.0 months	3.4 months	4.1 months
Quasi-drugs	2,340	2,221	1,976	1,938	1,968
Of which: Number of approved applications filed in or after April 2004	2,339	2,220	1,976	1,938	1,968
Median review time (for the applications filed in or after April 2004)	5.0 months	4.8 months	5.2 months	5.0 months	4.9 months
Total	6,141	7,663	5,617	6,060	6,270
Of which: Number of approved applications filed in or after April 2004	6,106	7,631	5,573	6,013	6,237

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

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

Reviews Conducted for Generic Drugs and Others by Fiscal Year

Classification	Fiscal Year	Applications	Approved	Withdrawals, etc.	Under review
Generic drugs	FY 2008	3,893	1,980	199	4,489
	FY 2009	2,354	3,271	223	3,343
	FY 2010	3,062	2,633	224	3,540
	FY 2011	2,892	3,091	165	3,175
	FY 2012	4,077	3,421	190	3,644
OTC drugs	FY 2008	2,387	1,821	302	2,438
	FY 2009	1,759	2,171	136	1,890
	FY 2010	1,092	1,008	133	1,841
	FY 2011	1,130	1,031	92	1,848
	FY 2012	1,005	881	90	1,882
Quasi-drugs	FY 2008	2,414	2,340	189	1,575
	FY 2009	2,572	2,221	82	1,844
	FY 2010	2,297	1,976	135	2,030
	FY 2011	2,212	1,938	82	2,222
	FY 2012	2,117	1,968	74	2,297

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

Note 2:The following numbers were corrected because errors in the summation were found.

Generic drugs

In "under review" for FY 2008, "4,488" was corrected to "4,489."
In "under review" for FY 2009, "3,342" was corrected to "3,343."
In "under review" for FY 2010, "3,539" was corrected to "3,540."

OTC drugs

In "under review" for FY 2008, "2,439" was corrected to "2,438."
In "under review" for FY 2009, "1,891" was corrected to "1,890."
In "withdrawals, etc." for FY 2010, "138" was corrected to "133."
In "under review" for FY 2010, "1,842" was corrected to "1,841."

Quasi-drugs

In "applications" for FY 2009, "2,571" was corrected to "2,572."

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

OTC drugs

New category of application	1	2	3-1	3-2	3-3	4	5-1	5-2	5-3	5-4	6	7-1	7-2	8	Total
Filed in FY 2012	0	0	1	0	0	8	0	3	1	10	7	65	9	891	995
Approved in FY 2012	0	0	0	0	0	15	0	4	0	2	2	46	4	778	851

Category of application	Insecticides	Total
Filed in FY 2012	10	10
Approved in FY 2012	9	9

Former category of application	1	2	3	4-1	4-2	OTC test agents	Total
Approved in FY 2012	0	0	5	5	11	0	21

Quasi-drugs

Category of application	1, 3	2	Total
Filed in FY 2012	72	2,045	2,117
Approved in FY 2012	44	1,924	1,968

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

Note 2:Categories of application are as follows:

OTC drugs

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

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

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

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

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

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

- The median regulatory review times for approved products in FY 2012 were 5.9 months for generic drugs (target, 10 months), 4.1 months for OTC drugs (target, 8 months), and 4.9 months for quasi-drugs (target, 5.5 months), showing target achievement for all categories.

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

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Generic drugs	601	1,004	1,040	1,118	1,188

- For generic drugs, PMDA conducted 1,188 inspections to confirm compliance with GLP, GCP, and other standards for product applications, by collating them with raw data such as test records, laboratory notebook, case report forms, etc.

(iii) Efficient conduct of clinical trial consultations

a. Improvement of pre-application consultations for generic drugs

- The Second Mid-term Plan stipulates that PMDA should establish a new pre-application consultation for generic drugs by FY 2013 that is different from the existing simple consultation. In January 2012, PMDA started to provide consultations on quality for generic drugs and on bioequivalence of generic drugs on a trial basis, and 10 consultations were provided in FY 2012. PMDA intends to deal with 2 consultations a month on a trial basis continuously in FY 2013.

Number of Consultations for Generic Drugs

	FY 2011	FY 2012
Conducted consultations	3	10
Withdrawals	0	0
Total (conducted consultations and withdrawals)	3	10

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

Number of Consultations for Generic Drugs by Consultation Category in FY 2012

Consultation category	Conducted consultations	Withdrawals	Total (conducted consultations and withdrawals)
Consultations on bioequivalence of generic drugs	8	0	8
Quality consultation for generic drugs	2	0	2
Total	10	0	10

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

- PMDA started to offer pre-development and pre-application consultations for OTC drugs on a trial basis in FY 2010 based on opinions from the industry associations. Among them, PMDA started to offer consultations on appropriateness of development of new OTC drugs 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 from FY 2011. Because the number of consultations in FY 2012 decreased as compared to those in the previous year, PMDA intends to improve the consultation service by referring to the opinions from the industry associations, etc.

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

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

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

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2012

Consultation category	Conducted consultations	Withdrawals	Total (conducted consultation and withdrawal)
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	3	0	3
Total	4	0	4

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

- PMDA exchanged opinions with the Japan Cosmetic Industry Association (JCIA) to identify the needs for pre-application consultations for quasi-drugs. PMDA intends to continue the interaction with JCIA, including the need for consultation service.

Medical devices

- Based on the "Action Program to Accelerate Reviews of Medical Devices" formulated in December 2008, PMDA took various measures with the aim of resolving the lag of 19 months that exists in the process up to approval of new medical devices between Japan and the US (consisting of 12 months for development and 7 months for review of applications).

(i) Appropriate and prompt reviews

a. Structure for clinical trial consultations and reviews

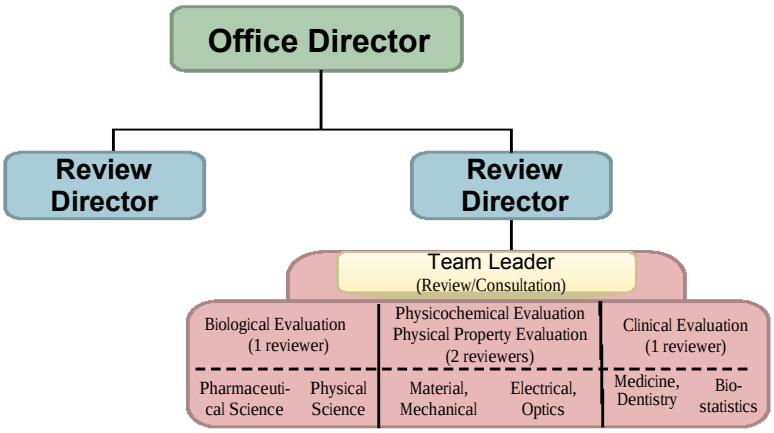
Review Performance for FY 2012 (medical devices and in vitro diagnostics)

(1) Number of Expert Discussions conducted: 77 (of which, 51 through document-based discussions, 26 through meetings)
(2) Applications deliberated at the Committee on Medical Devices and in vitro Diagnostics (under PAFSC): 19
Applications reported to the Committee on Medical Devices and in vitro Diagnostics (under PAFSC): 323 (of which, 292 for medical devices and 31 for in vitro diagnostics)

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

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

Organization Chart for Reviews of New Medical Devices



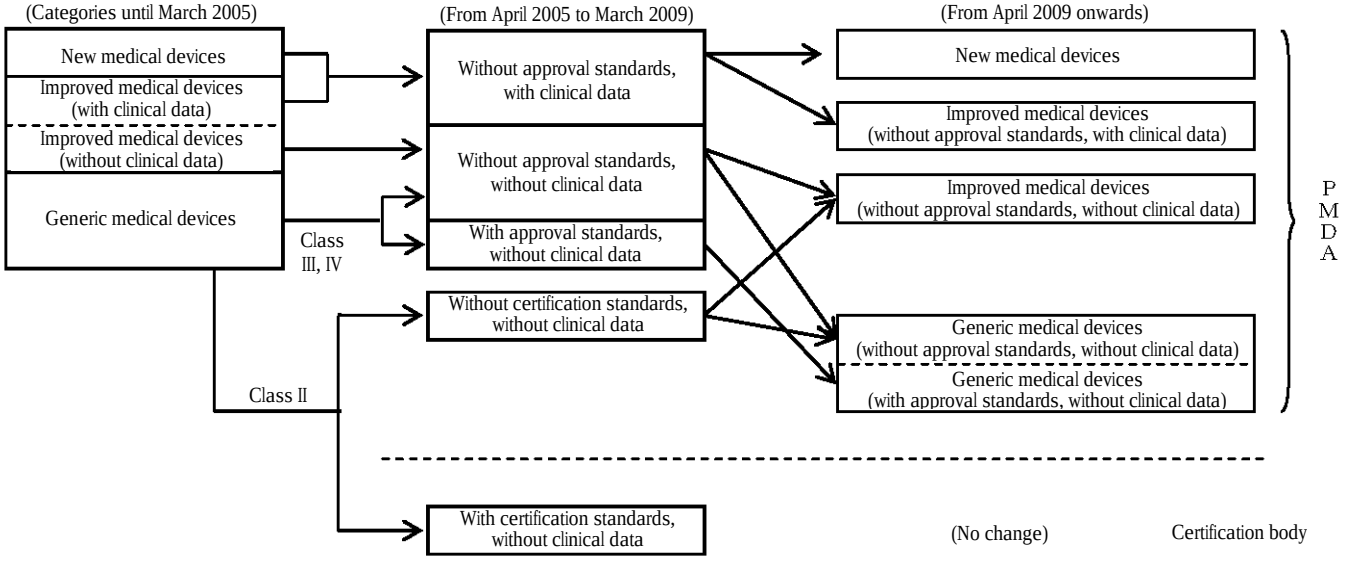
- PMDA increased the number of medical device reviewers based on the Action Program to Accelerate Reviews of Medical Devices. In order to enhance the review system, more reviewers were allocated mainly to the review categories where rapid processing was likely to be difficult, according to situations such as the status of processing of product applications.

- Reviews of new medical devices were conducted upon establishing a team to each review category as shown below:

Review Categories Covered by the Offices of Medical Devices

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

- PMDA conducted clinical trial consultations for new medical devices based on the team-reviewed guidance plan drafted by the Review Director as well as the consultation leader and the deputy consultation leader in charge, who were appointed in a review team.
- With the enforcement of the Pharmaceutical Affairs Act, as revised in April 2009, the categories of application were reclassified.



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

b. Introduction of the 3-track review system

- As one of the efforts to upgrade and accelerate reviews, PMDA fully implemented the 3-track review system (new medical devices, improved medical devices, and generic medical devices) in FY 2011. In FY 2012, PMDA was committed to further entrenching the system based on the experiences in the previous year.

c. Reinforcement of the progress management of reviews

- In order to conduct reviews and related services promptly and appropriately to achieve the target review time as specified in the Mid-term Plan, PMDA ensured that the Progress Management Committee for Reviews and Related Services hold meetings once every 3 months so that the Chief Executive and other executivets of PMDA could accurately grasp the progress of reviews and related services and support to improve the progress. The Committee thus monitored operational progress, and particularly for new medical devices, etc., comprehensively considered relevant information and approaches. The Committee advanced the consideration on policies for solving operational challenges.
- 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 2012. In the meetings, opinions for the advancement of the system were exchanged, information on the overall review status for new medical devices and associated issues were shared, measures addressing challenges and future approaches were examined, and the detailed review status of new medical devices and other products under review were informed (11 meetings were held in FY 2012).

  At the "Review Segment Committee for Progress Management," the Director of the Center for Product Evaluation and Associate Center Director provided necessary guidance, taking into account reports from office directors of review divisions, and efforts to widely disseminate the results of the investigation of issues and improvement measures for controversial products within review segments were newly started at the end of the FY 2012.

d. Standardization and transparency of review

- To clarify review standards, PMDA posted the following two documents on basic considerations for review on its website: "Points to Consider in Preparing Applications for New Medical Devices, etc." and "Points to Consider in Preparing Applications for Improved Medical Devices." Both were published in FY 2008 and revised in association with subsequent modifications to the 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 the website the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices)" which is a revised version of the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices and improved medical device)" published in FY 2009, and introduced at workshops to ensure that it was thoroughly acknowledged. PMDA posted on its website the following guidance documents: "Points to Consider in Preparing Data for Applications of Improved Medical Devices" for improved medical devices, "Points to Consider in Preparing Data for Applications of Generic Medical Devices," and "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices" for generic medical devices. PMDA also presented these guidance documents in workshops to thoroughly disseminate them.

e. Consultations and reviews based on medical care needs

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

* A total of 1,378 PMDA staff members participated in 414 academic conferences and seminars held in Japan.

- In order to encourage manufactures and distributors of medical devices to promote the development of medical devices that have been approved in Europe and the U.S. but not yet approved in Japan, the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Need (chaired by Dr. Soichiro Kitamura, President Emeritus of National Cerebral and Cardiovascular Center) was established in the MHLW in October 2006. The study group has been actively conducting investigations. PMDA has cooperated for the operation of the study group, and provided clinical trial consultations and review of product applications taking into account investigation results by the study group. Through this initiative, 3 medical devices were approved in FY 2012.

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. Close links between consultations and reviews are maintained and teams are flexibly organized as necessary.

g. Promotion of digitization in reviews

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

(ii) Introduction of new review systems

a. Introduction of prior assessment consultation

- To preliminarily evaluate the quality, efficacy and safety of medical devices from the development stage, PMDA started to offer prior assessment consultations as a pilot scheme in October 2010, and formally implemented in FY 2012.

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 64 products (excluding the period for GCP/GLP inspections) approved in FY 2012 was not more than 2 months.

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 for medical devices, the Committee on Medical Device Approval Standards held four meetings in FY 2012.

  The numbers of standards (established and revised) for approval and certification reported to MHLW in FY 2012 were as follows:

Reported in:	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	Total
Approval standards	6	7	5	2	6	6	5	37
Certification standards	0	14	86	64	294	84	67	609
Review guidelines	0	1	2	6	0	0	0	9

The number of standards established by MHLW in FY 2012 based on the reports from PMDA is shown below:

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

Established in:	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	Total
Approval standards	0	17	8	10	-2*	5	3	0	0	41
Certification standards	363	9	24	0	17	68	274	67	2	824
Review guidelines	0	0	0	0	3	1	4	0	0	8

* *In FY 2008, two of the established approval standards were switched to the certification standards making the value a negative number.*

List of Approval Standards and Certification Standards for Medical Devices (FY 2012)

Certification standards (2 established), approval standards (0 established), review guidelines (0 established)	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 264 dated November 20, 2012	Proposed certification standards for low frequency electro acupuncture device
MHLW Ministerial Announcement No. 435 dated July 20, 2012	Proposed certification standards for angiographic catheters, etc.

- The PMDA website for the information service on medical device standards provides the latest information on the certification standards and approval standards in relation to JIS, ISO/IEC as their components, MHLW Notifications, and Japanese Medical Device Nomenclature (JMDN), etc. 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 minor change notifications are not required, and 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 cooperated with MHLW for the issuance of "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 for changing raw materials.
- PMDA appropriately responded to questions raised by marketing authorization holders during consultations concerning the necessity, or not, of clinical data in accordance with the notifications, etc. issued by MHLW.
- In order to clarify the scope of one product, PMDA conducted simple consultations, etc. based on the notifications "Partial Revision of 'Points to Consider in Filing Applications for Medical Devices' (PFSB/ELD/OMDE Notification No.1224007 dated December 24, 2010)" and "Handling for Filing Applications for Dental Implants (PFSB/ELD/OMDE Notification No. 0713-1 dated July 13, 2012)."

d. Equivalence review of generic medical devices

- PMDA continuously conducted the equivalence review of generic medical devices filed in FY 2012 based on the notification titled "Points to Consider in Preparing Applications for Generic Medical Devices" (PFSB/ELD/OMDE Notification No.0327004 dated March 27, 2009).

e. Support for the development of certification standards, etc.

- PMDA supported the development and revision of certification standards by MHLW. A total of 2 certification standards were established in FY 2012, and a total of 54 certification standards were revised in the same year.

(iii) Efforts to solve the device lag

- The targets for total review time, regulatory review time, and applicant's time for medical device applications filed on or after April 1, 2004 were set up, and then both the regulatory authorities and applicants have been making efforts toward the achievement of the targets for review time.
- Review teams consisting of reviewers with expertise in pharmaceutical science, physical science, engineering, medicine, dentistry, veterinary medicine, biostatistics, etc., conducted reviews of submitted applications for new medical devices and improved medical devices.

  (Note) New medical devices: Medical devices subject to re-examination (medical devices that have a clearly different structure, usage, indications, performance, etc., as compared to existing approved medical devices or certified medical devices).
  Improved medical devices: Medical devices that do not fall under "new medical devices" or "generic medical devices," and are not novel enough to be subject to re-examination, nor are substantially equivalent to existing medical devices in terms of structure, usage, indications, or performance.

- For improved medical devices, PMDA reinforced the progress management while making efforts to reduce the backlog of applications pending completion of review. Specifically, reasons were identified for the prolonged review of products for which application was filed in past years, and reminder notices were frequently sent to applicants if their responses to PMDA's inquiries were delayed.
- For reviews of generic medical devices, PMDA introduced the buddy system in which an experienced reviewer and a newcomer 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 has conducted reviews intensively, and for categories with many products under review, PMDA flexibly operate the buddy system without boundaries between categories in order to accelerate reviews. Under the system, one reviewer is allowed to help another reviewer as far as there are similarities in the products they are reviewing.

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

- 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 the purpose of improving environments for the smooth conduct of global clinical trials, PMDA participated in the Harmonization by Doing (HBD) project which has been undertaken by both Japan and the US, and had discussions on the conduct of global clinical trials, the development of common protocols between Japan and the US, and the standardization of post-marketing surveillance database. In addition, continuously from the previous year, PMDA made efforts to accelerate reviews by exchanging information with the US FDA on review and consultation services. As part of the HBD activities, PMDA participated in scientific sessions held at academic conferences such as TCT (Transcatheter Cardiovascular Therapeutics) and CRT (Cardiovascular Research Technologies) Conferences, and discussed the challenges in the development of new medical devices with the industry, government, and academia.
- Toward the achievement of the target regulatory review times, PMDA made efforts to process the backlog of applications pending completion of review, while enhancing progress management of reviews of applications newly submitted so that the reviews could be accelerated.

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

  By carrying out the measures mentioned above, PMDA has endeavored to achieve the target total review time.
- The status of reviews for medical devices in FY 2012 is shown below:

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

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

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	28.8	13.9	15.1	4.3	9.3
Regulatory review time [months]	5.8	6.0	5.3	2.9	7.2
Applicant's time [months]	-	7.7	10.7	1.3	3.4
Number of approved applications	4	3	3	6	5

Note 1:Products covered were those for which applications were filed in or after FY 2004. Note 2: Because the target applicant's time was set up beginning in FY 2009, no previous values are available.

- In FY 2012, the median total review time for priority review products was 9.3 months, showing achievement of the target.

  The median regulatory review time was 7.2 months, and the median applicant's time was 3.4 months.

- 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 2012, 5 priority review products (all were new medical devices) were approved.

- A priority review status is given to a medical device regarded as having particularly high medical need. New requests for designation for priority review were made for 3 products in this fiscal year. Two out of the 3 products received priority review designation, and the remaining request was withdrawn.

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

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

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	14.4	11.0	16.5	9.7	12.7
Regulatory review time [months]	9.8	6.8	7.1	5.1	5.4
Applicant's time [months]	-	7.1	8.2	3.4	5.0
Number of approved applications	12	33	15	27	41

Note 1:Products covered were those for which applications were filed in or after FY 2004. Note 2: Because the target applicant's time was set up beginning in FY 2009, no previous values are available.

- In FY 2012, the median total review time for standard review products was 12.7 months, showing achievement of the target. Meanwhile, the number of approvals increased substantially.

  The median regulatory review time was 5.4 months, and the median applicant's time was 5.0 months.

- PMDA reviewed the submitted product applications in the order of receipt, giving full consideration to the target review time.
- The number of product applications under review at the end of FY 2012 was 61 (including 4 orphan medical devices and 4 priority review products that is not an orphan medical device).

Review Status of New Medical Devices by Fiscal Year of Application

New medical devices (Filed in)	Applications	Approved	withdrawal	Under review
On or before 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 (2)	6	0 [-2]
FY 2008	32	30 (2)	2	0 [-2]
FY 2009	24	19 (2)	3	2 [-2]
FY 2010	28	23 (2)	2	3 [-2]
FY 2011	42	34 (24)	1	7 [-24]
FY 2012	64	15 (15)	0	49 [49]
Total	445	267 (47)	117	61 [17]

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:Values in parentheses in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2012 (included in values on their left).

Note 4:Values in brackets indicate difference from the status reported in FY 2011.

Number of Applications Processed and Time Spent in Each Review Process

	Review process	1. From receipt of applications to product briefing session (formerly initial meeting)	2. From product briefing session to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2012	Number of processed applications	25	24	29	46
	Median total review time [days]	31.0	308.0	82.0	6.0

Note 1:The median total review times are the sum of the regulatory review time and applicants' time.

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

Note 3:Values are of applications filed in or after April 2004.

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

- Improved medical devices (with clinical data) refer to medical devices on which clinical trial data are required for regulatory review, among improved medical devices.

Review Times for Improved Medical Devices (with Clinical Data)

- The review status of improved medical devices (with clinical data) in FY 2012 was as follows.

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	-	17.2	15.5	13.9	17.3
Regulatory review time [months]	-	10.4	7.6	7.0	7.9
Applicant's time [months]	-	6.6	7.6	7.2	8.8
Number of approved applications	–	30	40	55	44

Note 1:Products covered were those for which applications were filed in or after FY 2004. Note 2: Applications filed in or before FY 2008 have been re-categorized in this table according to the new categorization implemented from FY 2009.

Note 3:Because the target for this category was set up beginning in FY 2009, previous values are not available.

- The number of improved medical devices (with clinical data) approved in FY 2012 was 44, and the median total review time for these applications was 17.3 months, showing non-achievement of the target time. Also, the number of approved applications decreased because the backlog of applications pending completion of review was strenuously processed as discussed below.

  The median regulatory review time was 7.9 months, and the median applicant's time was 8.8 months.

- For improved medical devices (with clinical data), the target total review time was not achieved in FY 2012 because the backlog of applications pending completion of review was strenuously processed, but the number of products under review for which application was filed in or before FY 2011 was substantially reduced.

  However, the backlog of applications has not been cleared, and therefore PMDA intends to further accelerate the process of the backlog of applications.

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

Improved medical devices (with clinical data) (Filed in)	Applications	Approved	Withdrawals	Under review
FY 2009	34	33 (3)	1	0 [-3]
FY 2010	34	32 (2)	1 (1)	1 [-3]
FY 2011	26	15 (14)	2 (2)	9 [-16]
FY 2012	42	6 (6)	2 (2)	34 [34]
Total	136	86 (25)	6 (5)	44 [12]

Note 1:The number of applications was counted based on the categorization of the day the application was filed or the request was received.

Note 2:The number of approved products includes those approved in other medical device categories.

Note 3:Values in parentheses indicate those processed in FY 2012 (included in values on their left).

Note 4:Values in brackets indicate difference from the status reported in FY 2011.

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

- Improved medical devices (without clinical data) refer to medical devices on which clinical trial data are not required for regulatory review, among improved medical devices.

Review Times for Improved Medical Devices (without Clinical Data)

- The review status of improved medical devices (without clinical data) in FY 2012 was as follows.

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	-	13.2	14.5	13.3	9.7
Regulatory review time [months]	-	8.5	8.0	5.6	4.8
Applicant's time [months]	-	3.9	6.2	6.5	4.7
Number of approved applications	–	158	182	218	229

Note 1:Products covered were those for which applications were filed in or after FY 2004. Note 2: Applications filed in or before FY 2008 have been re-categorized in this table according to the new categorization implemented from FY 2009.

Note 3:Because the target for this category was set up beginning in FY 2009, previous values are not available.

- There were 229 improved medical devices (without clinical data) approved in FY 2012, and the median total review time was 9.7 months, showing non-achievement of the target, but the number of applications approved in FY 2012 was the largest since FY 2009.

  The median regulatory review time was 4.8 months, and the median applicant's time was 4.7 months.

- For improved medical devices (without clinical data), the target total review time was not achieved in FY 2012 because the backlog of applications pending completion of review was strenuously processed, but the number of products under review for which application was filed in or before 2011 was substantially reduced.

  However, the backlog of applications has not been cleared, and therefore PMDA intends to further accelerate the process of the backlog of applications.

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

Improved medical devices (without clinical data) (Filed in)	Applications	Approved	Withdrawals	Under review
FY 2009	137	121 (11)	15 (3)	1 [-14]
FY 2010	165	125 (20)	21 (12)	19 [-32]
FY 2011	176 (-1)	136 (98)	10 (8)	30 [-106]
FY 2012	211	70 (70)	5 (5)	136 [136]
Total	689	452 (199)	51 (28)	186 [-16]

Note 1:The number of applications was counted based on the categorization of the day the application was filed or the request was received.

Note 2:From the number of applications in FY 2011, 1 application was deleted since team review category at the time of filing application was changed.

Note 3:The number of approved products includes those approved in other medical device categories.

Note 4:Values in parentheses indicate those processed in FY 2012 (included in values on their left).

Note 5:Values in brackets indicate difference from the status reported in FY 2011.

e. Review times for generic medical devices

- Generic medical devices refer to medical devices that are regarded as substantially equivalent to existing approved medical devices in terms of structure, usage, indications, and performance.

Review Times for Generic Medical Devices

- The review status of generic medical devices in FY 2012 is as follows:

Targets

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

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

Results

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Total review time [months]	-	12.9	11.0	5.0	4.0
Regulatory review time [months]	-	5.9	5.1	2.5	1.6
Applicant's time [months]	-	3.6	4.7	2.3	2.3
Number of approved applications	–	1,797	1,391	907	1,216

Note 1:Products covered were those for which applications were filed in or after FY 2004. Note 2: Applications filed in or before FY 2008 have been re-categorized in this table according to the new categorization implemented from FY 2009.

Note 3:Because the target for this category was set up beginning in FY 2009, previous values are not available.

- There were 1,216 generic medical devices approved in FY 2012, and the median total review time was 4.0 months, showing achievement of the target. At the same time, the number of approvals was increased.

  The median regulatory review time was 1.6 months, and the median applicant's time was 2.3 months. Applications filed between FY 2009 and FY 2011, in addition to those filed in FY 2012, were processed in the current fiscal year, which led to an increase in the number of approved applications. At the same time, the target review times were achieved as shown above. This probably means that acceleration of product review contributed to the results.

Review Status of Generic Medical Devices by Fiscal Year of Application

Generic medical devices (Filed in)	Applications	Approved	Withdrawals	Under review
FY 2009	1,126	1,023 (46)	69 (16)	34 [-62]
FY 2010	1,020	869 (103)	71 (16)	80 [-119]
FY 2011	995 (1)	864 (366)	43 (26)	88 [-392]
FY 2012	1,075	707 (707)	9 (9)	359 [359]
Total	4,216	3,463 (1,222)	192 (67)	561 [-214]

Note 1:The number of applications was counted based on the categorization of the day the application was filed or the request was received.

Note 2:The number of applications in FY 2011 includes 1 added application for which team review category at the time of making application was changed.

Note 3:The number of approved products includes those approved in other medical device categories.

Note 4:Values in parentheses indicate those processed in FY 2012 (included in values on their left).

Note 5:Values in brackets indicate difference from the status reported in FY 2011.

(iv) Efficient provision of clinical trial consultations

a. Provision of priority consultations

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

b. Acceleration of the procedure for clinical trial consultations

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

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

Number of Consultations Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	76	110	112	141	173
(Medical devices)	74	104	105	136	165
(In vitro diagnostics)	2	6	7	5	8
Withdrawals	2	1	1	4	3
(Medical devices)	2	1	1	4	3
(In vitro diagnostics)	0	0	0	0	0
Total (conducted and withdrawn consultations)	78	111	113	145	176
(Medical devices)	76	105	106	140	168
(In vitro diagnostics)	2	6	7	5	8

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

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	–	–	2	3	3
(Medical devices)	–	–	2	3	3
(In vitro diagnostics)	–	–	0	0	0
Withdrawals	–	–	0	0	0
(Medical devices)	–	–	0	0	0
(In vitro diagnostics)	–	–	0	0	0
Total (conducted and withdrawn consultations)	–	–	2	3	3
(Medical devices)	–	–	2	3	3
(In vitro diagnostics)	–	–	0	0	0

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Conducted consultations	–	0	0	0	0
Withdrawals	–	0	0	0	0
Total (conducted and withdrawn consultations)	–	0	0	0	0

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

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

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

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

- In FY 2012, PMDA conducted a total of 176 consultations (including 3 withdrawals).
- A total of 173 clinical trial consultations (excluding prior assessment consultations and consultations on pharmacogenomics/biomarkers; including 3 withdrawals) were carried out in FY 2012. The goal to be achieved by FY 2013 is to secure the yearly capability to process 200 consultations and provide all consultations requested. In FY 2012, PMDA basically provided all of the consultations requested.
- PMDA aimed to complete the process from conduct of clinical trial consultation to finalization of meeting records within 30 business days for 60% of products subjected to consultation. In FY 2012, the target was achieved in 159(89.3%) of 178 consultations.

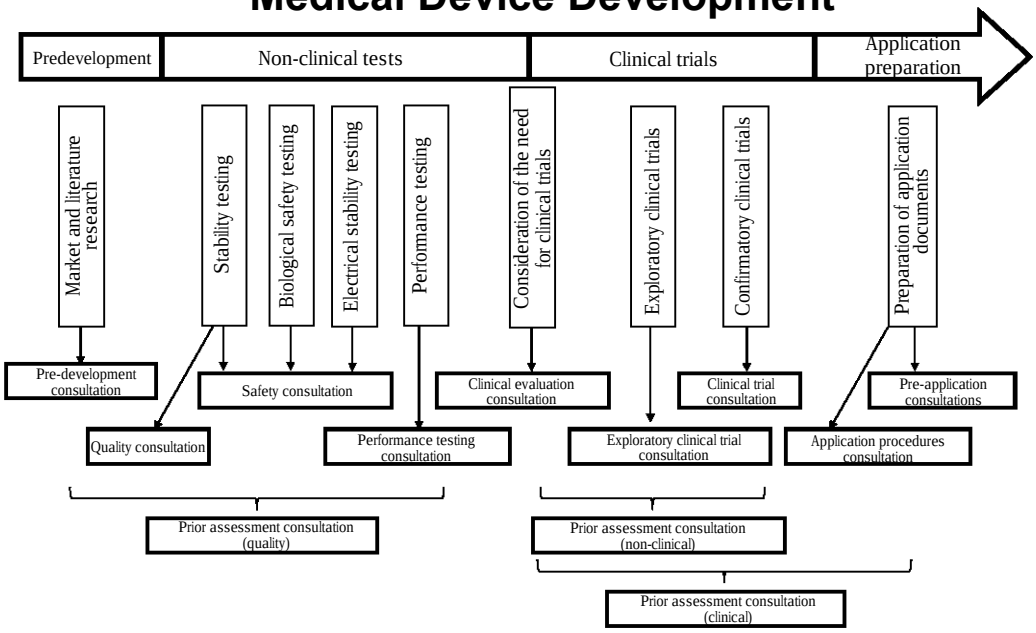
Number of Consultations for Medical Devices by Category in FY 2012

Consultation category	Conducted consultations	Withdrawals	Total (conducted and withdrawn consultations)
Pre-development consultation for medical devices	77	2	79
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	10	0	10
Clinical evaluation consultation for medical devices	27	1	28
Exploratory clinical trial consultation for medical devices	1	0	1
Clinical trial consultation for medical devices	30	0	30
Pre-application consultation for medical devices	3	0	3
Application procedure consultation for medical devices	6	0	6
Additional consultation for medical devices	3	0	3
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)	2	0	2
Prior assessment consultation for medical devices (clinical)	1	0	1
Pre-development consultation for in vitro diagnostics	0	0	0
Quality consultation for in vitro diagnostics	1	0	1
Consultation on conformity with standards for in vitro diagnostics	0	0	0
Clinical evaluation consultation for in vitro diagnostics	3	0	3
Clinical performance study consultation for in vitro diagnostics	2	0	2
Pre-application consultation for in vitro diagnostics	1	0	1
Application procedure consultation for in vitro diagnostics	0	0	0
Additional consultation for in vitro diagnostics	1	0	1
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	173	3	176

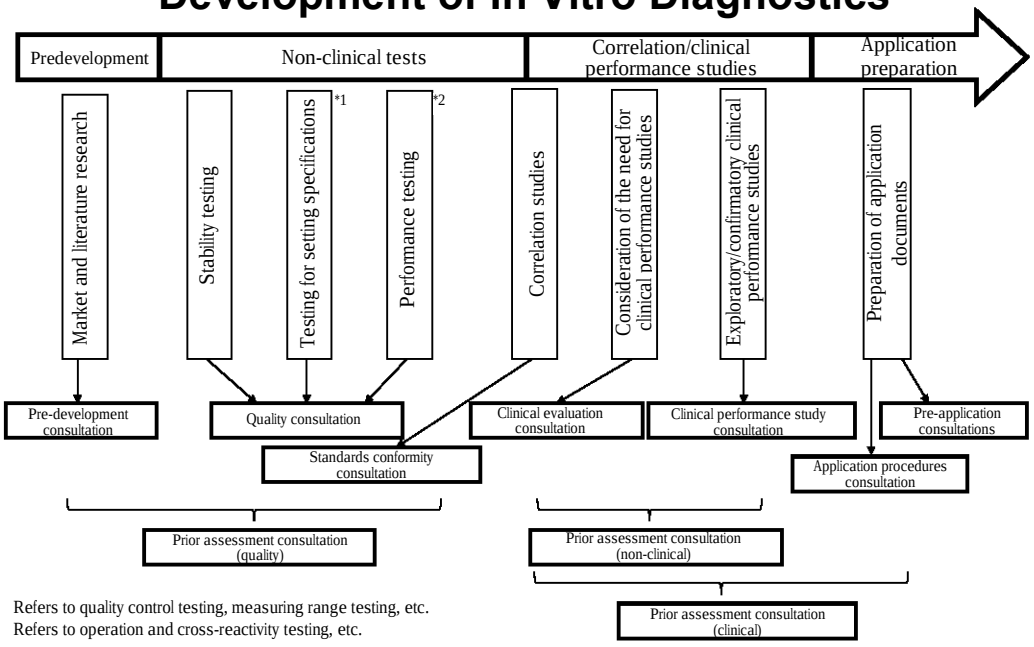
d. Expansion of consultation categories

- Since FY 2007, in order to promote product development and speed up reviews by providing detailed advice that meets various needs at each stage, the clinical trial consultations on medical devices and in vitro diagnostics have been improved to provide specific advice for each development stage.
- PMDA started prior assessment consultations to preliminarily evaluate the quality, efficacy and safety of devices from the development stage as a pilot scheme in October 2010, and formally started to offer these consultations in FY 2012.

Consultations Offered in the Course of Medical Device Development



Consultations Offered in the Course of Development of In Vitro Diagnostics



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

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

(v) Promotion of evaluation of new technologies

a. Utilization of external experts

- See (v)-a [New drugs].
- The number of Expert Discussions conducted in FY 2012 was 77 (of which, 51 through document-based discussions; 26 through meetings).

