THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2011

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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.

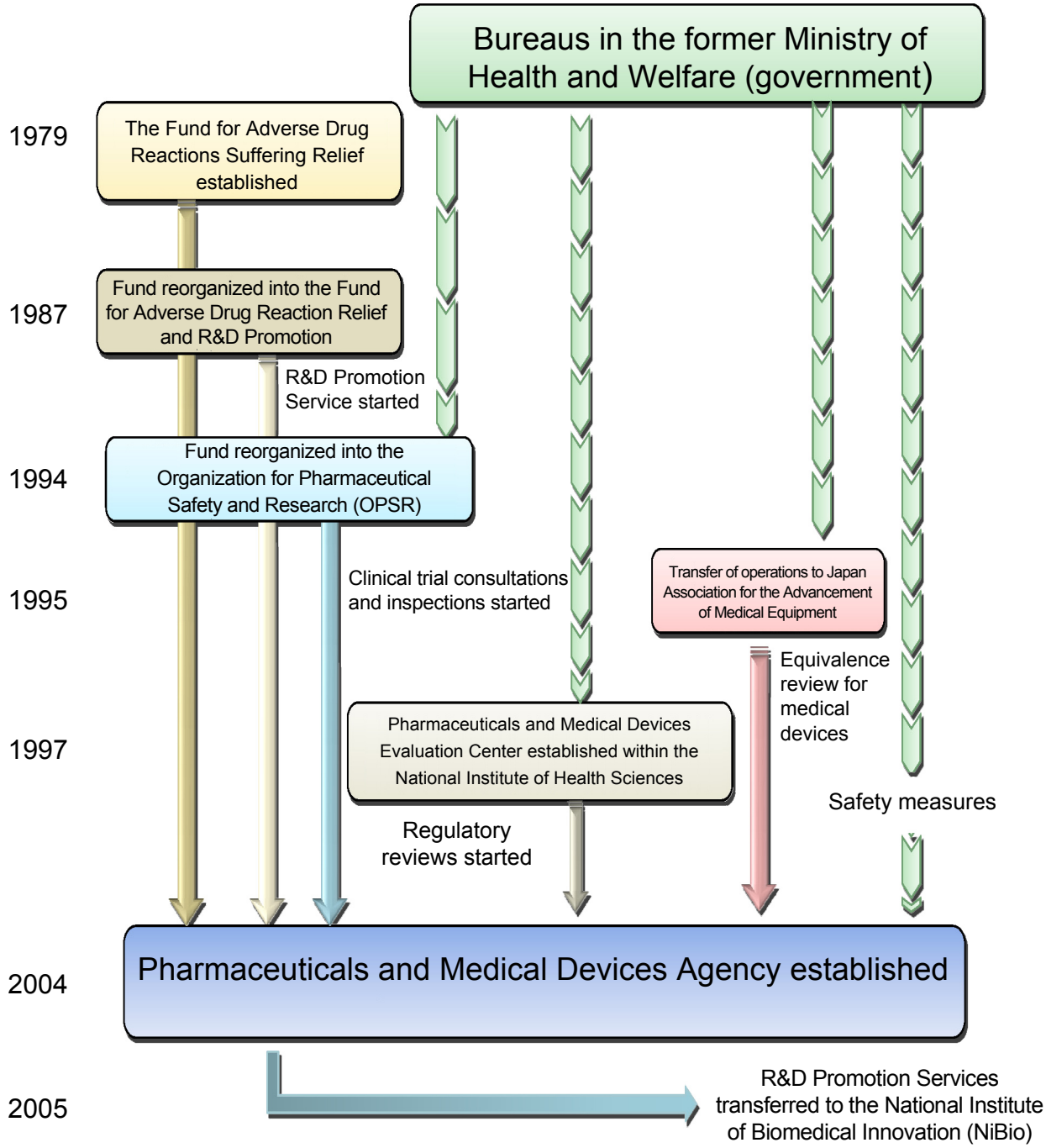
  In the midst of these situations, the Cabinet adopted the Special Service Agency Restructuring Plan in December 2001, in which it was decided that the OPSR should be dissolved and that the Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated 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, reviews of applications for confirmation of the quality and safety of cell- and tissue-based products prior to the first-in-man study, 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).

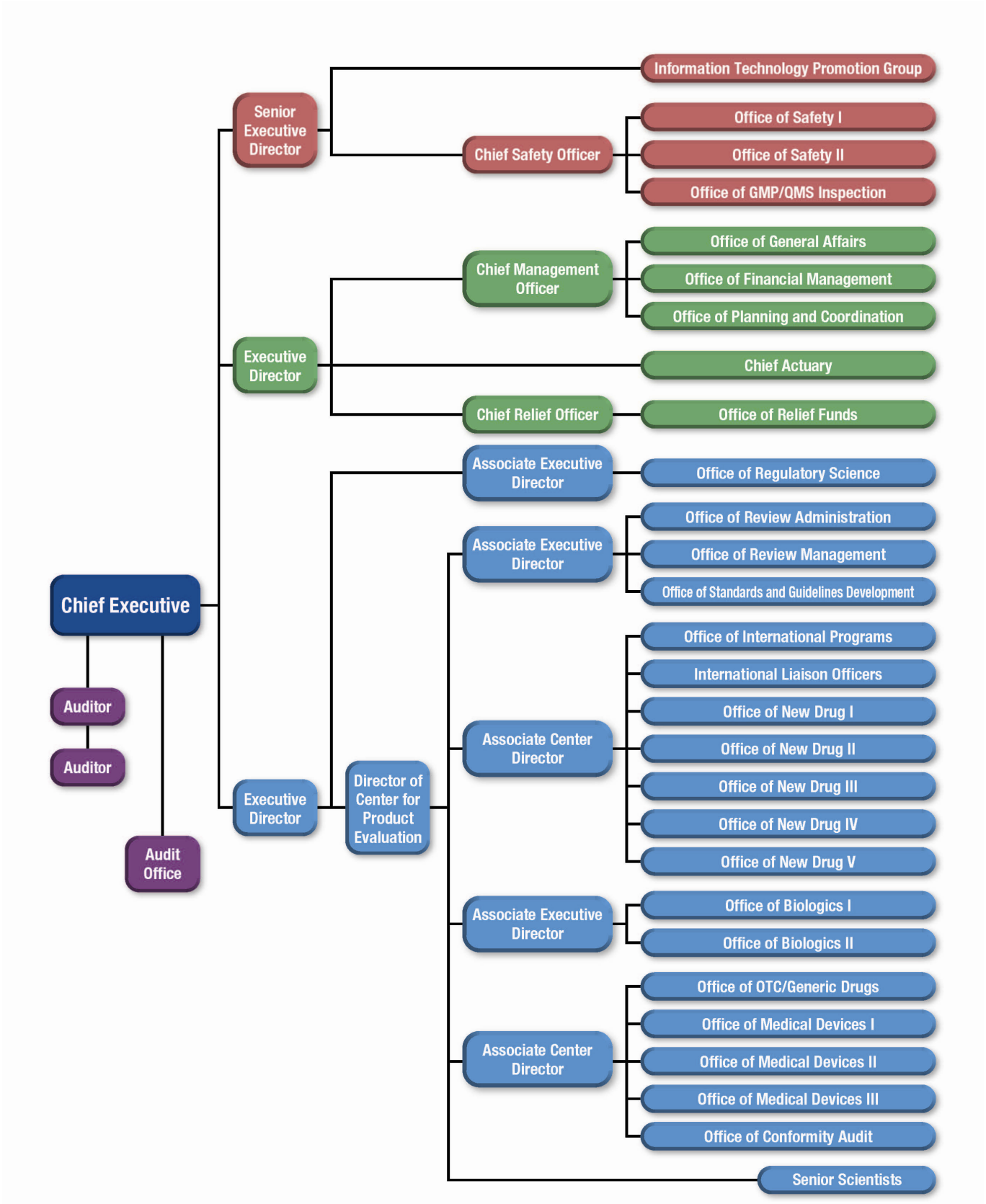
- PMDA conducts research for developing various standards, such as the Japanese Pharmacopoeia (JP), which is set forth in the Pharmaceutical Affairs Act (Research for Standards Development).

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, 2012)]



II. OPERATING PERFORMANCE FOR FY 2011

PART 1 Development of Fiscal Year 2011 Plan

1.1. Development and Implementation of Fiscal Year 2011 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.

- PMDA developed a plan for FY 2011 and submitted it to the Minister of Health, Labour and Welfare at the end of FY 2010 to carry out its operations in accordance with this plan. The FY 2011 plan was also developed based on the Second Mid-term Targets and Mid-term Plan as well as the results of the evaluation of the operating performance for FY 2010 provided by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW), and taking into account opinions from the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications (MIC) and results of budget screening by the Government Revitalization Unit (GRU).

1.2. Results of the Evaluation on Operating Performance for FY 2010

- 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 September 2, 2011, PMDA received the Results of the Evaluation on Operating Performance for FY 2010 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 2010" was released on the PMDA website, and was also reported at the Advisory Council Meeting held on November 9, 2011.

Results of Evaluation on the 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: FY2009 performance	Results of evaluation: FY2010 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	A	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 (2) Proactive public relations activity toward familiarity with the Relief System (3) Securing of efficient management of the consultation office	6	Provision of information on the System and strengthening of the consultation system	A	A
	(4) Promotion of improved efficiency of operations using databases (5) Promotion of expeditious processing of relief applications	7	Expeditious processing of applications and improvement of the system	A	A
	(6) Promotion of collaboration with the review/safety offices (7) Appropriate conduct and expansion of health and welfare services	8	Conduct of cross-functional collaboration and health and welfare services	A	A
	(8) Appropriate conduct of relief services for SMON patients and patients infected with HIV from blood preparations (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	9	Conduct of relief services for SMON patients and patients infected with HIV through blood preparations	A	A
	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)	A	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 collectiing, and systematization of organising, assessing and analysing 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 (2) Ensuring security	18	Personnel matters and establishment of security	A	A

Evaluation scale on performance of Incorporated Administrative Agency of MHLW			FY2009 performance	FY2010 performance
	S	Significantly exceeding the level prescribed in the midterm-plan	0	2
	A	Exceeding the level prescribed in the midterm-plan	18	16
	B	Somewhat exceeding the level prescribed in the midterm-plan	0	0
	C	Slightly below the level prescribed in the midterm-plan	0	0
	D	Below the level prescribed in the midterm-plan, therefore requiring drastic improvements	0	0

- The results of the evaluations 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 December 9, 2011, highlighting the following issues concerning the evaluation results for PMDA:

  Opinion from the Commission of MIC on the results of the evaluation for FY 2010

  With regard to PMDA's drug review process for fiscal years 2009 and 2010, 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."

  In the results of the evaluation by the Committee of MHLW, the item of "expeditious operation" was assessed as "S" (Significantly exceeding the level prescribed in the Mid-term Plan) based on the fact that "regarding new drug review, the median total review time for priority review products was 9.2 months against the target of 10 months, and the median total review time for standard review products was 14.7 months against the target of 16 months, showing that both are significantly exceeding the targets." However, the applicant's time in the total review time for standard review products was 6.4 months against the target of 5 months for FY 2010, which is below the target. Despite this fact, PMDA did not analyze the factors leading to the non-achievement or clearly present improvement measures, and the Committee of MHLW did not comment on this matter either.

  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. In the case of non-achievement of targets, 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. Review of System/Organization of Incorporated Administrative Agencies

- In September 2011, the "Subcommittee for Incorporated Administrative Agency Reform" was established under the control of the GRU. This subcommittee and its three working groups reviewed the system and organization of incorporated administrative agencies, holding hearings with related government ministries and agencies, incorporated administrative agencies, etc. Three sessions of hearings with PMDA were held in October 2011.

  The results of the discussion were compiled in the Subcommittee's report entitled "Review of System/Organization of Incorporated Administrative Agencies" on January 19, 2012. The Cabinet adopted the "Basic Policy for Review of System/Organization of Incorporated Administrative Agencies" on January 20, 2012.
- The necessary measures to implement this reform shall be taken toward the shift to the new system and organization in April 2014.

* Basic Policy for Review of System/Organization of Incorporated Administrative Agencies (adopted by the Cabinet on January 20, 2012) [excerpt]
[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 thorough agency evaluation system based on external viewpoints, and minimization of national burden.

- PMDA will proceed with discussions on the shift to the new organization, taking account of the policy adopted by the Cabinet.

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 2011, 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, from December 2011 to January 2012, PMDA executives conducted interviews 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 where management decisions by the Chief Executive are promptly reflected in operations.

- To this end, consecutively from FY 2010, 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 February 2012, the executives conducted interviews with office directors regarding the future actions on important issues at respective offices.

- 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 reviewed and future work policies were discussed 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 (five meetings were held during FY 2011).

- 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 2011), 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.

- Lunch meetings have been held between the Chief Executive and employees of each office to promote exchange of views regarding issues that each office faces and employees' requests.

- PMDA convened two opinion exchange sessions on new drugs (August 2011 and January 2012) and two opinion exchange sessions on drug safety (July 2011 and January 2012) with the pharmaceutical industry.