- PMDA had discussions with external experts on issues raised in clinical trial consultations and application reviews for cellular and tissue-based products. At the Cellular and Tissue-based Products Subcommittee of the Science Board, PMDA heard opinions from external experts regarding cross-sectional themes and had discussion. In addition, PMDA exchanged opinions regarding regulations on cellular and tissue-based products and discussion themes at ICH, etc. by making use of telephone conferences with EMA, FDA, etc. and gatherings at international conferences.

b. Support for the development of national guidelines

- See (v)-b [New drugs].
- PMDA worked cooperatively with MHLW to develop the "Guidance for the Evaluation of Emerging Technology Medical Devices (Orthopedic Customized Artificial Knee Joint Prosthesis and RNA Profiling-based Diagnosis Systems)" publicly made known by MHLW in November 2012 (PFSB/ELD/OMDE Notification No. 1120-5 dated November 20, 2012), and promoted to disseminate the notification.
- PMDA worked with the MHLW to develop the "Guidance for the Evaluation of Emerging Technology Medical Devices (Autologous iPS Cell-derived Retinal Pigment Epithelium Cells, Activity Function Recovery Devices, Medical Devices for the Treatment of Critical Ischemic Diseases of Lower Extremities) (draft)" in the MHLW's project for creation of guidance for the evaluation of emerging technology medical devices. Public comment was invited on this draft guidance for one month from March 2013.

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

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

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

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

e. Support for the Super Special Consortia for development of state-of-the-art medicine

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

Inspections

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

(i) Efficient conduct of GLP/GCP/GPSP inspections and data integrity assessment

- PMDA issued notifications from the Chief Executive dated October 12, 2012 regarding document-based compliance assessments for product applications and GCP on-site inspections, as well as document-based compliance assessments for documents submitted for re-examination and re-evaluation and GPSP on-site inspections.

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

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

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

Notification on the procedure for inspections related to re-examinations and re-evaluations of medical devices: PMDA Notification No. 1012066

- PMDA efficiently conducted on-site and document-based inspections and data integrity assessment concerning the studies and data submitted in applications for new drugs and medical devices, to determine whether such data were collected in compliance with the requirements of the Ministerial Ordinance on Good Laboratory Practice (GLP), the Ministerial Ordinance on Good Clinical Practice (GCP), and the data integrity standards for products applications.
- In line with the revision of the notification on operation of GCP (October 2011), PMDA revised the "Checklist for GCP on-site and document-based inspections and data integrity assessment for new drugs" and released it.
- PMDA conducted 99 GCP on-site inspections (at companies) for new drugs (the number is those of active ingredients) in FY 2012, and 98 (99.0%) of them were conducted in conjunction with document-based inspections.
- Although a standard administrative processing time for GLP/GCP/GPSP inspections has not been set, PMDA worked hard to make sure that the inspection processing time did not affect the review time of applications for individual products.

a. Promotion of document-based inspection on sites

- PMDA introduced a method in FY 2009 whereby its staff members visit companies for document-based compliance assessments for new drugs. In FY 2012, 100 inspections (84.0%) were conducted by this company-visit, out of the total of 119 inspections (the numbers are those of active ingredients).

b. Introduction of the GCP system inspection

- As a part of investigation on the GCP system inspection, PMDA released the EDC Management Sheet (for sponsors/marketing authorization holders) and the EDC Inspection Check List (for medical institutions) for the purpose of effectively and efficiently checking the operation processes using EDC. Regarding the method of inspection using such management sheet, PMDA issued PMDA/CPE Notification No. 0327001 dated March 27, 2013 by the Director for Center for Product Evaluation, and disseminated the notification.

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

- With regard to document-based compliance assessments for non-clinical studies of medical devices, PMDA held "Workshop on document-based compliance assessments for non-clinical studies of medical devices" for applicants, to improve the reliability of application documents and accelerate document-based assessments. In the workshop, points to consider, etc. for the conduct of appropriate studies were presented, based on examples that were actually seen in inspections.
- In FY 2012, 1,263 document-based inspections/data integrity assessments and 1 GCP on-site inspection were completed.

(ii) Efficient conduct of GPSP/GPMSP inspections and data integrity assessment for re-examination

- PMDA conducts document-based and on-site inspections and data integrity assessment as to whether or not data submitted for re-examination of approved new drugs and new medical devices had been collected and prepared in compliance with the data integrity standards for product applications and the requirements of the Ministerial Ordinance on Good Post-Marketing Study Practices (GPSP) or the Ministerial Ordinance on Good Post-Marketing Surveillance Practice (GPMSP).

  In FY 2012, the number of completed assessment was 112 for new drugs and 15 for new medical devices.

- PMDA conducts data integrity assessment as to whether or not data submitted for re-evaluation of approved drugs had been collected and generated in compliance with the data integrity standards for product applications, etc., but there were no products subject to the data integrity assessment for re-evaluation in FY 2012.

Number of GLP/GCP/GPSP Compliance Assessments

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Document-based assessments	1,543	2,140	2,359	2,437	2,737
New drugs	293	246	251	280	286
Generic drugs	601	1,004	1,040	1,118	1,188
Medical devices	649	890	1,068	1,039	1,263
GCP on-site inspections	198	175	171	149	197
New drugs	182	164	158	140	187
Generic drugs	15	10	10	8	9
Medical devices	1	1	3	1	1
Document-based assessment for re-examination	83	66	138	111	127
New drugs	83	66	135	109	112
New medical devices	–	–	3	2	15
GPSP inspections	79	65	135	109	112
New drugs	79	65	135	109	112
New medical devices	–	–	–	–	–
Document-based assessments for re-evaluation	–	–	–	–	–
GLP inspections	43	26	30	32	39
Drugs	32	18	26	23	29
Medical devices	11	8	4	9	10

Note 1: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.

Note 2:For annual numbers of GPSP inspections, the table shows those of GPMSP inspections for FY 2008, and those of GPMSP or GPSP inspections from FY 2009 and onward.

(iii) Efficient conduct of GMP/QMS inspections

a. Background of GMP/QMS inspections

- Based on the amended Pharmaceutical Affairs Act that came into effect on April 1, 2005, compliance of methods for manufacturing control and quality control at manufacturing sites for drugs, etc., with requirements specified in the Ministerial Ordinance on GMP for Drugs and Quasi-drugs*, and/or Ministerial Ordinance on QMS for Medical Devices and In Vitro Diagnostics† is a pre-requisite for approval. Therefore, in addition to the manufacturing sites already licensed by the Minister of Health, Labour and Welfare, the following manufacturing sites became subject to inspection by PMDA: (1) foreign manufacturing sites related to all products that require regulatory approval; and (2) domestic manufacturing sites for new drugs, new medical devices and Class IV medical devices (high-risk medical devices such as pacemakers).

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

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

b. Building of the inspection system

- PMDA continued to recruit GMP/QMS inspectors and the number of inspectors was 45 as of April 1, 2012. In the areas of drugs and quasi-drugs, PMDA carried forward the construction of the system to supervise quality management by measures such as establishment of an inspection quality assurance group, taking into account the accession to PIC/S (Pharmaceutical Inspection Cooperation Scheme: An international organization on GMP inspections, centering on European countries). In addition, PMDA enriched training programs such as external workshops in order to strengthen the inspection system for cellular and tissue-based products.
- The administrative processing status of GMP/QMS inspections in FY 2012 is shown below:

GMP/QMS Inspections Conducted under the Revised Pharmaceutical Affairs Act

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

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

	FY 2012				
	Applications	Completed		Withdrawals	In progress
Drugs *	1,582	1,593	(198)	40	821
In vitro diagnostics	64	48	(0)	0	16
Quasi-drugs	6	2	(0)	2	3
Medical devices	999	954	(81)	3	37
Total	2,651	2,597	(279)	45	877

* *Excluding in vitro diagnostics.*

Note: Values in parentheses show the numbers of on-site inspections out of completed inspections.

- The administrative processing times of GMP/QMS inspections in FY 2012 are shown below:

Median Processing Time of GMP/QMS Inspections

	FY 2008		FY 2009		FY 2010	
	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 *	155 days	100 days	162 days	91 days	118 days	63 days
In vitro diagnostics	117 days	46 days	110 days	56 days	117 days	62 days
Quasi-drugs	156 days	29 days	154 days	108 days	-	-
Medical devices	131 days	59 days	142 days	56 days	145 days	69 days

	FY 2011		FY 2012	
	Total processing time (median)	PMDA processing time (median)	Total processing time (median)	PMDA processing time (median)
Drugs *	147 days	77 days	176 days	90 days
In vitro diagnostics	83 days	38 days	100 days	36 days
Quasi-drugs	-	-	219 days	71 days
Medical devices	113 days	21 days	84 days	44 days

* *Excluding in vitro diagnostics.*

- The processing status of inspections of manufacturing facilities conducted in FY 2012 at domestic manufacturing sites licensed by the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Sites, is shown below:

Number of Inspections of Buildings and Facilities for Domestic Manufacturing Sites

	FY 2008		FY 2009		FY 2010		FY 2011		FY 2012	
Drugs *	8	(6)	40	(25)	20	(19)	25	(19)	15	(9)
In vitro diagnostics	2	(2)	4	(2)	1	(1)	3	(3)	1	(1)
Medical devices	1	(1)	2	(1)	3	(3)	0	(0)	2	(1)
Total	11	(9)	46	(28)	24	(23)	28	(22)	18	(11)

* *Excluding in vitro diagnostics.*

Note: Values include withdrawn applications. Values in parentheses show the number of on-site inspections out of the total inspection cases.

- PMDA conducts for-cause inspections, questioning, and sampling with regard to domestic manufacturers, etc., under instructions from the MHLW. The number of for-cause inspections conducted in FY 2012 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs *	13	12	6	12	13
In vitro diagnostics	1	3	2	3	1
Medical devices	0	0	1	0	0

* *Excluding in vitro diagnostics.*

- PMDA conducts simple consultations on GMP/QMS inspections. The number of simple consultations on GMP/QMS inspections conducted in FY 2012 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

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

* *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

Note: Breakdown of FY 2012: (Europe) France, Ireland, UK, Netherlands, Italy, Finland, Austria, Germany, Czech, Ukraine, Lithuania (North, Central and South America), USA (including Puerto Rico); (Asia, Oceania) China, India, South Korea, Taiwan, Indonesia, Israel

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

	Europe	North, Central and South America	Asia	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

Note: Breakdown of FY 2012: (Europe) Ireland, UK, Italy, France; (North, Central and South America) United States (including Puerto Rico), Canada, Mexico, Costa Rica; (Asia) Israel

- The number of inspections of manufacturing facilities conducted in FY 2012 at foreign manufacturing sites based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below:

Number of Inspections of Buildings and Facilities for Foreign Manufacturing Sites

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs *	294	390	230	579	530
In vitro diagnostics	69	40	27	60	68
Quasi-drugs	39	41	26	72	62
Medical devices	1,191	910	677	1,187	1,751
Total	1,593	1,381	960	1,898	2,411

* *Excluding in vitro diagnostics.*

Note: Values include withdrawn applications. All cases were document-based inspections.

- PMDA conducts for-cause inspections, questioning, and sampling with regard to foreign manufacturers, etc., under instructions from MHLW. The number of for-cause inspections conducted in FY 2012 is shown below:

Number of For-cause Inspections (Foreign Manufacturing Sites)

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs *	2	1	1	1	4
In vitro diagnostics	0	0	0	0	0
Medical devices	1	0	4	1	1
Total	3	1	5	2	5

* *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	Total
Europe	France	6	5	6	1	3	2	23
	Denmark	3	2	2	0	0	0	7
	Ireland	2	5	3	2	0	1	13
	UK	4	1	3	0	0	1	9
	Netherlands	1	1	5	0	0	2	9
	Spain	3	1	1	0	0	0	5
	Italy	2	5	3	2	0	1	13
	Belgium	1	2	4	3	1	0	11
	Austria	0	2	2	0	1	2	7
	Finland	0	0	2	0	0	1	3
	Germany	0	3	7	0	3	1	14
	Sweden	0	1	0	0	0	0	1
	Romania	0	1	0	0	0	0	1
	Czech	0	0	0	0	0	1	1
	Ukraine	0	0	0	0	0	1	1
	Lithuania	0	0	0	0	0	1	1
	Slovenia	0	2	1	0	0	0	3
	Portugal	0	0	0	3	0	0	3
	Greece	0	0	0	0	1	0	1
	Turkey	0	0	0	1	0	0	1
	Subtotal	22	31	39	12	9	14	127
North, Central and South America	USA	22	14	18	23	6	14	97
	Canada	0	2	2	1	0	0	5
	Mexico	0	1	0	0	1	0	2
	Argentina	0	2	0	0	0	0	2
	Subtotal	22	19	20	24	7	14	106
Asia	China	5	11	25	10	20	16	87
	India	1	12	4	7	4	4	32
	Singapore	2	4	0	0	0	0	6
	South Korea	0	3	9	10	18	14	54
	Indonesia	0	0	0	0	0	1	1
	Taiwan	0	2	6	1	1	2	12
	Thailand	0	0	2	0	1	0	3
	Vietnam	0	0	0	1	1	0	2
	Israel	0	0	0	0	0	1	1
	New Zealand	0	0	1	0	0	0	1
	Subtotal	8	32	47	29	45	38	199
Grand Total		52	82	106	65	61	66	432

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

Note 2:Puerto Rico was included in 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	Total
Europe	Ireland	0	6	0	4	1	3	14
	UK	0	1	0	0	1	0	2
	Italy	0	2	0	2	1	1	6
	Netherlands	0	1	0	1	0	0	2
	Switzerland	0	1	1	0	0	0	2
	Spain	0	1	0	0	0	1	2
	France	1	1	1	1	1	4	9
	Denmark	0	0	1	0	0	0	1
	Austria	0	0	0	0	0	1	1
	Belgium	0	0	0	0	0	1	1
	Subtotal	1	13	3	8	4	11	40
North, Central and South America	USA	10	16	27	19	12	21	105
	Mexico	0	1	0	0	1	0	2
	Brazil	0	0	1	0	0	0	1
	Canada	0	0	0	0	1	1	2
	Costa Rica	0	0	0	0	1	0	1
	Subtotal	10	17	28	19	15	22	111
Asia	China	0	0	3	0	0	1	4
	South Korea	0	0	0	1	0	0	1
	Thailand	0	0	0	0	0	1	1
	Singapore	0	0	2	0	0	0	2
	Philippines	0	0	0	0	0	2	2
	Israel	0	0	0	0	1	0	1
	Subtotal	0	0	5	1	1	4	11
Grand Total		11	30	36	28	20	37	162

Note 1:Not including for-cause inspections at foreign manufacturing sites under Article 75-4 of the Pharmaceutical Affairs Act.
Note 2:Puerto Rico was included in USA.

d. Coordination between GMP/QMS inspections and reviews

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

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

(i) Improvement of training program

a. Consideration of the method of training evaluations

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

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

- PMDA conducted training programs with observation of surgery using medical devices such as pacemakers, biological heart valves, and catheters for placing transvascular stents. A hands-on training using orthopedic medical devices was also provided. For the acquisition of basic knowledge about medical devices, a second-class ME technical training was also provided (21 employees).

  A training program (RMP study meeting, pharmacoepidemiology) for safety measures staff was also provided with the support of the safety division.

c. Lectures and guidance given by skilled experts

- In order to educate the staff from the broad perspective required for reviews and safety measures, PMDA invited domestic and overseas experts to provide the following training opportunities: lectures in which product development activities design/management of medical devices, etc. at companies are presented, and special training lectures including training for respective review parts with the cooperation of the National Institute of Health Sciences (NIHS) (32 times); training on regulations such as the Pharmaceutical Affairs Act to learn the regulatory system, etc. (once); and a training course on clinical study design to lean biostatistics (10 times).

d. Education and training of GMP/QMS inspectors

- GMP/QMS inspectors of PMDA participated in the Regulatory Affairs and Hygienic Control Training Program at the National Institute of Public Health, a training program hosted by the Parenteral Drug Association (PDA), a joint GMP/QMS mock inspection training program provided by MHLW, a workshop on sterilization validation of medical devices, etc. PMDA also conducted GMP on-site training programs at drug manufacturing facilities and dispatched two inspectors to two facilities with cooperation of relevant organizations.

e. Improvement of training in clinical practice

- In order to enable planning of safety measures in line with the clinical practice, PMDA dispatched five staff members to one medical institution to do practical training for pharmacists at hospitals.

f. Visits to manufacturing facilities

- PMDA conducted on-site training programs, such as visits to drug/medical device manufacturing facilities (5 facilities) and university laboratory (1 facility).

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

a. Promotion of Joint Graduate School Program

- In order to contribute to the diffusion of regulatory science and provision of information, PMDA promoted the Joint Graduate School Program and approached universities. PMDA concluded the joint graduate school agreement with 6 universities (Note 2) in FY 2012, in addition to the 11 partner universities (Note 1). In April 2011, PMDA accepted one graduate student from Gifu Pharmaceutical University as a pre-doctoral fellow to provide research guidance, etc.

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

  (Note 2) Osaka University (Graduate School of Medicine/Graduate School of Pharmaceutical Sciences), Kyoto Pharmaceutical University (Graduate School of Pharmaceutical Sciences), Okayama University (Graduate School of Medicine, Dentistry and Pharmaceutical Sciences), Nagoya University (Graduate School of Medicine), Nagoya City University (Graduate School of Pharmaceutical Sciences), Hokkaido University (Graduate School of Medicine)

- As a part of efforts to promote the recognition of regulatory science, PMDA made arrangement and sent PMDA staff to give lectures upon request from universities, etc. (FY 2012: 20 universities, 48 lectures).

b. Development of internal rules associated with the Joint Graduate School Program

- PMDA developed its internal rules in FY 2009 to accept students from joint graduate schools, and accepted one student from a joint graduate school as a pre-doctoral fellow on April 1, 2011.

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

- PMDA has worked to foster personnel familiar with regulatory science through personnel exchanges with research institutions including universities based on the initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products (a project funded by MHLW), and has also promoted cooperation in research projects on methods for evaluating the efficacy and safety of products developed using advanced technologies. In FY 2012, PMDA conducted personnel exchanges with 21 universities, etc., accepted 18 researchers as specially-appointed experts (including non-regular employees), and dispatched 30 employees (including non-regular employees).

(iii) Promotion of responding to advanced technologies through cross-sectional projects, etc.

a. Support for the development of evaluation guidelines

- For the purpose of making clear scientific principles for reviews of drug and medical device applications, thereby promoting product development, promoting international collaboration on review standards, etc., and accelerating reviews, in FY 2012, PMDA newly set up in vitro companion diagnostic devices project, the post-approval manufacturing changes project, and the microdose trials project. PMDA helped MHLW to develop product evaluation guidelines through activities of 11 cross-sectional projects/working groups for standards development within PMDA, which are orphan drug working group, pediatric drug working group, the QbD assessment project, the project on the innovative statistical strategies for new drug development, the nanomedicine initiative project, the global clinical trial project, the cardiovascular risk evaluation project, and the PMDA Omics project, in addition to the three projects mentioned above.
- PMDA gave presentations on activities of the cross-sectional projects at academic conferences, etc. as PR purposes, and also exchanged opinions with experts regarding evaluation policies, etc.

b. Contribution to establishment of internationally harmonized methods

- In FY 2012, in order to investigate respective issues on the PMDA's cross-sectional projects: in vitro companion diagnostic device project, pediatric drugs working group, orphan drug working group, QbD assessment project, nanomedicine initiative project, PMDA Omics project, etc., PMDA performed telephone conferences, preliminary meetings, etc. and exchanged opinions with experts from regulatory authorities in the EU and the US. The project team members also participated in presentation sessions and panel discussions in international academic conferences, and thus contributed to the processes toward global harmonization.

(iv) Promotion of proper conduct of clinical trials

- PMDA exchanged opinions on GCP or the conduct of clinical trials with healthcare professionals at medical institutions, etc., which were subject to GCP on-site inspections, after completion of the inspections.
- In order to enhance understanding of the proper conduct of clinical trials, PMDA held GCP Workshops in Tokyo and Osaka targeting drug development and regulatory affairs personnel, auditors of pharmaceutical companies and site management organizations (SMOs) as well as healthcare professionals. In the Workshops, PMDA representatives presented cases that are frequently pointed out as findings in document-based compliance assessment or GCP on-site inspections. The workshop materials were posted on PMDA's website to inform concerned parties of them. Also, PMDA staff members gave presentations at academic conferences, etc. attended by healthcare professionals to exchange opinions with concerned parties.

Number of GCP Workshop Participants

Location	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Tokyo	1,338	1,165	1,048	1,086	1,254
Osaka	543	461	455	418	471
Total	1,881	1,626	1,503	1,504	1,725

(v) Promotion of provision of information such as review reports

a. Improvement of provision of information

- In promoting proper use of drugs and medical devices and ensuring transparency of reviews, PMDA has, with the understanding and cooperation of relevant companies, released information on reviews of new drug applications, including review reports, on the Medical Product Information page of its website, in collaboration with MHLW.
- PMDA worked with MHLW to develop Notifications (draft), etc. to publicly release re-examination reports, and started posting re-examination reports of new drugs and new medical devices in FY 2009 and FY 2010, respectively, on its website.
- In order to make information on PMDA's reviews and safety measures available to foreign users, PMDA has created and released the English version of review reports on its English website. In FY 2012, the Agency created and released the English translations of 7 review reports.

b. Release of information related to review reports

(Review reports on new drugs)

- Based on the submitted information, new drugs are classified into 2 categories: those that are to be deliberated in the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (hereinafter referred to as "deliberation products") and those that are to be reported to the Drug Committees of PAFSC (hereinafter referred to as "report products"). Both "review reports" that describe details and results of reviews, and "summaries of product applications" that summarize submitted data, for deliberation products are subject to public release, whereas "review reports" for report products are subject to public release. The information is posted on the PMDA website upon conferring with the relevant companies regarding the contents released for each product, based on the Notification Issued from ELD, PFSB at MHLW.
- In FY 2012, PMDA released 131 review reports (median time from approval to release, 5 days), 77 summaries of product applications (median time from approval to release, 39 days) and 21 re-examination reports (median time from result notification to release, 0 day).

  The percentage of review reports released within one month after approval was 100% (86.5% in FY 2011) and the percentage of summaries of product applications released within 3 months after approval was 100% (90% in FY 2011).

(Review reports on new medical devices)

- In FY 2012, PMDA released 11 review reports (median time from approval to release, 8 days), 15 summaries of product applications (median time from approval to release, 83 days) and 13 re-examination reports (median time from result notification to release, 4 days).

  The percentage of review reports released within one month after approval was 81.8% (58.3% in FY 2011) and the percentage of summaries of product applications released within 3 months after approval was 73.3% (50.0% in FY 2011).

(Review reports on OTC drugs and quasi-drugs)

- It was decided that PMDA should publicly release review reports on OTC drugs and quasi-drugs, following the issuance of the PFSB/ELD Notification dated March 31, 2006, which specified publication procedures, etc. This Notification was amended on October 31, 2008 to publish

summaries of product applications as well. In FY 2012, PMDA released 5 review reports and 5 summaries of product applications on OTC drugs. There were no released reports for quasi-drugs.

c. Securing of impartiality in the utilization of external experts

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

d. Improvement of quality of review/safety operations by enhancement of information systems

- PMDA constructed the prototype system of medical device database (tentative name) and on-site verifications based on specifications developed by the MHLW's Study Group Meeting for Basic Investigation of International Information Exchange System on Medical Devices.

(vi) Promotion of international activities

- PMDA has been proactively promoting international activities in line with the PMDA International Strategic Plan developed in February 2009, aiming to proceed with the activities in a planned and systematic manner in cooperation with MHLW. In October 2011, PMDA established the PMDA International Vision to clarify the concrete goals to be attained in the next 5 to 10 years while achieving the PMDA International Strategic Plan. Based on the PMDA International Vision and PMDA International Strategic Plan, PMDA intends to meet the needs of Japanese people and people around the world for drugs and medical devices, thereby contributing to international society.

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

- In order to build a mechanism for sharing information, etc., relating to consultations, reviews, and post-marketing safety measures in cooperation with the US and the EU, PMDA has had discussions with the U.S. FDA and the EC/EMA, gathered information on review systems and safety measures, etc., and also exchanged information on methods of operations, etc., in collaboration with the MHLW.
- PMDA dispatched its employees as liaison officers to the US Pharmacopoeia and the EMA, in order to gather information and exchange views.
- PMDA participated in the 7th Summit of Heads of Medicines Regulatory Agencies held in Manaus (Brazil) in November 2012, and exchanged opinions on pharmaceutical regulatory affairs with regulators in various countries including the U.S. FDA and EMA.
- PMDA participated in "Swissmedic 10th Anniversary International Regulatory Symposium" held in Switzerland in September 2012, and had discussions with people from regulatory agencies in various countries including U.S. FDA and EMA regarding a wide range of themes such as roles of regulatory agencies and handling of future transformation of the world.

- PMDA concluded a confidentiality arrangement with Brazil, Italy, and France in November 2012 to develop a framework to share information. In February 2013, PMDA extended the term of the confidentiality arrangement with EC/EMA by 5 years and decided to automatically update the term every 5 years after that to make it possible to share information continuously.
- In May 2012, PMDA held the first bilateral meeting with Indonesian National Agency of Drug and Food Control (NADFC), and agreed on construction of a close collaborative relationship for the future. Also in February 2013, PMDA held the "First Japan-Indonesia Symposium" in Indonesia, and exchanged opinions on pharmaceutical regulations, pharmacovigilance, and GDP in both countries.
- In February 2013, PMDA held a bilateral meeting with the Food and Drug Administration Thailand (FDA THAILAND), and agreed on development of a mutual collaborative relationship.

b. Strengthening of activities for international harmonization

- In FY 2012, PMDA continued to actively participate in international harmonization initiatives for drugs such as ICH*. PMDA improved the consistency of Japanese standards with international standards, such as those for preparing data for regulatory submission, which were agreed upon among Japan, the US, and the EU in ICH Meetings, thereby promoting further international harmonization.
- Toward the development of international standards and the international regulatory harmonization, PMDA actively participated in Steering Committee Meetings and Expert Working Group Meetings of ICH, Steering Committee Meetings and Expert Working Group Meetings of IGDRP*, Steering Committee Meetings of APEC LSIF RHSC*, and the Expert Working Group Meetings of PDG*.

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

- In FY 2012, in the area of medical devices, PMDA continued to actively participate in Steering Committee Meetings and Expert Working Group Meetings of GHTF*, Steering Committee Meetings and Working Group Meetings of IMDRF*, Steering Committee Meetings and Working Group Meetings of HBD*, ISO*, etc. GHTF terminated its activities in December 2012. As Japan was the last chair of GHTF, PMDA supported the organization of regular meetings and the annual meeting, in addition to conventional activities including preparation of guidance documents in cooperation with related countries.

    * GHTF: Global Harmonization Task Force
    * HBD: Harmonization by Doing (for regulations on medical devices in Japan and US)
    * ISO: International Organization for Standardization
    * IMDRF: International Medical Devices Regulators Forum

- For HBD, PMDA supported activities of each working group as a co-chair with the US academia, and contributed to regulatory harmonization on a practical level through teleconferences or meetings of respective working groups. Particularly, through the HBD project, "Collaborative Consultations and Review of Premarketing Applications Pilot Program," PMDA made efforts to resolve the "device lag" between Japan and the US by sharing information with the US FDA regarding specific issues raised in the process of product review.

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

* ICH
  - Carcinogenicity (S1)
  - Photosafety Evaluation of Pharmaceuticals (S10)
  - Impurities: Guideline for Metal Impurities (Q3D)
  - Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions (Q4B)
  - Q&A on GMP for Active Pharmaceutical Ingredients (Q7 IWG)
  - Development and Manufacture of Drug Substances (Q11)
  - Q&A on CTD-Quality Documents (CTD-Q)
  - Informal Quality Brainstorming
  - MedDRA Term Selection: Points to Consider (M1 PtC WG)
  - Electronic Standards for Transmission of Regulatory Information (M2)
  - Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (M7)
  - Electronic Common Technical Document (M8)
  - Data Elements and Standards for Drug Dictionaries (M5)
  - Data Elements for Transmission of Individual Case Safety Reports (E2B [R3])
  - Q&A on Structure and Content of Clinical Study Reports (E3 IWG)
  - Clinical Safety Data Management: Periodic Safety Update Reports (PSUR) for Marketed Drugs (E2C [R2])
  - Q&A on the Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs (E14-IWG)
* PDG: Pharmacopoeial Discussion Group (Japan, U.S. and Europe): Tokyo conference and Rockville conference
* MedDRA (Medical Dictionary for Regulatory Activities) Steering Committee Meeting
* ISO TC/215 (health informatics)
* HL7 (standards for interoperability of health information technology)
* ICCR (International Cooperation on Cosmetics Regulations)
* IGDRP: International Generic Drug Regulators Pilot: Washington DC conference and Nanchang conference
* CIOMS (Council for International Organizations of Medical Sciences) Working Group
* Working Group on Good Laboratory Practice (GLP) of OECD
* WHO ICDRA (International Conference of Drug Regulatory Authorities)
* WHO INN (international nonproprietary names) meeting
* APEC LSIF RHSC (Life Science Innovation Forum, Regulatory Harmonization Steering Committee): Singapore conference and Jakarta conference

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

* ISO
  - ISO/TC/194 (Biological evaluation of medical devices)
  - ISO/TC/106 (Dentistry)
* GHTF
  - SG1 (Premarket evaluation)
  - SG1 IVD-subgroup (Premarket IVD regulation)
  - SG2 (Post-market surveillance/vigilance)
  - SG3 (Quality systems)
  - SG4 (Auditing)
  - SG5 (Clinical safety/performance)
* 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 Identifier)

- NCAR (National Competent Authority Report)
- Recognized Standards

* AHWP (Asian Harmonization Working Party)

* GMDN (Global Medical Device Nomenclature)

- PMDA held 5 Expert Discussion meetings on drug names and reported 21 Japanese accepted names (JAN) to MHLW. Five consultations on applications for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in April and October 2012.

c. Promotion of personnel exchanges

- Based on the Administrative Rules on Overseas Training, PMDA dispatched one employee to the OECD. PMDA selected the employee after soliciting personnel who were willing to be dispatched (OECD: 1 employee, FDA, NCI/NIH: 1 employee).
- PMDA received three foreign trainees from the Indonesia's NADFC. PMDA also accepted government research teams from China and Taiwan and provided explanations regarding Japanese pharmaceutical regulations.
- PMDA held a training seminar for people from overseas regulatory authorities, and provided training on the services of the Agency, post-marketing safety measures and relief system for drugs and medical devices, with examples, etc.

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

- Since FY 2011, PMDA has reinforced English training to improve the communication skills in English of employees, and provided a practical business English program (13 members) or an intermediate English program (19 members), according to the employee's English proficiency. The training was improved by setting more stringent selection criteria for applicants and by introducing rules for reimbursement of tuition fees once paid by the trainees according to the rate of attendance, which resulted in an increase in the rate of attendance for training and an enhancement in the trainees' English conversation skills.

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

- PMDA made efforts to improve the provision of English information by taking measures such as posting news releases every month on its English website.
- In order to provide information on its reviews and related services and safety measures to international audiences, PMDA has created and released English translations of the review reports and safety information on its website. In FY 2012, the Agency prepared and published English translations of 7 review reports. PMDA also created the English version of the lists of approved new drugs/new medical devices, and released them approximately once every quarter of the year.
- At the DIA Annual Meetings, etc. held in Japan, the US, and Europe, PMDA's speakers gave presentations on the Agency's reviews and safety measures to improve the international recognition of PMDA, and also made booth exhibitions for the publicity of PMDA's services.
- PMDA has introduced its cross-sectional projects on its English website. Particularly, PMDA conducted PR activities and provided activity information of the global clinical trial project and the nanomedicine initiative project, in which members cooperated with MHLW to develop guidance in

the present fiscal year. PMDA posted the English translation of the Administrative Notice on global clinical trials, at the time of issuance of the Japanese original Administrative Notice.

f. Promotion of global clinical trials

- In order to reduce the drug lag, PMDA has promoted global clinical trials, and has conducted consultations and reviews based on a document titled “Basic Principles on Global Clinical Trials” (PFSB/ELD Notification dated September 28, 2007) which clarifies basic concepts to conduct global clinical trials.

  Of 556 clinical trial notifications submitted in FY 2012, 130 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of cases	82	113	134	121	130

- PMDA intends to take an active approach to global clinical trials. In FY 2012, it carried out 64 consultations on global clinical trials for drugs with new active ingredients.

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

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of cases	51	56	66	73	64

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

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

- In order to improve the safety of marketed drugs and medical devices, and to enable patients and healthcare professionals to use them properly, PMDA collects and examines safety information efficiently, processes the information speedily, plans appropriate safety measures and provides easy-to-understand safety information promptly, to ensure that reviews and safety measures function in an inseparable manner.
- There were approximately 310,000 reports on adverse reactions and infections caused by drugs and approximately 24,000 reports on medical device malfunctions/infections caused by medical devices submitted to PMDA from within and outside of Japan in FY 2012. PMDA inputs the collected information into a database and shares such information with MHLW. In addition, PMDA monitors information on new measures taken for medical products by foreign regulatory agencies, including FDA and EMA, to consider and evaluate its responses to domestic products on a daily basis, while reviewing academic literature to analyze, share and evaluate information on adverse reactions. In addition, PMDA is making efforts to take effective safety measures for drugs and medical devices in the post-marketing stage by enhancing cooperation between the review offices and safety offices, as well as between the relief office and safety offices.
- Based on daily reviews conducted by the product safety teams, PMDA assesses and reviews such reports on adverse 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. Issues

that require a particularly urgent measure are responded to immediately in cooperation with MHLW.

- The numbers of reports submitted to MHLW for products judged to require safety measures (in terms of the number of active ingredients for drugs, and the number of generic names for medical devices), such as revision of package inserts, are as follows.