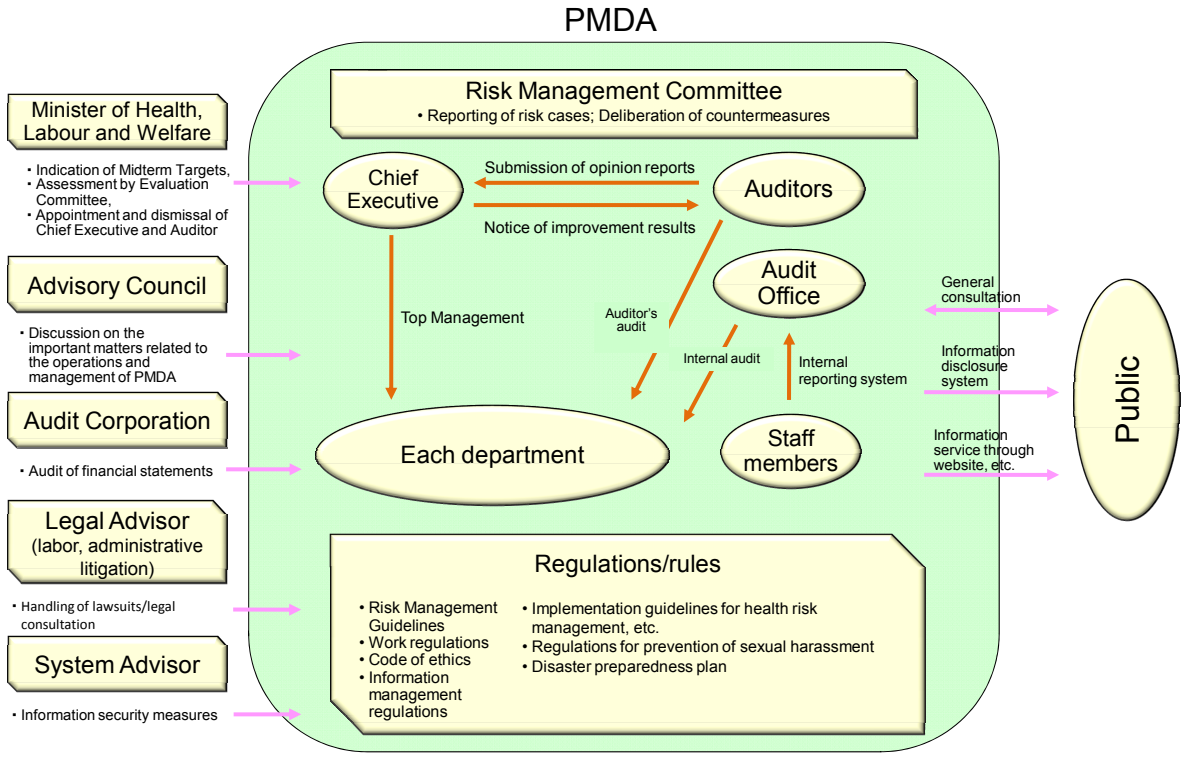
  Also, regarding medical devices and in vitro diagnostics, PMDA helped the MHLW to hold the regular opinion exchange forum on regulatory affairs for medical devices (July 2011) and to manage and hold the Action Program Review Committee's meetings (July and December 2011).

- The Risk Management Committee meetings were held once a month to allow the directors to discuss PMDA's risks. PMDA has also reviewed the rules for taking documents out of its offices.

  PMDA has continued the efforts to familiarize the executives and employees with risk management in accordance with the risk management manual which was revised. 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.

PMDA Risk Management System



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 cosmetic products, 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.

- PMDA developed the PMDA International Vision (October 11, 2011) that provides a concrete goal to be attained in the coming five to ten years while achieving the PMDA International Strategic Plan developed in 2009 as a basic policy for its overall international activities. In this way, PMDA aims at enhancing its abilities as one of the world's top level regulatory agencies, building close partnerships with Asian countries, and proactively contributing to international harmonization of standards, etc.

- From the viewpoint of proactively promoting regulatory science research and making use of its outcomes for PMDA's operations, PMDA developed the Basic Concept on Regulatory Science in PMDA (October 2011). Based on this Basic Concept, PMDA intends to carry forward international harmonization and play expected roles for the world, in addition to ensuring transparency and impartiality and enhancing public confidence.

- PMDA reorganized three divisions (the Division of Standards for Drugs and Division of Standards for Medical devices in the Office of Review Management, the Drug Master File Management Section in the Administration Division I of the Office of Review Administration) into the Office of Standards and Guidelines Development. The new office is responsible for the integrated management of the projects across multi-offices in PMDA, including the project for standards/review guidelines development. The reorganization is expected to lead to a consistent and efficient project management and extensive sharing of information within PMDA.

2.1.(3) Advisory Council meetings

- To create opportunities for exchanges 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 providing recommendations and improvement measures for 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 2011 are as follows.

Advisory Council—FY 2011

Agenda for the 1st Meeting (June 28, 2011)

(1) Annual Report for FY 2010
(2) Financial Report for FY 2010
(3) New Projects for FY 2011
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(6) Review of restrictions on career move of PMDA employees to the private sector after their resignation
(7) Others

Agenda for the 2nd Meeting (November 9, 2011)

(1) Results of the evaluation of operating performance for FY 2010 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Reinforcement of the system for medical device review
(3) Promotion of regulatory science
(4) Exchange of human resources
(5) Promotion of internationalization
(6) Status of new projects for FY 2011
    1) Project for promoting Pharmaceutical Affairs Consultation on R&D Strategy
    2) Project for developing the medical information database infrastructure
    3) Risk management plan
(7) Employment status of personnel from the private sector
(8) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(9) Others

Agenda for the 3rd Meeting (March 14, 2012)

(1) Fiscal year 2012 plan (draft)
(2) Budget for FY 2012 (draft)
(3) Revision of the rule for restrictions on employment of personnel from the private sector
(4) Review of restrictions on career move of PMDA employees to the private sector
(5) Recent main efforts
(6) Efforts toward further reinforcement of PMDA operations
(7) Status of PMDA’s responses to opinions, etc. provided at Advisory Council meetings in FY 2011
(8) Review of system/organization of incorporated administrative agencies (adopted by the Cabinet)
(9) Summary on revision of laws and regulations, including Pharmaceutical Affairs Act (A report by the Sub-committee on Reform of Regulatory Systems for Drugs, etc. of the Health Sciences Council, MHLW)
(10) Employment status of personnel from the private sector
(11) Cash contributions and contract money, etc., received by external experts commissioned for Expert Discussions
(12) Others

Committee on Relief Services—FY 2011

Agenda for the 1st Meeting (June 27, 2011)

(1) Annual Report for FY 2010
(2) Fiscal year 2011 plan
(3) Others

Agenda for the 2nd Meeting (December 21, 2011)

(1) Results of the evaluation of operating performance for FY 2010 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Operating performance by the end of October 2011
(3) Results of questionnaire for special functioning hospitals
(4) Status of efforts at medical institutions
(5) Others

Committee on Review and Safety Operations—FY 2011

Agenda for the 1st Meeting (June 28, 2011)

(1) Annual Report for FY 2010
(2) Financial Report for FY 2010
(3) New Projects for FY 2011
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(6) Review of restrictions on career move of PMDA employees to the private sector after their resignation
(7) Others

Agenda for the 2nd Meeting (December 20, 2011)

(1) Results of the evaluation of operating performance for FY 2010 (provided by the Evaluation Committee for Incorporated Administrative Agencies of MHLW)
(2) Operating performance by the end of October 2011 and issues to be addressed hereafter
(3) Employment status of personnel from the private sector
(4) Cash contributions, etc., received by external experts commissioned for Expert Discussions, etc.
(5) Others

- The above meetings were open to the public, and the minutes and materials relating to the meetings 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) 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 to adopt 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.

  (1,081 external experts are commissioned as of March 31, 2012)

- 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. (103 external experts are commissioned as of March 31, 2012)

- 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 the external experts, PMDA developed the “Rules for Convening Expert Discussions etc. by the Pharmaceuticals and Medical Devices Agency” (December 25, 2008) as a rule for the conflict of interests. The establishment of this rule enables PMDA to ensure the transparency by releasing review reports and information on the conflict of interests of commissioned external experts, and also allows outside parties to check the decision making process. Reports are made to the Advisory Council and the Committee on Review and Safety Operations regarding the cash contributions and contract money received by the external experts to whom PMDA has asked to participate in Expert Discussions on reviews and safety measures.

- In progressing with 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. Assistance for the development of the Optimization Plan for Operations and Systems were also commissioned to private companies.

- PMDA has continued to appoint a person who has advanced professional expertise regarding information systems in general as well as knowledge of pharmaceutical affairs as information system advisor, in order to ensure consistency and coordination of operations relating to the Agency’s information systems.

2.1.(5) Standardization of operating procedures

- In order to effectively utilize non-regular staff and limit the number of regular staff through standardizing various operating procedures, 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.(6) Development of databases

- In FY 2011, 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 are required to be broadly disseminated to the public are posted on the following website:
  http://www.pmda.go.jp/operations/notice.html

2.1.(7) 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 2nd revised version of the Plan in June 2011 and carried out tasks for building appropriate systems for PMDA operations based on this Plan.

  In FY 2011, design and development of the next review system were carried out in line with the results of the system requirements definition which was completed by FY 2010.

  In addition, PMDA decided to optimize the systems related to safety measures and relief services. For that purpose, the Agency created requirements definition for system development, while conducting 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 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 2011 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 2011 budget reflected about 9% reduction from the FY 2008 budget, and was added with for the expenses as listed below. However, the budget allocations for the listed expenses incurred starting in FY 2009 and FY 2010 were reduced by about 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, and FY 2011 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 2011, in order to more efficiently execute 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 papers, thereby reducing procurement costs.

  Consequently, PMDA successfully reduced general and administrative expenses by 16.7% of its budget size which was subject to more efficient budget control, even excluding the factor of 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 2011 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 2011 budget reflected about 3% 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 and FY 2010 were reduced by about 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 recommendations of the Council for Science and Technology Policy

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

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

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

- In FY 2011, 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 7.8% compared to the budget size which was subject to more efficient budget control, even excluding the budget amounts unused due to non-achievement of the target number of new employees and a smaller number of overseas GMP on-site inspections than initially expected.

2.2.(3) Competitive bidding

- PMDA promoted bidding for all contracts by measures such as shifts to general competitive bidding based on the Plan for the Review of Optional Contracts, etc. As a result, the ratio of competitive contract schemes, including competitive request for proposals and invitations to bid, to the total of all contracts increased by 15.7% in terms of the number of bids and 10.6% in terms of the monetary amount compared to the previous fiscal year.

	FY 2010	FY 2011	Change
General competitive bidding (including competitive request for proposals and invitation to bids)	116 bids (65.9%) 3,310 million yen (65.4%)	115 bids (81.6%) 4,892 million yen (76.0%)	-1 bid (15.7%) 1,582 million yen (10.6%)
Non-competitive optional contracts	60 bids (34.1%) 1,753 million yen (34.6%)	26 bids (18.4%) 1,546 million yen (24.0%)	-34 bids (-15.7%) -207 million yen (-10.6%)
Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	45 bids (25.6%) 296 million yen (5.8%)	10 bids (7.1%) 94 million yen (1.5%)	-35 bids (-18.5%) -202 million yen (-4.3%)
Total	176 bids 5,063 million yen	141 bids 6,438 million yen	-35 bids 1,375 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 2011, regarding the appropriateness of contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 4 meetings in FY 2011 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 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 2011, the collection rates achieved for ADR contributions, infection contributions, and safety measure contributions were 99.8%, 100%, and 99.6%, respectively.

FY 2011 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	714	713	99.9%	4,330
	MAHs of pharmacy-compounded drugs	6,707	6,694	99.8%	7
	Total	7,421	7,407	99.8%	4,337
Infection contributions	MAHs of approved biological products	92	92	100%	785
Post-marketing safety measures contributions	MAHs of drugs	621	620	99.8%	1,083
	MAHs of medical devices	2,169	2,149	99.1%	213
	MAHs of drugs/medical devices	205	205	100%	1,300
	MAHs of pharmacy-compounded drugs	6,707	6,694	99.8%	7
	Total	9,702	9,668	99.6%	2,603

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 contributions for adverse drug reaction fund and trends in the liability reserve

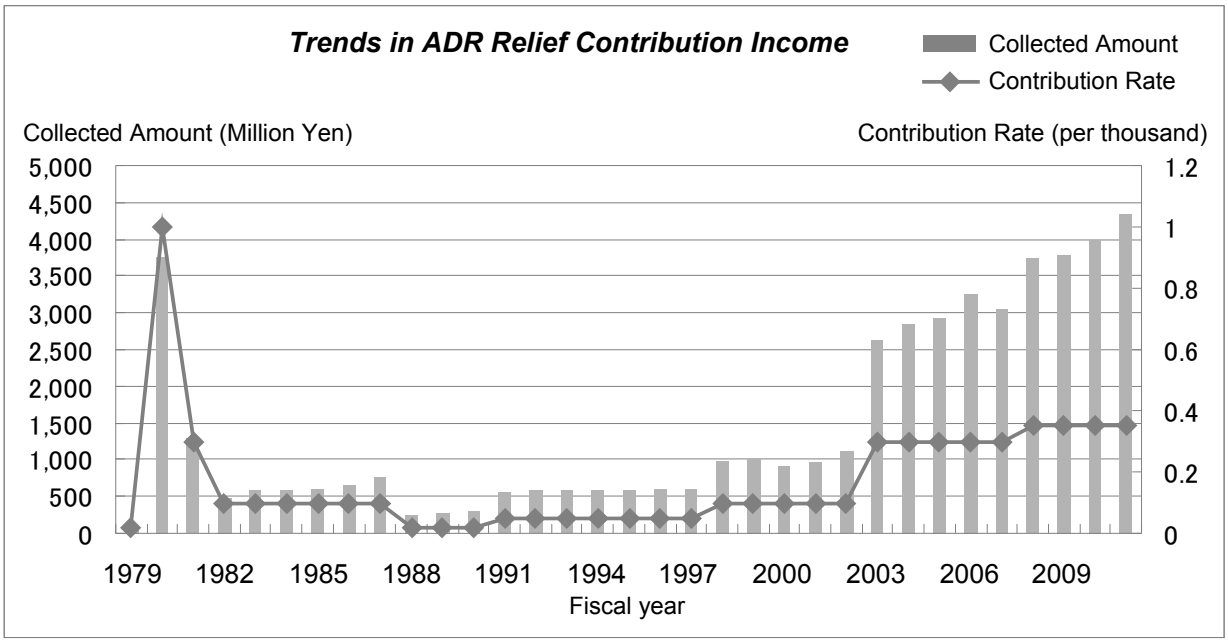
a. Adverse drug reaction fund

- To fund the relief service for adverse drug reactions, PMDA has collected contributions to the adverse drug reaction fund from marketing authorization holders of approved drugs. In FY 2011, the contribution rate applied to such marketing authorization holders was set at 0.35/1000 and the collected amount was 4,337 million yen.

(Million yen)

Fiscal Year	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
MAHs of drugs [Number of MAHs]	3,049 [762]	3,722 [752]	3,783 [742]	3,984 [716]	4,330 [713]
MAHs of pharmacy-compounded drugs [Number of MAHs]	8 [8,309]	8 [8,015]	8 [7,598]	7 [7,082]	7 [6,694]
Total amount	3,057	3,730	3,790	3,991	4,337
Contribution rate	0.3/1000	0.35/1000	0.35/1000	0.35/1000	0.35/1000

- The income of the adverse drug reaction fund and the contribution rate since the establishment of this service are shown below.