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs	151	260	339	185	198
Medical devices	37	62	19	17	15
Medical safety *	4	4	5	6	6

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

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

		FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs	Directions for revision to precautions in package insert	141	254	339	185	198
	Posting articles and cases on PMDSI*	20	29	32	41	36
Medical devices	Directions for revision to precautions in package insert or issuance of notifications on self-check	4	4	3	5	4
	Posting articles on PMDSI	2	5	3	4	1

* *Pharmaceuticals and Medical Devices Safety Information*

- As collaborative activities with the review offices, the Offices of Safety I and II evaluate adverse drug reactions reported via early post-marketing phase vigilance (EPPV) in cooperation with reviewers of product applications. Staff members of the safety offices also participate in the review process (clinical trial consultations, assessment of post-marketing surveillance plans, review of draft package inserts, Expert Discussions, etc.) of new drugs and new medical devices. With the cooperation 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 has been provided to the safety offices so that the information can be used for the safety measures.
- In FY 2012, PMDA made the following efforts to appropriately collect, organize, and examine the reports on adverse drug reactions, etc. and reports on medical device malfunctions, etc. submitted by companies 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 companies

  c. Encouraged staff members to attend academic conferences (a total of 302 participants) and gathered information through the academic conferences that they participated in

  d. Regularly held liaison meetings on both drugs and medical devices every week with MHLW

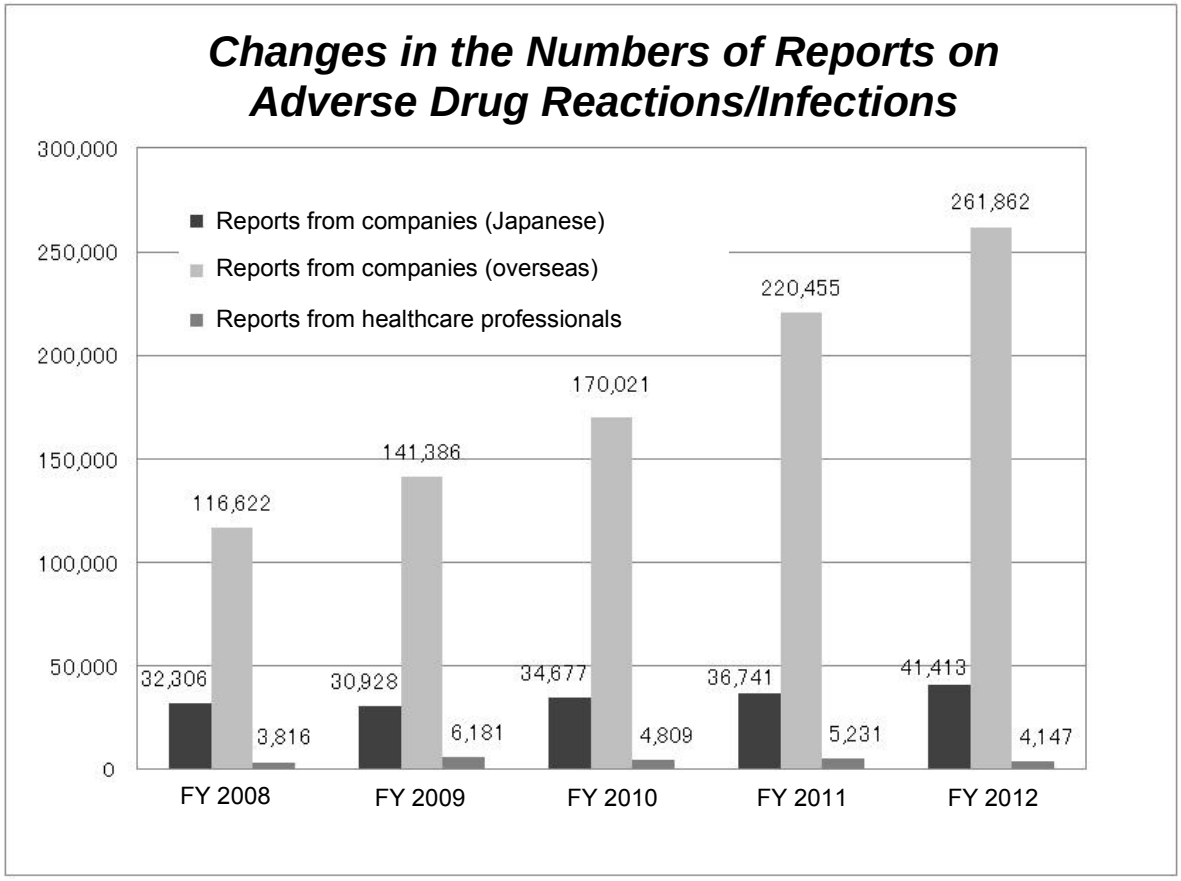
- PMDA's information management system for adverse drug reactions and the safety measures support system will need to be in accord with ICH-E2B (R3), which is the next international data exchange rules for adverse reaction reporting. In FY 2012, PMDA continuously operated a pilot system to verify them.

Collection of adverse reaction reports, etc.

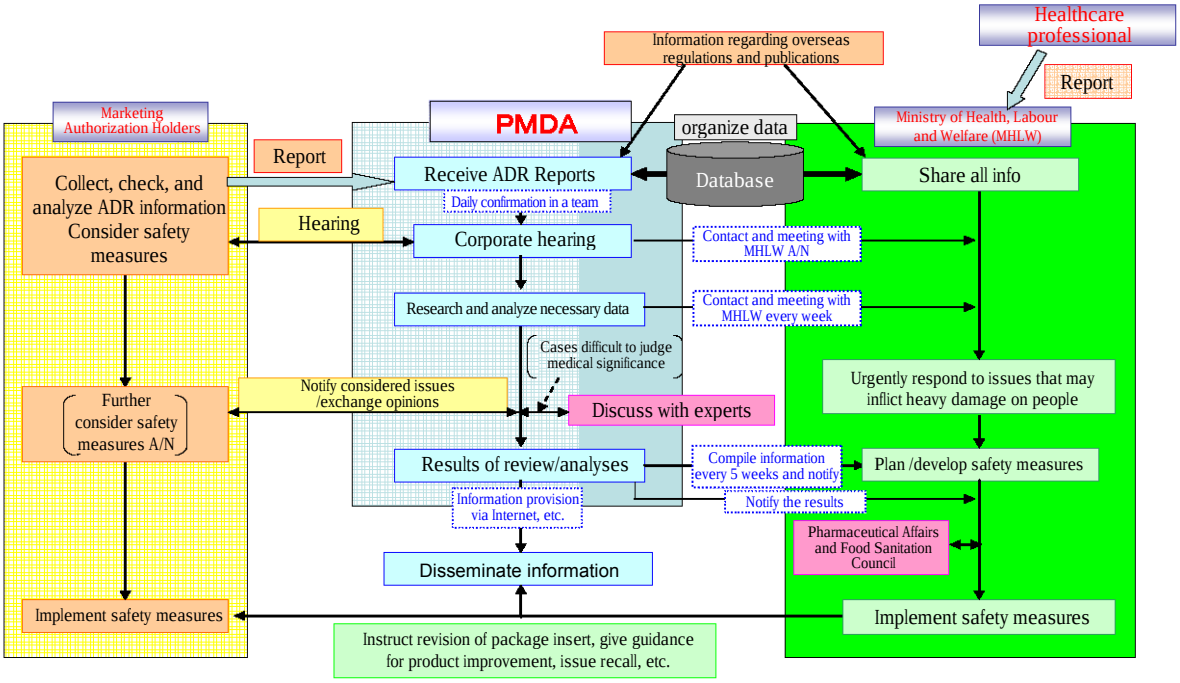
1-1) Number of reports relating to drugs

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Reports from companies	151,726	175,285	207,772	260,473	306,410
(cases of adverse drug reactions, Japanese)	(31,455)	(30,814)	(34,578)	(36,641)	(41,254)
(cases of infections caused by drugs, Japanese)	(851)	(114)	(99)	(100)	(159)
(cases of adverse drug reactions, foreign)	(116,592)	(141,364)	(169,994)	(220,410)	(261,823)
(cases of infections caused by drugs, foreign)	(30)	(22)	(27)	(45)	(39)
(research reports)	(855)	(933)	(940)	(841)	(884)
(foreign safety measure reports)	(869)	(930)	(1,033)	(1,347)	(1,134)
(periodic infection reports)	(1,074)	(1,108)	(1,101)	(1,089)	(1,117)
Reports from healthcare professionals	3,816	6,181	4,809	5,231	4,147
(1) Safety information reporting system	3,816	3,721	3,656	3,388	3,304
(2) Three vaccines/influenza *		2,460	1,153	1,843	843
Total	155,542	181,466	212,581	265,704	310,557

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



Flowchart for Processing Adverse Reaction Reports



1-2) Reports on side effects associated with influenza vaccines

With regard to the Influenza A (H1N1) Vaccination Program started in October 2009, a scheme was created for the central government to be immediately informed of serious side effects after vaccination in accordance with Basic Policy of Influenza A (H1N1) Vaccination (established on October 1, 2009 and revised on December 15, 2009, Japanese Government Task Force on Influenza A [H1N1]). The number of side effect reports collected according to this scheme is shown in the above table in 1-1). PMDA organized and evaluated these side effects cases, and contributed to the safety evaluation of vaccines in MHLW.

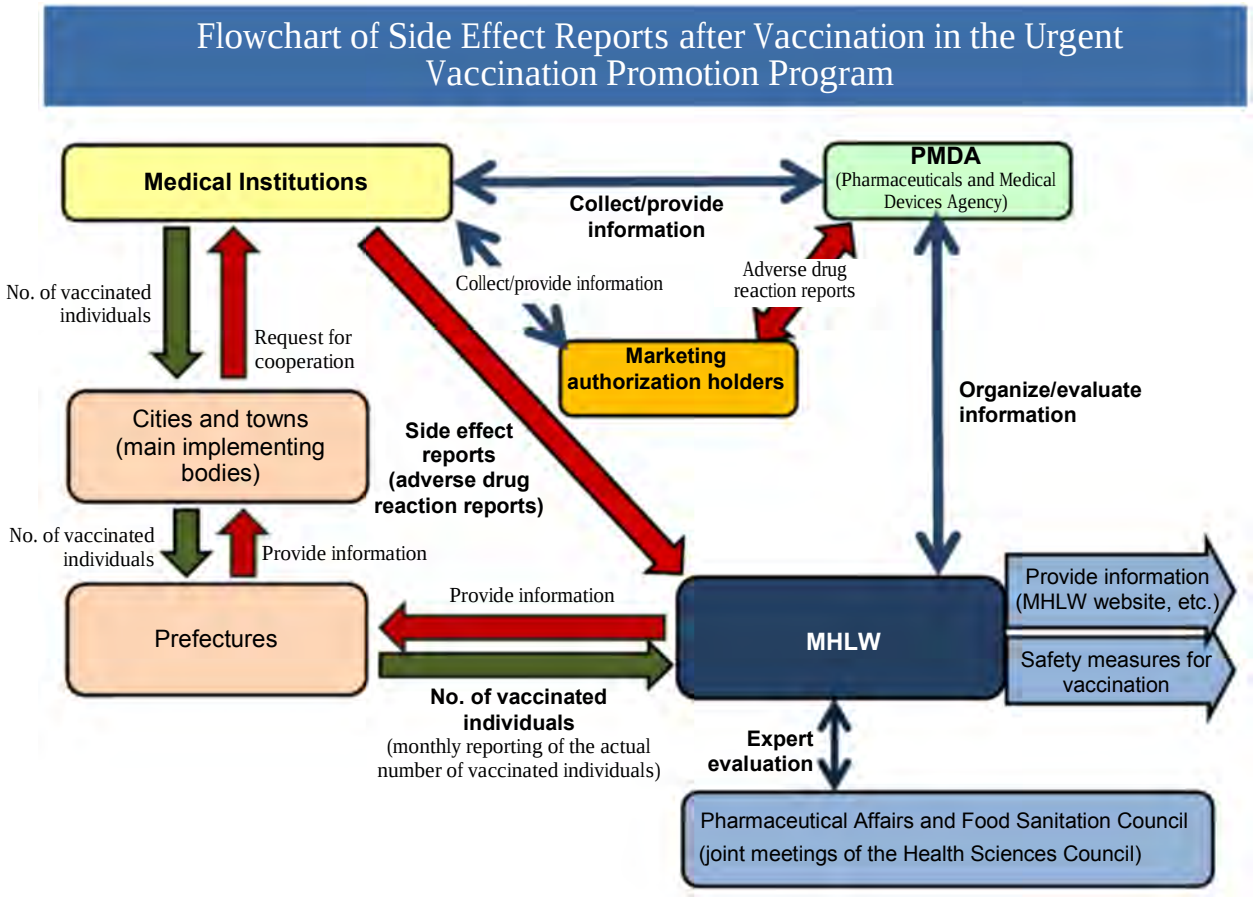
It was decided to handle influenza A (H1N1) as ordinary seasonal influenza from April 1, 2011 onwards, and consequently the Program was completed. However, in accordance with HSB Notification No. 0929-3 from the Health Service Bureau of MHLW and PFSB Notification No. 0929-8, dated September 29, 2011, "Reporting of Side Effects of Influenza Vaccination," side effects after influenza vaccination have been promptly reported and evaluated under a similar scheme.

Side effect reports	FY 2009	FY 2010	FY 2011	FY 2012
Influenza Vaccines	2,460	684	558	305

1-3) Reports on side effects associated with vaccines according to Urgent Vaccination Promotion Program

A scheme for the central government to be immediately informed of serious side effects after vaccination with cervical cancer vaccine, Hib vaccine and pediatric pneumococcal conjugate vaccine has been established in accordance with the "Procedure for Urgent Vaccination Promotion" (Appendix to "Implementation of Urgent Vaccination Promotion Program for Cervical Cancer Vaccine, etc.," HSB Notification No. 1126-10 and PFSB Notification No. 1126-3, dated November 26, 2010, as partially revised on March 31, 2011) (see the scheme below). The number of side effect reports collected according to this scheme is shown in the following table. PMDA organized and evaluated these side effects, and contributed to the safety evaluation of vaccines in MHLW.

Number of side effect reports	FY 2010	FY 2011	FY 2012
Cervical cancer vaccine	176	765	258
Hib vaccine	135	210	154
Pediatric pneumococcal conjugate vaccine	158	310	126



1-4) Adverse drug reaction reports from patients

The necessity of establishment of a system which enables utilization of information from patients for safety measures is described in the final recommendations by the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings that were compiled in April 2010. Also in the report by the Investigational Sub-committee on Revision of Pharmaceutical Regulatory Systems of the Health Science Council which was compiled in January 2012, it is suggested that information on adverse drug reactions should be obtained from patients for utilization.

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. Such reports are to be used for the purpose of carrying forward safety measures for drugs such as identifying trends in occurrence of adverse reactions to drugs. Based on reports and questionnaire results collected during the trial period, PMDA intends to revise the reporting system and then formally start receiving reports.

The number of patient adverse drug reaction reports collected in FY 2012 is shown in the following table.

	FY 2011	FY 2012
Adverse drug reaction reports from patients	30	154

1-5) PMDA's detailed investigation on reports from medical institutions (excluding side effect reports)

Regarding death/serious cases among adverse reactions, etc. reported from medical institutions, the necessity of development of a system to conduct necessary investigations such as direct inquiries to healthcare professionals had been pointed out in the final recommendations by the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings that were compiled in April 2010.

PMDA developed a system to conduct follow-up investigations of reports from medical institutions. In addition, PMDA examined the mechanism for feedback to companies, etc., prepared necessary notifications, and then started making inquiries to medical institutions regarding fatal cases from 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 serious cases are subject to detailed investigation.

The number of cases in which PMDA has conducted detailed investigation to date is shown in the following table.

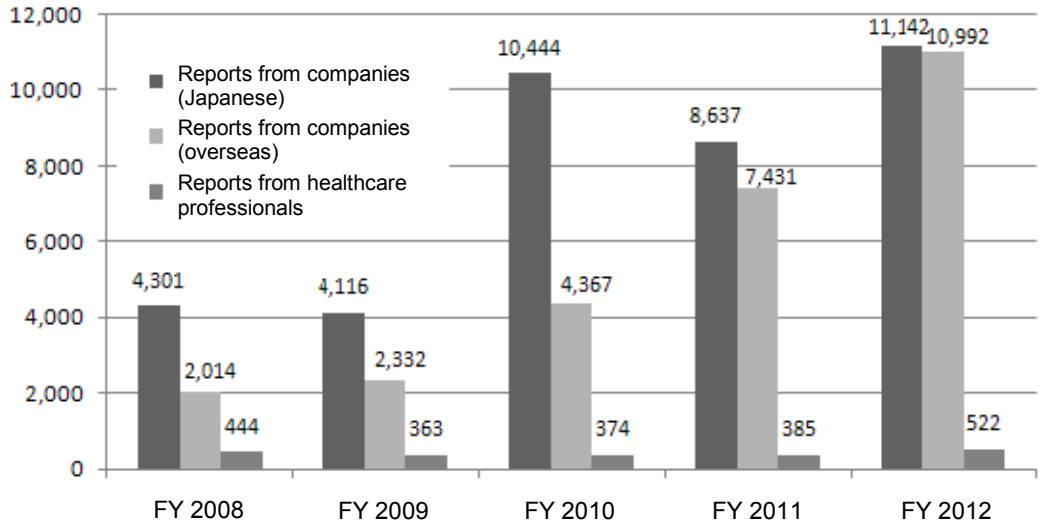
	FY 2010	FY 2011	FY 2012
Number of cases in detailed investigation	75	613	663

Among adverse drug reactions/infections that were reported from healthcare professionals to the Minister of Health, Labour and Welfare, PMDA investigated some reported cases, by making inquiries or other means. PMDA started sharing the information on individual cases of adverse drug reactions in these reports via the Internet (using a server dedicated for the information sharing) in November 2011 with marketing authorization holders of the primary suspected drugs of the reported cases.

2) Number of reports relating to medical devices

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Reports from companies	7,137	7,344	15,874	17,192	23,643
(cases of malfunctions of medical devices, Japanese)	(4,301)	(4,114)	(10,444)	(8,637)	(11,242)
(cases of malfunctions of medical devices, foreign)	(2,014)	(2,332)	(4,367)	(7,431)	(10,992)
(cases of infections caused bymedical devices, Japanese)	(0)	(2)	(0)	(0)	(0)
(research reports)	(10)	(6)	(27)	(2)	(3)
(foreign safety measure reports)	(748)	(831)	(978)	(1,060)	(1,337)
(periodic infection reports)	(64)	(59)	(58)	(62)	(69)
Reports from healthcare professionals	444	363	374	385	522
Total	7,581	7,707	16,248	17,577	24,165

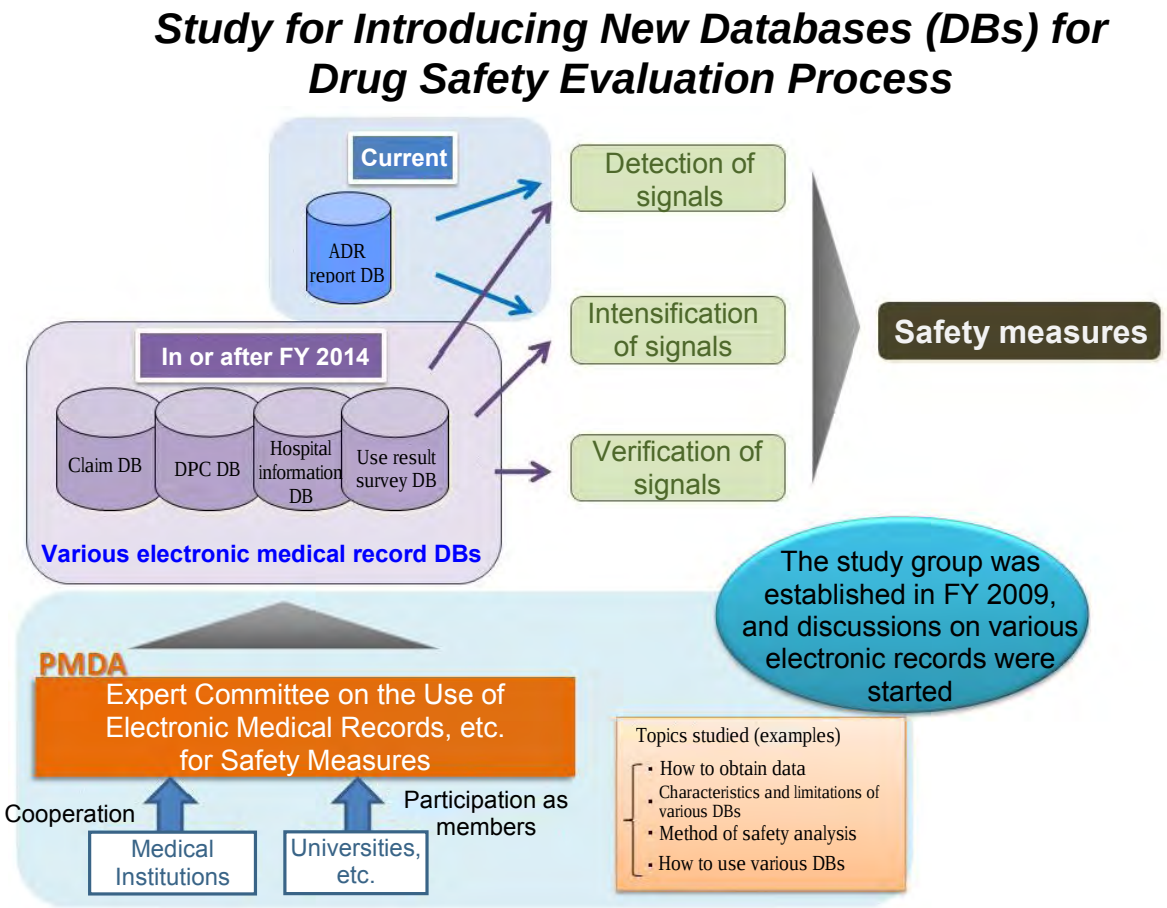
Changes in the Numbers of Reports on Medical Device Malfunctions/infections



(ii) Sophistication of safety measures

a. Use of electronic medical records, etc.

- In accordance with the Second Mid-term Plan, PMDA plans to build an infrastructure to access the databases of medical records including health insurance claim data (hereinafter referred to as "claim data") by FY 2013, and then perform pharmacoepidemiological analyses to evaluate pharmaceutical risks quantitatively. The Agency intends to start making use of such infrastructure on a trial basis in FY 2011, and establish a system for conducting investigations on the incidence of adverse drug reactions and pharmacoepidemiological analyses by FY 2013.
- PMDA named the investigation to utilize electronic medical records, etc. for safety measures "MIHARI Project," and started evaluating each type of data such as claim data and hospital information system data in terms of their advantages/disadvantages and feasibility and limitations in FY 2009. PMDA established the Expert Committee on the Use of Electronic Medical Records, etc. for Safety Measures as the evaluation body composed of external experts, and conducted various pilot studies while obtaining advice. In FY 2012, the pilot studies were continuously conducted mainly to explore appropriate analytical methods and to evaluate the usability, limitations, etc. of each data source (see the following table).



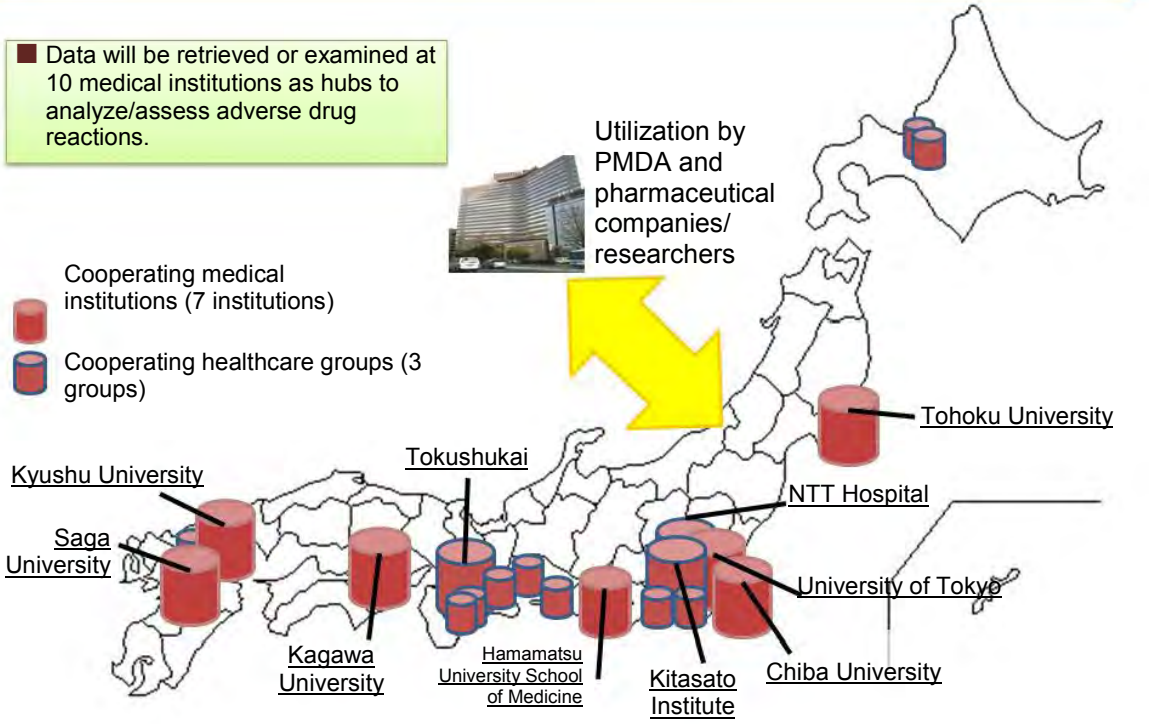
Data sources	Study started in	Study	Design
Claim data (commerciall y available DB, small-scale)	FY 2009	Data characterization	Patients with anaphylaxis were identified by using ICD-10 codes and analyses were performed by sex, age, primary disease, procedure, therapeutic agent, etc. (The report has already been posted on the Medical Product Information web page)
	FY 2010	Actual condition of prescription of drugs	Patients who were prescribed any one of the following four drugs were identified and analyses of respective drugs were performed. 1. Amantadine 2. Thiamazole 3. Paroxetine 4. Anti-influenza agents (The report has already been posted on the Medical Product Information web page. Partly presented in an academic conference)
	FY 2010	Survey on effects of safety measures	Patients who were prescribed any one of the following four drugs were identified and analyses were performed for safety measures taken during the follow-up period. 1. Amantadine (contraindicated in dialysis patients) 2. Thiamazole (periodic blood tests) 3. Paroxetine (prescription limited in patients under 18 years) 4. Anti-influenza agents (prescription limited in patients under age) (The report has already been posted on the Medical Product Information web page. Partly presented in an academic conference)
	FY 2010	Risk assessments of adverse drug reactions	Risk assessments were performed for the following two known associations of drugs and adverse reactions (presented in academic conference). 1. Osteoporosis associated with steroids (Cohort study/ Nested Case-Control study) 2. Drug-induced parkinsonism associated with antipsychotic agents (Nested Case-Control study)
	FY 2010	Signal detection by pharmacoepidemiolo gical method	Signal detection was performed by using SSA† for a known association between a drug and an adverse reaction (drug-induced parkinsonism associated with antipsychotic agents) (presented in an academic conference). † SSA: Symmetry Sequence Analysis
	FY 2010	Signal detection by data mining	Signal detection by using the data mining method was examined in collaboration with an external contractor. (The report has been already posted on the Medical Product Information web page)
	FY 2011	Actual condition of prescription of drugs	Patients who were prescribed any one of the following three drugs/drug groups were identified and analyses of respective drugs/drug groups were performed. 1. Antimicrobial drugs (for pediatrics) 2. Doxorubicin 3. Monobasic sodium phosphate monohydrate/anhydrous dibasic sodium phosphate
	FY 2011	Survey on influences of safety measures	Patients who were prescribed monobasic sodium phosphate monohydrate and anhydrous dibasic sodium phosphate were identified and analyses were performed for safety measures taken during the follow-up period.
	FY 2011 - 2012	Risk assessments	Risk assessments were performed for the following two associations of drugs and adverse reactions (presented in an academic conference). 1. Association between the use of atypical antipsychotic drugs and glucose metabolism disorder (Cohort study/ Nested Case-Control study) 2. Association between the use of thiazide diuretics and glucose metabolism disorder (Nested Case-Control study)

Data sources	Study started in	Study	Design
	FY 2011 - 2012	Signal detection by data mining	Signal detection (hypothesis extraction) by using the data mining method was examined in collaboration with an external contractor.
	FY 2012	Signal detection by pharmacoepidemiological method (SSA)	Assessment of the precision of signal detection was performed by using SSA for an association between a drug and an adverse reaction
DPC (Diagnosis Procedure Combination) data	FY 2010	Analysis of data profile	Patients with anaphylaxis were identified by using ICD-10 codes and analyses were performed by sex, age, primary disease, prescription, procedure, etc.
	FY 2011	Actual condition of prescription of drugs	Patients who were prescribed any one of the following three drugs/drug groups were identified and analyses of respective drugs/drug groups were performed. 1. Antimicrobial drugs (for pediatrics) 2. Doxorubicin 3. Sorafenib
	FY 2011	Survey on influences of safety measures	Patients who were prescribed sorafenib were identified and analyses were performed for safety measures taken during the follow-up period.
Hospital information data(HIS)	FY 2009 - 2011	Data characterization	The data was characterized with the cooperation of five medical institutions. Six types of adverse drug reactions were identified and analyzed (Partly presented in an academic conference).
	FY 2010 - 2011	Examination of validity of outcome definition	Cases of an adverse drug reaction were identified from the database and checked by a medical record review, with the cooperation of two medical institutions, and the validity of outcome definition was evaluated (Presented in academic conference).
	FY 2012	Survey on influences of safety measures	Patients who were prescribed sitagliptin were identified, and safety measures related to combined use with sulfonylurea were analyzed. (Presented in academic conference)
	FY 2012	Risk assessments	Risk assessments were performed for the following two associations of drugs and adverse reactions with the cooperation of 6 medical institutions. 1. Association between the use of vancomycin and liver disorder 2. Association between the use of sitagliptin and acute renal failure
	FY 2012	Examination of validity of outcome definition	Validity of definition from outcome was examined using clinical laboratory values for the following four outcomes with the cooperation of 6 medical institutions: 1. Diabetes mellitus 2. Hyperlipidemia 3. Hyperthyroidism 4. Acute renal failure/Acute renal disorder Validity of outcome definition was examined using medical records on "Acute renal failure/Acute renal disorder" with the cooperation of 2 medical institutions.

- In FY 2011, the "Project for developing infrastructure for medical information database " was started. The purpose of this project is to build a database at 10 cooperating medical institutions nationwide such as university hospitals, selected by MHLW through open recruitment, of electronic medical information retained by the medical institutions. The project aims at establishing a link system of the medical information databases covering 10 million patients nationwide in the future. In this project, PMDA assumes the role of establishing the system among the cooperating medical institutions. The Agency also intends to develop its internal analysis system to utilize this database for safety measures (see the diagram).

Project for Developing the Medical Information Database Infrastructure

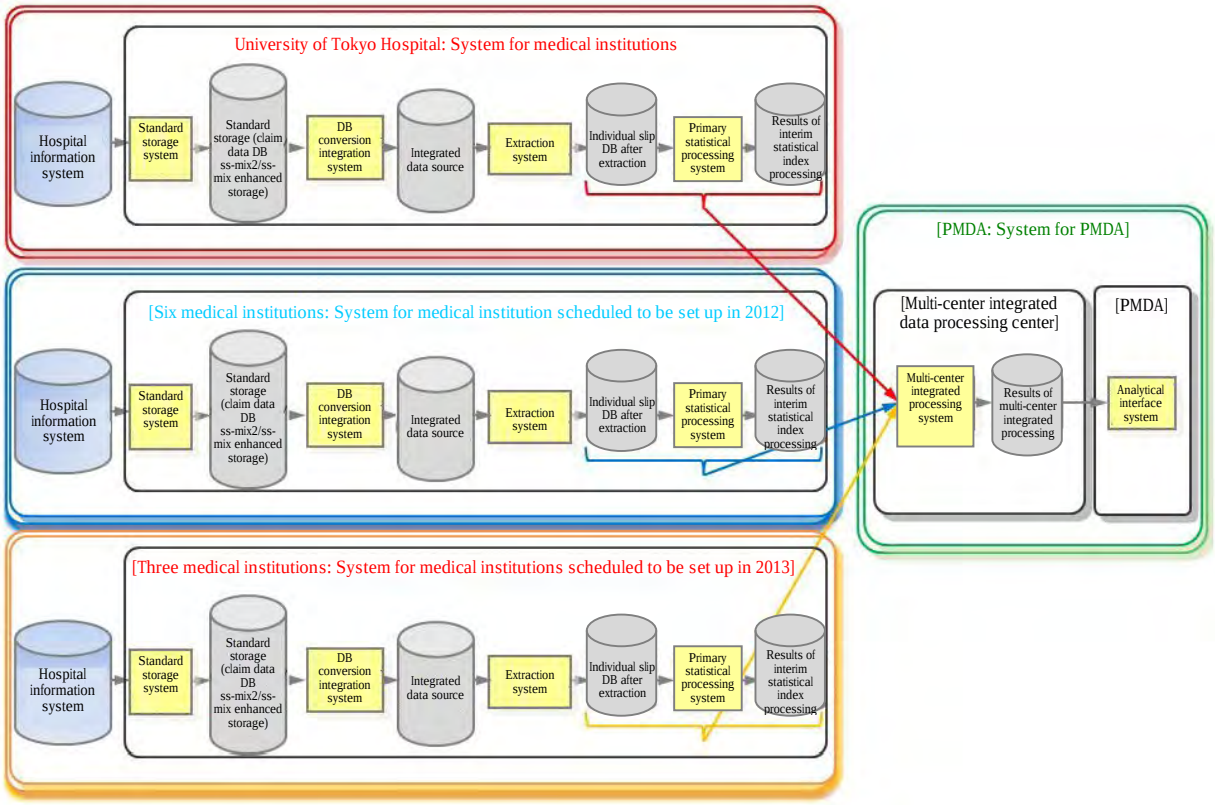
Hubs of the medical information database will be established at 10 university hospitals/group hospitals, etc. nationwide, with the aim of collecting data covering 10 million patients



- The establishment of the medical information database is scheduled to be carried forward sequentially from FY 2011 to FY 2013, with the aim of establishment of themedical database hubs at 7 cooperating medical institutions in FY 2012 and at 3 medical institutions in FY 2013.

  To date, PMDA started the development of its internal systems such as the analysis interface system, while initiating the development of systems at the University of Tokyo Hospital, one of the cooperating medical institutions. The Agency also upgraded the existing hospital information system at the University of Tokyo Hospital as a preparation for the introduction of the planned database system. In FY 2012, the development of the PMDA's system and hospital information system were completed and introduced to PMDA and the University of Tokyo Hospital, respectively. PMDA also started to upgrade hospital information systems in the 6 cooperating medical institutions. In FY 2013, PMDA intends to similarly introduce the system to 3 more cooperating medical institutions (see the diagram).

Outline of the Medical Information Database



b. Digitization of information on adverse drug reactions and its use for safety measures

- In accordance with the Second Mid-term Plan, PMDA intends to computerize information on adverse reactions, such as adverse drug reaction reports and information from drug use-results surveys, and build databases in order to make use of digitized information in the development of safety measures.
- The database of drug use-results surveys is continuously under consideration by the pharmaceutical companies who are providers of data for the surveys.

c. Sophistication of the data mining method

- In accordance with the Second Mid-term Plan, PMDA plans to proactively make use of the data mining method in organizing, evaluating, and analyzing information on adverse drug reactions, in order to detect adverse drug reactions at an early stage and take measures to prevent further events. PMDA also intends to improve the approach on an as-needed basis by referring to overseas examples.

Reference: What Is the Data Mining Method?

The data mining method is technology that extracts, from among a large amount of data accumulated in the database, highly correlative events that occur frequently and simultaneously. The term "data mining" refers to the process of retrieving, or "mining," only useful information from the database.

Specifically, the data mining method is used for detecting "combinations of drugs and adverse drug reactions that are likely to have a causal relationship (signals)" from the database of individual cases of adverse drug reactions.

- In FY 2012, the method of change-point analysis that captures the occurrence tendency (time-series changes in the number of reports on adverse drug reactions) which started to be reviewed in FY 2009 was organized in terms of the applicability for different uses. In FY 2013, the method will be continuously reviewed toward its practical use.

Reference: What Is the Change-Point Analysis?

An analysis method to search for a time-series change-point by dividing the sequence of data over time into two time domains and finding a time point where the tendency may radically change.

For example, this analysis finds out a time point where the number of reports per month may rapidly increase for a certain combination of drug and adverse drug reaction.

d. Collection and evaluation of data on medical devices subject to tracking (implantable ventricular-assist devices [IVAD])

- In accordance with the Second Mid-term Plan, PMDA intends to build a system for collecting and evaluating time-series data on the operational status of implantable ventricular-assist devices, which was adopted from among high-risk implantable medical devices subject to tracking, as a pilot study. Data to be collected include the incidence rate of malfunctions of the device. PMDA plans to appropriately use the system for developing safety measures, etc.

Reference: What are Medical Devices Subject to Tracking?

Medical devices for which it is obligatory for a marketing authorization holder, etc., to create and store records of contact information of the users so that prompt and appropriate responses can be taken easily if a malfunction occurs with the medical device. Under the Pharmaceutical Affairs Act, such devices are categorized as designated medical devices.