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

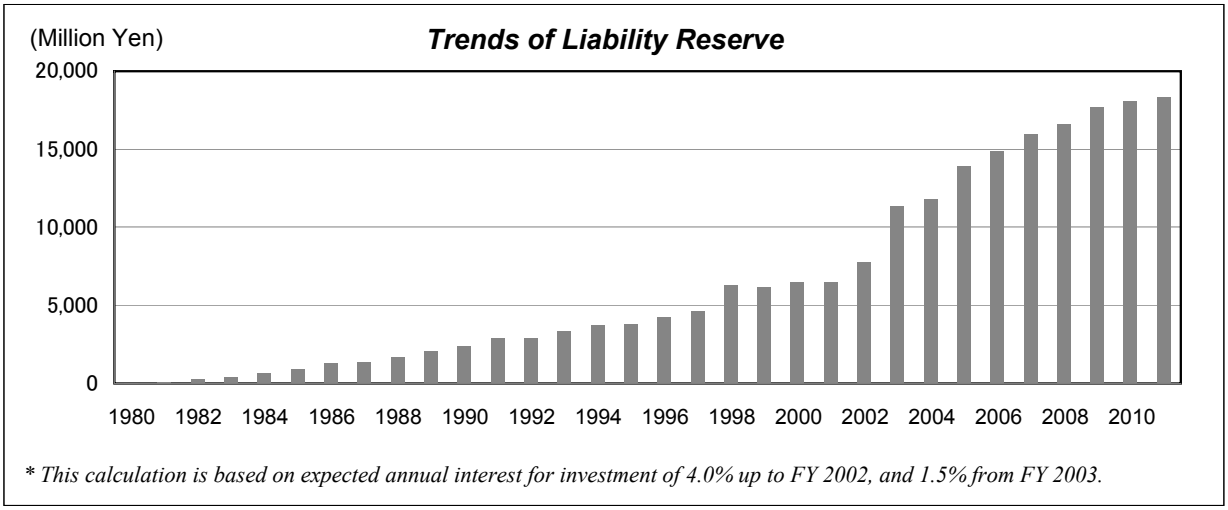
- To fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from marketing authorization holders of approved biological products. In FY 2011, the contribution rate applied to such marketing authorization holders was set at 1/1000 and the collected amount was 785 million yen.

(Million yen)

Fiscal year	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
MAHs of approved biological products [Number of MAHs]	574 [98]	620 [96]	631 [97]	693 [93]	785 [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 2011 was 18,326 million yen.



** This calculation is based on expected annual interest for investment of 4.0% up to FY 2002, and 1.5% from FY 2003.*

(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 2011, 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 2,603 million yen.

(Million yen)

Fiscal year	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
MAHs of drugs/ medical devices [Number of MAHs]	1,219 [3,094]	1,284 [3,053]	2,354 [3,019]	2,530 [2,922]	2,596 [2,974]
MAHs of pharmacy-compounded drugs [Number of MAHs]	8 [8,297]	8 [8,013]	8 [7,594]	7 [7,082]	7 [6,694]
Total amount	1,227	1,292	2,362	2,537	2,603
Contribution rate	0.11/1000	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)

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

- The personnel expenses for FY 2011 were reduced by approximately 8.4% (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 of the reform of the remuneration structure of national government employees.

- PMDA compared the remuneration system for its staff for FY 2010 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.

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

* *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 their self-starting and proactive efforts to achieve the "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 were a 7% reduction in the duration of overtime work, a 49% reduction in the number of taxi tickets used (a 51% reduction in terms of the monetary amount) and a 21% reduction in utility cost.

- In order to continuously take the measures in and after FY 2012, PMDA released the "Reinforcement of the efforts to reduce unnecessary expenditures" as partially revised on the basis of various efforts made in FY 2011. PMDA also developed the "Standard of practice for taking more efficient cost-cutting measures" as a behavioral indicator, and notified it to all staff members.

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 a weekly basis to make use of it to improve management of operations.

- Among the 1,958 inquiries that PMDA received in FY 2011, 664 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 2011	1,800 (639)	1 (0)	157 (25)	0 (0)	1,958 (664)

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 2011.

- In addition, PMDA developed a consultation manual to handle complaints, etc., from relevant companies. From among the complaints received, PMDA is reviewing those that would be helpful in improving its operations.

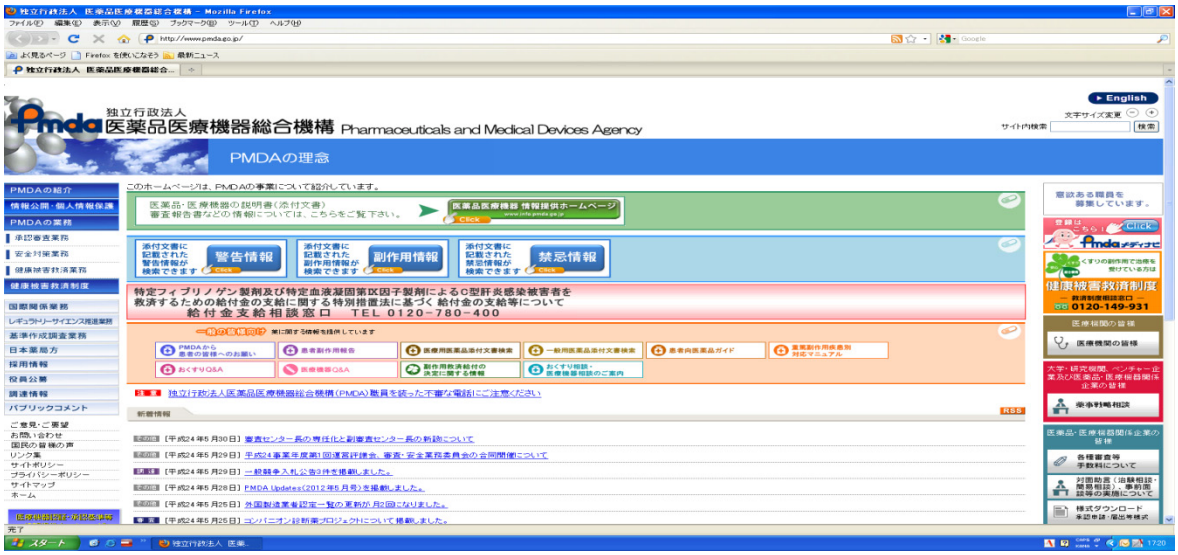
2.3.(3) Improvement in the PMDA website

- PMDA has prepared and posted on its website the Annual Report for FY 2010, which discloses the Agency's operating performance for FY 2010.

- 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.

- Taking into account opinions on the convenience of the website from visitors/users, PMDA improved its website, such as by using more easily viewable banners for the links to the Medical Product Information web page on which package inserts, review reports, etc. are posted.



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 2011, PMDA created leaflets to introduce PMDA to the general public, and distributed them at events in various locations.

  In the occasion of "Drug and Health Week," PMDA conducted PR activities with the use of transportation advertisements such as large-size posters posted in train stations, and also 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 8 prefectures.

  PMDA also issued monthly 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 (19 times in Japan and 3 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 2011, the number of requests increased by 21.3% compared to the previous fiscal year. PMDA appropriately processed them in accordance with the relevant laws and regulations.

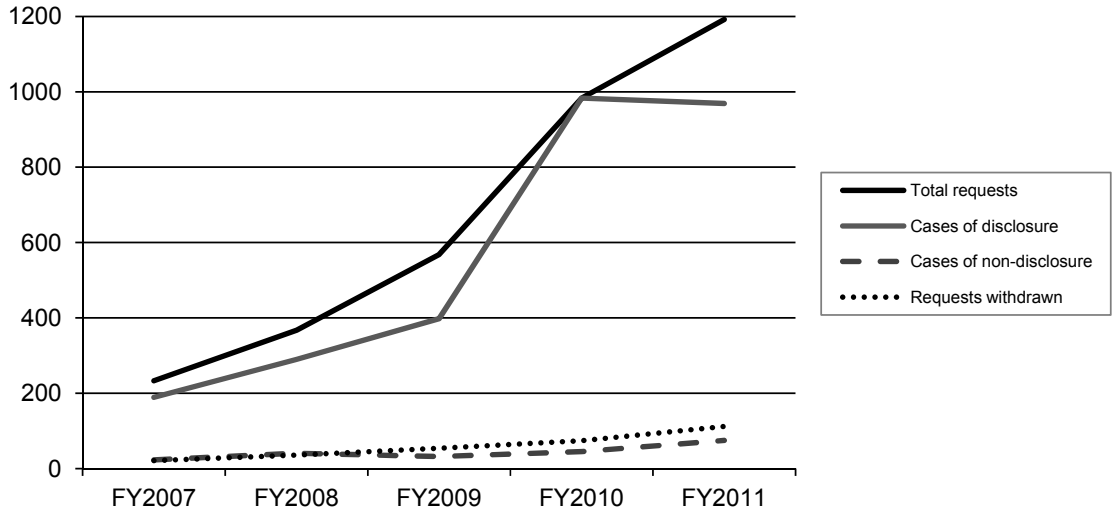
Number of Requests for Disclosure of Agency Documents (Unit: Case)

(Unit: Case)

	Total requests	Requests withdrawn	Decisions*					Objections	Carry-over into FY 2012 **
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer about existence/non-existence of the document		
FY 2007	233	21	7	182	1	22	0	2	0
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	152

**: 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 2012 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 2007	FY 2008	FY 2009	FY 2010	FY 2011	Examples
Product application review	189	315	479	902	1046	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post marketing safety	44	52	89	78	139	ADR reports
Others	0	0	0	3	7	
Total	233	367	568	983	1192	

Note: The numbers include requests that were withdrawn or 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 2012
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer about existence/ non-existence of the document		
FY 2007	3	0	2	1	0	0	0	0	0
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

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 2011, PMDA conducted internal audits on the management status of documents, the management status of cash and cash equivalents, and the status of compliance with the rule 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 2010, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2011 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 2010" on the website in September 2011.

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 raise, and promotion, to enhance the morale of employees.

- To this end, PMDA appropriately reflected the results of personnel evaluation during the period from April 2010 to March 2011 in pay raise, etc. as of July 2011. 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 four years have passed since the introduction, PMDA began to review the system to implement it in a more appropriate manner.

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 2011, 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 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 2011. 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 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 a 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 sessions of training program by inviting lecturers from organizations of adverse drug reaction sufferers and organizations of patients

(vii) On-site training programs, such as visits to drug manufacturing facilities (3 facilities), medical device manufacturing facilities (4 facilities), and IRB of medical institutions (including hands-on training, workshops, etc.)

2) Specialized Training Course

(i) Dispatch of a total of 92 employees (63 in Japan, 29 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 (39 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.

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

(iv) Dispatch of 27 employees to technical training programs conducted by external institutions (e.g., educational course on Pharmaceutical Regulatory Science of the University of Tokyo, Training Course for Experts of Pharmaceutical Affairs)

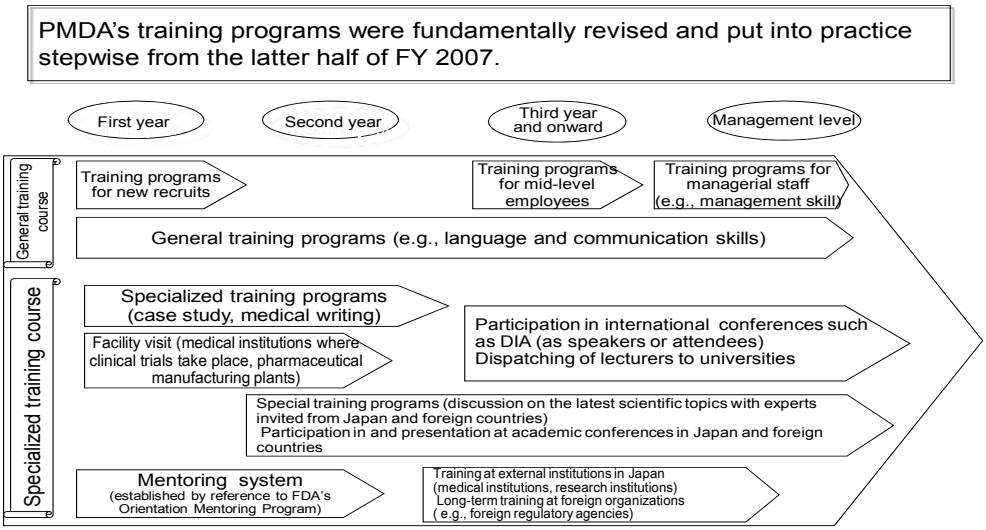
(v) Medical device training including observation of surgery and hands-on use of pacemakers, biological heart valves, and catheters for transvascular placement of stents, etc. A hands-on training on orthopedic medical devices was also provided.

(vi) Dispatch of 11 employees to three medical institutions for practical training of pharmacists conducted at hospitals and practical training at pharmacies to learn the clinical practice

(vii) Dispatch of one employee to an accounting training course sponsored by the Accounting Center, Ministry of Finance to improve administrative processing skills. Also, 11 employees attended a grade 2 or 3 bookkeeping course. Logical thinking training was conducted for administrative staff members who are on main career tracks.

(viii) Conduct of on-site GMP training programs at drug manufacturing facilities and dispatch of one employee to one facility in cooperation with 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.

- In FY 2011, personnel change and career progression were implemented in line with the basic policies for the PMDA Career Paths that were developed in March 2011.

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

- It is an important task to recruit capable persons with professional expertise while paying due attention to the neutrality and 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 2011 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2011 (as of April 1, 2012)

1) Technical employees (3 public recruitments)
   Number of applicants 491
   Number of employments 30

2) Administrative employees (1 public recruitment)
   Number of applicants 196
   Number of employments 4

FY 2011 Recruitment Activities

- PMDA information sessions
  February: Two sessions in Tokyo and one session in Osaka (total: 255 participants)
  May to June: Two sessions in Tokyo and one session in Osaka (total: 213 participants)
  September to October:
  Two sessions in Tokyo and one session in Osaka (total: 178 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 information sessions, etc.
- Information to be posted on job information websites
  - Website presenting job offers for new graduates in 2013 (NIKKEI NAVI 2013, My NAVI 2013, RIKUNABI 2013)
  - Total number of distributed direct mails: 149,876
- Recruitment advertising via academic journals
  - "Japan Medical Journal", "Japanese Journal of Pharmaceutical Health Care and Sciences", "FARUMASHIA (the Pharmaceutical Society of Japan)", "Journal of Japan Society of Mechanical Engineers", Collection of Articles from the Japanese Society of Computational Statistics, Proceedings of Lectures at the Annual Meetings of the Japanese Federation of Statistical Science Associations, Computational Statistics Seminar Textbook

Numbers of Executives and Regular Employees

	April 1, 2009	April 1, 2010	April 1, 2011	April 1, 2012	At the end of the effective period for the Second Mid-term Plan (end of FY 2013)
Total	521	605	648	678	751
Review Department	350	389	415	438	
Safety Department	82	123	133	136	
Relief Department	32	34	34	* 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 (excluding Associate Executive Director responsible for Office of Regulatory Science), Associate Center Directors, 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, Offices of Biologics I and II, 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).