- In FY 2012, PMDA continued the "Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS)" project based on the protocols that were developed under the industry-government-academia collaboration in the First Mid-term Plan. PMDA developed a web-based entry system and implementation structures at participating medical institutions, and started data collection in June 2010. As of April 1, 2013, 167 patients (115 for IVAD, 52 for extra-corporeal VAD) have been enrolled at 22 participating institutions. The number of enrolled patients and other data has been updated on the PMDA's Medical Product Information web page.

e. Evaluation of malfunctions of medical devices

- In accordance with the Second Mid-term Plan, PMDA intends to develop methods for scientific evaluation of medical devices by ascertaining the incidence of device malfunctions that may unavoidably occur at a certain rate due to the nature of the device rather than to its structural defects.
- As a part of this development, PMDA has been continuously conducting a pilot study on coronary stents from the effective period of the First Mid-term Plan. Data from a study (26 institutions, about 16,000 enrolled patients, 3- to 5-year follow-up period) in patients who underwent percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) operation have been collected through an external contract organization.
- In FY 2012, PMDA completed data collection over a follow-up period of five years. Data collection was completed from 15,759 patients (13,562 patients with PCI, 2,197 patients with CABG [excluding patients who did not give their consent]) at 26 institutions as of March 29, 2013.
- PMDA plans to continuously enhance post-marketing safety by actively working on safety measures that are capable of "prediction and prevention" through scientific evaluation and analysis. The approaches include efficient analyses of adverse drug reactions with the use of the data mining method to detect signals, introduction of the risk management plan that is a system to monitor safety information on a product throughout its lifetime, from the development to post-marketing stages, and utilization of electronic medical records.

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

a. Access to information on adverse drug reactions, etc. relating to a company's own products

- PMDA investigates information of adverse drug reactions, etc. which has been reported to the regulatory authorities but not informed to companies by medical institutions. The Agency has operated a system which enables companies to access and download SGML files in conformity with ICH-E2B on such adverse drug reactions from the PMDA website intended for companies so that the companies can analyze and respond to the information, and has provided information of investigation results to share with the companies.

b. Responses to consultation requests from companies

- In order to contribute to the improvement of post-marketing safety measures in companies, PMDA responded to requests for various consultations (on drugs, medical devices, and medical safety) from companies. Specifically, these medical safety consultations were 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 2012 is shown below:

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Drugs	559	619	752	670	704
Medical devices	283	247	171	163	179
Medical safety	172	142	83	59	80

- Consultations conducted in FY 2011 are mainly on the names of new drugs, packaging/labeling, and near-incident cases for drugs/medical devices. PMDA responded to all consultations in an appropriate and prompt manner.

c. Release of information on drug risk under evaluation

- From the viewpoint of further enhancing safety measures for drugs, PMDA releases (1) risk information which was suggested by accumulated information and may lead to revision of precautions in package inserts, etc. and (2) risk information which have attracted attention from foreign regulatory authorities, academic societies, etc. and are under evaluation by MHLW/PMDA. These types of information is posted on the Medical Product Information web page as appropriate from July 2011, as preliminary information that may lead to safety measures such as revision of precautions.

d. Public release of adverse drug reaction cases

- PMDA has publicly released adverse drug reaction reports that were submitted by companies in and after April 2004 on its Medical Product Information web page sequentially since January 2006. In March 2012, PMDA began to expand data items and reports to be released so that the contents can be more easily utilized by related parties.

  Currently, PMDA is releasing all domestic adverse drug reaction reports 4 months after reporting in principle. The following data items from the reports are released: "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 adminstration," "a single-dose," "start date of administration," "end date of administration," "action against suspected drug," "adverse events (onset date)," "presence/absence of recurrence due to re-administration," "outcome," "suspected concomitant drug," and "other concomitant drug."

  PMDA has also released reports of cases about which PMDA conducted investigations such as making inquiries, from among adverse drug reaction/infection reports submitted from healthcare professionals to the Minister of Health, Labour and Welfare.

  By the end of March 2013, PMDA posted 254,392 reports submitted up to November 2012.

- In addition, in April 2012, PMDA started providing the data sets of adverse reaction reports (including expanded items/reports) exported into the CSV format for public release. The database had been available only in line listing format. As a result, the data can be used for research and studies.

- The time from receiving adverse reaction reports to release was maintained for a 4-month period, showing that the target period for FY 2012 was achieved.

e. Public release of medical device malfunction cases

- From among the contents of all reports on medical device malfunctions that were submitted by companies in or after April 2004, PMDA has publicly released their fiscal year reported, gender, age, outcome, generic name, condition of the medical device, and adverse event experienced by patient on its Medical Product Information web page, since March 2006. By the end of March 2013, PMDA posted 73,012 reports submitted up to September 2012.

f. Prompt release of package inserts and related notifications directing their revision for prescription drugs on the PMDA website

- By the end of FY 2012, PMDA posted 12,435 package inserts of prescription drugs on the Medical Product Information web page. Upon the issuance of notifications directing for revision of a package insert by the government, PMDA posted the notifications on its website within 2 days of receiving such information, and provided a link to the corresponding package insert.

g. Provision of information relating to instructions for use of medical devices

- For medical devices, PMDA has made instructions for use publicly available since FY 2005. The Agency released 17,539 instructions for use by the end of FY 2012. Also, the Agency has posted notifications directing the revision of instructions for use within 2 days of the issuance of such information, and routinely provided links to the corresponding instructions for use.

h. Provision of information relating to package inserts of OTC drugs

- Regarding OTC drugs, the revised Pharmaceutical Affairs Act came into effect in June 2009. Prior to the enforcement, the government developed systems for providing advice and consultation according to the risk level of OTC drugs, secured qualifications of professionals engaged in selling drugs, and improved the environment that supports provision of proper information and consultation. As a part of the efforts, PMDA started posting package inserts of OTC drugs on the website in March 2007. A total of 10,158 package inserts are available on the website as of the end of FY 2012.

i. Package insert information for in vitro diagnostics

- As described above, information on package inserts of prescription drugs, medical devices, and OTC drugs are provided on the Medical Product Information web page to ensure their correct usage. In FY 2008, package insert information for in vitro diagnostics also began to be posted. A total of 4,054 package inserts are available on the website as of the end of FY 2012.

j. Provision of manuals for management of individual serious adverse drug reactions

- The manuals for management of individual serious adverse drug reactions prepared by MHLW in its initiative of comprehensive actions for serious adverse drug reactions have been made available on the PMDA website since November 2006. As of the end of FY 2011, manuals for a total of 75 diseases 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.

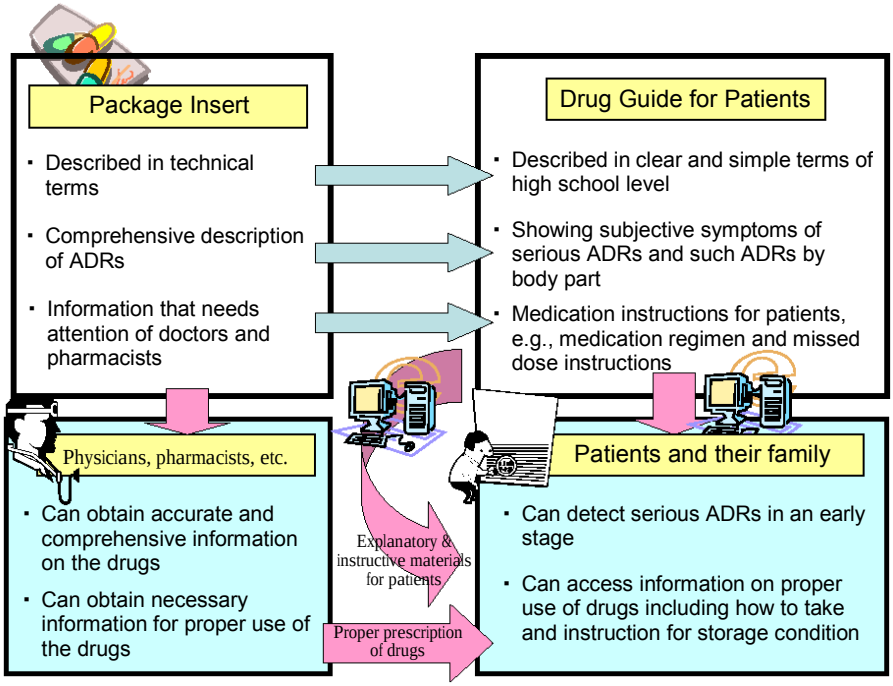
  The MHLW's initiative of comprehensive actions for serious adverse drug reactions was terminated in FY 2010, and consequently, no information was added to the manual in FY 2012,

but the manuals are reviewed for a future revision.

k. Provision of Drug Guides for Patients

- The Drug Guide for Patients is intended to promote proper understanding of prescription drugs among patients and to enable detection of serious adverse reactions at an earlier stage. The Guides have been available on the PMDA website since January 2006. In FY 2012, the drug guides for 54 active ingredients (for which a drug guide had to be developed following the revision of precautions, or which were newly marketed) were added to the Drug Guide database, and a total of 417 active ingredients in 2,453 products (1,748 package inserts) were posted by the end of FY 2012.
- In accordance with the "Guidelines for Developing the Drug Guide for Patients" (PFSB Notification dated June 30, 2005), PMDA has reviewed and revised the Drug Guide for Patients while continuously obtaining advice from experts ("Research on How to Provide Patients and People with Drug Safety information," a study supported by the Health and Labour Sciences Research Grant).

Package Inserts for Prescription Drugs and Drug Guide for Patients



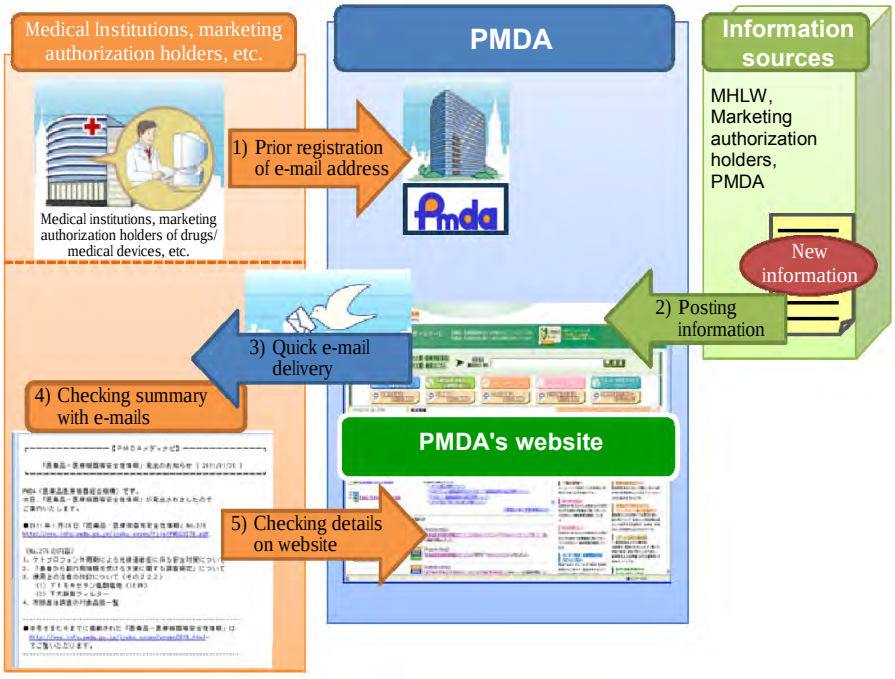
l. Provision of information from the PMDA's Medical Product Information web page

- Among safety information that are issued on a daily basis, PMDA promptly posts important information such as revision of PRECAUTIONS on its Medical Product Information web page (http://www.info.pmda.go.jp/), and distributed the information by e-mail (PMDA medi-navi) to healthcare professionals and relevant people in companies upon issuing the information. PMDA also posts various safety information including package inserts, on the Medical Product Information web page to enhance and reinforce the provision of safety information.
- PMDA improved its website by adding new contents such as RMP, informing maintenance schedules, etc., thereby making the website more user-friendly.

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

- The "Pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)" which provides safety information such as revisions to package inserts and Class I recalls, is provided via e-mail to healthcare professionals who subscribe to the service. To enhance its public recognition and increase the number of subscribers, PMDA reinforced the PR activities by conducting magazine advertisement using its character, listing advertisement, and academic conference presentations.
- A total of 84,146 e-mail addresses were registered as of the end of March 2013 (increased by about 28,500/year in FY 2012). Approximately 26,000 subscribers were at hospitals and clinics, 25,000 were pharmacies, 5,700 were dentist clinics or other medical facilities, and 13,000 were marketing authorization holders and distributors.
- In June 2011, PMDA started to provide "My Drug List for Safety Update" as an additional function of PMDA medi-navi. As of the end of March 2013, 6,414 subscribers have been registered.
- This service enables users to prepare a customizable drug list on the website. In this service, when users register necessary drugs (My Drugs), a list of links to package inserts, interview forms, and drug guides for patients, etc., of My Drugs is displayed. Furthermore, there are functions such as a warning mark being displayed, in case where any safety information such as Dear Healthcare Professional Letters is issued for any registered drug.

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



PMDA medi-navi by Content in FY 2012

Contents of e-mails	Number of cases
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letter)	1
Recalls (Class I)	18
Pharmaceuticals and Medical Devices Safety Information	11
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	7
Approval information (medical devices)	10
Approval information (prescription drugs)	69
Notifications on drugs, Notifications on medical devices	11
Information on proper use of drugs	21
Information on drug risk under evaluation	11
MHLW notification on medical safety measures	10
Information released by MHLW	1
Information on products submitted for public knowledge-based applications that are covered by insurance	5
Notice of decision on payment/non-payment of adverse reaction relief benefits	4
Others	4
Total	207

n. Provision of medical safety information

- PMDA has been extracting, evaluating, and examining near-incident cases associated with drugs and medical devices from the "Project Report on Collection of Medical Incident Information," "Annual Report of the Project to Collect and Analyze Near-incident Cases from Pharmacies," etc. published by the Japan Council for Quality Health Care. In FY 2012, 2,964 cases associated with drugs and 274 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 3,238 cases for which deliberations were completed by MHLW, the details of the cases were posted on the PMDA's Medical Product Information web page as shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 3,238 cases	2,964	274
1) Cases in which safety measures for the use of drugs/medical devices taken by the marketing authorization holders etc. were considered necessary or possible.	2	0
2) Cases in which measures have already been taken, or are currently under consideration, by the marketing authorization holder etc.	27	29
3) Cases in which information is insufficient for the marketing authorization holder to consider safety measures, or cases that were likely to have resulted from human errors or human factors.	2,935	245

- Since November 2007, PMDA has issued PMDA Medical Safety Information, which provides precautions for safe use of medical products using charts so that healthcare professionals can easily understand, by referring to opinions given by healthcare professionals such as physicians, pharmacists, nurses, and clinical engineers and specialists in fields such as ergonomics. The information addresses events that were reported repeatedly or led to issuance of revisions to package inserts, among near-incident cases and adverse drug reaction and malfunction reports. In FY 2012, the following 7 issues of PMDA Medical Safety Information were posted on the Medical Product Information web page.

Volume No.	Month and year published	PMDA Medical Safety Information titles
No.30	April 2012	Precautions in Handling of Endotracheal Tubes
No.31	May 2012	Precautions in Handling of Radiopharmaceuticals for Injection
No.32	June 2012	Precautions in Handling of Closed Suction Catheters
No.33	September 2012	Burn Accidents during Surgery
No.34	October 2012	Precautions in Handling of Glycerin Enema
No.35	October 2012	Precautions in Handling of Tracheostomy Tubes
No.36	March 2013	Cases of Tube or Line Removal

o. Information provision in English

- To promote provision of information on safety measures to overseas users, PMDA posted newly-translated information into English, such as that on drug risk under evaluation, as "PMDA Risk Communications" on its English website. The Agency also continued to translate into English the PMDA Medical Safety Information, the PMDA Request for Proper Use of Drugs, and the Pharmaceuticals and Medical Devices Safety Information issued by MHLW, to post the translations on its English website.

p. Conduct of post-marketing safety measures workshops

- At various workshops and academic conferences, PMDA gave presentations on the approaches to improvement and strengthening of safety measures, the safety measures including recent revisions of precautions in package inserts, the effective use of the Medical Product Information web page, and PMDA's consultation services.

q. Conduct of 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 2012, the number of persons receiving consultations was 9,679 (12,558 calls) for drugs, and 700 (733 calls) for medical devices.
- PMDA started consultations for generic drugs in May 2007, and has received requests for consultations from general customers and healthcare professionals such as physicians and pharmacists. In FY 2012, the number of persons receiving consultations was 493. General consumers accounted for 89.7% of them, whereas physicians/pharmacists accounted for 5.5%. PMDA has been providing consultation cases 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]), which has held meetings twice a year since July 2008.

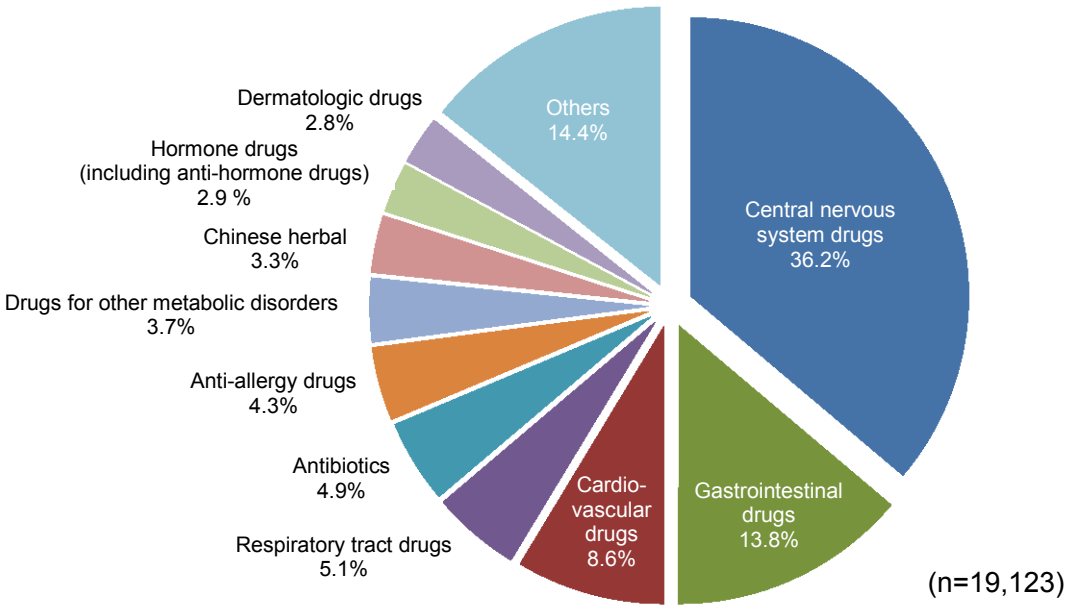
Number of Consultations on Drugs/Medical Devices

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Consultations on drugs	8,479 [34.9 cases/day]	9,316 [38.5 cases/day]	8,846 [36.4 cases/day]	8,945 [36.7 cases/day]	9,679 [39.5 cases/day]
(of which, consultations on generic drugs)	(143)	(687)	(617)	(453)	(493)
Consultations on medical devices	639 [2.6 cases/day]	558 [2.3 cases/day]	574 [2.4 cases/day]	660 [2.7 cases/day]	700 [2.9 cases/day]

Contents of Consultations on Drugs

Contents of consultation	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
(1) Safety	6,347	5,727	5,553	5,146	5,267
	(50.6%)	(42.4%)	(45.0%)	(41.3%)	(41.9%)
(2) Indications	954	1,079	890	1,147	1,158
	(7.6%)	(8.0%)	(7.2%)	(9.2%)	(9.2%)
(3) Administration and Dosage	836	746	784	981	1,259
	(6.7%)	(5.5%)	(6.4%)	(7.9%)	(10.0%)
(4) Interactions	732	753	784	986	1,206
	(5.8%)	(5.6%)	(6.4%)	(7.9%)	(9.6%)
(5) Active Ingredients	214	251	181	199	222
	(1.7%)	(1.9%)	(1.5%)	(1.6%)	(1.8%)
Others	3,450	4,960	4,144	4,014	3,446
	(27.5%)	(36.7%)	(33.6%)	(32.1%)	(27.5%)
Total	12,533	13,516	12,336	12,473	12,558
	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)

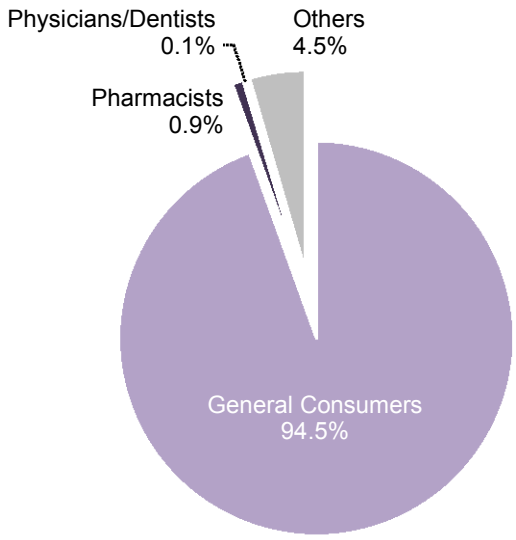
Number of Consultations on Drugs by Therapeutic Category (FY 2012)



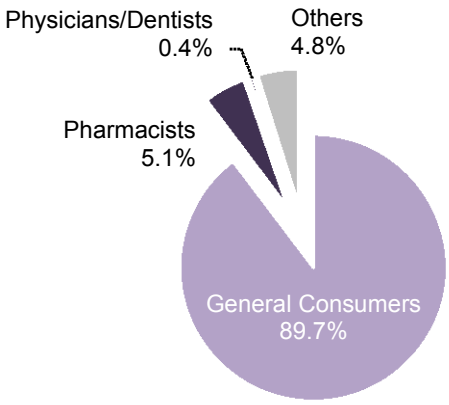
(n=19,123)

Breakdown of Persons Receiving Consultations on Drugs in FY 2012 (by Profession, etc.)

Consultations on drugs (n=9,679)

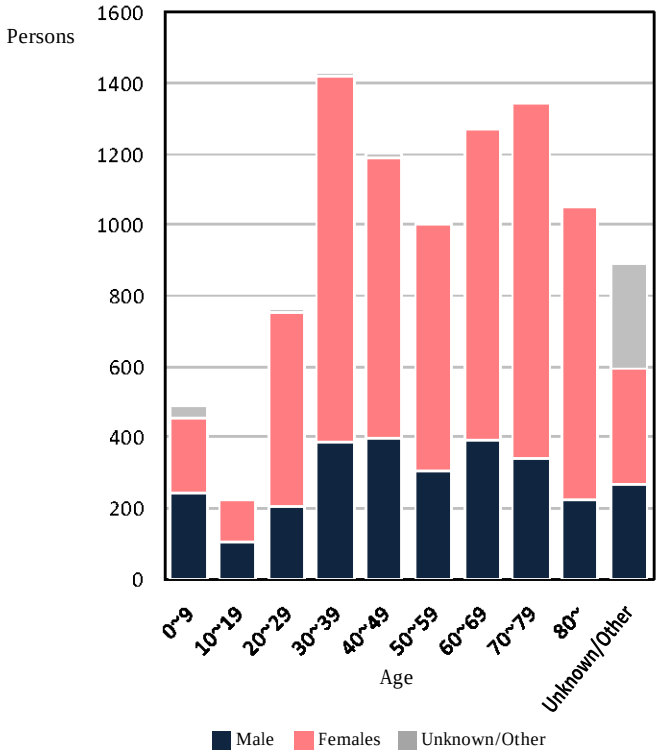


Consultations on generic drugs (n=493)

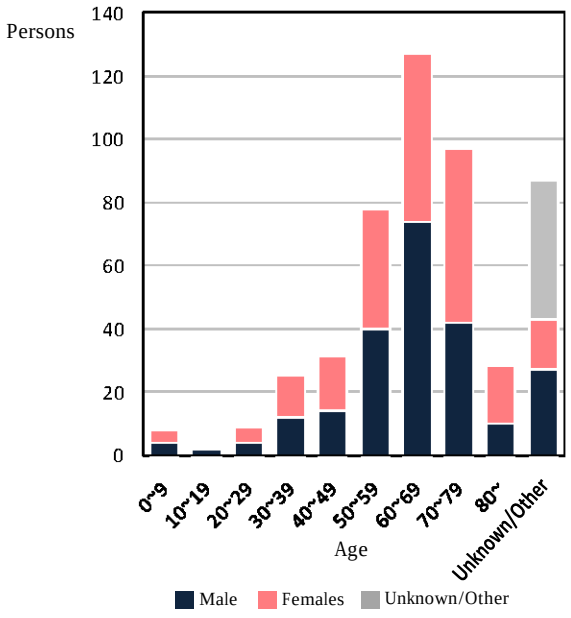


Breakdown of Persons Receiving Consultations on Drugs in FY 2012 (by Age/Gender) *

Consultations on drugs (n=9,679)



Consultations on generic drugs (n=493)

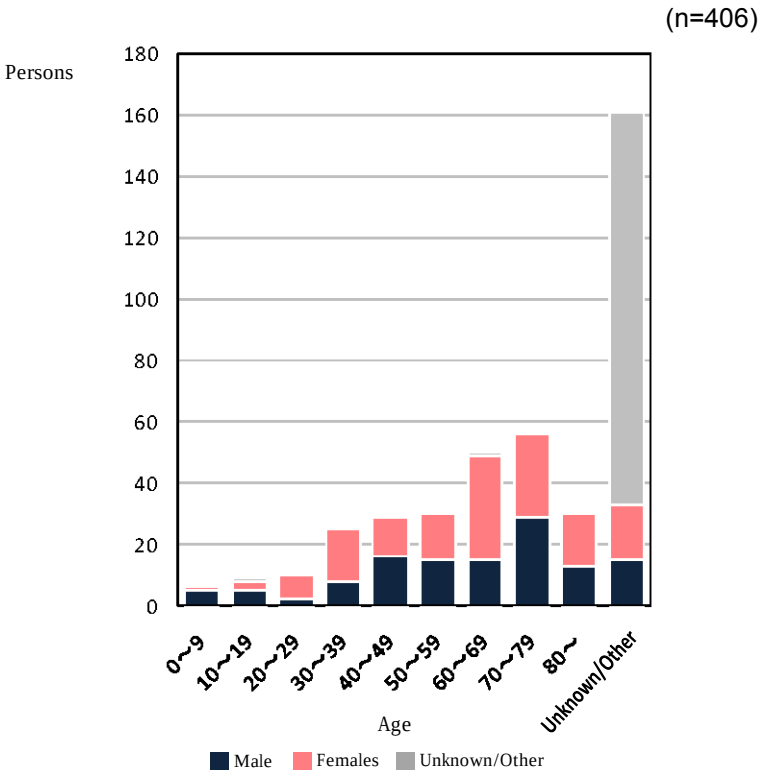


*Age and gender of the users of drugs are counted.

Contents of consultations on medical devices

Contents of consultation	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
(1) Safety	96 (10.6%)	74 (12.0%)	78 (12.5%)	85 (12.4%)	106 (14.5%)
(2) Indications	90 (10.0%)	59 (9.6%)	61 (9.8%)	69 (10.1%)	62 (8.5%)
(3) Performance	46 (5.1%)	27 (4.4%)	17 (2.7%)	24 (3.5%)	36 (4.9%)
(4) Directions for use	17 (1.9%)	15 (2.4%)	12 (1.9%)	10 (1.5%)	7 (0.9%)
Others	653 (72.4%)	441 (71.6%)	454 (73.0%)	498 (72.5%)	522 (71.2%)
Total	902 (100.0%)	616 (100.0%)	622 (100.0%)	686 (100.0%)	733 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2012 (by Age/Gender)**



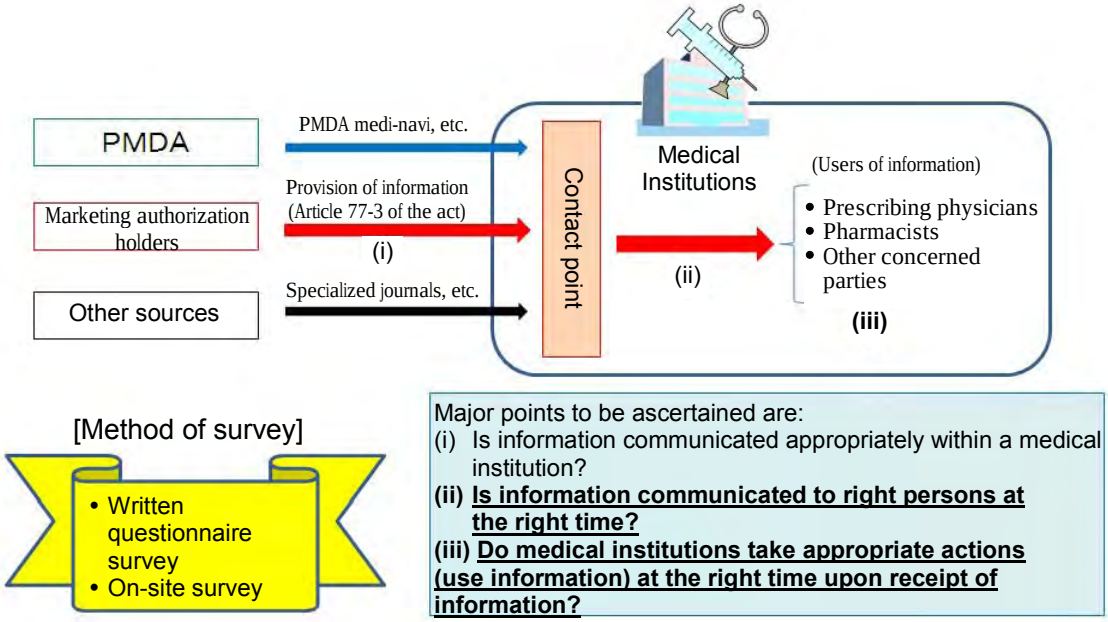
*** Summary of medical device users by age/gender consisting of general consumers and consultees of consumer affairs centers.*

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

- When a safety measure is taken, it is important that necessary safety information is appropriately communicated to and used by healthcare professionals in clinical settings. Accordingly, in FY 2010, PMDA started an investigation to ascertain the status of communication and use of safety information on drugs, etc. in medical institutions.

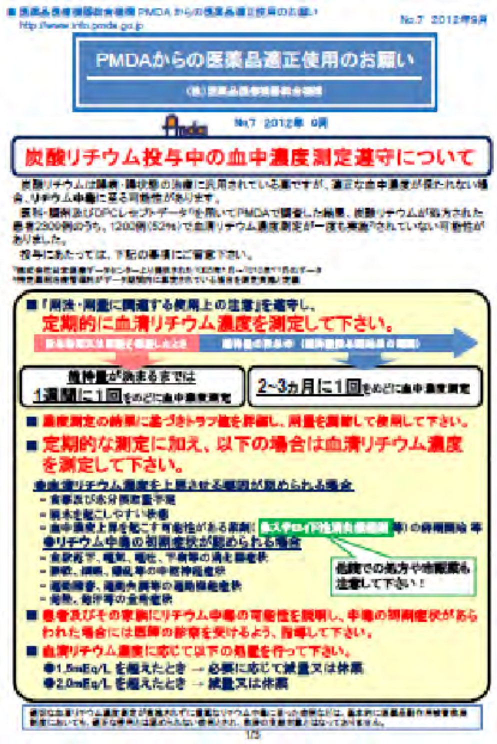
  PMDA conducted one mail-in questionnaire surveys among hospitals (8,679 institutions) nationwide in FY 2010, and another survey among 8,640 medical institutions in FY 2011 with different questionnaire items. The survey results up to FY 2011 were posted on the PMDA website. In FY 2012, PMDA newly included pharmacies as the targets of survey and conducted the survey among hospitals nationwide (8,536 institutions) and about a half of pharmacies nationwide (26,738 institutions). In this project, the survey was also conducted online in addition to the mail-in questionnaire. The results of the survey will be released as soon as they are finalized and efforts will be made to promote proper communication and use of information in medical institutions and pharmacies.

Survey to Ascertain the Status of Communication/Use of Information within Medical Institutions



s. Provision of the PMDA Request for Proper Use of Drugs

- If proper use (including doses and frequency as well as frequency of testing for adverse reaction monitoring) of a drug has already been recommended in its package insert or a company's document, but the drug was not used properly or testing was not properly conducted, patients cannot possibly receive relief benefits for adverse drug reactions. In order to avoid such a case, in FY 2010, PMDA started to provide information to healthcare professionals and related academic societies to promote proper use of drugs. In FY 2012, a total of 3 kinds of information, such as "Compliance with Measurement of Blood Lithium Level during Treatment with Lithium Carbonate," were provided.