** 34 as of May 1, 2012.*

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

- PMDA is careful to conduct appropriate personnel management so that suspicions 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 employment after resignation, and work restrictions for employees whose family members work in the pharmaceutical industry. PMDA conducts appropriate personnel management by keeping its staff members informed of these regulations.

- More specifically, PMDA prepared summaries and a Q & A list concerning relevant regulations, and made sure to thoroughly inform its staff of the rules during their new recruit training.

- PMDA re-edited the existing handbook in May 2011 to make it easier to use when referring to internal rules, etc., and distributed it to all executives and employees, etc.

- 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.

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 the 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 the 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 2011 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 revised relevant rules and 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	50	569
Within PMDA		862

Note: The numbers of registered companies and issued certificates as of the end of March 2012

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

3.1. Relief Fund Services

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 payment/non-payment of adverse reaction relief benefits on its website with due consideration to protecting personal information. Since February 2010, PMDA has posted cases approved/rejected in each month on its website in the following month.
  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 though 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 were created on the opening page of respective websites.

- For the purpose of carrying forward 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 2011 on its website.

- At the meeting of the Committee on Relief Services held on December 21, 2011, PMDA reported on the efforts of medical institutions to promote the use of the Relief System for Sufferers from Adverse Drug Reactions and the results of a questionnaire on the status of consultation service for adverse reactions set up at special functioning hospitals. The materials

are released on the website. Taking account of the results of the questionnaire survey, PMDA visited four special functioning hospitals to explain the relief system on site.

(ii) Improvement of brochures, etc.

- To make decision on payments promptly,

a) PMDA reviewed the descriptions of the brochure entitled “Do You Know about Relief Systems?”, which gives a clear explanation of the Relief Systems, based on the cases of benefits paid. The Agency distributed the revised brochure and posted the brochure (in PDF format) on its website in order to improve the convenience for users.

b) PMDA has been improving the instructions on the form of a medical certificate in order to make it easier for doctors to fill in. In FY 2011, the Agency newly prepared the instructions for shock/anaphylactoid symptoms and renal disorders, and also reviewed the instructions for medical certificates for disability pensions/pensions for raising handicapped children. Also, 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) PMDA prepared an instruction for preparation of claim forms, etc., enclosed it with the claim forms, etc. when sending them out, and posted it on its website.

3.1.(2) Proactive PR activities

Activities newly conducted in FY 2011

Request for cooperation to relevant organizations for MHLW administrative notices (e.g. utilization of materials of the relief system in materials of training)

In the 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, it is described that PMDA is willing to send materials explaining the relief system and dispatch lecturers. PMDA visited healthcare-related organizations, etc. (19 facilities) to request cooperation in the implementation of training for the relief system.

Activities conducted on site

(i) Academic conferences
PMDA conducted the following publicity activities at a total of 19 academic conferences:

◆ Poster presentations
- Annual Meeting of the Japanese Society of Pharmaceutical Health Care and Sciences

◆ Lectures/presentations
- Fall Meeting of Japanese Society of Allergology

◆ Distribution of brochures
- Spring Meeting of Japanese Society of Allergology
- Annual Meeting of Japanese Society of Neurology
- Annual Meeting of the Oto-Rhino-Laryngological Society of Japan

(ii) Training workshops

PMDA staff explained the Relief System at various workshops, such as:

- Clinical pharmacology workshops of the Society of Pharmacists of Japanese Red Cross
- Workshops for vaccination specialists (at 7 locations in Japan)
- Training course for the Care Section of the Tokyo Hospital Pharmacists Association
- Practical training courses of the Medical Safety Support Center (in Tokyo and Nagoya)

(iii) Request for cooperation to relevant organizations and government bodies

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

◆ Government bodies
- 2 prefectures
- 6 municipalities

◆ Public health centers
- 7 centers

◆ Medical Safety Support Center
- 2 prefectures
- 2 municipalities

◆ Medical Institutions
- 8 institutions

◆ Local medical associations/dental associations
- 3 associations

(iv) Others

- At the 25th Annual Meeting of the Japanese Society for AIDS Research, PMDA displayed posters, published information in the abstract journal, and distributed brochures, etc. about the Relief Systems.
- At the 13th Forum on Eradication of Drug-induced Sufferings (sponsored by the Japan Confederation of Drug-induced Sufferers Organizations), PMDA distributed leaflets and opened a consultation desk for the Relief Systems.

Activities conducted continuously

(i) PMDA utilized external consultants to implement efficient publicity.

(ii) In order to find out people's awareness toward the Relief Systems and provide effective publicity activities, PMDA conducted the awareness survey on the Relief System for Sufferers from Adverse Drug Reactions in the general public and healthcare professionals, and released the report on the survey results and the summary on the website. PMDA sent them out to prefectural governments and concerned bodies, etc.

- Survey period: Late-November 2011; Released on: March 13, 2012

Results of the awareness survey conducted in FY 2011 were as follows:

General public

FY 2011 Survey on “Relief System for Sufferers from Adverse Drug Reactions” (n=3,090)

I know it. (5.0%) I have heard of the name. (18.9%) Total: 23.9%

(Reference)

FY 2010 Survey on “Relief System for Sufferers from Adverse Drug Reactions” (n=21,000)

I know it. (5.1%) I have heard of the name. (13.8%) Total: 18.9%

Healthcare professionals

FY 2011 Survey on “Relief System for Sufferers from Adverse Drug Reactions” (n=3,412)

I know it. (50.2%) I have heard of the name. (32.5%) Total: 82.7%

(By job category)

	I know it.	I have heard of the name.	Total:
• Physicians	(47.0%)	(42.4%)	89.4%
• Pharmacists	(84.3%)	(14.1%)	98.4%
• Nurses	(20.7%)	(39.4%)	60.1%
• Dentists	(46.3%)	(37.3%)	83.6%

(Reference)

FY 2010 Survey on “Relief System for Sufferers from Adverse Drug Reactions” (n=3,377)

I know it. (53.1%) I have heard of the name. (27.9%) Total: 80.9%

(By job category)

	I know it.	I have heard of the name.	Total:
• Physicians	(50.2%)	(39.0%)	89.2%
• Pharmacists	(89.3%)	(9.8%)	99.1%
• Nurses	(21.1%)	(32.4%)	53.5%
• Dentists	(46.5%)	(36.2%)	82.7%

(iii) The original character "Doctor Q" was created. Also, a period of three months from September to November, 2011 covering the "Drug and Health Week (October 17 to 23)" was set up as an intensive publicity period, and a nationwide publicity campaign for the Relief Systems was carried out (some activities have been continuing even in the fiscal year starting in April 2012).
- Newspaper advertisement
- Billboard advertisement in train stations
- Internet advertisement (banner ads)
- Advertisement in professional journals (medical journals, medical newspapers)
- Advertisement at hospitals (in-house television broadcasting, leaflet placement)
- Distribution of and request for displaying publicity posters, etc. (dispensing pharmacies, drug stores)
- Distribution of leaflets (dispensing pharmacies)
- Utilization of PMDA website

(iv) PMDA posted a poster on the Relief Systems on its website (the poster can be downloaded from the website), as pharmacies are required to display such information.

(v) PMDA placed the publicity information on its website so that it can be downloaded from the website and put on medicine envelopes.

(vi) 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 so that it can be utilized in lectures, briefing sessions, etc. on the Relief System held at universities and hospitals.

(vii) PMDA conducted publicity activities using the brochure entitled “Do You Know about Relief Systems?”
- Enclosed the brochures in the Journal of Japan Medical Association (about 171,000 copies) and the Journal of Japan Pharmaceutical Association (about 101,000 copies).
- Posted the brochure in electronic medium (PDF format) on the website.
- Distributed the brochure to universities/colleges (colleges of pharmacy, faculties of pharmaceutical sciences), clinical training hospitals, university hospitals, nursing training schools, etc.
- PMDA requested the MR Education & Accreditation Center of Japan to distribute the brochure at the MR educational training conducted by the Center.

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

(ix) PMDA requested the Federation of Pharmaceutical Manufacturers' Associations of Japan to place the information on the Relief Systems in a magazine on drug safety updates (DSU) published by the Federation, and distributed the magazine to all medical institutions.

(x) 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 to relevant organizations, etc.

(xi) PMDA requested the Japan Red Cross 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 Center delivers blood products.

(xii) 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.

(xiii) PMDA placed the information on the Relief Systems in “medication record book” published by the Japan Pharmaceutical Association.

(xiv) 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.”

(xv) PMDA placed an article titled "Cases of Non-payment under the Relief System for Sufferers from Adverse Drug Reactions and Proper Use of Drugs" in the "Pharmaceuticals and Medical Devices Safety Information No. 286 (December 2011)" issued by the MHLW.

(xvi) 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).

(xvii) In FY 2011, PMDA placed the website address for the Relief Systems in the education material "What are Drug-Induced Sufferings?" which was distributed to junior high students nationwide by the MHLW.

Newspaper advertisement using the original character "Doctor Q"

Brochure "Do you know about Relief Systems?"

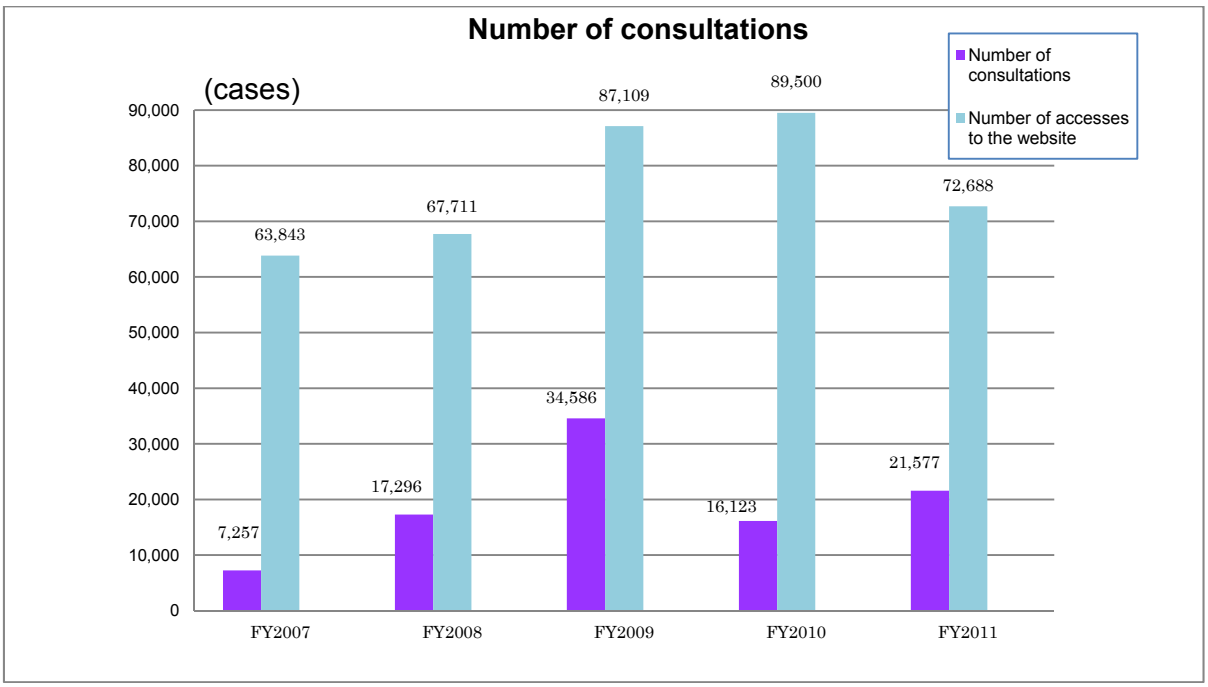
PR by using billboards in train stations

3.1.(3) Efficient management of the consultation service

- In FY 2011, the number of consultations at the Relief System Consultation Service was 21,577, with a ratio of 134% compared with the previous fiscal year (16,123 consultations).
- In FY 2011, the number of accesses to the website was 72,688, with a ratio of 81% compared with the previous fiscal year (89,500 accesses).
- The number of accesses to the feature page of the Relief System was 397,583.
- 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 2007	FY 2008	FY 2009	FY 2010	FY 2011	Compared with FY 2010
Number of consultations	7,257	17,296	34,586	16,123	21,577	134%
Number of accesses to the website	63,843	67,711	87,109	89,500	72,688	81%

*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. The number of consultations that were actually handled by PMDA were 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

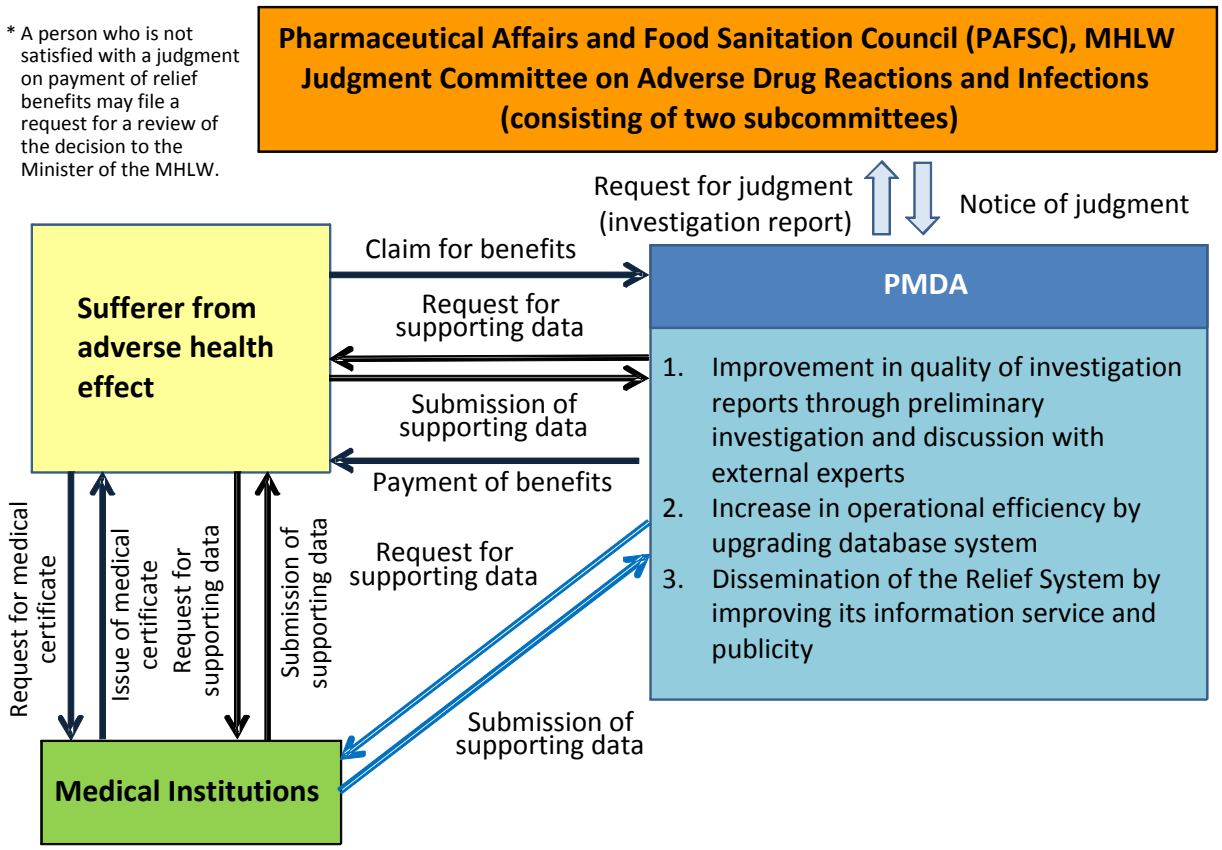
3.1.(4) Integrated management of information through databases

- To make operations more efficient and swift, PMDA upgraded the Integration and Analysis Systems for Databases on Relief Benefits services as follows:
  - Development of a database of current states of disability pension recipients, etc. and visualization of changes in disability grade
  - Enhancement of progress management by difficulty level of cases with the aim of administrative processing within 6 months.

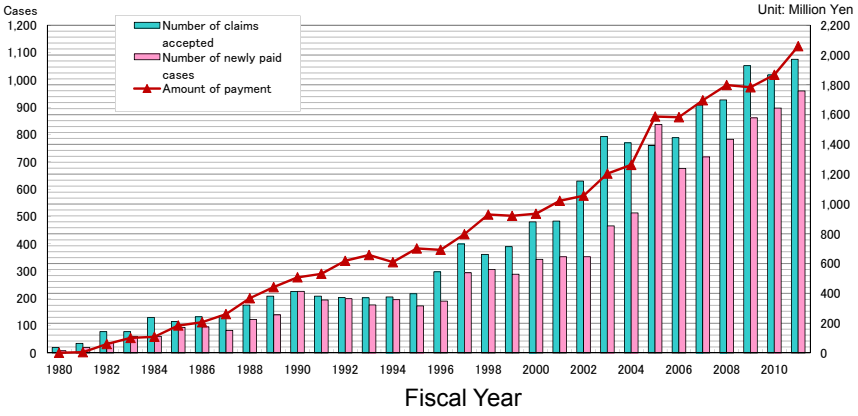
3.1.(5) Prompt processing of relief benefit claims

- 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 (MHLW) to make a medical and pharmaceutical judgment on the claim. For this purpose, the following operations are conducted: (i) Fact-finding investigations of the event included in the claim, (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



Payment of Relief Benefit



FY 2011

- Relief services for adverse drug reactions: 1,075 claims received, 1,103 cases for which judgment on approval/rejection was made (of which 959 were judged approved)
- Relief services for infections: 9 claims received, 7 cases for which judgment on approval/rejection was made (of which 3 were judged approved)

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 2011, PMDA planned to increase the number of claims judged within 6 months by 10% compared with FY 2010, while ensuring that 70% or more of claims are judged within 8 months of the standard administrative processing time. The meeting of the Judgment Committee on Adverse Drug Reactions and Infections scheduled to be held in March 2011 was cancelled due to the Great East Japan Earthquake. The number of claims judged within 8 months was 809, accounting for 73.3% of the total (Note). The number of claims judged within 6 months was 534, resulting in an increase of 23.0% compared with 434 claims judged in FY 2010. The percentage of claims judged within 6 months increased from 42.5% in FY 2010 to 48.4% in FY 2011, showing a steady progress toward achievement of the goal in the Second Mid-term Plan.

Note: A total of 70 claims scheduled to be on the agenda in March were deliberated at the meeting in May. Among them, 32 claims were judged within 8 months. When the duration of administrative processing was estimated, supposing that these 70 claims were deliberated at the meeting in March while using actual number of days of administrative processing for each case, the number of claims judged within 8 months was 60. When the results for FY 2011 were estimated by using the results of the above estimation, the number of claims judged within 8 months was 837, and the achievement rate was 75.9%.

(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 2011 is shown below.

(Unit: Cases)

Fiscal Year			FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of claims			908	926	1,052	1,018	1,075
Number of judged cases			855	919	990	1,021	1,103
		Approved	718	782	861	897	959
		Rejected	135	136	127	122	143
		Withdrawn	2	1	2	2	1
	Within 8 months	Number of cases	634	683	733	765	809
		Achievement rate*1	74.2%	74.3%	74.0%	74.9%	73.3%
	Within 6 months	Number of cases	367	355	360	434	534
		Achievement rate*2	42.9%	38.6%	36.4%	42.5%	48.4%
Cases in progress*3			677	684	746	743	715
Median processing time			6.4 months	6.5 months	6.8 months	6.4 months	6.1 months

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

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

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

b. Number of claims by type of benefit

The numbers of claims filed in FY 2011 by type of benefit are shown below.

(Unit: Cases)

Fiscal Year		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of claims		908	926	1,052	1,018	1,075
Types of benefits	Medical expenses	730	769	902	854	909
	Medical allowances	786	824	943	911	964
	Disability pensions	70	79	71	74	77
	Pensions for raising handicapped children	10	7	11	4	4
	Bereaved family pensions	33	26	36	46	47
	Lump-sum benefits for bereaved families	72	49	50	54	63
	Funeral expenses	105	78	83	100	107

Note: A single claim could include the payment of more than one type of benefit.

c. Judgment status by type of benefit

The number of approved cases and amounts of benefits in FY 2011 by type of benefit are shown below.

(Unit: thousand yen)

Types	FY 2007		FY 2008		FY 2009	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	603	67,603	659	75,339	763	86,666
Medical allowances	651	62,668	711	62,055	813	70,963
Disability pensions	42	730,007	27	747,362	26	804,251
Pensions for raising handicapped children	7	35,760	7	40,127	7	50,804
Bereaved family pensions	20	501,454	22	523,455	18	545,843
Lump-sum benefits for bereaved families	39	286,373	47	335,977	30	215,342
Funeral expenses	63	12,661	72	14,391	46	9,914
Total	1,425	1,696,525	1,545	1,798,706	1,703	1,783,783

Types	FY 2010		FY 2011	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	803	87,475	836	93,284
Medical allowances	837	71,142	895	75,198
Disability pensions	38	853,854	28	881,885
Pensions for raising handicapped children	5	44,210	6	49,606
Bereaved family pensions	31	583,501	35	614,318
Lump-sum benefits for bereaved families	29	214,081	47	328,093
Funeral expenses	63	12,927	80	16,006
Total	1,806	1,867,190	1,927	2,058,389

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 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 2011 is shown below.

(Unit: Case)

Fiscal Year		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of claims		9	13	6	6	9
Number of judged cases		5	11	10	7	7
	Approved	3	6	8	6	3
	Rejected	2	5	2	1	4
	Withdrawn	0	0	0	0	0
Cases in progress*		5	7	3	2	4
Achievement rate**		100.0%	100.0%	100.0%	85.7%	100.0%
Median processing time		3.8 months	5.2 months	5.4 months	6.9 months	4.4 months

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

** *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 2011 by type of benefit are shown below.

(Unit: Case)

Fiscal Year		FY 2009	FY 2008	FY 2009	FY 2010	FY 2011
Number of claims		9	13	6	6	9
Types of benefits	Medical expenses	7	11	5	5	6
	Medical allowances	8	13	6	5	8
	Disability pensions	1	0	0	1	0
	Pensions for raising handicapped children	0	0	0	0	1
	Bereaved family pensions	0	0	0	0	0
	Lump-sum benefits for bereaved families	0	1	0	1	0
	Funeral expenses	0	1	0	1	0

Note: A single claim could include the payment of more than one type of benefit.

c. Judgment status by type of benefit

The number of approved cases and amounts of benefits in FY 2011 by type of benefit are shown below.

(Unit: thousand yen)

Types	FY 2007		FY 2008		FY 2009		FY 2010		FY 2011	
	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	3	102	5	204	6	375	5	425	3	213
Medical allowances	3	352	6	386	8	567	5	384	3	282
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,378	–	2,378	–	2,378	–	2,378	-	2,370
Lump-sum benefits for bereaved families	–	–	1	7,135	–	–	1	7,160	–	–
Funeral expenses	–	–	1	199	–	–	1	193	–	–
Total	6	2,833	13	10,302	14	3,320	12	10,540	6	2,865

Note: Since the amounts are rounded off to the nearest thousand yen, the sum of 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 information on cases judged to be approved/rejected for relief benefits were provided to the Offices of Safety, etc. with due consideration to protecting personal information. In addition, PMDA conducted liaison meeting sessions about once a month between the Office of Relief Funds and Offices of Safety 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 also provided via e-mail in "PMDA medi-navi" to healthcare professionals, etc. who subscribe the e-mail service.

- PMDA promoted the collaboration between the "Relief System Consultation Service" and the "Drugs and Medical Devices Consultation Service" that is provided by the safety department, by clarifying their respective roles in consultation services.

- A link to the web page of the "Relief System for Sufferers from Adverse Drug Reactions" was set up in the web page of "Patient's Report for Adverse Drug Reactions."

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 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 is 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 2011, a survey was conducted in 62 persons, and also the results of the operating performance for FY 2010 were organized and sent to the members of the Committee on Relief Services and other concerned parties. The number of survey subjects with Reye syndrome was smaller compared with those with Stevens-Johnson syndrome, and therefore survey subjects for FY 2012 were reconsidered. As a result, it was decided that sufferers from Reye syndrome-like serious adverse health effects will be newly added to survey subjects. Also, the survey form was reviewed so that the results can be used for reviews of QOL improvement measures, etc.

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 (62 volunteers in FY 2011).

Investigative Research Team

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

(ii) Consultation Services to Address Mental Issues, etc.

The survey on the actual state of adverse health effects stemming from adverse drug reactions, 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 as a result, Consultation Services to Address Mental Issues, etc. was 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 2011, 56 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 drug(s) that is considered or suspected to have caused the adverse reaction to the card holder. In FY 2011, the card was issued to 431 persons. In addition, the explanatory text on the distribution of the benefit recipient card as proposed at the Committee on Relief Services was reviewed.

(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 services and measures for improving the QOL of sufferers.

In FY 2011, a survey was conducted in 189 persons, and also the results of the operating performance for FY 2010 were organized and sent to the members of the Committee on Relief Services and other concerned parties. Also, the survey form was reviewed toward FY 2012 so that the results can be used for reviews of QOL improvement measures, etc.

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 (189 volunteers in FY 2011).

Investigative 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

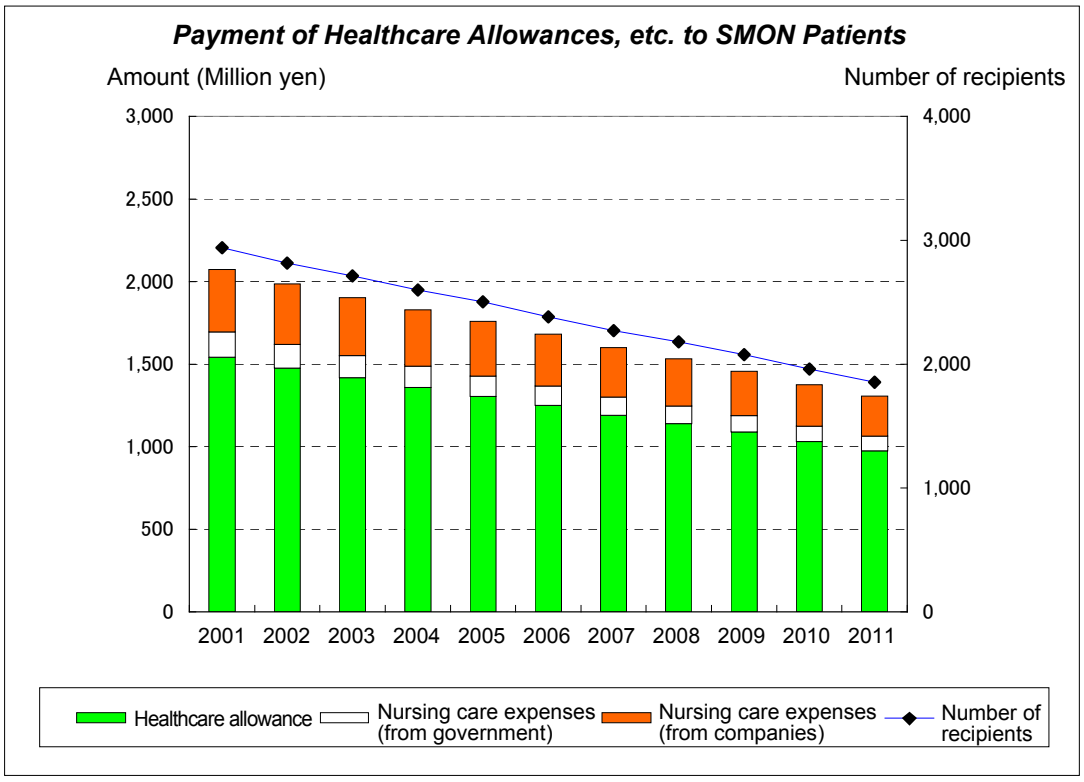
PMDA appropriately provided healthcare allowances, etc. to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

(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. In FY 2011, the number of patients receiving such allowances was 1,855, and the total amount paid was 1,306 million yen.