No.7 2012年9月

PMDAからの医薬品適正使用のお願い

No.7 2012年 9月

炭酸リチウム投与中の血中濃度測定遵守について

定期的に血清リチウム濃度を測定して下さい。

維持量が決まるまでは 1週間に1回をめどに血中濃度測定

2~3カ月に1回をめどに血中濃度測定

■ 定期的な測定に加え、以下の場合は血清リチウム濃度を測定して下さい。

■ 血清リチウム濃度に応じて以下の処置を行って下さい。

●1.5mEq/L を超えたとき → 必要に応じて減量又は休薬

●2.0mEq/L を超えたとき → 減量又は休薬

(Request for Proper Use of Drugs to patients)

Number of Information Documents Released on the PMDA's Medical Product Information Web Page as of the End of March 2013

Posted information	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Package insert information *1					
Prescription drugs	13,287	13,050	12,256	12,064	12,435
Medical devices	8,164	11,213	13,979	15,584	17,539
OTC drugs	8,356	9,513	9,884	10,136	10,158
In vitro diagnostics	2,237	3,301	3,984	3,994	4,054
Drug Guide for Patients *1	294 active ingredients (1,958 products)	312 active ingredients (1,920 products)	330 active ingredients (2,311 products)	363 active ingredients (1,951 products)	417 active ingredients (2,453 products)
Safety information issued by MHLW • Directions for revision of package inserts • Pharmaceuticals and Medical Devices Safety Information • Press release	350	376	409	438	464
Dear Healthcare Professional Letters (by pharmaceutical companies) *2	24	24	24	24	25
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])	51	61	71	81	91
Notification of safety measures for medical devices					
Notification on self-check	47	49	50	50	51
Notification of revisions of labeling	30	32	33	41	45
Other related notification	57	66	74	83	93
Information about case reports on suspected ADR	110,879	142,084	175,360	210,412	254,392
Information about case reports on suspected malfunction	42,405	46,551	51,169	62,898	73,012
Notification related to preventive measures for medical accidents	44	56	68	77	87
PMDA Medical Safety Information	9	15	22	29	36
Manuals for management of individual serious adverse drug reactions	38	63	63	75	75
Information on approved new drugs • Review reports, summaries of product applications	373 active ingredients (763 products)	445 active ingredients (895 products)	513 active ingredients (1,034 products)	592 active ingredients (1,189 products)	666 active ingredients (1,314 products)
A list of prescription drugs on which Quality Information Package (Orange Book) was published	811 active ingredients/ formulations (3,900 products)	811 active ingredients/ formulations (3,900 products)	811 active ingredients/ formulations (3,900 products)	811 active ingredients/ formulations (3,900 products)	811 active ingredients/ formulations (3,900 products)
Information on recalls of drugs or medical devices *3	3,448	1,979	1,977	2,299	1,907
Pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)					
E-mails issued *4	107	188	203	259	207
Subscribers	20,707	27,410	35,719	55,372	84,146
Number of site visitors *5	642 million	754 million	873 million	949 million	994 million

**1 Added or deleted as necessary*

**2 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 was indicated in and after October 2011.*

**3 Added as necessary; and deleted after two years in principle.*

**4 Accumulated total number of e-mails issued in each year*

**5 Total number of viewed files in each year*

III. SUPPLEMENTARY INFORMATION

Table 1. Products Approved in FY 2012 : New Drugs

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Jun. 22, 2012	1	Nexium Capsules 10 mg Nexium Capsules 20 mg (AstraZeneca K.K.)	Change Change	Esomeprazole magnesium hydrate	Drugs 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	Jun. 22, 2012	2	Emend Capsules 80 mg Emend Capsules 125 mg Emend Capsules Set (Ono Pharmaceutical Co., Ltd.)	Change Change Change	Aprepitant	Drugs with a new additional pediatric dosage for patients of 12 years or older. These drugs are indicated for the treatment of gastrointestinal symptoms (nausea and vomiting) associated with administration of antineoplastic drugs (cisplatin, etc.) (including delayed phase).
1	Jun. 29, 2012	3	Amitiza Capsules 24 μg (Sucampo Pharma. Ltd.)	Approval	Lubiprostone	A drug with a new active ingredient indicated for the treatment of chronic constipation (excluding constipation due to organic diseases).
1	Aug. 24, 2012	4	Pentasa Tablets 250 mg Pentasa Tablets 500 mg (Kyorin Pharmaceutical Co., Ltd.)	Change Change	Mesalazine	Drugs with a new dosage. These drugs are indicated for the treatment of ulcerative colitis.
1	Dec. 21, 2012	5	Radiogardase Capsule 500 mg (Nihon Medi-Physics Co., Ltd.)	Change	Iron (III) hexacyanoferrate (II)	A drug with a new additional indication for the treatment of thallium and thallium compound poisoning.
1	Dec. 25, 2012	6	Moviprep Combination Oral Solution (Ajinomoto Pharmaceutical Co., Ltd.)	Approval	N/A for this combination drug	A combination prescription drug with similar formulations to be used for bowel cleansing as a preparation for colonoscopy and large intestine surgery.
1	Dec. 25, 2012	7	Phosribbon Combination Granules (Zeria Pharmaceutical Co., Ltd.)	Approval	Monobasic sodium phosphate monohydrate/dibasic sodium phosphate anhydrous	A drug with a new indication and a new dosage in an additional dosage form for the treatment of hypophosphatemia. [Orphan drug]
1	Feb. 28, 2013	8	Minclea Catapasm for Internal Use 0.8% (Nihon Pharmaceutical Co., Ltd.)	Change	*l*-Menthol	A drug with a new additional indication for the inhibition of gastric peristalsis in endoscopic therapy for the upper gastrointestinal tract.
1	Mar. 25, 2013	9	Pentasa Suppositories 1 g (Kyorin Pharmaceutical Co., Ltd.)	Approval	Mesalazine	A drug in a new dosage form indicated for the treatment of ulcerative colitis (excluding severe cases).
1	Mar. 25, 2013	10	Acofide Tablets 100 mg (Zeria Pharmaceutical Co., Ltd.)	Approval	Acotiamide hydrochloride hydrate	A drug with a new active ingredient indicated for the treatment of postprandial fullness, upper abdominal bloating, and early satiation in functional dyspepsia.
2	May 25, 2012	11	Kaytwo Syrup 0.2% (Sannova Co., Ltd.)	Change	Menatetrenone	A drug with a new additional indication and a new dosage for the prevention of vitamin K-deficiency hemorrhage in neonates/infants. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
2	May 25, 2012	12	Inderal Tablets 10 mg Inderal Tablets 20 mg (AstraZeneca K.K.)	Change Change	Propranolol hydrochloride	Drugs with new additional pediatric dosages for extrasystole (supraventricular/ventricular), the prevention of paroxysmal tachycardia, atrial fibrillation with rapid ventricular response (bradycardiac effect), sinus tachycardia, atrial fibrillation, and the prevention of paroxysmal atrial fibrillation. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 22, 2012	13	Epadel Capsules 300 Epadel S300 Epadel S600 Epadel S900 (Mochida Pharmaceutical Co., Ltd.)	Change Change Change Change	Ethyl icosapentate	Drugs with a new dosage. These drugs are indicated for the treatment of hyperlipemia.
2	Jun. 22, 2012	14	Renivace Tablets 2.5 Renivace Tablets 5 Renivace Tablets 10 (MSD K.K.)	Change Change Change	Enalapril maleate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 22, 2012	15	Zestril Tablets 5 Zestril Tablets 10 Zestril Tablets 20 (AstraZeneca K.K.)	Change Change Change	Lisinopril hydrate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 22, 2012	16	Longes Tablets 5 mg Longes Tablets 10 mg Longes Tablets 20 mg (Shionogi & Co., Ltd.)	Change Change Change	Lisinopril hydrate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun.22, 2012	17	Norvasc Tablets 2.5 mg Norvasc Tablets 5 mg Norvasc OD Tablets 2.5 mg Norvasc OD Tablets 5 mg (Pfizer Japan Inc.) Amlodin Tablets 2.5 mg Amlodin Tablets 5 mg Amlodin OD Tablets 2.5 mg Amlodin OD Tablets 5 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change Change Change Change Change Change	Amlodipine besilate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	Jun. 22, 2012	18	Amlodipine Tab. 2.5 mg "Amel" Amlodipine Tab. 5 mg "Amel" Amlodipine OD Tab. 2.5 mg "Amel" Amlodipine OD Tab. 5 mg "Amel" (Kyowa Pharmaceutical Industry Co., Ltd.)	Change Change Change Change	Amlodipine besilate	Drugs with a new additional pediatric dosages. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 22, 2012	19	Enalart Fine Gran. 1% Enalart Tab. 2.5 mg Enalart Tab. 5 mg Enalart Tab. 10 mg (Kyowa Pharmaceutical Industry Co., Ltd.)	Change Change Change Change	Enalapril maleate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 22, 2012	20	Amlodipine Oral Jelly 2.5 mg "Towa" Amlodipine Oral Jelly 5 mg "Towa" Amlodipine OD Tablets 2.5 mg "Towa" Amlodipine OD Tablets 5 mg "Towa" Amlodipine Tablets 2.5 mg "Towa" Amlodipine Tablets 5 mg "Towa" (Towa Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change	Amlodipine besilate	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 29, 2012	21	Requip CR Tablets 2 mg Requip CR Tablets 8 mg (GlaxoSmithKline K.K.)	Approval Approval	Ropinirole hydrochloride	Drugs in new dosage forms and with a new dosage. These drugs are indicated for the treatment of Parkinson's disease.
2	Aug. 24, 2012	22	Plavix 25 mg Tablets Plavix 75 mg Tablets (Sanofi-Aventis K.K.)	Change Change	Clopidogrel sulfate	Drugs with a new additional indication for the treatment of the following ischemic heart disease for which percutaneous coronary intervention (PCI) is applied: ST elevation myocardial infarction.
2	Aug. 24, 2012	23	Diovan Tablets 20 mg Diovan Tablets 40 mg Diovan Tablets 80 mg Diovan Tablets 160 mg (Novartis Pharma K.K.)	Change Change Change Change	Valsartan	Drugs with a new additional pediatric dosage. These drugs are indicated for the treatment of hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Sep. 28, 2012	24	Lotriga Granular Capsule 2 g (Takeda Pharmaceutical Company Limited)	Approval	omega-3-acid ethyl esters	A drug with a new active ingredient indicated for the treatment of hyperlipidaemia.
2	Sep. 28, 2012	25	Aimix Combination Tablet LD Aimix Combination Tablet HD (Dainippon Sumitomo Pharma Co., Ltd.)	Approval Approval	Irbesartan/ amlodipine besilate	New combination drugs indicated for the treatment of hypertension.
2	Sep. 28, 2012	26	Plavix 25 mg Tablets Plavix 75 mg Tablets (Sanofi-Aventis K.K.)	Change Change	Clopidogrel sulfate	Drugs with a new additional indication and a new dosage for the suppression of embolus/thrombus formation in peripheral arterial diseases.
2	Nov. 21, 2012	27	Tracleer Tablets 62.5 mg (Actelion Pharmaceuticals Japan Ltd.)	Change	Bosentan hydrate	A drug with a new additional indication for the treatment of pulmonary arterial hypertension (WHO functional class II). [Orphan drug]
2	Dec. 21, 2012	28	Micamlo Combination Tablets BP (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Telmisartan/amlodipine besilate	A drug with a new dosage in an additional dosage form for the treatment of hypertension.
2	Dec. 25, 2012	29	Eliquis Tablets 2.5 mg Eliquis Tablets 5 mg (Bristol-Myers K.K.)	Approval Approval	Apixaban	Drugs with a new active ingredient indicated for prevention of ischemic stroke and systemic embolism in patients with nonvalvular atrial fibrillation.
2	Feb. 28, 2013	30	Livalo Tablets 1 mg Livalo Tablets 2 mg Livalo Tablets 4 mg (Kowa Company, Ltd.)	Change Change Change	Pitavastatin calcium	Drugs with a new dosage indicated for the treatment of hypercholesterolemia and familial hypercholesterolemia.
2	Feb. 28, 2013	31	Grtpa Inj. 6,000,000 Grtpa Inj. 12,000,000 Grtpa Inj. 24,000,000 (Mitsubishi Tanabe Pharma Corporation) Activacin for Injection 6,000,000 Activacin for Injection 12,000,000 Activacin for Injection 24,000,000 (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change Change Change Change	Alteplase (genetical recombination)	Drugs with a new indication and a new dosage for the improvement of functional impairment in association with acute phase of Ischemic cerebrovascular disorder (within 4.5 hours after onset). [Public knowledge-based application after PAFSC's preliminary assessment]
2	Feb. 28, 2013	32	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 migraine attack. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Mar. 25, 2013	33	Nouriast Tablets 20 mg (Kyowa Hakko Kirin Co., Ltd.)	Approval	Istradefylline	A drug with a new active ingredient indicated for the improvement of wearing-off phenomenon in patients with Parkinson's disease on treatment with levodopa-containing products.
2 & 3-1	Dec. 25, 2012	34	[1] Neupro Patch 2.25 mg [2] Neupro Patch 4.5 mg [3] Neupro Patch 9 mg [4] Neupro Patch 13.5 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval	Rotigotine	[1] [2] Drugs with a new active ingredient indicated for the treatment of Parkinson's disease and moderate to severe idiopathic restless legs syndrome. [3] [4] Drugs with a new active ingredient indicated for the treatment of Parkinson's disease.
3-1	Jun. 22, 2012	35	Lyrica Capsules 25 mg Lyrica Capsules 75 mg Lyrica Capsules 150 mg (Pfizer Japan Inc.)	Change Change Change	Pregabalin	Drugs with a new additional indication and a new dosage for the treatment of pain associated with fibromyalgia. [Priority review]

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Aug. 24, 2012	36	Strattera Capsule 5 mg Strattera Capsule 10 mg Strattera Capsule 25 mg Strattera Capsule 40 mg (Eli Lilly Japan K.K.)	Change Change Change Change	Atomoxetine hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of attention-deficit/hyperactivity disorder (AD/HD) in adults.
3-1	Sep. 28, 2012	37	Zyprexa for Intramuscular Injection 10 mg (Eli Lilly Japan K.K.)	Approval	Olanzapine	A drug with a new route of administration indicated for the treatment of acute agitation associated with schizophrenia.
3-1	Sep. 28, 2012	38	Diacomit Drysyrup 250 mg Diacomit Drysyrup 500 mg Diacomit Capsules 250 mg (Meiji Seika Pharma Co., Ltd.)	Approval Approval Approval	Stiripentol	Drugs with a new active ingredient indicated for use in conjunction with clobazam and sodium valproate as adjunctive therapy of refractory generalized tonic-clonic and clonic seizures in patients with Dravet's syndrome whose seizures are not adequately controlled with clobazam and sodium valproate. [Orphan drug]
3-1	Nov. 21, 2012	39	Botox for Injection 50 Units Botox for Injection 100 Units (GlaxoSmithKline K.K.)	Change Change	Botulinum toxin type A	Drugs with a new route of administration and an additional indication for the treatment of severe primary axillary hyperhidrosis.
3-1	Dec. 25, 2012	40	Choreazine Tablets 12.5 mg (Alfresa Pharma Corporation)	Approval	Tetrabenazine	A drug with a new active ingredient indicated for the treatment of chorea associated with Huntington's disease. [Orphan drug]
3-1	Feb. 28, 2013	41	Lyrica Capsules 25 mg Lyrica Capsules 75 mg Lyrica Capsules 150 mg (Pfizer Japan Inc.)	Change Change Change	Pregabalin	Drugs with a new indication for the treatment of neuropathic pain.
3-1	Mar. 25, 2013	42	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 a new additional indication and a new dosage for the treatment of acute exacerbation of multiple sclerosis. [Public knowledge-based application after PAFSC's preliminary assessment]
3-1	Mar. 25, 2013	43	Regtect Tablets 333 mg (Nippon Shinyaku Co., Ltd.)	Approval	Acamprosate calcium	A drug with a new active ingredient indicated for use as an aid for maintenance of abstinence in patients with alcohol dependence.
3-1	Mar. 25, 2013	44	Inovelon Tablets 100 mg Inovelon Tablets 200 mg (Eisai Co., Ltd.)	Approval Approval	Rufinamide	Drugs with a new active ingredient indicated for use as a concomitant therapy with other antiepileptic drugs to treat tonic and atonic seizures in patients with Lennox-Gastaut syndrome who have not responded sufficiently to other antiepileptic drugs. [Orphan drug]
3-2	Jun. 22, 2012	45	Penles Tape 18 mg (Nitto Denko Corporation)	Change	Lidocaine	A drug with a new additional indication and a new dosage for pain relief at the resection of molluscum contagiosum.
3-2	Sep. 28, 2012	46	Eylea Intravitreal Injection 40 mg/mL Eylea Intravitreal Injection Kit 40 mg/mL (Bayer Yakuhin, Ltd.)	Approval Approval	Aflibercept (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of age-related macular degeneration associated with subfoveal choroidal neovascularization.
3-2	Sep. 28, 2012	47	Methapain Tablet 5 mg Methapain Tablet 10 mg (Teikoku Seiyaku Co., Ltd.)	Approval Approval	Methadone hydrochloride	Drugs with a new active ingredient indicated for achieving analgesia of moderate to severe pain associated with various types of cancer which can not be managed by treatment with other strong opioid analgesics.
4	May 25, 2012	48	Finibax for Intravenous Infusion 0.25 g Finibax for Intravenous Infusion 0.5 g Finibax Kit for Intravenous Infusion 0.25 g (Shionogi & Co., Ltd.)	Change Change Change	Doripenem hydrate	Drugs with a new additional pediatric dosage and with a new additional indication for the treatment of purulent meningitis.
4	May 25, 2012	49	Viccillin 0.25 g for Injection Viccillin 0.5 g for Injection Viccillin 1 g for Injection Viccillin 2 g for Injection (Meiji Seika Pharma Co., Ltd.)	Change Change Change Change	Ampicillin sodium	Drugs with a new additional indication for *Listeria monocytogenes* as an applicable microorganism and with new additional pediatric and neonate dosages. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Jun. 22, 2012	50	Meiact MS Fine Granules 10% for Pediatric (Meiji Seika Pharma Co., Ltd.)	Change	Cefditoren pivoxil	A drug with a new additional dosage for the treatment of pneumonia, otitis media, and sinusitis.
4	Jun. 22, 2012	51	Zithromac Intravenous Use 500 mg Zithromac Tablets 250 mg (Pfizer Japan Inc.)	Change Change	Azithromycin hydrate	Drugs with a new additional indication and a new dosage for the treatment of pelvic inflammatory diseases.
4	Aug. 10, 2012	52	Flagyl Oral Tablet 250 mg (Shionogi & Co., Ltd.)	Change	Metronidazole	A drug with new additional indications and a new dosage for the treatment of anaerobic bacterial infection, infectious enteritis, amoebic dysentery, and *Giardia lamblia* infection. [Public knowledge-based application after PAFSC's preliminary assessment]

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Aug. 10, 2012	53	Baktar Combination Tablets Baktar Combination Granules (Shionogi & Co., Ltd.) Bactramin Combination Tablet Bactramin Combination Granule (Chugai Pharmaceutical Co., Ltd.)	Change Change Change Change	Sulfamethoxazole/ trimethoprim	Drugs with a new additional indication and a new dosage for the treatment and prevention of Pneumocystis pneumonia. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Aug. 10, 2012	54	Unasyn-S for Intravenous Use 0.75 g Unasyn-S for Intravenous Use 1.5 g Unasyn-S Kit for Intravenous Use 1.5 g Unasyn-S Kit for Intravenous Use 3 g (Pfizer Japan Inc.)	Change Change Change Change	Sulbactam sodium/ampicillin sodium	Drugs with new additional indications for *Streptococcus Pneumoniae* and *Moraxella catarrhalis* as applicable microorganisms. A new dosage has been added to enable high-dosage use for severe infections.
4	Sep. 28, 2012	55	Tobi Inhalation Solution 300 mg (Novartis Pharma K.K.)	Approval	Tobramycin	A drug with a new route of administration indicated for the improvement of symptoms associated with respiratory infection caused by *Pseudomonas aeruginosa* in cystic fibrosis patients.
4	Sep. 28, 2012	56	Zosyn for Intravenous Injection 2.25 Zosyn for Intravenous Injection 4.5 (Taiho Pharmaceutical Co., Ltd.)	Change Change	Tazobactam/ piperacillin hydrate	Drugs with new additional indications for the treatment of peritonitis, intraperitoneal abscess, cholecystitis, and cholangitis.
4	Sep. 28, 2012	57	Tygacil Injection 50 mg (Pfizer Japan Inc.)	Approval	Tigecycline	A drug with a new active ingredient indicated for the treatment of deep skin infection, chronic pyoderma, secondary infection of trauma, burn, and surgical wounds, secondary infection of erosion and ulcer, peritonitis, intraperitoneal abscess, and cholecystitis. [Priority review]
4	Nov. 21, 2012	58	Zyvox Tablets 600 mg Zyvox Injection 600 mg (Pfizer Japan Inc.)	Change Change	Linezolid	Drugs with a new additional pediatric dosage. These drugs are indicated for sepsis, deep skin infection, chronic pyoderma, secondary infection of trauma, burn, and surgical wounds, and pneumonia. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Dec. 25, 2012	59	Malarone Combination Tablets (GlaxoSmithKline K.K.)	Approval	Atovaquone/proguanil hydrochloride	A new combination drug with a new active ingredient indicated for the treatment and prevention of malaria. [Priority review]
4	Dec. 25, 2012	60	Ameparomo Capsules 250 mg (Pfizer Japan Inc.)	Approval	Paromomycin sulfate	A drug with a new active ingredient indicated for the treatment of intestinal amoebiasis.
4	Feb. 21, 2013	61	Famvir Tab. 250 mg (Asahi Kasei Pharma Corporation)	Change	Famciclovir	A drug with a new additional indication and a new dosage for the treatment of herpes simplex.

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Feb. 21, 2013	62	(1) Takepron capsules 15 Takepron capsules 30 (2) Takepron OD Tablets 15 Takepron OD Tablets 30 (Takeda Pharmaceutical Company Limited) (3) Omepral Tablets 10 Omepral Tablets 20 (AstraZeneca K.K.) (4) Omeprazon Tablets 10 mg Omeprazon Tablets 20 mg (Mitsubishi Tanabe Pharma Corporation) (5) Omeprazole Tablets 10 mg "Mylan" Omeprazole Tablets 20 mg "Mylan" (Mylan Seiyaku Ltd.) (6) Pariet Tablets 10 mg (Eisai Co., Ltd.) (7) Rabeprazole Na Tablets 10 mg "Ohara" (Ohara Pharmaceutical Co., Ltd.) (8) Nexium Capsules 10 mg Nexium Capsules 20 mg (AstraZeneca K.K.) (9) Pasetocin Capsules 125 Pasetocin Capsules 250 (10) Pasetocin Tablets 250 (Kyowa Hakko Kirin Co., Ltd.) (11) Sawacillin Capsules 125 Sawacillin Capsules 250 (12) Sawacillin Tablets 250 (Astellas Pharma Inc.) (13) Amolin Capsules 125 Amolin Capsules 250 (14) 10% Amolin Fine Granules (Takeda Pharmaceutical Company Limited) (15) Clarith tab. 200 (Taisho Pharmaceutical Co., Ltd.) (16) Klaricid Tablets 200 mg (Abbott Japan Co., Ltd.) (17) Clarithromycin Tab. 200 mg "Mylan" (Mylan Seiyaku Ltd.) (18) Clarithromycin Tablets 200 mg "Takata" (Takata Seiyaku Co., Ltd.) (19) Flagyl Oral Tablet 250 mg (Shionogi & Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change	(1)(2) Lansoprazole (3)(4)(5) Omeprazole (6)(7) Rabeprazole sodium (8) Esomeprazole magnesium hydrate (9)(10)(11)(12)(13)(14) Amoxicillin hydrate (15)(16)(17)(18) Clarithromycin (19) Metronidazole (20) Lansoprazole/amoxicillin hydrate/clarithromycin (21) Lansoprazole/amoxicillin hydrate/metronidazole	Drugs with a new additional indication for the treatment of gastritis induced by *Helicbacter pylori* infection.
			(20) Lansap 400 Lansap 800 (21) Lampion Pack (Takeda Pharmaceutical Company Limited)	Change Change Change		
5	Dec. 21, 2012	63	Minirinmelt OD Tablets 120 μg Minirinmelt OD Tablets 240 μg (Ferring Pharmaceuticals Co., Ltd.)	Change Change	Desmopressin acetate hydrate	Drugs with a new indication and a new dosage for the treatment of central diabetes insipidus.
5	Dec. 25, 2012	64	Toviaz Tablet 4 mg Toviaz Tablet 80 mg (Pfizer Japan Inc.)	Approval Approval	Fesoterodine fumarate	Drugs with a new active ingredient indicated for the treatment of urinary urgency, urinary frequency, and urge urinary incontinence associated with overactive bladder.
5	Dec. 25, 2012	65	Minirinmelt OD Tablets 60 μg (Ferring Pharmaceuticals Co., Ltd.)	Approval	Desmopressin acetate hydrate	A drug with a new indication and a new dosage in an additional dosage form for the treatment of central diabetes insipidus.
5	Mar. 25, 2013	66	Magsent Injection 100 mL Magnesol for Intravenous Injection 20 mL Magsent Injection Syringe 40 mL (Toa Pharmaceuticals Co., Ltd.)	Change Change Change	Magnesium sulfate hydrate/glucose	Drugs with a new additional indication and a new dosage for the prevention and treatment of eclampsia in patients with severe pregnancy-induced hypertension. [Public knowledge-based application after PAFSC's preliminary assessment]
5	Mar. 25, 2013	67	Voluven Solution for Infusion 6% (Fresenius Kabi Japan K.K.)	Approval	Hydroxyethylated starch 130000	A drug with a new active ingredient indicated for maintenance of circulating blood volume.
5	Mar. 25, 2013	68	Neoxy Tape 73.5 mg (Hisamitsu Pharmaceutical Co., Inc.)	Approval	Oxybutynin hydrochloride	A drug with a new route of administration and new indications for the treatment of urinary urgency, urinary frequency, and urge urinary incontinence associated with overactive bladder.

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	May 25, 2012	69	Thaled Capsule 50 Thaled Capsule 100 (Fujimoto Pharmaceutical Corporation)	Change Change	Thalidomide	Drugs with a new additional indication and a new dosage for the treatment of erythema nodosum leprosum. [Orphan drug]
6-1	May 25, 2012	70	Nasonex Nasal 50 µg 56 sprays Nasonex Nasal 50 µg 112 sprays (MSD K.K.)	Change Change	Mometasone furoate hydrate	Drugs with a new additional pediatric dosage for the treatment of allergic rhinitis.
6-1	Jun. 22, 2012	71	Symbicort Turbuhaler 30 doses Symbicort Turbuhaler 60 doses (AstraZeneca K.K.)	Change Change	Budesonide/formoterol fumarate hydrate	Drugs with a new dosage for inhalation as needed in addition to periodic inhalation as a maintenance therapy. These drugs are indicated for the treatment of bronchial asthma (when a combination treatment of an inhaled steroid and a long-acting beta-2 agonist is needed).
6-1	Jun. 29, 2012	72	Kolbet Tablets 25 mg (Toyama Chemical Co., Ltd.) Careram Tablets 25 mg (Eisai Co., Ltd.)	Approval Approval	Iguratimod	Drugs with a new active ingredient indicated for the treatment of rheumatoid arthritis.
6-1	Jun. 29, 2012	73	Oxis 9 µg Turbuhaler 28 doses Oxis 9 µg Turbuhaler 60 doses (AstraZeneca K.K.)	Approval Approval	Formoterol fumarate hydrate	Drugs with a new indication and a new dosage for the alleviation of various symptoms due to airway obstructive impairment in chronic obstructive pulmonary diseases (chronic bronchitis and emphysema).
6-1	Aug. 10, 2012	74	Humira 40 mg for S.C. Injection Syringe 0.8 mL (Abbott Japan Co., Ltd.)	Change	Adalimumab (genetical recombination)	A drug with a new additional indication for the treatment of rheumatoid arthritis (including prevention of structural joint damage).
6-1	Aug. 10, 2012	75	Symbicort Turbuhaler 30 doses Symbicort Turbuhaler 60 doses (AstraZeneca K.K.)	Change Change	Budesonide/formoterol fumarate hydrate	Drugs with a new additional indication and a new dosage for the relief of symptoms of chronic obstructive pulmonary diseases (chronic bronchitis, emphysema).
6-1	Sep. 28, 2012	76	Seebri Inhalation Capsules 50 µg (Novartis Pharma K.K.)	Approval	Glycopyrronium bromide	A drug 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	Nov. 21, 2012	77	MaQaid Intravitreal Injection 40 mg (Wakamoto Pharmaceutical Co., Ltd.)	Change	Triamcinolone acetonide	A drug with a new additional indication and a new dosage for the treatment of diabetic macular edema.
6-1	Dec. 25, 2012	78	Cimzia 200 mg Syringe for S.C. Injection (UCB Japan Co., Ltd.)	Approval	Certolizumab pegol (genetical recombination)	A drug with a new active ingredient indicated for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not sufficiently responded to conventional treatments.
6-1	Dec. 25, 2012	79	Dellegra Combination Tablets (Sanofi K.K.)	Approval	Fexofenadine hydrochloride/ pseudoephedrine hydrochloride	A new combination drug indicated for the treatment of allergic rhinitis.
6-1	Mar. 25, 2013	80	Neoral 10 mg Capsules Neoral Solution 10% Neoral 25 mg Capsules Neoral 50 mg Capsules (Novartis Pharma K.K.)	Change Change Change Change	Ciclosporin	Drugs with a new indication and a new dosage for the treatment of non-Behcet's, non-infectious uveitis (active non-infectious uveitis in the intermediate or posterior area in patients who have not responded sufficiently to conventional treatments and may involve deterioration of visual acuity). [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Mar. 25, 2013	81	Ciclosporin Cap. 10 mg "Mylan" Ciclosporin Cap. 25 mg "Mylan" Ciclosporin Cap. 50 mg "Mylan" Ciclosporin Fine Granules 17% "Mylan" (Mylan Seiyaku Ltd.)	Change Change Change Change	Ciclosporin	Drugs with a new indication and a new dosage for the treatment of non-Behcet's, non-infectious uveitis (active non-infectious uveitis in the intermediate or posterior area in patients who have not responded sufficiently to conventional treatments and may involve deterioration of visual acuity). [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Mar. 25, 2013	82	Xeljanz Tablets 5 mg (Pfizer Japan Inc.)	Approval	Tofacitinib citrate	A drug with a new active ingredient for the treatment of rheumatoid arthritis in patients who have not sufficiently responded to conventional treatments.
6-1	Mar. 25, 2013	83	Actemra 162 mg Syringe for SC Injection Actemra 162 mg Auto-injector for SC Injection (Chugai Pharmaceutical Co., Ltd.)	Approval Approval	Tocilizumab (genetical recombination)	Drugs with a new route of administration indicated for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not sufficiently responded to conventional treatments.
6-2	Jun. 22, 2012	84	NovoRapid 100 U/ml (Novo Nordisk Pharma Ltd.)	Change	Insulin aspart (genetical recombination)	A drug with a new route of administration and a new dosage. This drug is indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	Jun. 29, 2012	85	Tenelia Tablets 20 mg (Mitsubishi Tanabe Pharma Corporation)	Approval	Teneligliptin hydrobromide hydrate	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Jun. 29, 2012	86	Somatuline Subcutaneous Injection 60 mg Somatuline Subcutaneous Injection 90 mg Somatuline Subcutaneous Injection 120 mg (Teijin Pharma Limited)	Approval Approval Approval	Lanreotide acetate	Drugs with a new active ingredient for the improvement of hypersecretion of growth hormone and IGF-I (somatomedin-C) and related symptoms in acromegaly and pituitary gigantism (when surgical therapies are not sufficiently effective or are difficult to perform).
6-2	Aug. 24, 2012	87	Growject BC for Injection 8 mg Growject for Injection 8 mg Growject for Injection 1.33 mg (JCR Pharmaceuticals Co., Ltd.)	Change Change Change	Somatropin (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of SGA (small-for-gestational age) dwarfism not associated with epiphyseal closure.
6-2	Sep. 28, 2012	88	Suiny Tab. 100 mg (Sanwa Kagaku Kenkyusho Co., Ltd.) Beskoa Tab. 100 mg (Kowa Pharmaceutical Co. Ltd.)	Approval Approval	Anagliptin	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Sep. 28, 2012	89	Tresiba Flex Touch Tresiba Penfill (Novo Nordisk Pharma Ltd.)	Approval Approval	Insulin degludec (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
6-2	Sep. 28, 2012	90	Buphenyl Tablet 500 mg Buphenyl Granule 94% (CMIC Holdings, Co., Ltd.)	Approval Approval	Sodium phenylbutyrate	Drugs with a new active ingredient indicated for the treatment of urea cycle disorder. [Orphan drug]
6-2	Dec. 25, 2012	91	L-Cartin FF Oral Solution 10% L-Cartin FF Injection 1000 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval	Levocarnitine	Drugs with a new active ingredient indicated for the treatment of carnitine deficiency.
6-2	Dec. 25, 2012	92	Ryzodeg Combination Injection FlexTouch Ryzodeg Combination Injection Penfill (Novo Nordisk Pharma Ltd.)	Approval Approval	Insulin degludec (genetical recombination)/insulin aspart (genetical recombination)	New combination drugs indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
6-2	Dec. 25, 2012	93	Actonel Tablets 75 mg (Ajinomoto Pharmaceutical Co., Ltd.) Benet Tablets 75 mg (Takeda Pharmaceutical Company Limited)	Approval Approval	Sodium risedronate hydrate	Drugs with a new dosage in a new additional dosage form. These drugs are indicated for the treatment of osteoporosis.
6-2	Feb. 28, 2013	94	Equa Tablets 50 mg (Novartis Pharma K.K.)	Change	Vildagliptin	A drug with a new indication for the treatment of type 2 diabetes mellitus.
6-2	Feb. 28, 2013	95	Surepost Tablets 0.25 mg Surepost Tablets 0.5 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change	Repaglinide	Drugs with a new indication for the improvement of postprandial changes of blood glucose in type 2 diabetes mellitus.
6-2	Feb. 28, 2013	96	Denotas Chewable Combination Tablets (Nitto Pharmaceutical Industries, Ltd.)	Approval	Precipitated calcium carbonate/cholecalciferol/ magnesium carbonate	A combination prescription drug with a similar formulation indicated for the treatment and prevention of hypocalcemia in association with administration of RANKL inhibitors (e.g. denosumab [genetical recombination]) [Expedited review]
6-2	Mar. 25, 2013	97	Trazenta Tablets 5 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Change	Linagliptin	A drug with a new indication for the treatment of type 2 diabetes mellitus.
6-2	Mar. 25, 2013	98	Pralia Subcutaneous Injection 60 mg Syringe (Daiichi Sankyo Company, Limited)	Approval	Denosumab (genetical recombination)	A drug with a new indication and a new dosage for the treatment of osteoporosis.
6-2	Mar. 25, 2013	99	Onglyza Tablets 2.5 mg Onglyza Tablets 5 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval	Saxagliptin hydrate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Mar. 25, 2013	100	Metreleptin for Subcutaneous Injection 11.25 mg "Shionogi" (Shionogi & Co., Ltd.)	Approval	Metreleptin (genetical recombination)	A drug with a new active ingredient for the treatment of lipodystrophy. [Orphan drug]
In vivo diagnostics	May 25, 2012	101	Thyrogen for Intramuscular Injection 0.9 mg (Sato Pharmaceutical Co., Ltd.)	Change	Thyrotropin human alfa (genetical recombination)	A drug with a new additional indication for adjunctive treatment for radioiodine ablation of thyroid tissue remnants in patients who have undergone a near-total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of distant metastatic thyroid cancer. [Orphan drug]
In vivo diagnostics	Aug. 10, 2012	102	Sonazoid for Injection 16 μL (Daiichi Sankyo Company, Limited)	Change	Perflubutane	A drug with a new additional indication as a contrast agent for breast mass lesion in ultrasonography.
In vivo diagnostics	Mar. 25, 2013	103	Alabel Oral 1.5 g (Nobelpharma Co., Ltd.) Alaglio Internal Medicine 1.5 g (SBI Pharmaceuticals Co., Ltd.)	Approval Approval	Aminolevulinic acid hydrochloride	Drugs with a new active ingredient indicated for the visualization of tumor tissues during tumorectomy for malignant glioma. [Orphan drug]
Oncology drugs	Jun. 29, 2012	104	Gonax 80 mg for Subcutaneous Injection Gonax 120 mg for Subcutaneous Injection (Astellas Pharma Inc.)	Approval Approval	Degarelix acetate	Drugs with a new active ingredient indicated for the treatment of prostate cancer.
Oncology drugs	Jun. 29, 2012	105	Inlyta Tablets 1 mg Inlyta Tablets 5 mg (Pfizer Japan Inc.)	Approval Approval	Axitinib	Drugs with a new active ingredient indicated for the treatment of unresectable or metastatic renal cell carcinoma.
Oncology drugs	Aug. 10, 2012	106	Sutent Capsule 12.5 mg (Pfizer Japan Inc.)	Change	Sunitinib malate	A drug with a new additional indication and a new dosage for pancreatic neuroendocrine tumour. [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	Sep. 28, 2012	107	Gliadel for Intracerebral Implant 7.7 mg (Nobelpharma Co., Ltd.)	Approval	Carmustine	A drug with a new active ingredient indicated for the treatment of malignant glioma. [Orphan drug]
Oncology drugs	Sep. 28, 2012	108	Votrient Tablets 200 mg (GlaxoSmithKline K.K.)	Approval	Pazopanib hydrochloride	A drug with a new active ingredient indicated for the treatment of soft tissue sarcoma. [Orphan drug]
Oncology drugs	Nov. 21, 2012	109	Afinitor Tablets 5 mg Afinitor Tablets 2.5 mg (Novartis Pharma K.K.)	Change Change	Everolimus	Drugs with new additional indications and a new dosage for the treatment of renal angiomyolipoma associated with tuberous sclerosis complex and subependymal giant cell astrocytoma associated with tuberous sclerosis complex. [Orphan drug]
Oncology drugs	Dec. 21, 2012	110	Erbitux Injection 100 mg (Merck Serono Co., Ltd.)	Change	Cetuximab (genetical recombination)	A drug with a new additional indication for the treatment of head and neck cancer. [Priority review]
Oncology drugs	Dec. 21, 2012	111	Velcade Injection 3 mg (Janssen Pharmaceutical K.K.)	Change	Bortezomib	A drug with a new route of administration indicated for the treatment of multiple myeloma.
Oncology drugs	Dec. 25, 2012	112	Afinitor Dispersible Tablet 2 mg Afinitor Dispersible Tablet 3 mg (Novartis Pharma K.K.)	Approval Approval	Everolimus	Drugs with a new additional indication and a new dosage in an additional dosage form for the treatment of subependymal giant cell astrocytoma associated with tuberous sclerosis complex (currently in the reexamination period). [Orphan drug]
Oncology drugs	Feb. 21, 2013	113	Abraxane I.V. Infusion 100 mg (Taiho Pharmaceutical Co., Ltd.)	Change	Paclitaxel	A drug with new additional indications and a new dosage for the treatment of gastric cancer and non-small cell lung cancer.
Oncology drugs	Feb. 21, 2013	114	Gemzar Injection 200 mg Gemzar Injection 1 g (Eli Lilly Japan K.K.) Gemcitabine for I.V. infusion 200 mg "Yakult" Gemcitabine for I.V. infusion 1 g "Yakult" (Takata Seiyaku Co., Ltd.) Gemcitabine for i.v. infusion 200 mg "Sawai" Gemcitabine for i.v. infusion 1 g "Sawai" (Sawai Pharmaceutical Co., Ltd.) Gemcitabine for I.V. Infusion 200 mg "NK" Gemcitabine for I.V. Infusion 1 g "NK" (Nippon Kayaku Co., Ltd.) Gemcitabine for I.V. Infusion 200 mg "Hospira" Gemcitabine for I.V. Infusion 1 g "Hospira" (Hospira Japan Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change	Gemcitabine hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of relapsed or refractory malignant lymphoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 21, 2013	115	Taxol Injection 30 mg Taxol Injection 100 mg (Bristol-Myers K.K.) Paclitaxel Inj. 30 mg/5 mL "NK" Paclitaxel Inj. 100 mg/16.7 mL "NK" (Nippon Kayaku Co., Ltd.) Paclitaxel Injection 30 mg "Sawai" Paclitaxel Injection 100 mg "Sawai" Paclitaxel Injection 150 mg "Sawai" (Sawai Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change	Paclitaxel	Drugs with new additional indications and a new dosage for the treatment of relapsed or refractory germ cell tumors (testicular tumors, ovarian tumors, extragonadal tumors). [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 21, 2013	116	Leunase Injection 5000 Leunase Injection 10000 (Kyowa Hakko Kirin Co.. Ltd.)	Change Change	L-Asparaginase	Drugs with a new route of administration. These drugs are indicated for acute leukemia (including blast crisis of chronic leukemia) and malignant lymphoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 25, 2013	117	Campto 40 mg for I.V. infusion Campto 100 mg for I.V. infusion (Yakult Honsha Co., Ltd.) Topotecin Intravenous Drip Infusion 40 mg Topotecin Intravenous Drip Infusion 100 mg (Daiichi Sankyo Company, Limited) Irinotecan Hydrochloride Intravenous Drip Infusion 40 mg "Sawai" Irinotecan Hydrochloride Intravenous Drip Infusion 100 mg "Sawai" (Sawai Pharmaceutical Co., Ltd.) Irinotecan Hydrochloride I.V. Infusion 40 mg "Taiho" Irinotecan Hydrochloride I.V. Infusion 100 mg "Taiho" (Taiho Pharmaceutical Co., Ltd.) Irinotecan Hydrochloride I.V. Infusion 40 mg "Hospira" Irinotecan Hydrochloride I.V. Infusion 100 mg "Hospira" (Hospira Japan Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change	Irinotecan hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of pediatric malignant solid tumor. [Public knowledge-based application after PAFSC's preliminary assessment]