Fiscal Year		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of recipients		2,269	2,180	2,075	1,960	1,855
Amount paid (thousand yen)		1,601,134	1,531,745	1,457,724	1,375,622	1,306,329
Break down	Healthcare allowances	1,191,245	1,140,517	1,089,491	1,031,376	975,567
	Allowance for nursing care expenses (from companies)	299,108	284,981	268,749	250,946	241,890
	Allowance for nursing care expenses (from government)	110,781	106,247	99,485	93,300	88,872

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)

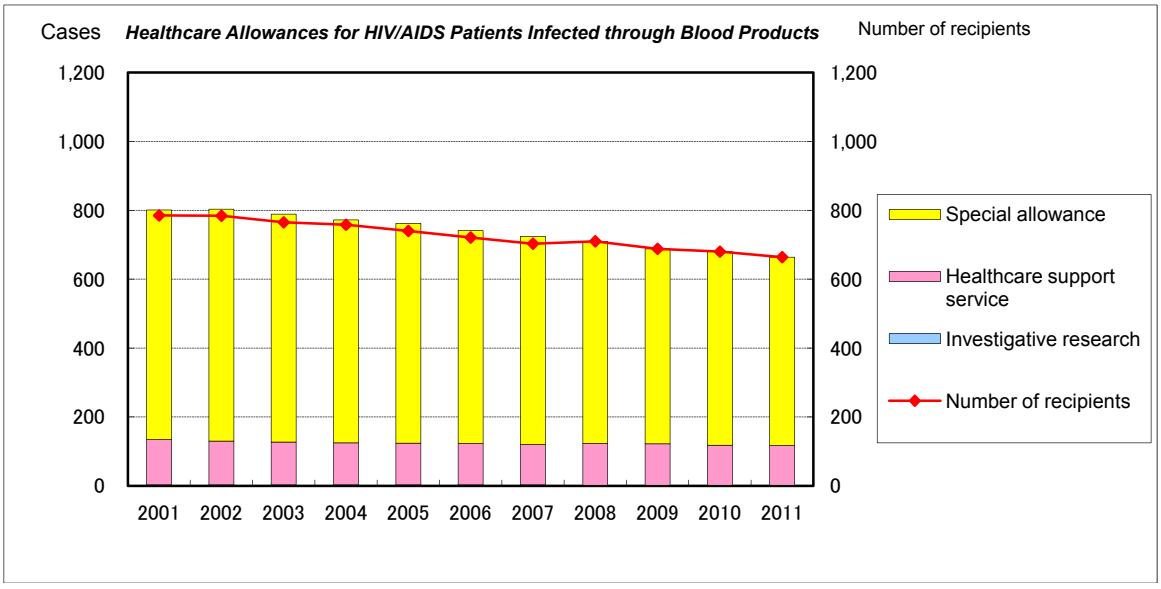
- PMDA provides allowances relating to the following 3 services for HIV-positive patients affected through blood products under commission of the relevant organization. In FY 2011, 547 HIV-positive patients received allowances relating to the investigative research, 115 AIDS patients

received allowances relating to the healthcare support service and 2 AIDS patients received special allowances. The total number of patients receiving allowances relating to the 3 services was 664, and the total amount paid was 519 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 2007		FY 2008		FY 2009	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	603	327,857	586	320,122	566	313,676
Healthcare support services	117	224,796	121	211,800	120	210,600
Special allowance	3	8,084	2	6,300	2	6,300
Total	723	560,737	709	538,222	688	530,576

Fiscal Year	FY 2010		FY 2011	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	562	309,355	547	302,763
Healthcare support services	116	206,100	115	210,000
Special allowance	2	6,300	2	6,276
Total	680	521,755	664	519,039



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 220, with 4,732 million yen as the total amount paid in FY 2011.

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of recipients	108	660	661	305	220
(Of which: number of recipients of additional payment)	(0)	(4)	(22)	(20)	(20)
Amount paid (Thousand yen)	2,360,000	13,632,000	13,748,000	6,293,000	4,732,000
(Of which: amount of additional payment)	(0)	(68,000)	(272,000)	(324,000)	(268,000)
Number of consultations (cases)	16,814	3,607	894	1,286	674

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 2011 plan.

3.2.(1) Accelerated Access to the Latest Drugs and Medical Devices

New drugs

- Based on the 5-year Strategy for Creating Innovative Drugs and Medical Devices (dated April 26, 2007) and the roadmap for expediting reviews, PMDA have taken various measures with the aim of resolving the lag of 2.5 years between approval of new drugs in the United States (US) and approval in Japan, by FY 2011.

(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 2004, the Pharmaceuticals and Medical Devices Agency (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 the system were made.

  1) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency (PMDA) was established through the integration of three separate organizations that were responsible for reviews and related services.

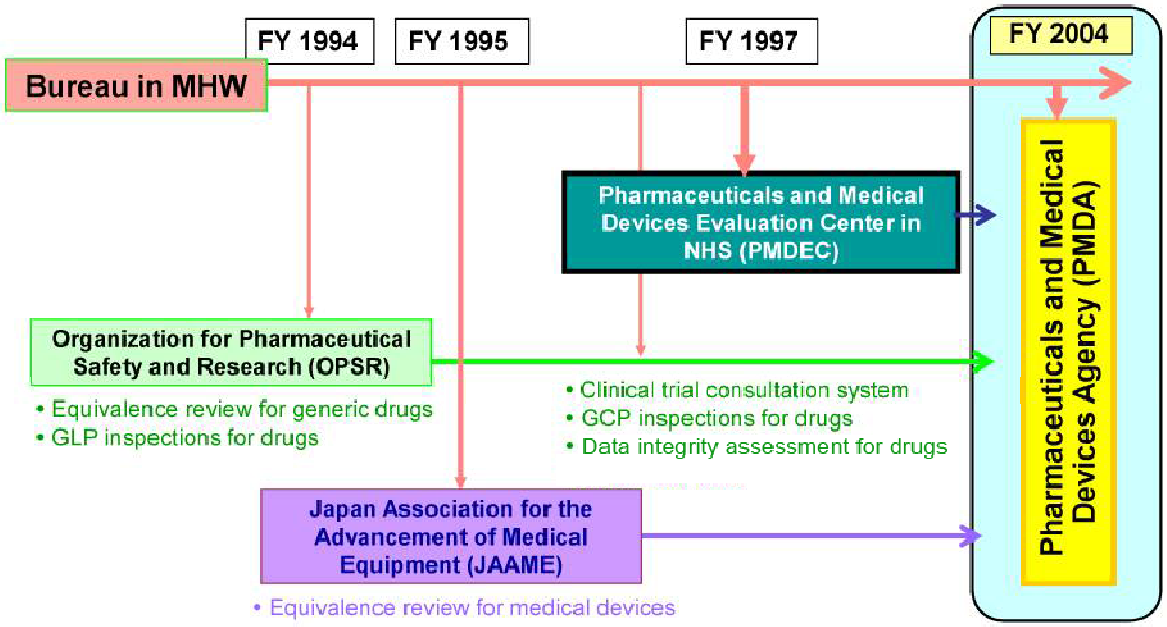
  2) Substantial increase in the number of its staff including reviewers.

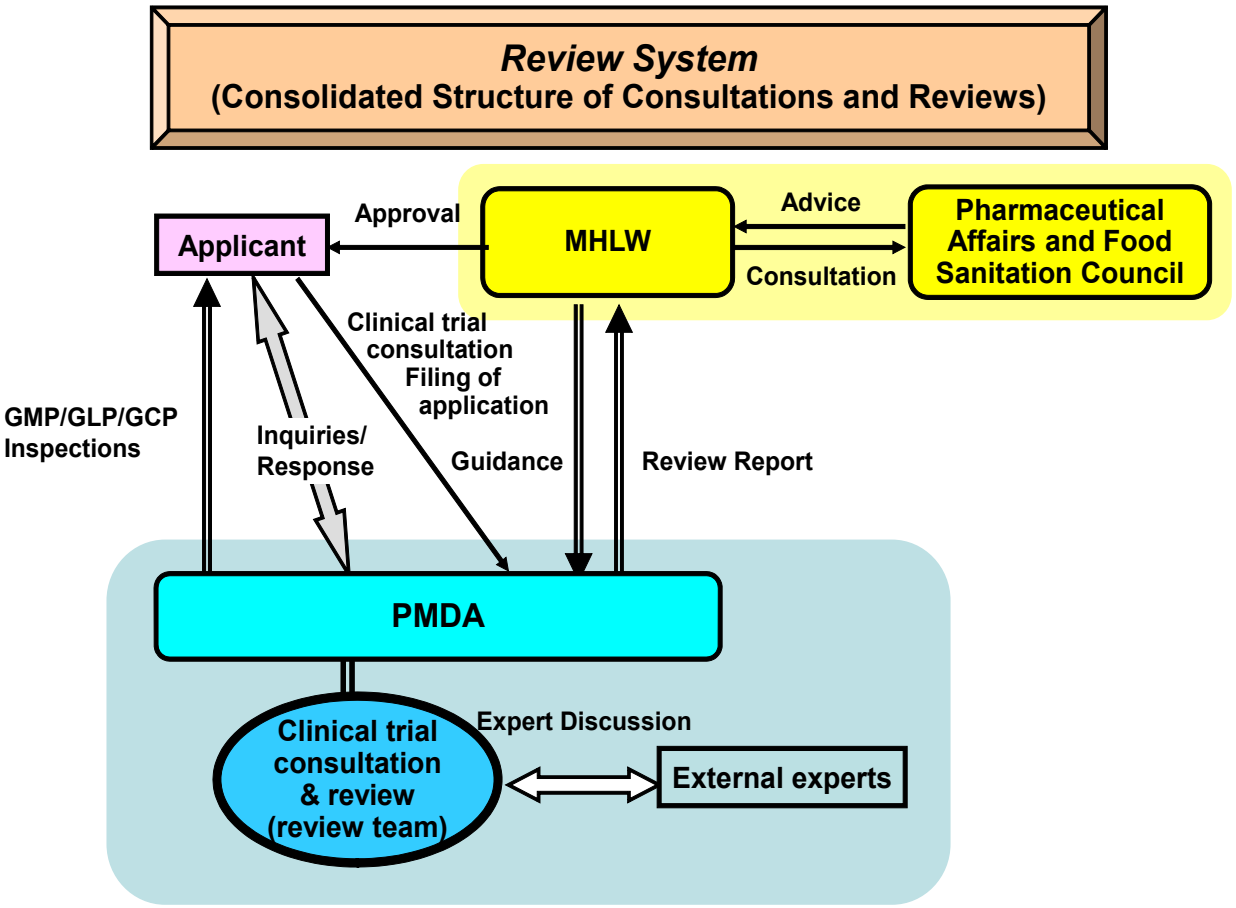
  3) Introduction of a system in which the process from clinical trial consultations until reviews is conducted by the same team with the same staff members.

  4) Enhancement of reviews of biological and biotechnology-derived products.

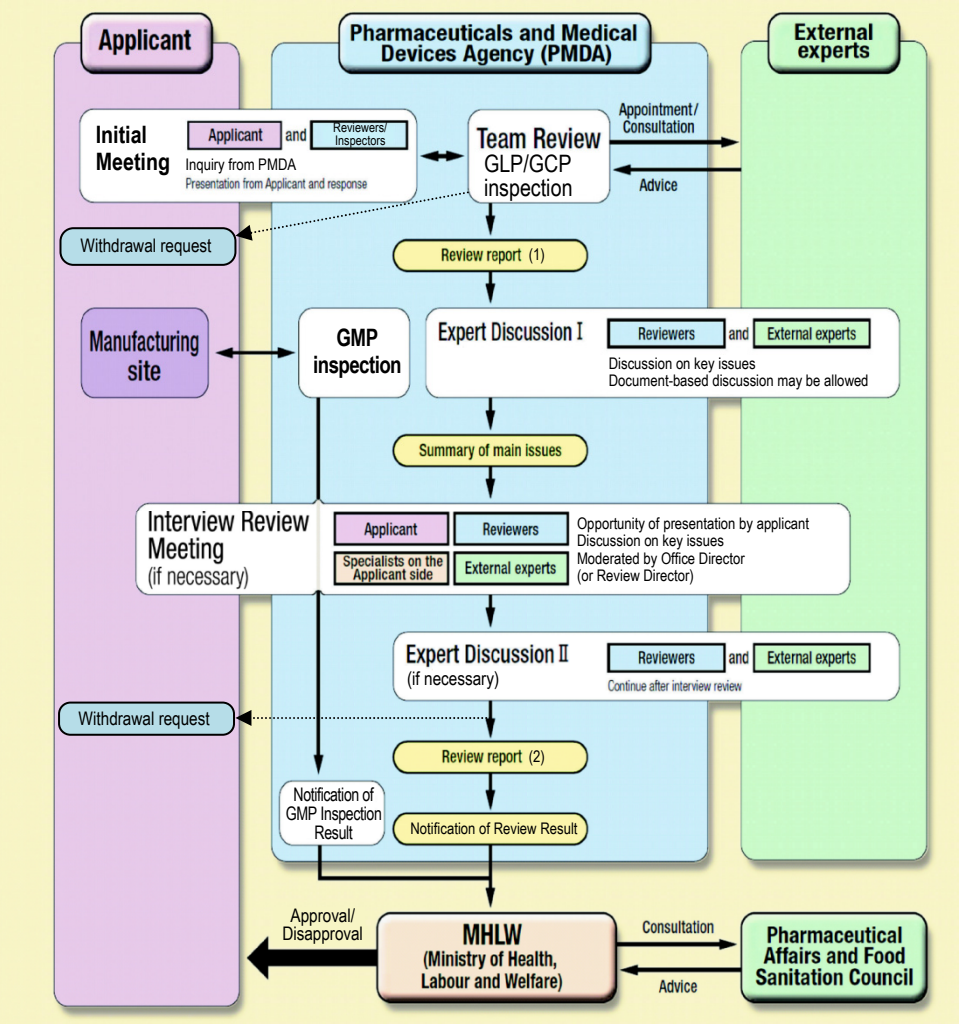
  5) Reinforcement of functions for reviewing medical devices.

Transition of approval review system on drugs and medical devices





Flowchart of review process



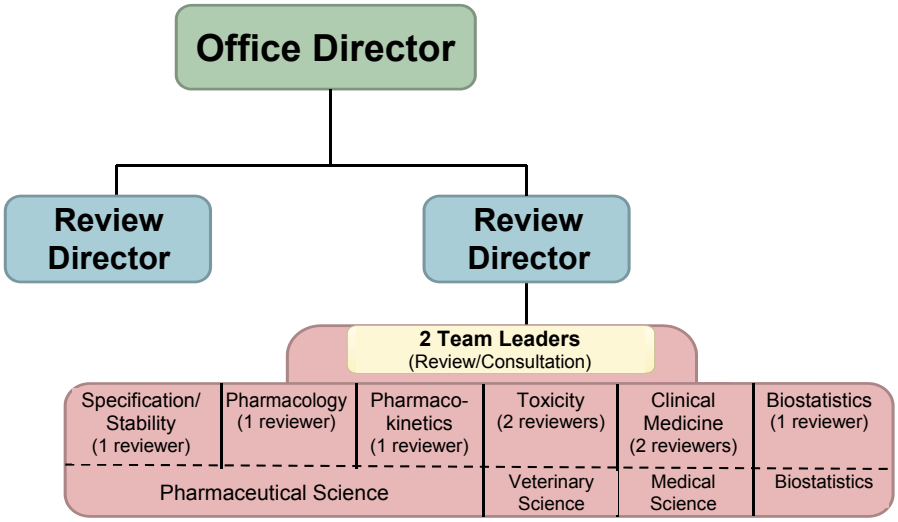
Review Performance for FY 2011 (drugs)

(i) Number of Expert Discussions conducted: 180 (of which, 137 through document-based discussions, 43 through meetings)

(ii) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 69
Applications reported to the Drug Committees (under PAFSC): 50

- 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, medicine, veterinary medicine, biostatistics, or other specialized courses. The review team is typically comprised of team leader(s), deputy team leader(s), and reviewers specialized 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
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

- 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 2011, 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 constantly convened in FY 2011. 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 (10 meetings were held in FY 2011).

  The office directors of review divisions also assessed the operational progress on a routine basis. Based on the reports from these office directors, the Director and Associate Center Director of the Center for Product Evaluation provided necessary guidance at the Review Segment Committee for Progress Management.

- 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 review to them.

c. Standardization of review

- To provide basic considerations for reviewers, the “Points to be Considered by the Review Staff Involved in the Evaluation Process of New Drug” was released in FY 2008 from the perspective of clarification of review standards. This information was then explained to reviewers and was also posted on the PMDA website.

d. Consultations and reviews based on medical care needs

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

  Note: A total of 1,137 PMDA staff members participated in 338 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, Director of National Hospital Organization Nagoya Medical 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.

- For cellular and tissue-based products that are developed with state-of-the-art technology such as pharmacogenomics and regenerative medicine, there is an extremely high need for advice on product development and regulatory submission, as there are only a few precedents for such types of product development.

In order to respond to these needs, PMDA continued to conduct consultations on pharmacogenomics/biomarkers that were started in FY 2009 to qualify biomarkers, etc., and prepared for adding a new consultation category to deal with the plans of studies to be conducted to prepare data for biomarker qualification.

e. Consistency between clinical trial consultations and reviews

- In order to ensure the consistency between clinical trial consultations and reviews, PMDA flexibly organizes teams where necessary while maintaining the connection between consultations and reviews. All of the clinical trial consultations involved the participation of members of the relevant review team.

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 on use results that have been obtained by marketing authorization holders, etc.

  Already-approved drugs that have been specified by the Minister of Health, Labour and Welfare are re-evaluated for the 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, the 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, 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 2011, 81 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Products that underwent re-examination		95	235	164	115	81
Re-evaluation	Products that underwent re-evaluation for drug efficacy	0	0	0	0	0
	Products that underwent re-evaluation for quality	434	89	12	53	0

Note: Number of products for which re-examination was completed 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.)*

- This new application/review system enables the PMDA staff to manage the 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 2011 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 were compiled. In addition, a procurement specification sheet was prepared and developers were selected for the design and development to be implemented from the second half of FY 2011 to FY 2013.

  2) Upgrading of the user fees management function, etc. for the review support system for drugs, etc.

     - In order to promote the optimization of review operations for drugs, etc., PMDA made the following changes to the system: improvement of the screen to manage the receipt of on-site inspection user fees, addition of the function to manage the collection of travel expenses for on-site inspection, addition of the function to manage user fees collected as miscellaneous incomes, and improvement of the screen to manage the receipt of GCP inspection fees for generic drugs.

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

     - Since an increasing number of medical devices will be transferred to the category of the third-party certification scheme, PMDA expects to accept an increased number of reports from third-party certification bodies. Taking this into account, since FY 2010, PMDA has been developing a method of submission of reports through the Web application platform for medical devices which is compatible with the new application/review system. Since it took time to form a necessary consensus with the medical device industry as the end user, the contract for the system development was extended for an extra 3 months in FY 2011.

  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, an IT literacy training (Microsoft Access 2007, Excel 2007) was carried out for a total of 65 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 to the Electronic Common Technical Document (eCTD) with a higher level of security and put it into operation. 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 2011, the Japanese Pharmacopoeia Draft Committee held a total of 76 meetings, and posted information on the PMDA website to seek public comments regarding 253 official monographs (77 new articles, 176 amendments, 4 deletions), 11 general tests (2 new tests, 9 amendments), 18 ultraviolet-visible reference spectra, 29 infrared reference spectra, 9 reference information (3 new information, 6 amendments), amendments to other General Notices, and partial revision of the General Rules for Preparations as a draft of Supplement 1 to the 16th edition of the Japanese Pharmacopoeia (JP) (scheduled to be published as a Ministerial Announcement in September, 2012).

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

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

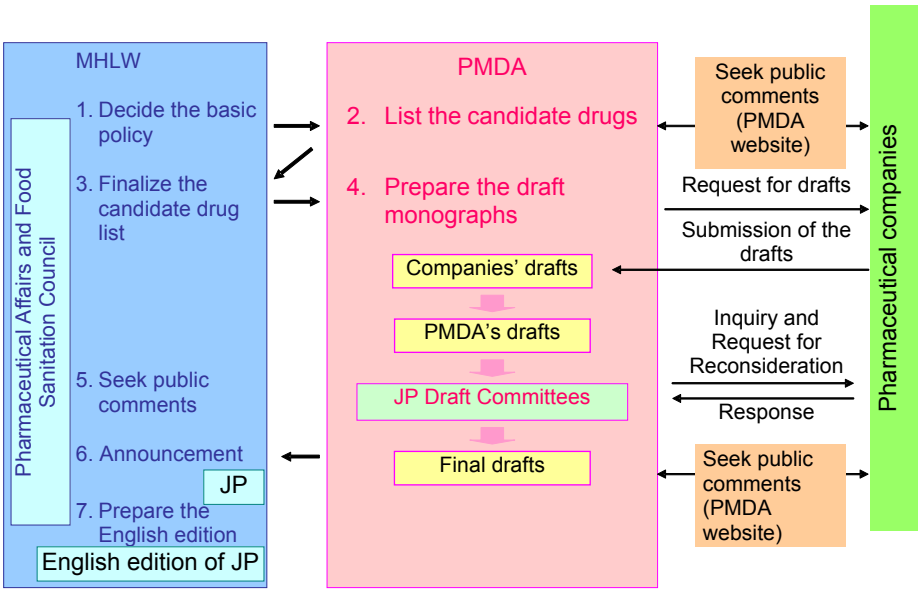
Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for General Notices, General Rules for Preparations, General Rules for Crude Drugs, General Tests, Processes, and Apparatus, and General Information. PMDA usually provides those drafts to MHLW 6 months before the normal publication. In FY 2011, PMDA reported the draft of Supplement 1 to the 16th edition (scheduled to be published as a Ministerial Announcement in September 2012) to MHLW in March 2011.

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
Month and year announced	March 2006	September 2007	March 2009	September 2009	July 2010	March 2011
New monographs	102	90	1	106	0	106
Amendments	272	171	1	122	2	330
Deleted monographs	8	6	0	1	0	15
Total number of monographs	1,483	1,567	1,568	1,673	1,673	1,764

- 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)

Flow of Revision of Japanese Pharmacopoeia



(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 was formally implemented in FY 2011. In FY 2011, 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 (6 consultation items; same hereinafter), Category 3-1, 1 product (5); Category 3-2, 2 products (8), Category 6-1, 1 product (4); Category 6-2, 1 product (5); Oncology drugs, 1 product (1); Biological products, 2 products (4).
  (* When consultations were provided for an identical product in the first and second halves of the year for different consultation items, it was included as 1 product).

b. Introduction of the system of risk managers

- To consistently monitor the safety of drugs from the clinical trial stage to 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, and they were involved in the activities such as safety evaluation of new drugs by review teams and the preparation of the reports on cancellation of conditions for approval in relation to post-marketing surveillance.

(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 for 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, medicine, veterinary 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 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	12.3 (19.4)	15.4 (19.1)	11.9 (24.5)	9.2 (12.6)	6.5 (9.2)
Regulatory review time [months]	4.9 (7.7)	7.3 (8.3)	3.6 (6.7)	4.9 (6.8)	4.2 (5.5)
Applicant's time [months]	6.5 (12.0)	6.8 (11.4)	6.4 (15.9)	3.4 (7.6)	2.0 (4.7)
Number of approved applications	20	24	15	20	50

Note 1: Products covered were those for which applications were filed in or after FY 2004. The numbers of applications are expressed on an active ingredient basis. See Products Approved in FY 2011 in the Supplementary Information for details.

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

Note 3: For FY 2010 and later, 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 for New Drug Applications Excluding Those for Unapproved Drugs Submitted based on Public Knowledge (FY 2010 and later)

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

- 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 50 applications were approved in FY 2011 in this category (including 32 public knowledge-based applications as recommended by the Study Group on Unapproved and Off-label Drugs of High Medical Need).

- In FY 2011, 6 applications requesting priority reviews were submitted for drugs regarded as having particularly high medical need. Of the 6 applications submitted, 2 were judged to be "eligible" for priority review, and 2 were "not eligible," and 2 were currently under consideration as of the end of FY 2011.

- The median total review time for priority review products in FY 2011 was 6.5 months, the median regulatory review time was 4.2 months, and the median applicant's time was 2.0 months, all showing the achievement of the target.

  Among approved applications in FY 2011, priority review products accounted for 38%, showing a higher percentage than for FY 2010 (18%).

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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	20.7 (29.5)	22.0 (27.6)	19.2 (24.8)	14.7 (22.7)	11.5 (15.7)
Regulatory review time [months]	12.9 (17.7)	11.3 (18.5)	10.5 (15.3)	7.6 (10.9)	6.3 (8.2)
Applicant's time [months]	7.9 (11.2)	7.4 (14.1)	6.7 (10.7)	6.4 (12.2)	5.1 (9.6)
Number of approved applications	53	53	92	92	80

Note 1: Products covered above are those for which applications were filed in or after FY 2004. The numbers of applications are expressed on an active ingredient basis. See Products Approved in FY 2011 in the Supplementary Information for details.

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

- In FY 2011, the median total review time for standard review products was 11.5 months, showing a reduction compared with 14.7 months in FY 2010. The median regulatory review time was 6.3 months, showing a reduction of 1.3 months compared with 7.6 months in FY 2010. The median applicant's time was 5.1 months, showing a reduction of 1.3 months compared with 6.4 months in FY 2010.

- PMDA reviewed the submitted product applications in the order of acceptance, giving full consideration to the target review time.

Processing Time by Review Process in Standard Review (Median Regulatory Review Time)

	From application to initial meeting	From initial meeting to inquiries on key issues	From inquiries on key issues to Expert Discussion	From Expert Discussion to approval
FY 2011	1.6 months (1.8 months) 29 applications	0.4 months (0.7 months) 27 applications	2.3 months (3.7 months) 69 applications	2.0 months (2.7 months) 80 applications

Note 1: Values are calculated based on the applications filed in or after April 2004.
Note 2: Values in parentheses are reference values (80th percentile).

- The number of applications under review at the end of FY 2011 was 106 (including 12 applications for orphan drugs; 9 public knowledge-based applications for unapproved drugs; 3 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	Withdrawn	Under review
On or before Mar 31, 2004	140	108 (0)	0 (0)	28 (0)	4 [0]
FY 2004	87	78	0	9	0
FY 2005	57	50	0	7	0
FY 2006	102	92 (0)	0 (0)	9 (0)	1 [0]
FY 2007	92	78	0	14	0
FY 2008	81	76 (0)	0 (0)	4 (1)	1 [-1]
FY 2009	106	87 (18)	1 (1)	18 (4)	0 [-23]
FY 2010	116 (-2)	101 (85)	0 (0)	11 (9)	4 [-94]
FY 2011	123	27 (27)	0 (0)	0 (0)	96 [96]
Total	904	697 (130)	1 (1)	100 (14)	106 [-22]

Note 1: The number of applications in FY 2010 includes 2 deleted applications (the 2 applications were changed from team review category to administrative review category during the review).
Note 2: Values in parentheses in the columns of "Approvedn parentheses in indicate those processed in FY 2011 (included in values on their left).
Note 3: Values in brackets indicate difference from the status reported in FY 2010.

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 2011	Number of processed applications	43	50	86	130
	Median total review time	63.0 days	173.0 days	26.0 days	45.0 days

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

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- In FY 2011, there were no requests for designation for priority consultations of drugs that are considered to have particularly high medical necessity. PMDA conducted a total of 4 priority consultations for designated ingredients.

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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations	281	315	370	390	447
Withdrawals	21	23	23	44	30
Total (conducted and withdrawn consultations)	302	338	393	434	477

Number of Prior Assessment Consultations for Drugs Conducted

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations	-	-	33	30	33
Withdrawals	-	-	0	0	0
Total (conducted and withdrawn consultations)	-	-	33	30	33

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations	-	-	1	1	1
Withdrawals	-	-	0	0	0
Total (conducted and withdrawn consultations)	-	-	1	1	1

Number of Consultations on Drug Product Eligibility for Priority Review Conducted

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations	-	-	-	-	2
Withdrawals	-	-	-	-	0
Total (conducted and withdrawn consultations)	-	-	-	-	2

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 2011, PMDA conducted a total of 477 consultations (including 30 withdrawals).