Review Category*	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Mar. 25, 2013	118	Endoxan for Injection 100 mg Endoxan for Injection 500 mg (Shionogi & Co., Ltd.)	Change Change	Cyclophosphamide hydrate	Drugs with a new additional indication and a new dosage for the treatment of pheochromocytoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 25, 2013	119	Dacarbazine Injection 100 (Kyowa Hakko Kirin Co., Ltd.)	Change	Dacarbazine	A drug with a new additional indication and a new dosage for the treatment of pheochromocytoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 25, 2013	120	Oncovin for Inj. 1 mg (Nippon Kayaku Co., Ltd.)	Change	Vincristine sulfate	A drug with a new additional indication and a new dosage for the treatment of pheochromocytoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 25, 2013	121	Hydrea Capsules 500 mg (Bristol-Myers K.K.)	Change	Hydroxycarbamide	A drug with new additional indications for the treatment of essential thrombocythemia and polycythemia vera. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 25, 2013	122	Arzerra for I.V. infusion 100 mg Arzerra for I.V. infusion 1000 mg (GlaxoSmithKline K.K.)	Approval Approval	Ofatumumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory CD20-positive chronic lymphocytic leukemia. [Orphan drug]
Oncology drugs	Mar. 25, 2013	123	Evoltra Intravenous Drip Infusion 20 mg (Genzyme Japan K.K.)	Approval	Clofarabine	A drug with a new active ingredient for the treatment of recurrent or refractory acute lymphoblastic leukemia. [Orphan drug]
Oncology drugs	Mar. 25, 2013	124	Stivarga tablets 40 mg (Bayer Yakuhin, Ltd.)	Approval	Regorafenib hydrate	A drug with a new active ingredient indicated for the treatment of unresectable advanced or recurrent colorectal cancer. [Priority review]
AIDS drugs	May 18, 2012	125	Edurant Tablets 25 mg (Janssen Pharmaceutical K.K.)	Approval	Rilpivirine hydrochloride	A drug with a new active ingredient indicated for the treatment of HIV-1 infection. [Orphan drug]
AIDS drugs	Mar. 25, 2013	126	Stribild Combination Tab. (Japan Tobacco Inc.)	Approval	Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate	A new combination drug with a new active ingredient indicated for the treatment of HIV-1 infection. [Orphan drug]
Biologicals	Apr. 27, 2012	127	Imovax Polio Subcutaneous Injection (Sanofi Pasteur)	Approval	Inactivated poliomyelitis vaccine (Salk vaccine)	A drug with a new active ingredient indicated for the prevention of acute poliomyelitis. [Expedited review]
Biologicals	Jul. 27, 2012	128	Tetrabik Subcutaneous Injection Syringe (The Research Foundation for Microbial Diseases of Osaka University)	Approval	Adsorbed diphtheria-purified pertussis-tetanus-inactivated polio (Sabin strain) combined vaccine	A drug with a new active ingredient indicated for the prevention of pertussis, diphtheria, tetanus, and acute poliomyelitis.
Biologicals	Jul. 27, 2012	129	Quattrovac Subcutaneous Injection Syringe (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Adsorbed diphtheria-purified pertussis-tetanus-inactivated polio (Sabin strain) combined vaccine	A drug with a new active ingredient indicated for the prevention of pertussis, diphtheria, tetanus, and acute poliomyelitis.
Vaccines	Mar. 15, 2013	130	Aimmugen (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change	Freeze-dried inactivated tissue culture hepatitis A vaccine	A drug with a new pediatric dosage. The drug is indicated for the prevention of hepatitis A.
Vaccines	Mar. 26, 2013	131	Adsorbed Influenza Vaccine (H5N1) "Seiken" 1 mL (Denka Seiken Co., Ltd.)	Approval	Adsorbed influenza vaccine (H5N1)	A drug with a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
Blood products	Mar. 25, 2013	132	Normosang Infusion 250 mg (CMIC Holdings Co., Ltd.)	Approval	Hemin	A drug with a new active ingredient indicated for the improvement of symptoms of acute attack in patients with acute porphyria. [Orphan drug]
Bio-CMC	Nov. 21, 2012	133	Filgrastim BS Injection 75 μg Syringe "Mochida" Filgrastim BS Injection 150 μg Syringe "Mochida" Filgrastim BS Injection 300 μg Syringe "Mochida" (Mochida Pharmaceutical Co., Ltd.) Filgrastim BS Injection 75 μg Syringe "F" Filgrastim BS Injection 150 μg Syringe "F" Filgrastim BS Injection 300 μg Syringe "F" (Fuji Pharma Co., Ltd.)	Approval Approval Approval Approval Approval Approval	Filgrastim (genetical recombination)	Follow-on biologics indicated for mobilization of hematopoietic stem cells to peripheral blood, promotion of increases in neutrophil count at the time of hematopoietic stem cell transplantation, and the treatment of neutropenia caused by cancer chemotherapy, neutropenia which affects the treatment of human immunodeficiency virus (HIV) infection, neutropenia associated with myelodysplastic syndrome, neutropenia associated with aplastic anemia, and congenital/idiopathic neutropenia.
Bio-CMC	Feb. 28, 2013	134	Filgrastim BS Inj. 75 μg Syringe "NK" Filgrastim BS Inj. 150 μg Syringe "NK" Filgrastim BS Inj. 300 μg Syringe "NK" (Nippon Kayaku Co., Ltd.) Filgrastim BS Injection 75 μg Syringe "Teva" Filgrastim BS Injection 150 μg Syringe "Teva" Filgrastim BS Injection 300 μg Syringe "Teva" (Teva Pharma Japan Inc.)	Approval Approval Approval Approval Approval Approval	Filgrastim (genetical recombination) [filgrastim biosimilar 2]	Follow-on biologics indicated for mobilization of hematopoietic stem cells to peripheral blood, promotion of increases in neutrophil count at the time of hematopoietic stem cell transplantation, and the treatment of neutropenia caused by cancer chemotherapy, neutropenia which affects the treatment of human immunodeficiency virus (HIV) infection, neutropenia associated with myelodysplastic syndrome, neutropenia associated with aplastic anemia, and congenital/idiopathic neutropenia.

Table 2. Products Approved in FY 2012: New Medical Devices

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-1	Apr. 6, 2012 Total review time: 282 days Regulatory review time: 244 days	Nov. 1, 2011 Foreign clinical study results	1	XIENCE PRIME Drug-eluting Coronary Stent System (Abbott Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting stent coated with everolimus to inhibit the neointimal proliferation and a delivery catheter. The improvements from the company's predicate device are the different strut and the new stent lengths, 33 mm and 38 mm. Clinical studies were conducted to evaluate the efficacy and safety of this product in patients with symptomatic ischemic heart disease. (The original product is in a reexamination period)
3-1	Jul. 9, 2012 Total review time: 69 days Regulatory review time: 45 days	- No clinical study results	2	Nobori (Terumo Corporation)	Change	Instrument & apparatus 7 Coronary stent	A coronary stent used for treatment of patients with symptomatic ischemic heart diseases who have a new coronary lesion (a lesion length of 30 mm or less) with a reference vessel diameter of 2.5-3.5 mm. An application for a partial change to alter the test specifications for the drug (biolimus). (A partial change during the reexamination period)
3-1	Jul. 27, 2012 Total review time: 854 days Regulatory review time: 327 days	Oct. 15, 2009 Foreign clinical study results	3	MOMA Ultra (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	A device to prevent distal emboli, which is used for capture and removal of obstructing materials such as thrombi during percutaneous carotid artery stenting with dilatation of 2 balloons to occlude the common carotid artery and external carotid artery. Clinical studies were conducted by using the pre-improvement product to confirm the efficacy and safety of this product for patients at a high surgical risk of complications of carotid artery endarterectomy.
3-1	Sep. 6, 2012 Total review time: 385 days Regulatory review time: 291 days	Jun. 1, 2012 Global clinical trial and domestic clinical study results	4	Promus Element Plus Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting stent coated with everolimus to inhibit the neointimal proliferation and a delivery catheter. The stent with a diameter of 2.25 mm included in this product is the first coronary stent in Japan which is used for elective cases in patients with symptomatic ischemic heart diseases due to de novo lesions in native coronary arteries with a reference vessel diameter of 2.25-2.50 mm. Clinical studies were conducted to confirm the efficacy and safety of this product for small vascular lesions.
3-1	Nov. 29, 2012 Total review time: 49 days Regulatory review time: 47 days	- No clinical study results	5	MOMA Ultra (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	A device to prevent distal emboli, which is used for capture and removal of obstructing materials such as thrombi during percutaneous carotid artery stenting with dilatation of 2 balloons to occlude the common carotid artery and external carotid artery. An application for a partial change to change the specifications, etc. of endotoxin test. (A partial change during the reexamination period)
3-1	Dec. 5, 2012 Total review time: 433 days Regulatory review time: 195 days	- Domestic clinical study results	6	Misago (Terumo Corporation)	Approval	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nickel-titanium alloy stent used for bail-out treatment (for acute or impending occlusion caused by failure in percutaneous angioplasty) and a delivery system to deliver the stent to the site of the lesion, for the treatment of symptomatic arterial diseases in the superficial femoral artery region. A clinical study was conducted to evaluate the efficacy and safety in bail-out treatment for stenosis or occlusion of the superficial femoral artery. (The original product is in a reexamination period)
3-1	Mar. 7, 2013 Total review time: 463 days Regulatory review time: 390 days	Nov. 1, 2011 Domestic clinical study results	7	XIENCE PRIME SV Drug-eluting Coronary Stent System (Abbott Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting stent coated with everolimus to inhibit the neointimal proliferation and a delivery catheter. This product is used for elective cases in patients with symptomatic ischemic heart diseases due to *de novo* lesions in native coronary arteries with a reference vessel diameter of 2.25-2.50 mm. Clinical studies were conducted to evaluate the efficacy and safety of this product for small vascular lesions. (The original product is in a reexamination period)
3-2	Sep. 28, 2012 Total review time: 470 days Regulatory review time: 109 days	May. 27, 2010 Domestic clinical study results	8	Neuroform Stent (Stryker Japan K.K.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	An intracranial artery stent (for treatment of cerebral aneurysm) used to prevent coil migration in coil embolization for wide-necked cerebral aneurysm. "Codman Enterprise VRD (Approval No. 22200BZX00078000)", an already-approved similar medical device, has a stent with a closed cell structure, but this product is characterized by a stent with an open cell structure. Clinical studies were conducted to evaluate the efficacy and safety of this product for patients with wide-necked cerebral aneurysm. (The original product is in a reexamination period)

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	Sep. 28, 2012 Total review time: 458 days Regulatory review time: 317 days	Sep. 9, 2003 Domestic clinical study results	9	AMPLATZER Vascular Plug (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthetic material to promote vascular embolization which is used to occlude blood vessels and reduce, block, or alter blood flow by inserting and placing it transdermally in arteries/veins, except blood vessels in the heart and the skull. Clinical studies were conducted to confirm the efficacy and safety of this product for occlusion of vascular lesions, alteration of blood flow, and hemostasis for hemorrhagic lesions.
3-2	Nov. 21, 2012 Total review time: 100 days Regulatory review time: 38 days	- No clinical study results	10	Penumbra System (Medico's Hirata Inc.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A catheter for removal of emboli in the central circulation system to be used to restore the blood flow by aspirating thrombi in patients in acute phase of cerebral infarction who fail intravenous infusion of a tissue plasminogen activator (t-PA). An application for a partial change to prolong the expiration period. (A partial change during the reexamination period)
3-2	Dec. 27, 2012 Total review time: 505 days Regulatory review time: 348 days	- Domestic clinical study results	11	Kawasumi Najuta Thoracic Stent Graft System (Kawasumi Laboratories, Incorporated)	Approval	Instrument & apparatus 7 Aortic stent graft	This product consists of a stent graft and delivery system used for endovascular treatment of thoracic aortic aneurysm. For the product, 64 kinds of stent skeletons are set up as basic shapes by making differences in stent length, curvature, and torsion angle in order for it to fit the site and shape of the aorta where the product is placed. A straight-type or a tapered-type graft is sutured and fixed in accordance with the diastolic diameter of this stent skeleton, and fenestration is present or absent in a graft; and therefore there are 952 patterns of stent grafts depending on the combination. A clinical study was conducted to evaluate the efficacy and safety in the treatment of thoracic aortic aneurysm.
3-2	Mar. 22, 2013 Total review time: 493 days Regulatory review time: 199 days	- Clinical evaluation report	12	Serescue (Astellas Pharma Inc.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A porous gelatin sponge plate was developed as a vascular embolization material. Users cut this plate to an appropriate size using the sterilized medical knife, medical scissors, etc. with consideration of the vascular diameter of the site to be applied, suspend it with an appropriate amount of a contrast medium, and deliver it to the site in the blood vessel via a catheter to block the blood flow or to support forming an embolus. In this way, the hemostatic effect is expected for bleeding to which direct pressure cannot be applied from the body surface. A clinical evaluation report summarizing the results of literature searches on the efficacy and safety of transcatheter hemostasis using a gelatin sponge equivalent to this product was submitted.
3-2	Mar. 29, 2013 Total review time: 499 days Regulatory review time: 194 days	Jun. 18, 2007 Domestic clinical study results	13	AMPLATZER Vascular Plug II (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthetic material for embolization in vessels consisted of a self-expandable plug with a nitinol mesh wire of a cylindrical form, a push wire to send the plug to a target site, and a loader that stores the plug in the expanded state. It blocks a blood vessel by being percutaneously inserted and placed in the arteries and veins except blood vessels in the heart and the skull, and reduces, blocks or alters the blood flow. A major difference from the approved "AMPLATZER Vascular Plug" (Approval No. 22400BZX00361000) is a change in the plug shape from a simple cylindrical shape to a shape composed of three cylindrical blocks. The change intends to shorten the time for vascular occlusion by creating many barriers against the blood flow and adding size variations. Results from Japanese clinical studies using the approved product were submitted to evaluate the efficacy and safety of this product in patients with occlusion of vascular lesions, patients indicated for alternation of blood flow, and patients indicated for hemostasis of hemorrhagic lesions. (The original product is in a reexamination period)
3-2	Jan. 28, 2013 Total review time: 374 days Regulatory review time: 247 days	- Domestic clinical study results	14	Bronchial Blocker EWS (Harada Corporation)	Approval	Instrument & apparatus 7 Bronchial blocker	A silicone resin bronchial blocker that is used to fill the bronchi and close fistula in patients who have refractory and inoperable, secondary pneumothorax, prolonged airleak following pneumectomy or other fistula. Clinical studies were conducted to evaluate the efficacy and safety of this product for the target diseases. [Orphan device]
4	May. 31, 2012 Total review time: 168 days Regulatory review time: 85 days	Dec. 19, 2008 (Approval of application corresponding to the present partial change) No clinical study results	15	Vagus Nerve Stimulation Device VNS System (Nihon Kohden Corporation)	Change	Instrument & apparatus 12 Vagus nerve stimulation device with anti-seizure effects	An electrical stimulation device to stimulate vagus nerve as an adjuvant therapy to reduce the frequency of seizures for patients with drug-resistant epilepsy who have refractory epileptic seizures. An application for a partial change to add a lead which is intended to improve fatigue durability. (A partial change during the reexamination period)

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	Jun. 25, 2012 Total review time: 1666 days Regulatory review time: 446 days	Aug. 1, 2003 Foreign clinical study results	16	Thermogard System (ZOLL Circulation, Inc.)	Approval	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheter balloon in which a perfusion fluid (physiological saline) circulates in patients who need body temperature management. The product consists of a main device to deliver the perfusion fluid whose temperature is adjusted in the thermostatic chamber of the product and a central venous catheter with a perfusion-type balloon. Clinical studies were conducted to evaluate the performance and adverse events of this product when used in the human body.
4	Sep. 7, 2012 Total review time: 263 days Regulatory review time: 161 days	- No clinical study results	17	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device used to improve circulation until heart transplantation in patients with severe heart failure for whom heart transplantation is indicated. This application for a partial change was filed to alter the alarm and to add a small, light controller, etc. (A partial change during the reexamination period) [Orphan device]
4	Nov. 7, 2012 Total review time: 57 days Regulatory review time: 40 days	- No clinical study results	18	DuraHeart Left Ventricular Assist System (Terumo Corporation)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device system to be used to improve the blood circulation until heart transplant is performed in patients who have severe cardiac failure for which heart transplant is indicated, show continuous decompensation in spite of drug therapy or circulation assist techniques, such as the use of an external ventricular assist system, and for whom it is considered difficult to survive without heart transplant. An application for a partial change in order that the power connector will not easily come off, in accordance with the Instruction 1 given at the time of approval; "Continuously examine measures for reducing power disruption risk, and consider revising the specifications of the product." (A partial change during the reexamination period) [Orphan device]
4	Nov. 29, 2012 Total review time: 513 days Regulatory review time: 131 days	Apr. 21, 2008 Domestic and foreign clinical study results	19	Implantable ventricular assist device HeartMate II (Thoratec Corporation)	Approval	Instrument & apparatus 7 Implantable ventricular assist device	The first axial-flow implantable ventricular assist device system in Japan to be used to improve the blood circulation until heart transplant is performed in patients who have severe cardiac failure for which heart transplant is indicated, show continuous decompensation in spite of drug therapy or circulation assist techniques, such as the use of an external ventricular assist system, and for whom it is considered difficult to survive without heart transplant. A clinical study was conducted in the US to evaluate the efficacy and safety of this product, and a domestic clinical study was conducted to evaluate the efficacy and safety in Japan where healthcare environments are different from those in the US.
4	Nov. 29, 2012 Total review time: 139 days Regulatory review time: 91 days	- Foreign clinical study results	20	CapSure Sense MRI Lead (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead used by connecting them to an implantable cardiac pacemaker. The patients implanted the device can conditionally undergo an MRI scan. Efficacy and safety evaluations of this product were performed based on the results of overseas clinical studies of the original product "CapSure FIX MRI Lead (approval No.: 22400BZX00132000)." (The original product is in a reexamination period)
4	Nov. 29, 2012 Total review time: 139 days Regulatory review time: 99 days	- No clinical study results	21	Medtronic Advisa MRI (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker to be used by connecting it to electrodes placed within the heart. An application for a partial change to add the pacemaker lead "CapSure Sense MRI Lead." which is newly available for connection, as a compatible medical device. (A partial change during the reexamination period)
4	Dec. 26, 2012 Total review time: 159 days Regulatory review time: 49 days	Aug. 23, 2007 No clinical study results	22	Thermogard System (ZOLL Circulation, Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheter balloon in which a perfusion fluid (physiological saline) circulates in patients who need fever control. An application for partial changes including modification of the compressor in the main device and partial deletion of options for flow rate settings. (A partial change during the reexamination period)

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	Mar. 22, 2013 Total review time: 451 days Regulatory review time: 295 days	Jan. 4, 2008 Domestic clinical study results	23	NaviStar RMT ThermoCool (Johnson & Johnson K.K.)	Approval	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 by other ways. This device is manipulated with "Magnetic Navigation System Niobe" (Approval No. 22500BZX00103000). It also has an irrigation system that flows with saline from an irrigation hole at the tip electrode. The clinical study was conducted to evaluate the efficacy and safety of manipulating it by the Magnetic Navigation System Niobe.
4	Mar. 22, 2013 Total review time: 451 days Regulatory review time: 295 days	Jan. 26, 2006 Domestic clinical study results	24	NaviStar RMT (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter for the radiofrequency catheter ablation and for the electrophysiological study; it is used to treat supraventricular tachycardia. This device is manipulated with "Magnetic Navigation System Niobe" (Approval No. 22500BZX00103000). The clinical study was conducted to evaluate the efficacy and safety of manipulating it by the Magnetic Navigation System Niobe.
4	Feb. 19, 2013 Total review time: 419 days Regulatory review time: 163 days	- Clinical evaluation report	25	Evia T Series Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. This device was newly applied as an implantable cardiac pacemaker which is compatible with MRI. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Feb. 19, 2013 Total review time: 419 days Regulatory review time: 163 days	- Clinical evaluation report	26	Evia Series Pro (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker connected with electrodes placed within the heart. The patients implanted with the device can conditionally undergo an MRI scan. This device was newly applied as an implantable cardiac pacemaker which is compatible with MRI. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Feb. 19, 2013 Total review time: 419 days Regulatory review time: 163 days	- Clinical evaluation report	27	Solia S (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. This device was newly applied as a pacemaker lead which is compatible with MRI. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Feb. 19, 2013 Total review time: 419 days Regulatory review time: 163 days	- Clinical evaluation report	28	Solia T (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker leads	An endocardial implantable pacemaker lead connected with an implantable cardiac pacemaker. The patients implanted with the device can conditionally undergo an MRI scan. This device was newly applied as a pacemaker lead which is compatible with MRI. A clinical evaluation report was submitted to evaluate the safety of this device in MRI scans. (The original product is in a reexamination period)
4	Mar. 29, 2013 Total review time: 210 days Regulatory review time: 60 days	Aug. 23, 2007 No clinical study results	29	Thermogard System (ZOLL Circulation Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheter balloon in which a perfusion fluid (physiological saline) circulates in patients who need fever control. An application for partial change to add a catheter introducer kit to components. (A partial change during the reexamination period)
6-2	Jun. 25, 2012 Total review time: 278 days Regulatory review time: 216 days	- (No application filed for pustular psoriasis in US) Domestic clinical study results	30	Adacolumn (JIMRO Co., Ltd.)	Change	Instrument & apparatus 7 Purifier for blood cell removal	A extracorporeal column for improving pathological conditions by adsorption/apheresis of white blood cells, mainly granulocytes in the peripheral blood, and suppressing inflammatory reactions. An application for a partial change to add the improvement of clinical symptoms of pustular psoriasis to the indications. A clinical study was conducted to evaluate the efficacy and safety of this product in patients with moderate or severe pustular psoriasis. [Orphan medical 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
6-2	Jul. 31, 2012 Total review time: 319 days Regulatory review time: 230 days	Feb. 25, 2009 Domestic clinical study results	31	RENASYS Wound Therapy System (Smith & Nephew Wound Management K.K.)	Approval	Medical products 4 Negative pressure wound therapy system	A negative pressure wound therapy system to promote wound healing by maintaining a local negative-pressure environment, protecting wounds, and removing exudative fluid, infectious material, etc. for patients with refractory wounds who have not responded to existing treatments or are considered to not be responding. Clinical studies were conducted to evaluate the efficacy and safety of this product for acute, subacute, and chronic refractory wounds. (The original product is in a reexamination period)
6-2	Sep. 12, 2012 Total review time: 104 days Regulatory review time: 95 days	- No clinical study results	32	KYPHON BKP System (Medtronic Sofamor Danek Co., Ltd.)	Change	Instrument & apparatus 58 Single-use vertebral body restoration device	A treatment system used in percutaneous kyphosis correction in acute painful spinal compression fracture performed for restoration of the height of fractured vertebral body, fixation of the vertebral body, and pain relief. An application for a partial change to add a new size of a component of the single-use vertebral body restoration device and manufacturing sites. (A partial change during the reexamination period)
6-2	Sep. 28, 2012 Total review time: 2080 days Regulatory review time: 436 days	Nov. 17, 2006 Foreign clinical study results	33	Natrelle Breast Implant (Allergan Japan K. K.)	Approval	Medical products 4 Gel-filled artificial breast	A gel-filled breast in which silicone gel is filled in a shell made of silicone elastomer which repairs or forms the shape of a breast after insertion into the application site. It is used for breast reconstruction surgery or augmentation mammaplasty. Clinical studies were conducted to evaluate the efficacy and safety of this product when used for breast reconstruction surgery, augmentation mammaplasty, and revision surgery.
6-2	Sep. 28, 2012 Total review time: 309 days Regulatory review time: 147 days	- No clinical study results	34	V.A.C.ATS Therapy System (KCI K.K.)	Change	Medical products 4 Negative pressure wound therapy system	A negative-pressure wound therapy system to promote wound healing by maintaining the local negative-pressure environment, protect wounds, and remove exudative fluid, infectious material, etc. for patients with refractory wounds who have not responded to existing treatments or are considered to not be responding. An application for partial changes for addition of manufacturing sites and updating of approved matters regarding sizes, raw materials, etc. (A partial change during the reexamination period)
6-2	Oct. 22, 2012 Total review time: 39 days Regulatory review time: 28 days	- No clinical study results	35	KYPHON BKP System (Medtronic Sofamor Danek Co., Ltd.)	Change	Instrument & apparatus 58 Single-use vertebral body restoration device	A treatment system used in percutaneous kyphosis correction in acute painful spinal compression fracture performed for restoration of the height of fractured vertebral body, fixation of the vertebral body, and pain relief. Addition of a manufacturing site. (A partial change during the reexamination period)
6-2	Nov. 12, 2012 Total review time: 60 days Regulatory review time: 28 days	- No clinical study results	36	KYPHON BKP Bone Cement HV-R (Medtronic Sofamor Danek Co., Ltd.)	Change	Medical products 4 Orthopedic bone cement	A therapeutic spinal bone cement used in percutaneous kyphosis correction in acute spinal compression fracture performed for restoration of the height of fractured vertebrae, fixation of the vertebral body, and pain relief. This product is used with KYPHON BKP System. Addition of a manufacturing site. (A partial change during the reexamination period)
6-2	Dec. 18, 2012 Total review time: 280 days Regulatory review time: 102 days	Dec. 7, 2007 No clinical study results	37	VertaPlex Bone Cement (Stryker Japan K.K.)	Change	Medical products 4 Orthopedic bone cement	The product is used in percutaneous vertebroplasty to mitigate pain in patients with malignant spinal tumor such as painful metastatic bone tumor and myeloma who have not responded to conventional therapy. An application for a partial change to change the setting time (hardening time). (A partial change during the reexamination period)
6-2	Mar. 22, 2013 Total review time: 387 days Regulatory review time: 143 days	- Domestic clinical study results	38	Conduit for Nerve Regeneration Nerbridge (Toyobo Co., Ltd.)	Approval	Medical products 4 Collagen-using absorbent nerve regeneration-inducing material	A polyglycolic acid conduit filled with sponge-like collagen which is inserted into defects of the peripheral nerves that have been ruptured or broken because of injuries, etc. in order to induce regeneration of the nerve and reconstruct the function by bridging both ends of nerve. A prospective clinical study was conducted to evaluate the efficacy and safety of this product in patients with peripheral nerve defect on the distal wrist.

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	Oct. 18, 2012 Total review time: 385 days Regulatory review time: 235 days	Feb. 18, 2009 Foreign clinical study results	39	da Vinci SI Surgical System (Intuitive Surgical Inc.)	Approval	Instrument & apparatus 12 Surgical robot, operation unit	A device to assist the surgeon's manipulation of endoscopic surgical devices when endoscopic surgery is performed in areas of general digestive surgery, thoracic surgery (except cardiac surgery), urology, and gynecology. Improvement from the original product "da Vinci Surgical System (approval No.: 22100BZX01049000)" includes downsizing of the surgeon consoles and enabling setting of the position of movement according to the needs of the surgeon. In addition, as a secondary function, two surgeons can manipulate the device, when two surgeon consoles are connected. Results of clinical studies using the original product were submitted to explain the extrapolability to efficacy and safety evaluation of this product. (The original product is in a reexamination period)
8	Mar. 22, 2013 Total review time: 451 days Regulatory review time: 327 days	Jan. 15, 2003 Domestic clinical study results	40	Magnetic Navigation System Niobe (Siemens Japan K.K.)	Approval	Instrument & apparatus 51 Cardiac Mapping System Workstation	A guiding system that navigates "NaviStar RMT ThermoCool" (Approval No. 22500BZX00104000) or "NaviStar RMT" (Approval No. 22500BZX00107000), both of which are exclusive catheters to this system, to a target region in intervention procedures. Clinical studies were conducted to evaluate the efficacy and safety of manipulating these exclusive catheters with this device.
Biologics-2	Jul. 27, 2012 Total review time: 1068 days Regulatory review time: 200 days	- Domestic clinical study results	41	Jacc (Japan Tissue Engineering Co., Ltd.)	Approval	Instrument & apparatus 7 Human autologous cells and tissue	An autologous cultured cartilage to alleviate clinical symptoms by implanting it in the affected site of traumatic cartilage deficiency and osteochondritis dissecans (excluding knee osteoarthritis) in knee joints with a cartilage defective area of 4 cm2 or more for which there are no other treatment options. Chondrocytes isolated from the non-load-bearing site of a knee joint of patients by taking a small amount of cartilage tissue are three-dimensionally cultured in atelocollagen gel to obtain this product. Clinical studies were conducted to evaluate the efficacy and safety of this product for patients with traumatic cartilage deficiency, osteochondritis dissecans, and knee osteoarthritis.
Biologics-2	Sep. 28, 2012 Total review time: 1652 days Regulatory review time: 357 days	Nov. 21, 2003 Foreign clinical study results	42	Contegra Pulmonary Valved Conduit (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Artificial blood vessel with a bovine-derived valve	A conduit with a pulmonary valve made of bovine jugular veins which is used to repair/reconstruct the right ventricular outflow tract leading to the pulmonary arteries from the heart. A clinical study was conducted to evaluate the efficacy and safety of this product in children (aged under 18 years) with abnormality of the right ventricular outflow tract or functional failure of an already-implanted homograft, etc.
Cellular and tissue-based products	Dec. 27, 2012 Total review time: 59 days Regulatory review time: 37 days	- No clinical study results	43	Jacc (Japan Tissue Engineering Co., Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	This autologous cultured cartilage uses atelocollagen as a scaffolding material for culture. It is necessary to perform an allergy test for atelocollagen before applying this product. An application for partial changes, including addition of a syringe for intradermal tests of the atelocollagen as a component of this product, and change in biological ingredients in the raw materials. (A partial change during the reexamination period)
Cellular and tissue-based products	Mar. 29, 2013 Total review time: 205 days Regulatory review time: 102 days	- No clinical study results	44	Jace (Japan Tissue Engineering Co., Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	An autologous-cultured epidermis manufactured with epidermal cells derived from patients with severe burn injury and multiple biological materials. An application for partial changes, including change in the biological raw materials and addition of component(s). (A partial change during the reexamination period)
Specified Partial Change	Apr. 19, 2012 Total review time: 56 days Regulatory review time: 34 days	- No clinical study results	45	Zilver PTX Drug-eluting Peripheral Stent (Cook Japan Inc.)	Change	Instrument & apparatus 7 Drug-eluting femoral artery stent	A nitinol self-expanding stent to be inserted and placed at the site of a lesion to maintain the lumen of a femoropopliteal stenotic site and a delivery system used to deliver the stent to the site of the lesion. An application for a partial change to change the specification of paclitaxel, etc. (A partial change during the reexamination period)
Specified Partial Change	Sep. 28, 2012 Total review time: 73 days Regulatory review time: 51 days	- No clinical study results	46	CryoSeal Disposable Kit (Asahi Kasei Medical Co., Ltd.)	Change	Instrument & apparatus 7 Blood component separation kit	Blood component separation kit to be used to isolate/collect blood components in a sterile state when preparing a biological tissue adhesive from autologous plasma. Patients are to undergo preoperative autologous blood donation. The raw material of spike needles was changed. (A partial change during the reexamination period)

Table 3. Products Approved in FY 2012: 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	May 15, 2012 Total review time: 407 days Regulatory review time: 115 days	- Foreign clinical study results	1	Tecnis 1-Piece VB (AMO Japan K.K.)	Approval	Instrument & apparatus 72 Posterior chamber lens	A monofocal posterior chamber lens to be implanted in the posterior chamber of the eye as a substitute for the crystalline lens to correct the vision of the aphakic eye. As the raw materials, an ultraviolet absorbing agent and a violet light absorbing agent, both of which are new covalent materials, were added to acrylic-methacrylic cross-linked copolymer, a base material of the approved "Tecnis 1-Piece". A clinical study was conducted to evaluate the optical efficacy and safety of the new raw materials.
1	Oct. 30, 2012 Total review time: 246 days Regulatory review time: 140 days	Mar. 30, 2012 Domestic clinical study results	2	Dailies Total 1 (Ciba Vision Corporation)	Approval	Instrument & apparatus 72 Single-use colored contact lenses for correcting visual acuity	Single-use tinted contact lenses for correcting visual acuity. The silicone hydrogel lens is indicated for daily wear. The product has high oxygen transmissibility and uses a new material called Delefilcon A to improve the quality. The raw material has novelty, and a clinical study was conducted to evaluate the efficacy and safety of wearing this product for correction of visual acuity.
1	Dec. 26, 2012 Total review time: 512 days Regulatory review time: 118 days	- Domestic clinical study results	3	Four Seasons (Menicon Co., Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Reusable colored contact lenses for correcting visual acuity. The lens is indicated for daily wear and replaced in three-month intervals. A silicon-containing material which has oxygen transmissibility equivalent to or greater than the approved "Menicon Tinu" (Approval No. 21800BZZ10125000) is used for this product. The combination of major component monomers in the raw material has novelty, and a clinical study was conducted to evaluate the efficacy and safety of wearing this product for correction of visual acuity.
1	Dec. 26, 2012 Total review time: 348 days Regulatory review time: 236 days	- Domestic clinical study results	4	HOYA Vivinex iSert (HOYA Corporation)	Approval	Instrument & apparatus 72 Posterior chamber lenses with an injector	A posterior chamber lens with an injector, for which single focus posterior chamber lens that is inserted into the aphakic eye after cataract surgery is preloaded in an injector. With the haptics and the optics made of the same raw material, it has a casting one-piece structure. A major difference from the approved "HOYA iSert Micro (Approval No. 22200BZX00615000) is a change in the raw material of the posterior chamber lens to reduce the risk of capsule opacification. The raw material has novelty, and a clinical study was conducted to evaluate the optical efficacy and safety of this product in clinical use.
2	Feb. 14, 2013 Total review time: 637 days Regulatory review time: 116 days	Jun. 11, 1997 (Initial approval) Nov. 15, 2004 (Addition of GTR method) Aug. 9, 2005 (Change in manufacturing process) Domestic clinical study results	5	Geistlich Bio-Gide (Geistlich Pharma AG)	Approval	Medical products 4 Absorbent periodontal tissue regeneration material	An absorbent material using collagen derived from porcine membrane (originated in Switzerland) as a raw material. It is used in combination with autologous bone or bone substitute in guided (periodontal) tissue regeneration (GTR) for a defective part of the alveolar bone as a protective membrane against epithelial migration to new bone. A clinical study was conducted to evaluate the efficacy and safety of the combined use of this product with a dental bone substitute.
3-1	May 18, 2012 Total review time: 1569 days Regulatory review time: 374 days	Feb. 16, 2006 Foreign clinical study results	6	Spider Protection Device (At the time of approval, ev3 K.K.; currently (post-approval transfer of approval), Covidien Japan Inc.)	Approval	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	A device to prevent distal emboli, which is used for capture and removal of obstructing materials such as thrombi during percutaneous carotid artery stenting. It is transdermally inserted into blood vessels and temporarily placed in the distal side of a lesion. Clinical studies were conducted to evaluate the efficacy and safety of this product in patients with angiostenosis in the carotid artery with the rate of stenosis of at least 70% (for asymptomatic patients) and at least 50% (for symptomatic patients).
3-1	May 18, 2012 Total review time: 1449 days Regulatory review time: 356 days	Jan. 24, 2007 Foreign clinical study results	7	PROTEGE Carotid Stent Set (At the time of approval, ev3 K.K.; currently [post-approval transfer of approval], Covidien Japan Inc.)	Approval	Instrument & apparatus 7 Stent for the carotid artery	A stent which is used to expand the carotid artery (common carotid artery, internal carotid artery) or maintain the lumen in patients who are at high risk for adverse events by surgical treatment (carotid endarterectomy), and a delivery catheter that transdermally delivers the stent to the site of stenosis in the carotid artery. Clinical studies were conducted to evaluate the efficacy and safety of this product in patients with angiostenosis in the carotid artery with the rate of stenosis of at least 70% (for asymptomatic patients) and at least 50% (for symptomatic patients).

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	May 18, 2012 Total review time: 364 days Regulatory review time: 242 days	Feb. 17, 2012 Domestic and foreign clinical study results	8	Resolute Integrity Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting stent coated with zotarolimus to inhibit the neointimal proliferation and a delivery catheter. The improvemjent from the approved "Endeavor Coronary Stent System" is the prolonged drug-eluting duration as a result of modification of the drug coating base material. A clinical study was conducted to evaluate the efficacy and safety of this product including such improvement in patients with symptomatic ischemic heart disease.
3-1	Jun. 25, 2012 Total review time: 620 days Regulatory review time: 280 days	- Clinical evaluation report	9	Expansor Balloon Catheter (Fuji Systems Corporation)	Approval	Instrument & apparatus 51 Balloon catheter for neuroendoscopy	A balloon catheter which is inserted through a working channel of the endoscopy to expand a puncture hole created by an endoscopic clamp, etc. during surgery for hydrocephalus using neuroendoscopy (ventriculostomy, laparoscopic fenestration of cyst, etc.). Because there is no balloon catheter indicated for this treatment, a clinical evaluation report summarizing the results of literature searches on the efficacy and safety of this treatment using the balloon catheter was submitted.
3-1	Sep. 28, 2012 Total review time: 277 days Regulatory review time: 235 days	- Foreign clinical study results	10	Kaname (Terumo Corporation)	Approval	Instrument & apparatus 7 Coronary stent	A cobalt-chromium alloy coronary stent which is used for the treatment of patients with symptomatic ischemic disease (including the treatment of acute or threatened coronary artery closure as a result of unsuccessful intervention) whose reference vessel diameter is in the range of 3.0 mm to 4.0 mm and who have new or restenosis coronary lesion (length of lesion up to 25 mm). Clinical studies were conducted to confirm the efficacy and safety of this product for the treatment of symptomatic ischemic disease.
3-1	Dec. 27, 2012 Total review time: 302 days Regulatory review time: 77 days	Apr. 13, 2012 Foreign clinical study results	11	Epic Vascular Stent (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Stent for iliac artery	This product consists of a self-expandable stent made of nickel-titanium alloy and its delivery system. The stent is transdermally inserted and placed in a blood vessel to maintain or expand the vascular lumen for the treatment of symptomatic vascular disease in the iliac artery such as stenotic lesion. The stent has a tandem structure, including closed cells at both ends and an open cell at the center in order to reduce a position gap when it is expanded. Clinical studies were conducted to confirm the efficacy and safety of this product for the treatment of symptomatic vascular disease in the iliac artery.
3-2	Jun. 27, 2012 Total review time: 565 days Regulatory review time: 139 days	Mar. 23, 2010 (Approval of application corresponding to the present partial change) Foreign clinical study results	12	Gore TAG Thoracic Endoprosthesis (W.L. Gore & Associates, Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	This product consists of a stent graft and delivery system used for endovascular treatment of thoracic aortic aneurysm. Application for a partial change to add a 45 mm-diameter stent graft, etc. A clinical study was conducted to evaluate the equivalence of the efficacy and safety between the existing stent graft and the added 45 mm-diameter stent graft.
3-2	Sep. 28, 2012 Total review time: 826 days Regulatory review time: 127 days	Mar. 5, 2009 Foreign clinical study results	13	Gore Excluder AAA Endoprosthesis (W.L. Gore & Associates, Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	This product consists of a stent graft and delivery system used for endovascular treatment of abdominal aortic aneurysm. Application for a partial change to add a 31 mm-diameter Trunk-Ipsilateral Leg, 32 mm-diameter Aortic Extender, etc. A clinical study was conducted to evaluate the equivalence of the efficacy and safety between the existing stent graft and the stent graft with the added diameter.
3-2	Nov. 27, 2012 Total review time: 1246 days Regulatory review time: 269 days	Oct. 23, 2007 Foreign clinical study results	14	Mitroflow (Sorin Biomedica Cardio S.r.l.)	Approval	Instrument & apparatus 7 Bovine pericardial valve	A bovine pericardial valve used to replace the aortic valve which has become dysfunctional due to disease, etc. Unlike the existing product, this product has a valve leaflet outside the stent frame. A clinical study was conducted to confirm that the efficacy and safety of this product in target patients are within the assumed range.
3-2	Mar. 29, 2013 Total review time: 407 days Regulatory review time: 237 days	Sep. 21, 2012 Foreign clinical study results	15	Relay Plus Thoracic Stent Graft System (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	This product consists of a stent graft and delivery system used for endovascular treatment of descending thoracic aortic aneurysm. The two covered stent rings at the proximal end of the stent graft are free from a spiral support wire, which allows independent bending at the proximal end. The placement position of the stent graft can be adjusted by keeping a bare stent on the proximal end with a holder at the tip in the delivery system. A clinical study was conducted to evaluate the efficacy and safety of this product for the treatment of descending thoracic aortic aneurysm in comparison with a control group treated with surgical procedures.

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	Apr. 24, 2012 Total review time: 407 days Regulatory review time: 237 days	- Foreign clinical study results	16	Thermocool Smarttouch (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter with the irrigation system used for radiofrequency catheter ablation and electrophysiological study. The contact force-sensing function is loaded at the tip of electrode; it is used to calculate and to display the degree of contact between the tip and the tissue. A clinical study was conducted to evaluate the behavior of contact force level in clinical use.
4	Jul. 26, 2012 Total review time: 848 days Regulatory review time: 314 days	- Clinical evaluation report	17	Linox Smart S DX (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A screw-type electrode lead that is used to conduct atrial sensing, ventricular sensing/pacing, anti-trancycardia pacing treatment and defibrillation with one lead. It consists of 1 defibrillation electrode, 3 ring electrodes and 1 screw electrode. A clinical evaluation report was submitted to evaluate that defibrillation is properly achieved when this product is used in clinical practice.
4	Aug. 24, 2012 Total review time: 534 days Regulatory review time: 344 days	Feb. 7, 2007 Clinical evaluation report	18	Servo Ventilator Series (Fukuda Denshi Co., Ltd.)	Change	Instrument & apparatus 6 Versatile artificial respirator	A versatile artificial ventilator that sends the mixed gas of oxygen and air to the lung through the oral or nasal cavity under the mechanical adjustment. In the application for a partial change, the assisted ventilation mode is added; the mode detects a patient's electrical activity of the diaphragm and drives a pressure support in line with respiratory timing. Furthermore, components needed for the mode are added. A clinical evaluation report of this device was submitted to evaluate that the support in line with respiratory timing is achieved in clinical use.
4	Oct. 30, 2012 Total review time: 193 days Regulatory review time: 141 days	May 28, 2008 Clinical evaluation report	19	NRG RF Transseptal Needle (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 47 Transseptal needle	A transseptal needle with an electrode to be used to create a puncture in interatrial septum in order to insert a catheter, etc. from the right atrium to the left atrium. The atrial septum is punctured by the tissue causarization with high-frequency energy generated from a dedicated high-frequency generator. In contrast to conventional transseptal needles, this device can puncture using high-frequency energy. A clinical evaluation report summarizing the clinical data of literature was submitted to evaluate the efficacy and safety of this product in comparison with conventional transseptal needles.
4	Oct. 30, 2012 Total review time: 181 days Regulatory review time: 99 days	Nov. 21, 2007 Clinical evaluation report	20	Medtronic Reveal XT (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 21 Implantable data recorder for electrocardiogram	An implantable electrocardiogram recorder, subcutaneously implanted to continuously monitor the electrocardiogram. This device detects, records and stores wave patterns of atrial fibrillation, and sends the information recorded in this product to a server through the approved "Medtronic CareLink Monitor" (Approval No. 21900BZX00664000); the functions are the major improvements from the approved device "Medtronic Reveal DX" (Approval No. 22000BZX01025000). A clinical evaluation report was submitted to evaluate that this product can detect atrial fibrillation.
4	Mar. 28, 2013 Total review time: 1554 days Regulatory review time: 577 days	Mar. 3, 2008 Foreign clinical study results	21	Niox Mino (Chest M.I., Inc.)	Approval	Instrument & apparatus 21 Nitric oxide analysis instrument	A measuring instrument used to measure the level of nitric oxide, used as a biomarker of eosinophic inflammation, in the expired air. In a clinical study, the measuring performance for the concentration of nitric oxide is evaluated on equivalence to predicate devices outside Japan, and the changes in the concentration of nitric oxide was compared before and after the treatment of inflammation.
4	Feb. 22, 2013 Total review time: 231 days Regulatory review time: 149 days	- Clinical evaluation report	22	FastView (Terumo Corporation)	Approval	Instrument & apparatus 51 Intravascular optical tomographic catheter	An intravascular optical coherence tomographic (OCT) catheter to conduct OCT of the coronary artery; it is connected to "Lunawave" (Approval No. 22500BZX00058000), an OCT image diagnosis equipment for exclusive use with this catheter. The broadband near-infrared light guided from the exclusive equipment is irradiated toward the circumferential direction from near the tip of the catheter. Then, the reflected from the vessel interferes with the reference light, and the interference signal is generated. This equipment obtains the cross-sectional images of blood vessels by Fourier-transforming the interference signal. A clinical evaluation report was submitted to evaluate the efficacy and safety of this equipment in clinical use.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
5	May 25, 2012 Total review time: 1123 days Regulatory review time: 397 days	Nov. 19, 2002 Foreign clinical study results	23	Monarc Transobturator System (American Medical Systems, Inc.)	Approval	Instrument & apparatus 30 Urinary incontinence treatment tape	This product consists of a mesh to be placed suburethrally and its introducer, both of which are intended to improve stress urinary incontinence in women caused by urethral hypermobility or intrinsic sphincter deficiency of the urethra. While the approved product is placed retropubically, this product is placed in the obturator foramen. A clinical study was conducted to evaluate the objective efficacy (pad weight test, cough stress test, etc.), subjective efficacy (QOL improvement), and safety of this product for stress urinary incontinence.
5	May 31, 2012 Total review time: 330 days Regulatory review time: 86 days	- Domestic clinical study results	24	Nipro Polyether Sulfone Dialyzer (Nipro Corporation)	Approval	Instrument & apparatus 7 Hollow-fiber dialyzer	A hollow-fiber dialyzer intended to remove fluid and uremic substances stored in the body due to uremia. It is indicated for patients whose renal function has markedly reduced due to chronic or acute renal failure, etc. Although this product uses the same membrane material as the approved products, because equivalence to the approved products was not demonstrated with regard to the performance profile, a clinical study was conducted to evaluate its performance profile.
5	Jul. 27, 2012 Total review time: 872 days Regulatory review time: 332 days	- Domestic clinical study results	25	Bipolar RFA System CelonPOWER (Olympus Medical Systems Corporation)	Approval	Instrument & apparatus 29 Radiofrequency ablation system	A device to be used to coagulate a malignant tumor of the liver with radiofrequency current. While the approved product is a monopolar system, this product is a bipolar system with two electrodes for one applicator. It also has a mode to energize up to 6 electrodes (15 pairs) sequentially by simultaneous puncture of up to 3 applicators. A clinical study was conducted to evaluate the necrogenic effect and safety of this product for hepatic malignancy.
5	Sep. 7, 2012 Total review time: 1036 days Regulatory review time: 427 days	Apr. 17, 2002 Clinical evaluation report	26	Cook Postpartum Balloon (Cook Japan Inc.)	Approval	Instrument & apparatus 51 Uterine balloon	A balloon used to relieve or stop uterine bleeding after delivery. There is no product that specializes in such intended use in Japan. Considering the fact that pressure hemostasis using a balloon such as this product is common in and out of Japan, a clinical evaluation report was submitted to evaluate the efficacy and safety of this product.
5	Feb. 19, 2013 Total review time: 358 days Regulatory review time: 80 days	- Domestic clinical study results	27	Double-balloon Endoscopy System (Fujifilm Corporation)	Approval	Instrument & apparatus 25 Balloon-guided small-intestine endoscopy system	A system that inserts an endoscope deep inside of the small intestine by using the technique to fold the intestinal tract with the combination of the endoscope, an over-tube with a balloon, a balloon to be attached to the endoscope and a balloon controller. A clinical study was conducted to verify the capability of this system to reach deep inside of the small intestine with the technique to fold the small intestine and to ensure the safety of the system.
6-1	Jul. 10, 2012 Total review time: 1489 days Regulatory review time: 444 days	Apr. 29, 2009 Clinical evaluation report	28	Biolox Option Head (B. Braun Aesculap Japan Co., Ltd.)	Approval	Medical products 4 Head prosthesis	A stem head made of a zirconia-toughened high-purity aluminum matrix composite (BIOLOX® Delta) and used in combination with the company's approved system and "Ceramic Hip System Delta". The raw material of this system is innovative as an artificial hip prosthesis in Japan. The equivalence of the shape between the approved products and this product was explained, and a clinical evaluation report was submitted to provide clinical evaluation of differences in the raw materials.
6-1	Jul. 10, 2012 Total review time: 1404 days Regulatory review time: 565 days	Nov. 20, 2008 (Delta head) Clinical evaluation report	29	Ceramic Hip System Delta (B. Braun Aesculap Japan Co., Ltd.)	Approval	Medical products 4 Total hip prosthesis	This product consists of a stem head made of a zirconia-toughened high-purity aluminum matrix composite (BIOLOX® Delta) and a liner for shelf operation. It is used in combination with the company's approved system. Although the raw material of this system is innovative as an artificial hip prosthesis in Japan, a clinical evaluation report was submitted to explain the equivalence of the shape between the approved products and this product and the clinical evaluation of differences in the raw materials.

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6-1	Sep. 28, 2012 Total review time: 161 days Regulatory review time: 96 days	Oct. 18, 2007 Clinical evaluation report	30	Restoration ADM (Stryker Japan K.K.)	Approval	Medical products 4 Artificial hip joint, acetabular component	This product consists of an acetabular cup and an acetabular insert used for hip replacement. The inner side of the acetabular insert is located on the femoral stem head, while the external side forms a bearing surface with the acetabular cup. This product was developed to increase the range of motion for the artificial hip prosthesis by the two bearing surfaces (dual-mobility) of the acetabular insert and to enhance the stability of the prosthesis because dislocation of the hip requires severer displacement of the femoral head in the vertical direction. A clinical evaluation report was submitted to evaluate the treatment outcome of the artificial hip prosthesis with the dual-mobility structure.
6-1	Nov. 21, 2012 Total review time: 601 days Regulatory review time: 400 days	Jan. 14, 2011 Clinical evaluation report	31	Active Articulation E1 (Biomet Japan, Inc.)	Approval	Medical products 4 Artificial hip joint, acetabular component	An acetabular liner used for hip replacement. It is used in combination with an acetabular cup and a femoral stem head. It is a dual-mobility system that has bearing surfaces both inside and outside the product. This double-mobility system enables increase of the range of motion and enhances the implant stability. It is made of ultra high molecular weight polyethylene which was given cross-linking treatment to enhance the resistance to abrasion, and was immersed in vitamin E to enhance the resistance to oxygen. A clinical evaluation report was submitted to evaluate the efficacy and safety of the dual-mobility structure.
6-1	Jan. 28, 2013 Total review time: 581 days Regulatory review time: 73 days	- Clinical evaluation report	32	Adler Hip Prosthesis System (Robert Reid Inc.)	Approval	Medical products 4 Total hip prosthesis	This product consists of a press-fit fixed stem, modular neck and head which are used on the femoral side and a cup and liner which are used on the acetabular side to replace the hip function in total hip replacement. Aluminum oxide (alumina) is adopted for the liner and head to improve the resistance to abrasion and toughness of the bearing surface, while the acetabular cup surface has a porous structure by layering technique to improve the synostosis. Since there have been concerns about a risk of breakage caused by a new raw material of alumina, a clinical evaluation report that evaluated the incidence of repeat replacement when this product was used for total hip replacement was submitted.
6-1	Jan. 28, 2013 Total review time: 356 days Regulatory review time: 109 days	- Clinical evaluation report	33	BIOLOX Delta Ceramic Head (Robert Reid Inc.)	Approval	Medical products 4 Head prosthesis	An artificial head prosthesis used to replace the hip function on the femoral side in total hip replacement. The raw material, shape and structure of this product are equivalent to those of the approved product "BIOLOX Delta Ceramic Femoral Head" (Approval No. 22300BZX00018000). A major difference is the acetabular liner, which is used in combination with this product, made of aluminum oxide (alumina). A clinical evaluation report that evaluated the incidence of repeat replacement, incidence of defects, etc. when this product and the alumina-made acetabular liner were used together was submitted.
6-1	Mar. 29, 2013 Total review time: 273 days Regulatory review time: 131 days	Dec. 23, 2010 (inner diameter 28 mm) Apr. 2, 2013 (inner diameter 36 mm) (inner diameter 32 mm: has not been applied in the US) Foreign clinical study results	34	Pinnacle Ceramic Liner (CERAMAX) (Johnson & Johnson K.K.)	Approval	Medical products 4 Artificial hip joint, acetabular component	A liner that costitutes an acetabular component used in total hip replacement. The major improvement is its raw material, an Alumina-Zirconia ceramic matrix composites (BIOLOX delta) that has better intensity than the conventional ceramic material. Used in combination with the company's artificial femoral head made by the same raw material, this product composes a ceramic-on-ceramic system. A clinical study was conducted to evaluate the usability and safety of this product in clinical use.
6-1	Mar. 29, 2013 Total review time: 273 days Regulatory review time: 154 days	Jul. 1, 2003 (excluding some sizes) Apr. 8, 2004 (some sizes) Nov. 30, 2006 (same as above) (36 mm 9/10 taper has not been applied in the US) Foreign clinical study results	35	BIOLOX Delta Ceramic Head (CERAMAX) (Johnson & Johnson K.K.)	Change	Medical products 4 Head prosthesis	An application for partial change to add "Pinnacle Ceramic Liner (CERAMAX)" (Approval No. 22500BZX00165000) as a liner to be combined with this product and add a head component with the bearing surface of 36 mm in diameter. A clinical study was conducted to evaluate the usability and safety of this product in combination with the aforementioned liner.

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	Jun. 26, 2012 Total review time: 358 days Regulatory review time: 167 days	- Domestic clinical study results	36	Refit (Hoya Corporation)	Approval	Medical products 4 Artificial bone using collagen	An artificial bone implant made of sponge-like low-crystalline calcium phosphate and swine collagen. It is intended to enhance the porosity and improve the elasticity and bioabsorption. Since this product is a new raw material, a clinical study was conducted to confirm the effect of this product to promote bone regeneration for bone defects is equivalent to or greater than the existing products.
6-2	Jul. 3, 2012 Total review time: 627 days Regulatory review time: 242 days	Mar. 31, 2000 Domestic clinical study results	37	Versajet S (Smith & Nephew Wound Management K.K.)	Approval	Instrument & apparatus 12 Hydraulic knife	A device to be used for wound debridement (acute wound, chronic wound and thermal burn), soft tissue debridement and cleaning of surgical wound site. With the high-pressure water flow and its Venturi effect, it enables debridement and cleaning of surgical wound site. While it has the same mechanism of tissue ablation as the approved product, a major difference is that this product was developed as a device for debridement. A clinical study was conducted to evaluate the efficacy and safety of this product in wound debridement.
6-2	Sep. 19, 2012 Total review time: 1267 days Regulatory review time: 775 days	- Clinical evaluation report	38	CARP-H System (Nakashima Medical Co., Ltd.)	Approval	Medical products 4 Artificial hip joint, femoral component	A femoral component of artificial hip prosthesis used for reconstruction of joint function in patients with femur head necrosis and coxarthrosis. While the shape and structure of this product are the same as those of the approved product, this product uses different raw materials for the compression bolt and cortical crew. A clinical evaluation report was submitted to confirm the efficacy and safety of hip replacement and bipolar hip arthroplasty using this product.
6-2	Sep. 28, 2012 Total review time: 1642 days Regulatory review time: 87 days	Jul. 23, 1986 Clinical evaluation report	39	Natrelle 133 Tissue Expander (Allergan Japan K.K.)	Approval	Medical products 4 Skin tissue expander	A device to be temporary implanted under the breast subcutaneous tissue or the pectoralis major muscle to facilitate placement of artificial breast in which purpose is to expand/extend the skin and tissues surrounding the breast prior to breast reconstruction surgery. A clinical evaluation report was submitted to confirm that the insertion of a round-type breast implant is possible after skin/tissue expansion using this product in breast reconstruction surgery.
6-2	Dec. 5, 2012 Total review time: 344 days Regulatory review time: 138 days	Aug. 7, 2009 Foreign clinical study results	40	SNaP Negative Pressure Wound Therapy System (Century Medical, Inc.)	Approval	Medical products 4 Single-use negative pressure wound therapy system	A negative pressure wound therapy system to promote wound healing by adding the controlled negative-pressure, protecting wounds, promoting granulation of the wound, and removing exudative fluid and infectious waste materials for patients with refractory wounds who have not responded to existing treatments or are considered not to be responding. This product is a portable device for single use and can be used for outpatients. Thus, a clinical study was conducted to evaluate the efficacy and safety of this product in outpatients.
6-2	Dec. 20, 2012 Total review time: 869 days Regulatory review time: 307 days	Jun. 6, 2005 Clinical evaluation report	41	CENTERPIECE OD Plate System (Medtronic Sofamor Danek Co., Ltd.)	Approval	Medical products 4 Fixation device placed in the spine	A fixation device placed in the spine. This product is used for laminectomy to maintain the location of the vertebral arch which is dilated from the lower cervical spine to the upper thoracic spine (C3 to Th3). It is used for the treatment of cervical spine diseases such as spondylitic myelopathy and ossification of posterior longitudinal ligament, spinal cord tumor, etc. It consists of a cervical spine plate and a cervical spine screw. While one-side open laminectomy is performed for the existing therapy using a titanium plate in the same way with this product, the form structure has been improved for this product to optimize the surgical technique. Since there is no other product with the similar form and structure, a clinical evaluation report was submitted to confirm the efficacy and safety of the surgical technique with this product.
6-2	Dec. 21, 2012 Total review time: 360 days Regulatory review time: 282days	Nov. 3, 2008 Domestic clinical study results	42	Osteoraptor HA Anchor (Smith & Nephew Endoscopy K.K.)	Approval	Medical products 4 Absorbable ligament anchor	This product consists of absorbable anchors made of poly-L-lactic acid and hydroxyapatite, suture and inserter. Multiple anchors are implanted in the bone to secure them to the bone by surgically suturing damaged, ruptured or exfoliated soft tissues such as tendons, ligaments or muscles. The point of improvement is that hydroxyapatite was mixed to poly-L-lactic acid, which is an absorbable material of the existing product. A clinical study was conducted to confirm the efficacy and safety of the aforementioned purpose and usage of this new absorbable material.

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	Jul. 24, 2012 Total review time: 589 days Regulatory review time: 346 days	Mar. 31, 2009 Clinical evaluation report	43	PEM Flex Solo II PET Scanner (Sceti K.K.)	Approval	Instrument & apparatus 10 Positron emission tomography device for nuclear medicine diagnosis	A positron CT device for nuclear medicine diagnosis; it images distribution of the pre-dosed radioactive agent that releases positive electrons in the breast. The breast is sandwiched by a tray with built-in gamma-ray scanner and the distribution of a radioactive agent is imaged. A clinical evaluation report was submitted to evaluate the images obtained when this product was applied to the breast.
8	Mar. 22, 2013 Total review time: 276 days Regulatory review time: 229 days	Sep. 22, 2009 Clinical evaluation report	44	Leksell Gamma Knife Perfexion (Elekta K.K.)	Change	Instrument & apparatus 10 Radionuclide system for stereotactic radiotherapy	A radioactive nuclide system for stereotactic radiotherapy; it is used for non-incisional surgery by gamma ray irradiation for the treatment of cerebral vascular disorder and brain tumor. In an application for partial change, a component that fixes and positions the patient head in a non-invasive manner is added. A clinical evaluation report was submitted to evaluate the positioning and re-positioning accuracy of the mouth piece which is prepared with respect to each patient.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs, etc., Directed by MHLW in FY 2012

Post-marketing safety measures implemented by MHLW in FY 2012

	Drugs	Medical devices
Revision of PRECAUTIONS directed	198	4
Information published in the Pharmaceuticals and Medical Devices Safety Information	36	1

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

Revision of PRECAUTIONS for Drugs Directed by MHLW in FY 2012

Date	Drug name
Apr. 24, 2012	1. Ibuprofen (oral dosage form) 2. Ibuprofen (suppository) 3. Flurbiprofen (oral dosage form) 4. Flurbiprofen axetil 5. Mosapride citrate hydrate 6. Liraglutide (genetical recombination) Exenatide 7. Iodine (prepodyne solution) 8. Iodine (drugs with an indication and dosage and administration as "use for dispensing of iodine tincture, dilute iodine tincture, compound iodine glycerin, etc.") 9. Alogliptin benzoate 10. Alogliptin benzoate/Pioglitazone hydrochloride 11. Sitagliptin phosphate hydrate 12. Vildagliptin 13. Canakinumab (genetical recombination) 14. Lomefloxacin hydrochloride (oral dosage form) 15. Raltegravir potassium 16. Acetaminophen 17. Isopropylantipyrine/Acetaminophen/Allylisopropylacetylurea/Anhydrous caffeine 18. Tramadol hydrochloride/Acetaminophen 19. Salicylamide/Acetaminophen/Anhydrous caffeine/Chlorpheniramine maleate (for adults) 20. Salicylamide/Acetaminophen/Anhydrous caffeine/Chlorpheniramine maleate (forpediatrics) 21. Salicylamide/Acetaminophen/Anhydrous caffeine/Promethazine Methylenedisalicylate (for adults) 22. Salicylamide/Acetaminophen/Anhydrous caffeine/Promethazine Methylenedisalicylate (for pediatrics) 23. Diprophylline/Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Diphenhydramine salicylate/Acetaminophen/Bromovalerylurea 24. Linagliptin 25. Bendamustine hydrochloride 26. Azacitidine 27. Sorafenib tosilate 28. Pivmecillinam hydrochloride 29. Cefcapene pivoxil hydrochloride hydrate (tablets) 30. Cefcapene pivoxil hydrochloride hydrate (fine granule for pediatrics) 31. Cefditoren pivoxil (tablets) 32. Cefditoren pivoxil (fine granule for pediatrics) 33. Cefteram pivoxil (tablets) 34. Cefteram pivoxil (fine granule for pediatrics) 35. Tebipenem pivoxil 36. Moxifloxacin hydrochloride (oral dosage form)

Date	Drug name
	37. Live attenuated human rotavirus vaccine, oral 38. Rotavirus vaccine, live, oral, petavalent 39. Preparations containing ibuprofen (OTC)
Jun. 5, 2012	1. Escitalopram oxalate 2. Aliskiren fumarate 3. Garenoxacin mesilate hydrate 4. Telaprevir 5. Ivermectin 6. Ropinirole hydrochloride 7. Trazodone hydrochloride 8. Azosemide 9. Hydralazine hydrochloride 10. Darunavir ethanolate
Jul. 10, 2012	1. Pregabalin 2. Methotrexate (tablets 2 mg, capsules) 3. Influenza HA Vaccine 4. Metformin hydrochloride 5. Eltrombopag olamine 6. Denosumab (genetical recombination) 7. Temsirolimus 8. Nilotinib hydrochloride hydrate 9. Voriconazole 10. Sitafloxacin hydrate 11. Ciprofloxacin Ciprofloxacin hydrochloride 12. Adefovir pivoxil 13. Famciclovir
Aug. 7, 2012	1. Suxamethonium chloride hydrate 2. Pamidronate disodium hydrate 3. Oxaliplatin 4. Ropinirole hydrochloride (extended release tablets) 5. Diazoxide 6. Zoledronic acid hydrate 7. Nelarabine 8. Varenicline tartrate
Sep. 11, 2012	1. Denosumab (genetical recombination)

Date	Drug name
Sep. 25, 2012	1. Diclofenac sodium (ophthalmic solution) 2. Levocabastine hydrochloride (ophthalmic solution) 3. Levocabastine hydrochloride (nasal solution) 4. Tetracosactide acetate (0.5 mg preparation) 5. Diclofenac sodium (dermatologic preparation) 6. Lithium carbonate 7. Cibenzoline succinate 8. Aliskiren fumarate 9. Propylthiouracil 10. Tegafur/Gimeracil/Oteracil potassium 11. Telaprevir 12. Tocilizumab (genetical recombination) 13. Over-the-counter drugs Preparation containing diclofenac sodium (dermatologic preparation)
Oct. 23, 2012	1. Inactivated Polio Vaccine
Oct. 30, 2012	1. Mexiletine hydrochloride (oral dosage form) 2. Mexiletine hydrochloride (injectable dosage form) 3. Imatinib mesilate 4. Ceftriaxone sodium hydrate 5. Acetaminophen 6. Isopropylantipyrine/Acetaminophen/Allylisopropylacetylurea/Anhydrous caffeine 7. Tramadol hydrochloride/Acetaminophen 8. Salicylamide/Acetaminophen/Anhydrous caffeine/Chlorpheniramine maleate 9. Diprophylline/Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Diphenhydramine salicylate/Acetaminophen/ Bromovalerylurea 10. Spironolactone 11. Dabigatran etexilate methanesulfonate 12. Rotavirus vaccine, Live, Oral, Pentavalent
Dec. 4, 2012	1. Pramipexole hydrochloride hydrate 2. Digoxin Deslanoside Methyldigoxin 3. Ambrisentan 4. Gelatin (sponge 2 cm x 6 cm x 0.7 cm, 8 cm x 12.5 cm x 1 cm) 5. Gelatin (sponge 5 cm x 2.5 cm, 10 cm x 7 cm) 6. Temozolomide 7. Pazopanib hydrochloride 8. Mogamulizumab (genetical recombination)

Date	Drug name
	9. Telaprevir 10. Gelatin (film)
Jan. 8, 2013	1. Sunitinib malate 2. Ryutanshakanto 3. Josamycin Josamycin propionate 4. Zanamivir hydrate 5. Glimepiride Pioglitazone hydrochloride/Glimepiride 6. Cefozopran hydrochloride 7. Cefotiam hydrochloride 8. Atazanavir sulfate Abacavir sulfate Indinavir sulfate ethanolate Etravirine Efavirenz Emtricitabine Emtricitabine/Tenofovir disoproxil fumarate Saquinavir mesilate Sanilvudine Didanosine Zidovudine Zidovudine/Lamivudine Darunavir ethanolate Tenofovir disoproxil fumarate Nevirapine Nelfinavir mesilate Fosamprenavir calcium hydrate Maraviroc Lamivudine (150mg, 300mg) Lamivudine/Abacavir sulfate Raltegravir potassium Ritonavir Rilpivirine hydrochloride Lopinavir/Ritonavir 9. Ryutanshakanto (OTC)
Feb. 19, 2013	1. Estradiol (Estrana, Julina, Divigel, Femiest) Estradiol benzoate Estradiol valerate Estradiol dipropionate Estriol (oral dosage form) Estriol tripropionate

Date	Drug name
	Conjugated estrogen Estradiol/Norethisterone acetate Estradiol/Levonorgestrel Testosterone/Estradiol Testosterone enanthate/Estradiol valerate Testosterone enanthate/Testosterone propionate/Estradiol valerate 2. Ethinylestradiol 3. Norethisterone/Mestranol (preparations with the indication for climacteric disturbance) 4. Propafenone hydrochloride 5. Purified human menopausal gonadotrophin Human menopausal gonadotrophin Human chorionic gonadotrophin Follitropin beta (genetical recombination) Follitropin alfa (genetical recombination) Estriol (injectable dosage form, preparations for vaginal application) Clomifene citrate Gonadorelin acetate (1.2 mg, 2.4 mg) Cyclofenil
Mar. 26, 2013	1. Gabapentin 2. Carbamazepine 3. Gabapentin enacarbil 4. Hydrochlorothiazide Candesartan cilexetil/Hydrochlorothiazide Telmisartan/Hydrochlorothiazide Valsartan/Hydrochlorothiazide Losartan potassium/Hydrochlorothiazide 5. Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Chlorpheniramine maleate Platycodon fluidextract/Glycyrrhiza extract/Plantago herb extract/ Peony root extract/Dihydrocodeine phosphate Dihydrocodeine phosphate/Ephedrine hydrochloride/Ammonium chloride 6. Diprophylline/Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Diphenhydramine salicylate/Acetaminophen/ Bromovalerylurea 7. Cherry bark extract/Codeine phosphate hydrate 8. Codeine phosphate hydrate 9. Dihydrocodeine phosphate 10. Denosumab (genetical recombination) 11. Sorafenib tosilate 12. Panitumumab (genetical recombination) 13. Doripenem hydrate 14. Telaprevir

Date	Drug name
	15. Recombinant adsorbed bivalent human papillomavirus-like particle vaccine (derived from Trichoplusia ni cells) 16. Interferon beta 1b (genetical recombination)
Mar. 29, 2013	1. Escitalopram oxalate 2. Sertraline hydrochloride 3. Duloxetine hydrochloride 4. Fluvoxamine maleate 5. Mirtazapine 6. Milnacipran hydrochloride

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 5. Revision of PRECAUTIONS for Medical Devices Directed by MHLW in FY 2012

Date	Title
Apr. 27, 2012	International Standardization of Hemoglobin A1c Measurements (a notification to Health and Medical Affairs Division in Prefectural Health Departments [Bureaus]) International Standardization of Hemoglobin A1c Measurements (a notification to marketing authorization holders of HbA1c analysis devices and in vitro diagnostics for measurement of HbA1c)
Nov. 7, 2012	Revision of PRECAUTIONS for Gastrointestinal Stents
Mar. 19, 2013	Revision of PRECAUTIONS related to Influences of Electromagnetic Waves from Battery Chargers of Electric Vehicles on Implantable Cardiac Pacemakers, etc.
Mar. 19, 2013	Provision of Information, etc. related to Influences of Electromagnetic Waves from Battery Chargers of Electric Vehicles on Implantable Cardiac Pacemakers, etc. (request) (to the Director of the Automobile Division, Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry) (to the Director of the Engineering Policy Division and Director of the Type Approval and Recall Division, Road Transport Bureau, Ministry of Land, Infrastructure, Transport and Tourism)

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 6. FY 2012 Pharmaceuticals and Medical Devices Safety Information (No. 290-300)

Date	No.	Contents
Apr. 25, 2012	290	1. Lookback Study onBlood Products for Transfusion 2. Drug-induced Serious Skin Disorders 3. Important Safety Information (1) Products Containing Acetaminophen (2) Cibenzoline Succinate (3) Triclofos Sodium, Chloral Hydrate (4) Metformin Hydrochloride (products with "Dosage and Administration" of maximum daily dosage of 2250 mg) 4. Revision of Precautions (No. 235) Pioglitazone Hydrochloride / Metformin Hydrochloride (and 14 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) 1. Increase of the Number of Cooperating Hospitals in the Project for “Japan Drug Information Institute in Pregnancy” 2. List of Errata for Pharmaceuticals and Medical Devices Safety Information No. 289
Jun. 27, 2012	291	1. Safety Measures for Cervical Cancer Prevention Vaccines 2. Important Safety Information (1) Alogliptin Benzoate, Alogliptin Benzoate/Pioglitazone Hydrochloride, Sitagliptin Phosphate Hydrate, Vildagliptin, Linagliptin (2) Exenatide, Liraglutide (Genetical Recombination) (3) Mosapride Citrate Hydrate (4) Iodine 3. Revision of Precautions (No. 236) Ibuprofen (oral dosage form) (and 29 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jul. 25, 2012	292	1. Launch of a pilot program of "Direct Patient Reporting System for Adverse Drug Reactions" 2. Important Safety Information (1) Ivermectin (2) Telaprevir (3) Garenoxacin Mesilate Hydrate 3. Revision of Precautions (No. 237) Escitalopram Oxalate (and 6 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
Aug. 29, 2012	293	1. Serious Adverse Associated with Over-the-counter Drugs 2. Important Safety Information (1) Pregabalin (2) Methotrexate (Tablet 2 mg, Capsule) (3) Influenza HA Vaccine 3. Revision of Precautions (No. 238) Metformin Hydrochloride (and 9 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Sep. 26, 2012	294	1. Proper Use of Contact Lenses and Prevention of Eye Disorders 2. Summary of Report on Adverse Reactions to the Influenza Vaccine in the 2011 Season 3. Important Safety Information (1) Oxaliplatin 4. Revision of Precautions (No. 239) Suxamethonium Chloride Hydrate (and 6 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 31, 2012	295	1. Serious Hypocalcaemia Associated with Denosumab (Genetical Recombination) 2. Important Safety Information (1) Denosumab (Genetical Recombination) (2) Tetracosactide Acetate (0.5 mg preparation) (3) Levocabastine Hydrochloride 3. Revision of Precautions (No. 240) Diclofenac Sodium (ophthalmic solution) (and 9others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Nov. 27, 2012	296	1. Summary of Payment / Non-payment of Adverse Drug Reactions Relief Benefits and Drugs with Many Cases of Improper Use 2. Important Safety Information (1) Imatinib Mesilate (2) Ceftriaxone Sodium Hydrate (3) Mexiletine Hydrochloride 3. Revision of Precautions (No. 241) Inactivated Poliomyelitis Vaccine (and 4 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 26, 2012	297	1. Surveillance on Dissemination and Utilization of Safety Information in Medical Institutions 2. Precautions for Using of Gastrointestinal Stents 3. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
Jan. 30, 2013	298	1. Partial Amendment of the "Guidance for Bar Code Labeling on Prescription Drugs" for the Prevention of Medical Accidents 2. Important Safety Information (1) Temozolomide (2) Telaprevir (3) Pramipexole Hydrochloride Hydrate (4) Mogamulizumab (Genetical Recombination) 3. Revision of Precautions (No. 242) Digoxin, Deslanoside, and Metildigoxin (and 5 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Feb. 27, 2013	299	1. Utilization of PMDA Medical Safety Information 2. Important Safety Information (1) Zanamivir Hydrate (2) Josamycin, Josamycin Propionate (3) Sunitinib Malate (4) Ryutanshakanto (for Ethical Use) 3. Revision of Precautions (No. 243) Glimepiride, Pioglitazone Hydrochloride / Glimepiride (and 4 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance (Reference) 1. Adverse DrugReaction Term "Anaphylaxis"
Mar. 27, 2013	300	1. Implementation of the "Risk Management Plan" 2. Revision of Precautions (No. 244) Estradiol (ESTRANA, Julina, DIVIGEL, FEMIEST) (and 4 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 7. FY 2012 PMDA Medical Safety Information

No.	Month and year published	Title
30	April 2012	Precautions in Handling of Endtracheal Tubes
31	May 2012	Precautions in Handling of Radiopharmaceuticals for Injection
32	June 2012	Precautions in Handling of Closed Suction Catheters
33	September 2012	Accidental Burns during Surgery
34	October 2012	Precautions in Handling of Glycerin Enemas
35	October 2012	Precautions in Handling of Tracheotomy Tubes
36	March 2013	Cases of Tube or Line Removal

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 8. List of User Fees (partially revised on October 1, 2012)

8-1. List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Pharmaceutical Affairs Act (Act No. 145, 1960)"

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		148,100	148,100
				Article 16, Paragraph 1, Item 1 (a)	
		Document		111,500	111,500
				Article 16, Paragraph 1, Item 1 (b)	
Change/addition of classification		On-site		97,400	97,400
				Article 16, Paragraph 1,Item 2 (a)	
		Document		55,300	55,300
				Article 16, Paragraph 1,Item 2 (b)	
Renewal of existing license		On-site		97,400	97,400
				Article 16, Paragraph 1,Item 3 (a)	
		Document		55,300	55,300
				Article 16, Paragraph 1,Item 3 (b)	
Assessment for foreign manufacturers' accreditation of drugs					
New accreditation		On-site		133,300 + travel expenses	133,300 + travel expenses
				Article 16, Paragraph 2, Item 1 (a)	
		Document		58,100	58,100
				Article 16, Paragraph 2, Item 1 (b)	
Change/addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16, Paragraph 2,Item 2 (a)	
		Document		39,700	39,700
				Article 16, Paragraph 2,, Item 2 (b)	
Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16, Paragraph 2,Item 3 (a)	
		Document		39,700	39,700
				Article 16, Paragraph 2,Item 3 (b)	
Review for approval of drugs (new approval)					
New drugs (No. 1) (non-orphan drugs)		First application products	23,788,100	6,559,600	30,347,700
			Article 17, Paragraph 1, Item 1 (a)-(1)	Article 17,Paragraph 2, Item 1 (a)	
		Line extension products	2,464,000	1,639,800	4,103,800
			Article 17, Paragraph 1, Item 1 (a)-(3)	Article 17,Paragraph 2, Item 1 (c)	
New drugs (No. 1) (orphan drugs)		First application products	19,934,100	3,286,000	23,220,100
			Article 17, Paragraph 1, Item 1 (a)-(2)	Article 17,Paragraph 2, Item 1 (b)	
		Line extension products	2,061,500	818,100	2,879,600
			Article 17, Paragraph 1, Item 1 (a)-(4)	Article 17,Paragraph 2, Item 1 (d)	
New drugs (No. 2) (non-orphan drugs)		First application products	11,353,100	2,463,200	13,816,300
			Article 17, Paragraph 1, Item 1 (a)-(5)	Article 17,Paragraph 2, Item 1 (e)	
		Line extension products	1,174,300	615,900	1,790,200
			Article 17, Paragraph 1, Item 1 (a)-(6)	Article 17,Paragraph 2, Item 1 (f)	
New drugs (No. 2) (orphan drugs)		First application products	9,345,700	1,232,500	10,578,200
			Article 17, Paragraph 1, Item 1 (a)-(7)	Article 17,Paragraph 2, Item 1 (g)	
		Line extension products	1,004,100	310,100	1,314,200
			Article 17, Paragraph 1, Item 1 (a)-(8)	Article 17,Paragraph 2, Item 1 (h)	
Generic prescription drugs (with inspections)			412,100	214,000	626,100
			Article 17, Paragraph 1, Item 1 (a)-(9)	Article 17,Paragraph 2, Item 1 (i)	
OTC drugs	Switch to OTC status, etc.	First application products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1 (a)-(10)		
		Line extension products	1,291,600		1,291,600
			Article 17, Paragraph 1, Item 1 (a)-(10)		
	Others		110,300		110,300
			Article 17, Paragraph 1, Item 1 (a)-(11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17, Paragraph 1, Item 1 (a)-(14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17, Paragraph 1, Item 1 (a)-(13)		
		Addition of series	60,300		60,300
			Article 17, Paragraph 1, Item 1 (a)-(12)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17, Paragraph 1, Item 1 (b) (c)		
New application for change or replacement of brand name			35,600		35,600
			Article 17, Paragraph 1, Item 1 (e)		

Classification				User fees		
				Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)						
	New drugs (No. 1) (non-orphan drugs)	Changes in indications, etc.	First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Others		205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17,Paragraph 2, Item 2 (c)	
	New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300	1,232,500	9,666,800
				Article 17, Paragraph 1, Item 2 (a)-(4)	Article 17,Paragraph 2, Item 2 (d)	
			Line extension products	875,600	310,100	1,185,700
				Article 17, Paragraph 1, Item 2 (a)-(5)	Article 17,Paragraph 2, Item 2 (e)	
		Others		132,700	109,800	242,500
				Article 17, Paragraph 1, Item 2 (a)-(6)	Article 17,Paragraph 2, Item 2 (f)	
	New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Others		205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17,Paragraph 2, Item 2 (c)	
	New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300	1,232,500	9,666,800
				Article 17, Paragraph 1, Item 2 (a)-(4)	Article 17,Paragraph 2, Item 2 (d)	
			Line extension products	875,600	310,100	1,185,700
				Article 17, Paragraph 1, Item 2 (a)-(5)	Article 17,Paragraph 2, Item 2 (e)	
		Others		132,700	109,800	242,500
				Article 17, Paragraph 1, Item 2 (a)-(6)	Article 17,Paragraph 2, Item 2 (f)	
	Generic prescription drugs (with inspections)	Changes in indications, etc.	First application products	10,190,500	2,463,200	12,653,700
				Article 17, Paragraph 1, Item 2 (a)-(1)	Article 17,Paragraph 2, Item 2 (a)	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17, Paragraph 1, Item 2 (a)-(2)	Article 17,Paragraph 2, Item 2 (b)	
		Changes based on guidelines, etc.		35,600		35,600
				Article 17, Paragraph 1, Item 2 (a)-(7)		
		Others		205,100	120,700	325,800
				Article 17, Paragraph 1, Item 2 (a)-(3)	Article 17, Paragraph 2, Item 2 (c)	
	OTC drugs	Switch to OTC status, etc. / Changes in indications, etc.	First application products	10,190,500		10,190,500
				Article 17, Paragraph 1, Item 2 (a)-(1)		
			Line extension products	1,057,400		1,057,400
				Article 17, Paragraph 1, Item 2 (a)-(2)		
		Changes based on guidelines, etc.		35,600		35,600
				Article 17, Paragraph 1, Item 2 (a)-(7)		
		Others		56,400		56,400
				Article 17, Paragraph 1, Item 2 (a)-(8)		
	In vitro diagnostics (without approval standards)			295,800		295,800
				Article 17, Paragraph 1, Item 2 (a)-(11)		
	In vitro diagnostics (with approval standards)		Basic	143,500		143,500
				Article 17, Paragraph 1, Item 2 (a)-(10)		
			Addition of series	31,900		31,900
				Article 17, Paragraph 1, Item 2 (a)-(9)		
	Quasi-drugs/cosmetics			35,600		35,600
				Article 17, Paragraph 1, Item 2 (b) (c)		

Classification					User fees		
					Review	Inspection	Total
GMP inspection of drugs							
Approval, partial change and manufacture for export		New drugs		Domestic		739,800 Article 17, Paragraph 4, Item 1 (b)-(1)	739,800
				Overseas		933,500 + travel expenses Article 17, Paragraph 4, Item 1 (b)-(2)	933,500 + travel expenses
		Biological drugs/Radiopharmaceuticals, etc.		Domestic		666,100 Article 17, Paragraph 4, Item 1 (a)-(1)	666,100
				Overseas		844,400 + travel expenses Article 17, Paragraph 4, Item 1 (a)-(2)	844,400 + travel expenses
		Sterilized drugs/Sterilized quasi-drugs		Domestic		201,300 Article 17, Paragraph 4, Item 1 (c)-(1)	201,300
				Overseas		229,800 + travel expenses Article 17, Paragraph 4, Item 1 (c)-(2)	229,800 + travel expenses
		Other Drugs/quasi-drugs		Domestic		141,200 Article 17, Paragraph 4, Item 1 (d)-(1)	141,200
				Overseas		155,400 + travel expenses Article 17, Paragraph 4, Item 1 (d)-(2)	155,400 + travel expenses
		Packaging, labeling, storage, external testing, etc.		Domestic		63,800 Article 17, Paragraph 4,Item 2 (a) and Paragraph 5, Item 1 (a)	63,800
				Overseas		84,800 + travel expenses Article 17, Paragraph 4,Item 2 (b) and Paragraph 5, Item 1 (b)	84,800 + travel expenses
Renewal of the above		Biological drugs/ Radiopharmaceuticals, etc.	Basic	Domestic		436,000 Article 17, Paragraph 4, Item 3 (a)-(1)	436,000
				Overseas		554,200 + travel expenses Article 17, Paragraph 4, Item 3 (a)-(2)	554,200 + travel expenses
			Addition of products	Domestic		30,500 Article 17, Paragraph 4, Item 3 (a)-(1)	30,500
				Overseas		30,500 Article 17, Paragraph 4, Item 3 (a)-(2)	30,500
		Sterilized drugs/ Sterilized quasi-drugs	Basic	Domestic		380,000 Article 17, Paragraph 4, Item 3 (b)-(1)	380,000
				Overseas		480,000 + travel expenses Article 17, Paragraph 4, Item 3 (b)-(2)	480,000 + travel expenses
			Addition of products	Domestic		12,400 Article 17, Paragraph 4, Item 3 (b)-(1)	12,400
				Overseas		12,400 Article 17, Paragraph 4, Item 3 (b)-(2)	12,400
		Other Drugs/ quasi-drugs	Basic	Domestic		336,500 Article 17, Paragraph 4, Item 3 (c)-(1)	336,500
				Overseas		409,400 + travel expenses Article 17, Paragraph 4, Item 3 (c)-(2)	409,400 + travel expenses
			Addition of products	Domestic		9,600 Article 17, Paragraph 4, Item 3 (c)-(1)	9,600
				Overseas		9,600 Article 17, Paragraph 4, Item 3 (c)-(2)	9,600
		Packaging, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	258,500
				Overseas		338,100 + travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	338,100 + travel expenses
			Addition of products	Domestic		6,700 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,700
				Overseas		6,700 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,700

Classification				User fees		
				Review	Inspection	Total
GLP inspection of drugs						
	GLP	Domestic			2,062,400	2,062,400
					Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	
		Overseas			2,282,600 + travel expenses	2,282,600 + travel expenses
					Article 17, Paragraph 3, Item 1 (b) and Paragraph 9, Item 2 (a)-(2)	
GCP inspection of drugs						
	New GCP	First application products	Domestic		2,723,200	2,723,200
					Article 17, Paragraph 3, Item 2 (a)	
			Overseas		3,011,900 + travel expenses	3,011,900 + travel expenses
					Article 17, Paragraph 3, Item 2 (b)	
		Line extension products	Domestic		720,800	720,800
					Article 17, Paragraph 3, Item 2 (c)	
			Overseas		751,800 + travel expenses	751,800 + travel expenses
					Article 17, Paragraph 3, Item 2 (d)	
	GCP inspection of generic drugs		Domestic		645,200	645,200
					Article 17, Paragraph 3, Item 2 (e)	
			Overseas		950,200 + travel expenses	950,200 + travel expenses
					Article 17, Paragraph 3, Item 2 (f)	
Re-examination of drugs						
	Re-examination	First application products		806,600	2,673,700	3,480,300
				Article 17, Paragraph 8, Item 1 (a)	Article 17, Paragraph 9, Item 1 (a)	
		Line extension products		271,500	892,100	1,163,600
				Article 17, Paragraph 8, Item 1 (b)	Article 17, Paragraph 9, Item 1 (b)	
	GPSP	First application products	Domestic		2,193,300	2,193,300
					Article 17, Paragraph 9, Item 2 (b)-(1)	
			Overseas		2,409,600 + travel expenses	2,409,600 + travel expenses
					Article 17, Paragraph 9, Item 2 (b)-(2)	
		Line extension products	Domestic		752,600	752,600
					Article 17, Paragraph 9, Item 2 (b)-(3)	
			Overseas		772,300 + travel expenses	772,300 + travel expenses
					Article 17, Paragraph 9, Item 2 (b) (4)	

8-2. List of user fees for reviews etc. of medical devices under the Pharmaceutical Affairs Act (Act No. 145, 1960)

Note: The lower rows in the User fees column indicate the applicable articles of the Cabinet Order on Fees related to the Pharmaceutical Affairs Act. *(Yen)*

Classification				User fees		
				Review	Inspection	Total
Assessment for manufacturing license of medical devices						
	New license		On-site		148,100	148,100
					Article 16, Paragraph 1, Item 1 (a)	
			Document		111,500	111,500
					Article 16, Paragraph 1, Item 1 (b)	
	Change/addition of classification		On-site		97,400	97,400
					Article 16, Paragraph 1, Item 2 (a)	
			Document		55,300	55,300
					Article 16, Paragraph 1, Item 2 (b)	
	Renewal of existing license		On-site		97,400	97,400
					Article 16, Paragraph 1, Item 3 (a)	
			Document		55,300	55,300
					Article 16, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers accreditation of medical devices						
	New accreditation		On-site		133,300 + travel expenses	133,300 + travel expenses
					Article 16, Paragraph 2, Item 1 (a)	
			Document		58,100	58,100
					Article 16, Paragraph 2, Item 1 (b)	
	Change/addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16, Paragraph 2, Item 2 (a)	
			Document		39,700	39,700
					Article 16, Paragraph 2, Item 2 (b)	
	Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16, Paragraph 2, Item 3 (a)	
			Document		39,700	39,700
					Article 16, Paragraph 2, Item 3 (b)	
Review for approval of medical devices (new approval)						
	Medical devices (with clinical data)	Class IV	New medical devices	8,705,500	664,500	9,370,000
				Article 17, Paragraph 1, Item 1 (d)-(1)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(2)	Article 17, Paragraph 2, Item 1 (j)	
		Class III	New medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(3)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1 (d)-(4)	Article 17, Paragraph 2, Item 1 (j)	
		Class II	New medical devices	6,213,000	664,500	6,877,500
				Article 17, Paragraph 1, Item 1 (d)-(3)	Article 17, Paragraph 2, Item 1 (j)	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17, Paragraph 1, Item 1 (d)-(4)	Article 17, Paragraph 2, Item 1 (j)	
	Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	2,355,400	68,500	2,423,900
				Article 17, Paragraph 1, Item 1 (d)-(7)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,767,700	68,500	1,836,200
				Article 17, Paragraph 1, Item 1 (d)-(8)	Article 17, Paragraph 2, Item 1 (l)	
		Class III	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
		Class II	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17, Paragraph 1, Item 1 (d)-(9)	Article 17, Paragraph 2, Item 1 (l)	
	Medical devices (with approval standards, without clinical data)	Class IV		429,200	68,500	497,700
				Article 17, Paragraph 1, Item 1 (d)-(5)	Article 17, Paragraph 2, Item 1 (k)	
		Class III		344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1 (d)-(6)	Article 17, Paragraph 2, Item 1 (k)	
		Class II		344,100	68,500	412,600
				Article 17, Paragraph 1, Item 1 (d)-(6)	Article 17, Paragraph 2, Item 1 (k)	
	Change of brand name			35,600		35,600
				Article 17, Paragraph 1, Item 1 (e)		

Classification			User fees		
			Review	Inspection	Total
Review for approval of medical devices (approval of partial changes to approved matters)					
Medical devices (with clinical data)	Class IV	New medical devices	4,357,500	664,500	5,022,000
			Article 17, Paragraph 1, Item 2 (d)-(1)	Article 17, Paragraph 2, Item 2 (g)	
		Improved medical devices	3,109,900	664,500	3,774,400
			Article 17, Paragraph 1, Item 2 (d)-(2)	Article 17, Paragraph 2, Item 2 (g)	
	Class III	New medical devices	3,109,900	664,500	3,774,400
			Article 17, Paragraph 1, Item 2 (d)-(3)	Article 17, Paragraph 2, Item 2 (g)	
		Improved medical devices	1,872,400	664,500	2,536,900
			Article 17, Paragraph 1, Item 2 (d)-(4)	Article 17, Paragraph 2, Item 2 (g)	
	Class II	New medical devices	3,109,900	664,500	3,774,400
			Article 17, Paragraph 1, Item 2 (d)-(3)	Article 17, Paragraph 2, Item 2 (g)	
		Improved medical devices	1,872,400	664,500	2,536,900
			Article 17, Paragraph 1, Item 2 (d)-(4)	Article 17, Paragraph 2, Item 2 (g)	
Medical devices (without approval standards, without clinical data)	Class IV	Improved medical devices	1,181,200	37,100	1,218,300
			Article 17, Paragraph 1, Item 2 (d)-(7)	Article 17, Paragraph 2, Item 2 (i)	
		Generic medical devices	884,200	37,100	921,300
			Article 17, Paragraph 1, Item 2 (d)-(8)	Article 17, Paragraph 2, Item 2 (i)	
	Class III	Improved medical devices	709,500	37,100	746,600
			Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
		Generic medical devices	709,500	37,100	746,600
			Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
	Class II	Improved medical devices	709,500	37,100	746,600
			Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
		Generic medical devices	709,500	37,100	746,600
			Article 17, Paragraph 1, Item 2 (d)-(9)	Article 17, Paragraph 2, Item 2 (i)	
Medical devices (with approval standards, without clinical data)	Class IV		217,600	37,100	254,700
			Article 17, Paragraph 1, Item 2 (d)-(5)	Article 17, Paragraph 2, Item 2 (h)	
	Class III		173,600	37,100	210,700
			Article 17, Paragraph 1, Item 2 (d)-(6)	Article 17, Paragraph 2, Item 2 (h)	
	Class II		173,600	37,100	210,700
			Article 17, Paragraph 1, Item 2 (d)-(6)	Article 17, Paragraph 2, Item 2 (h)	

Classification					User fees		
					Review	Inspection	Total
QMS inspection of medical devices							
	Approval, partial change and manufacture for export	New medical devices		Domestic		739,800 Article 17, Paragraph 4, Item 1 (b)-(1)	739,800
				Overseas		933,500 + travel expenses Article 17, Paragraph 4, Item 1 (b)-(2)	933,500 + travel expenses
		Biological medical devices, specially controlled medical devices (Class IV), etc.		Domestic		666,100 Article 17, Paragraph 4, Item 1 (a)-(1)	666,100
				Overseas		844,400 + travel expenses Article 17, Paragraph 4, Item 1 (a)-(2)	844,400 + travel expenses
		Sterilized medical devices		Domestic		201,300 Article 17, Paragraph 4, Item 1 (c)-(1)	201,300
				Overseas		229,800 + travel expenses Article 17, Paragraph 4, Item 1 (c)-(2)	229,800 + travel expenses
		Other medical devices		Domestic		141,200 Article 17, Paragraph 4, Item 1 (d)-(1)	141,200
				Overseas		155,400 + travel expenses Article 17, Paragraph 4, Item 1 (d)-(2)	155,400 + travel expenses
		Packaging, labeling, storage, external testing, etc.		Domestic		63,800 Article 17, Paragraph 4, Item 2 (a) and Paragraph 5, Item 1 (a)	63,800
				Overseas		84,800 + travel expenses Article 17, Paragraph 4, Item 2 (b) and Paragraph 5, Item 1 (b)	84,800 + travel expenses
	Renewal of the above	Biological medical devices, specially controlled medical devices (Class IV), etc.	Basic	Domestic		436,000 Article 17, Paragraph 4, Item 3 (a)-(1)	436,000
				Overseas		554,200 + travel expenses Article 17, Paragraph 4, Item 3 (a)-(2)	554,200 + travel expenses
			Addition of products	Domestic		30,500 Article 17, Paragraph 4, Item 3 (a)-(1)	30,500
				Overseas		30,500 Article 17, Paragraph 4, Item 3 (a)-(2)	30,500
		Sterilized medical devices	Basic	Domestic		380,000 Article 17, Paragraph 4, Item 3 (b)-(1)	380,000
				Overseas		480,000 + travel expenses Article 17, Paragraph 4, Item 3 (b)-(2)	480,000 + travel expenses
			Addition of products	Domestic		12,400 Article 17, Paragraph 4, Item 3 (b)-(1)	12,400
				Overseas		12,400 Article 17, Paragraph 4, Item 3 (b)-(2)	12,400
		Other medical devices	Basic	Domestic		336,500 Article 17, Paragraph 4, Item 3 (c)-(1)	336,500
				Overseas		409,400 + travel expenses Article 17, Paragraph 4, Item 3 (c)-(2)	409,400 + travel expenses
			Addition of products	Domestic		9,600 Article 17, Paragraph 4, Item 3 (c) (1)	9,600
				Overseas		9,600 Article 17, Paragraph 4, Item 3 (c)-(2)	9,600
		Packaging, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	258,500
				Overseas		338,100 + travel expenses Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	338,100 + travel expenses
			Addition of products	Domestic		6,700 Article 17, Paragraph 4, Item 3 (d)-(1) and Paragraph 5, Item 2 (a)	6,700
				Overseas		6,700 Article 17, Paragraph 4, Item 3 (d)-(2) and Paragraph 5, Item 2 (b)	6,700

Classification			User fees		
			Review	Inspection	Total
GLP Inspection of medical devices					
	GLP	Domestic		2,062,400	2,062,400
				Article 17, Paragraph 3, Item 1 (a) and Paragraph 9, Item 2 (a)-(1)	
		Overseas		2,282,600 + travel expenses	2,282,600 + travel expenses
				Article 17, Paragraph 3, Item 1 (b) and Paragraph 9, Item 2 (a)-(2)	
GCP inspection of medical devices					
	GCP	Domestic		635,300	635,300
				Article 17, Paragraph 3, Item 3 (a)	
		Overseas		918,400 + travel expenses	918,400 + travel expenses
				Article 17, Paragraph 3, Item 3 (b)	
Re-examination of medical devices					
	New medical devices		502,600	624,600	1,127,200
			Article 17, Paragraph 8, Item 2 (a)	Article 17, Paragraph 9, Item 1 (c)	
	Medical devices other than the new ones		51,600	624,600	676,200
			Article 17, Paragraph 8, Item 2 (b)	Article 17, Paragraph 9, Item 1 (c)	
	GPSP	Domestic		610,700	610,700
				Article 17, Paragraph 9, Item 2 (b)-(5)	
		Overseas		949,000 + travel expenses	949,000 + travel expenses
				Article 17, Paragraph 9, Item 2 (b)-(6)	

8-3. List of user fees under Article 4 of the Administrative Instructions for the Statement of Operating Procedures on Reviews and Related Services of the Pharmaceuticals and Medical Devices Agency

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	139,800 yen	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on bioequivalence testing, etc. for drugs	per consultation	556,000 yen	
	Safety consultation for drugs	per consultation	1,782,800 yen	
	Quality consultation for drugs	per consultation	1,478,300 yen	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,239,400 yen	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,186,100 yen	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,623,000 yen	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,222,500 yen	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,028,400 yen	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,274,200 yen	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,011,500 yen	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,515,700 yen	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,011,400 yen	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,513,000 yen	
	Consultation on protocols of clinical trials for reevaluation and re-examination of drugs	per consultation	3,320,600 yen	
	Consultation at completion of clinical trials for reevaluation and re-examination of drugs	per consultation	3,319,400 yen	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,675,600 yen	
	Additional consultation for drugs (orphan drugs)	per consultation	2,010,400 yen	
	Consultation on GLP/GCP compliance for drugs (non-orphan drugs)	per consultation	2,875,500 yen	
	Consultation on GLP/GCP compliance for drugs (orphan drugs)	per consultation	2,157,200 yen	
	Prior assessment consultation for drugs (quality)	per consultation	3,049,300 yen	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,061,100 yen	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,484,700 yen	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,497,400 yen	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	6,985,700 yen	
	Consultation on drug product eligibility for priority review	per consultation	823,300 yen	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	168,700 yen	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,026,400 yen	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,111,000 yen	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	921,900 yen	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	403,100 yen	
	Consultation on R&D strategy for drugs	per consultation	1,498,800 yen	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately)	per consultation	149,800 yen	
	Consultations on bioequivalence of generic drugs	per consultation	997,500 yen	
	Quality consultation for generic drugs	per consultation	491,800 yen	
	Pre-application consultation for switch OTC drugs	per consultation	1,501,100 yen	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	502,500 yen	
	Consultation on appropriateness of development of new OTC drugs	per consultation	199,100 yen	
	Pre-development consultation for medical devices	per consultation	135,200 yen	
	Safety consultation for medical devices (excluding biological medical devices)	per consultation	822,100 yen	
	Safety consultation for biological medical devices	per consultation	910,100 yen	
	Quality consultation for medical devices (excluding biological medical devices)	per consultation	775,400 yen	
	Quality consultation for biological medical devices	per consultation	921,400 yen	
	Performance testing consultation for medical devices	per consultation	845,900 yen	
	Clinical evaluation consultation for medical devices	per consultation	1,026,600 yen	
	Exploratory clinical trial consultation for medical devices	per consultation	1,105,300 yen	
	Clinical trial consultation for medical devices	per consultation	2,413,000 yen	
	Pre-application consultation for medical devices	per consultation	2,413,000 yen	
	Application procedure consultation for medical devices	per consultation	135,200 yen	
	Additional consultation for medical devices	per consultation	1,130,100 yen	
	Consultation on GLP/GCP compliance for medical devices	per consultation	772,900 yen	

(Yen)

			User fees		Timing of payment
Consultations					
Devices and in vitro diagnostics	Prior assessment consultation for medical devices (quality)		per consultation	2,982,300 yen	
	Prior assessment consultation for medical devices (non-clinical)		per consultation	2,982,300 yen	
	Prior assessment consultation for medical devices (clinical)		per consultation	4,490,800 yen	
	Consultation on R&D strategy for medical devices		per consultation	849,700 yen	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately*)		per consultation	84,900 yen	
	Pre-development consultation for in vitro diagnostics		per consultation	139,900 yen	
	Quality consultation for in vitro diagnostics		per consultation	345,500 yen	
	Consultation on conformity with standards for in vitro diagnostics		per consultation	442,800 yen	
	Clinical evaluation consultation for in vitro diagnostics		per consultation	675,400 yen	
	Clinical performance study consultation for in vitro diagnostics		per consultation	1,594,700 yen	
	Pre-application consultation for in vitro diagnostics		per consultation	1,594,700 yen	
	Application procedure consultation for in vitro diagnostics		per consultation	135,200 yen	
	Additional consultation for in vitro diagnostics		per consultation	927,500 yen	
	Prior assessment consultation for in vitro diagnostics (quality)		per consultation	2,982,300 yen	
	Prior assessment consultation for in vitro diagnostics (non-clinical)		per consultation	2,982,300 yen	
	Prior assessment consultation for in vitro diagnostics (clinical)		per consultation	4,490,800 yen	
	Consultation on preparation of documents for gene therapy products		per consultation	223,500 yen	
Simple consultations	Generic drugs		per consultation	21,000 yen	
	OTC drugs		per consultation	21,000 yen	
	Quasi-drugs (including pesticides and rodenticides)		per consultation	21,000 yen	
	Medical devices or in vitro diagnostics		per consultation	34,300 yen	
	Preparation of new drug applications		per consultation	21,000 yen	
	GMP/QMS inspection		per consultation	24,700 yen	
Assessment for designation of priority consultation products					
Assessment for designation of drugs for priority consultation			per application	818,800 yen	Request to PMDA after advanced payment
Assessment for designation of medical devices or in vitro diagnostics fo rpriority consultation			per application	818,800 yen	
GLP inspection of test facilities					
All test items (for drugs and medical devices)			per facility	3,023,800 yen	Request to PMDA after advanced payment
All test items (for drugs or medical devices)		Domestic	per facility	2,062,400 yen	
		Overseas	per facility	2,282,600 yen + travel expenses	
Limited test items			per facility	995,200 yen	
Additional compliance accreditation			per facility	932,600 yen	
Confirmation of certification on drugs, etc.					
GMP certification on investigational products (with on-site inspection)			per product of one facility	739,800 yen	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)			per product of one facility	15,100 yen	
Certification of drug products			per product	15,100 yen	
Other certifications			per matter of one product	8,400 yen	
Use of document storage rooms					
			per day per room	3,000 yen	Payment upon invoice sent from PMDA after the end of the period of use

* Universities/research institutions and venture companies meeting requirements specified separately.
They shall meet all of the following requirements 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