- To achieve the target of meeting all the demands 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 in the desired month, the date is arranged within one month before or after that month. In FY 2011, PMDA provided a total of 441 consultations (including 30 withdrawals), basically responding to all of the consultations requested.

- PMDA aimed to complete the process from a consultation to finalization of meeting records within 30 business days for 80% of all consultations conducted. In FY 2011, the process was completed within 30 business days for 405 (92.0%) out of 440 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 consultation is presented to the applicant beforehand (preliminary opinion disclosure system).

Number of Consultations for Drugs by Review Category in FY 2011

Review category	Actual results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs, etc.)	4	2	2	5	3	0	10	3	3	3	0	6	41
Category 6-2 (Hormone drugs)	2	3	4	4	5	8	6	2	2	2	5	1	44
Category 2 (Cardiovascular drugs)	4	4	6	7	3	3	5	4	7	4	3	1	51
Category 5 (Drugs for the urogenital system, etc.)	3	0	2	0	2	0	3	1	3	1	2	2	19
Radiopharmaceuticals	1	0	0	1	0	0	0	1	0	0	0	0	3
In vivo diagnostics	0	1	1	1	0	1	0	1	0	0	0	3	8
Category 3-1 (Central nervous system drugs, etc.)	7	4	2	6	5	3	3	6	3	0	2	8	49
Category 3-2 (Anesthetic drugs, etc.)	0	1	0	0	4	3	1	1	2	4	0	4	20
Category 4 (Antibacterial agents, etc.)	2	3	4	5	3	3	4	1	0	1	0	1	27
Category 6-1 (Respiratory tract drugs, etc.)	8	4	6	4	8	0	5	2	5	8	2	3	55
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Oncology drugs	7	5	3	4	6	3	9	11	11	1	3	9	72
Blood products	1	2	1	0	2	1	0	2	0	1	0	1	11
Bio-CMC	0	1	2	4	1	1	1	3	1	4	0	1	19
Biological products	1	1	1	2	0	1	6	2	2	1	5	2	24
Cellular and tissue-based products	0	1	0	0	0	0	0	1	0	0	0	1	3
[Re-listed] Prior assessment	0	0	0	0	3	6	9	0	1	6	0	8	33
[Re-listed] Drug product eligibility for priority review	0	0	0	0	0	0	1	0	0	1	0	0	2
Pharmacogenomics/biomarkers	1	0	0	0	0	0	0	0	0	0	0	0	1
GLP/GCP compliance	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	41	32	34	43	42	27	53	41	39	30	22	43	447
Withdrawals	3	2	2	2	0	7	1	1	6	1	2	3	30
Grand Total	44	34	36	45	42	34	54	42	45	31	24	46	477

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.

(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 the 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, 2012, the number of commissioned experts is 1,081 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2011 was 180 (of which, 137 through document-based discussions; 43 through meetings).

- In FY 2011, the PMDA Omics Project (POP) team held unofficial meetings with academia, companies, etc., as appropriate, to exchange opinions on pharmacogenomics, biomarkers, etc. The team also participated in related academic conferences to give presentations on drug development using pharmacogenomics, biomarkers, etc. and to exchange opinions.

b. Support to the development of national guidelines

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

  PMDA worked with MHLW to develop the "Guidance on the Evaluation for Quality of Antibody Drugs (Draft)," which became open for public comments in late March 2012. In addition, PMDA worked with MHLW to develop and release the Ministerial Notification titled "Guideline on the Development of Prototype Vaccine against Pandemic Influenza" (PFSB/ELD Notification No.1031-1 of the Evaluation and Licensing Division, PFSB, MHLW, dated October 31, 2011).

  PMDA worked with MHLW to develop the following five draft guidelines. The below-listed guidelines have been developed in the research project supported by the FY 2011 Health and Labour Sciences Research Grants (multidisciplinary research project on regulatory science for drugs, medical devices, etc.). The research 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. These draft guidelines became open for public comments in February 2012. MHLW will issue the notification on the guidelines after reviewing and considering the comments received.

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

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

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

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

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

  PMDA also participated in a working group of the expert committee for revision of guidelines on clinical research using human stem cells, under the Committee for Science and Technology, the Health Science Council, MHLW, and worked with MHLW to develop the

points to consider in terms of quality and safety evaluations of stem cells subject to the guidelines.

- The PMDA Omics Project (POP) team has collected information on the application of biomarkers, etc., to drug development, from a scientific standpoint, to promote appropriate personalized medicine. The team periodically held internal meetings and worked with MHLW, as appropriate, to handle the project. In FY 2011, the POP team provided consultations on pharmacogenomics/biomarkers to qualify biomarkers.

- In order to proactively conduct regulatory science research and make use of its outcomes for the Agency's operations, PMDA developed and announced the Basic Principles for Regulatory Science Research by PMDA (October 2011). Based on the Basic Principles, PMDA's internal rules for the conduct of regulatory science research at PMDA were developed with the aim of securing transparency and impartiality. PMDA published a paper discussing the concept of regulatory science in *Clinical Pharmacology Therapeutics*, an international scientific journal (July 2011) to promote international understanding.

c. Preliminary reviews on cellular and tissue-based products, 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. The preliminary reviews of cellular and tissue-based drugs and medical devices were abolished in July 2011.

Number of Applications for Preliminary Reviews and Number of Completed Reviews

	FY 2007		FY 2008		FY 2009		FY 2010		FY 2011	
	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases	No. of applications	No. of completed cases
Cellular and tissue-based products	2	2	1	0	2	2	0	1	1	1
Gene therapy products	0	2	1	0	0	2	1	1	1	0

- With regard to the use of genetically modified living organisms, preliminary reviews are conducted about approval of first-class use and confirmation of second-class 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. PMDA also worked with MHLW to revise the list of "GILSP* Genetically Modified Living Microorganisms Specified by the Minister of Health, Labour and Welfare Based on Appended Table 1 of the Ministerial Ordinance Providing Containment Measures to Be Taken in the Industrial Use within the Scope of Second-Class Use of Living Modified Organisms" (MHLW Ministerial Announcement No. 27 of 2004). The revision was publicly notified in November 11, 2011.
  *GILSP: good industrial large scale practice

Review under the Cartagena Act (Median Regulatory Review Time)

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
No. of preliminary reviews for first-class use Median review time	1 -	0 -	0 - months	0 - months	0 - months
No. of preliminary reviews for second-class use Median review time	8 -	24 -	11 2.5 months	13 2.5 months	15 2.0 months

Note 1: "First-class use" refers to cases where measures are not taken to prevent the release to the environment and "Second-class 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 institutes, and venture companies that have promising seed-stage resources. In addition to having briefing sessions in Osaka and Tokyo in August 2011 and in Sendai in October 2011, PMDA held individual orientations, and seminars at universities, etc., on the consultation service. Consequently, the number of consultation requests has been increasing. The figures as of March 31, 2012 are shown in the table below.

Requests for Pharmaceutical Affairs Consultations on R&D Strategy (as of March 31, 2012)

Consultations	Drugs (excluding CTP*)	Medical devices (excluding CTP)	CTP	Total (%)
Universities	15	2	2	19 (53%)
Companies/Ventures	2	1	4	7 (19%)
Research institutes/Others	5	1	4	10 (28%)
Total (%)	22 (61%)	4 (11%)	10 (28%)	36 (100%)

Pre-consultation meetings	Drugs (excluding CTP)	Medical devices (excluding CTP)	CTP	Total (%)
Universities	48	15	11	74 (46%)
Companies/Ventures	12	21	21	54 (32%)
Research institutes/Others	17	5	16	38 (22%)
Total (%)	77 (46%)	41 (25%)	48 (29%)	166 (100%)

Note: As for pre-consultation meetings, the second and subsequent meetings (if any) for the same product are also included in the figures.

**CTP: cellular and tissue-based products*

Individual orientations	Drugs (excluding CTP)	Medical devices (excluding CTP)	CTP	Others (for proxy applications for foreign companies/ *in vitro* diagnostics)	Total (%)
Universities	19	17	4	1	41 (34%)
Companies/Ventures	16	42	4	2	64 (53%)
Research institutes/Others	6	9	0		15 (13%)
Total	41 (34%)	68 (57%)	8 (7%)	3 (2%)	120 (100%)

Note: Including the number of individual orientations, etc., provided in briefing sessions. (Osaka, 32; Tokyo, 21; Sendai, 11; Fukushima, 5; Nagoya, 11)

e. Support to 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 2011. 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: 3 clinical trial consultations for drugs, 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.

Over-the-counter drugs and generic drugs

- To promote self-medication and wide use of generic drugs, in FY 2011, PMDA conducted presentation sessions in various symposia held for the general public and worked with MHLW to develop its Q&A document on generic drugs. PMDA posted on its website various materials, such as the Q&A document and handouts for briefing sessions in which PMDA staff members gave presentations.

(i) Appropriate and prompt reviews

a. Conduct of 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.

  Note: A total of 1,137 PMDA staff members participated in 338 domestic academic conferences and seminars.

b. Promotion of digitization in reviews

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

c. Development of the Japanese Pharmacopoeia

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

d. 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 2011. Based on the results of deliberation at the review committee, the PFSB Notification was issued on December 19, 2011, regarding the partial revision of the "Japanese Standards of Quasi-drug Ingredients 2006."

e. 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 active participation of reviewers in Expert Discussions and 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 prescription drugs (hereinafter "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 clearly 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 2011).

- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Generic drugs	3,278	1,980	3,271	2,633	3,091
Of which: Number of approved applications filed in or after April 2004	3,228	1,960	3,245	2,590	3,046
Median review time (for the applications filed in or after April 2004)	4.5 months	5.3 months	7.5 months	6.9 months	6.5 months
OTC drugs	1,329	1,821	2,171	1,008	1,031
Of which: Number of approved applications filed in or after April 2004	1,309	1,807	2,166	1,007	1,029
Median review time (for the applications filed in or after April 2004)	4.0 months	3.5 months	4.6 months	4.0 months	3.4 months
Quasi-drugs	2,236	2,340	2,221	1,976	1,938
Of which: Number of approved applications filed in or after April 2004	2,230	2,339	2,220	1,976	1,938
Median review time (for the applications filed in or after April 2004)	5.2 months	5.0 months	4.8 months	5.2 months	5.0 months
Total	6,843	6,141	7,663	5,617	6,060
Of which: Number of approved applications filed in or after April 2004	6,767	6,106	7,631	5,573	6,013

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	No. of applications	Approved	Withdrawal, etc.	Under review
Generic drugs	FY 2007	3,729	3,278	160	2,756
	FY 2008	3,893	1,980	199	4,488
	FY 2009	2,354	3,271	223	3,342
	FY 2010	3,062	2,633	224	3,539
	FY 2011	2,892	3,091	165	3,175
OTC drugs	FY 2007	1,377	1,329	113	2,167
	FY 2008	2,387	1,821	302	2,439
	FY 2009	1,759	2,171	136	1,891
	FY 2010	1,092	1,008	138	1,842
	FY 2011	1,130	1,031	92	1,848
Quasi-drugs	FY 2007	2,427	2,236	118	1,688
	FY 2008	2,414	2,340	189	1,575
	FY 2009	2,571	2,221	82	1,844
	FY 2010	2,297	1,976	135	2,030
	FY 2011	2,212	1,938	82	2,222

Note 1: For FY 2007, values in the Withdrawal etc. column include the number of products switched to other review categories during the review, but for FY 2008 and later, values do not include such products.

Note 2: Regarding the numbers for OTC drugs and quasi-drugs, some data were missing in the summation for FY 2009 and FY 2010, and therefore corrections were made as follows.

OTC drugs

In "under review" for FY 2009, "1,761" was corrected to "1,891."
In "withdrawals, etc." for FY 2010, "133" was corrected to "138."
In "under review" for FY 2010, "1,712" was corrected to "1,842."

Quasi-drugs

In "under review" for FY 2009, "1,824" was corrected to "1,844."
In "under review" for FY 2010, "2,010" was corrected to "2,030."

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 2011	0	0	0	0	0	16	0	2	0	3	6	89	16	989	1,121
Approved in FY 2011	0	0	0	0	1	6	0	4	0	2	11	73	8	869	974

Category of application	Insecticides	Total
Filed in FY 2011	9	9
Approved in FY 2011	6	6

Former category of application	1	2	3	4-1	4-2	OTC test agents	Total
Approved in FY 2011	0	4	20	2	25	0	51

Quasi-drugs

Category of application	1,3	2	Total
Filed in FY 2011	82	2,130	2,212
Approved in FY 2011	50	1,888	1,938

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 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 a new active ingredient (Direct OTC drugs)
2: Drugs with a new route 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 a new active ingredient 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 a new active ingredient
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 2011 were 6.5 months for generic drugs (target, 10 months), 3.4 months for OTC drugs (target, 8 months), and 5.0 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Generic drugs	1,135	601	1,004	1,040	1,118

- For generic drugs, PMDA conducted 1,118 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 during FY 2013 that is different from the existing simple consultation. In FY 2011, in consideration of the results of questionnaire surveys of industry associations conducted in 2010, PMDA started to receive requests for quality consultations for generic drugs and consultations on bioequivalence of generic drugs in October 2011. The consultations were provided on a trial basis from January 2012 onwards.

Number of Consultations for Generic Drugs

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

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

Number of Consultations for Generic Drugs by Consultation Category in FY 2011

Consultation category	Conducted consultations	Withdrawals	Total (conducted and withdrawn consultations)
Consultation on bioequivalence for generic drugs	1	0	1
Quality consultation for generic drugs	2	0	2
Total	3	0	3

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

- PMDA started to offer consultations on the appropriateness of development of OTC drugs on a full scale in FY 2011 as a pre-application consultation, based on opinions from industry associations. PMDA continued to provide pre-application consultations for Switch OTC drugs and consultations on key points of clinical trial protocols on a trial basis from FY 2010. In addition, PMDA conducted questionnaire surveys, etc., among pharmaceutical companies that received these consultation. PMDA intends to improve the consultation service by referring to the results of questionnaire surveys, and the opinions from industry associations, etc.

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

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

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 2011

Consultation category	Conducted consultations	Withdrawals	Total (conducted and withdrawn consultations)
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	16	2	18
Total	17	2	19

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 opinions on 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) Conduct of appropriate and prompt reviews

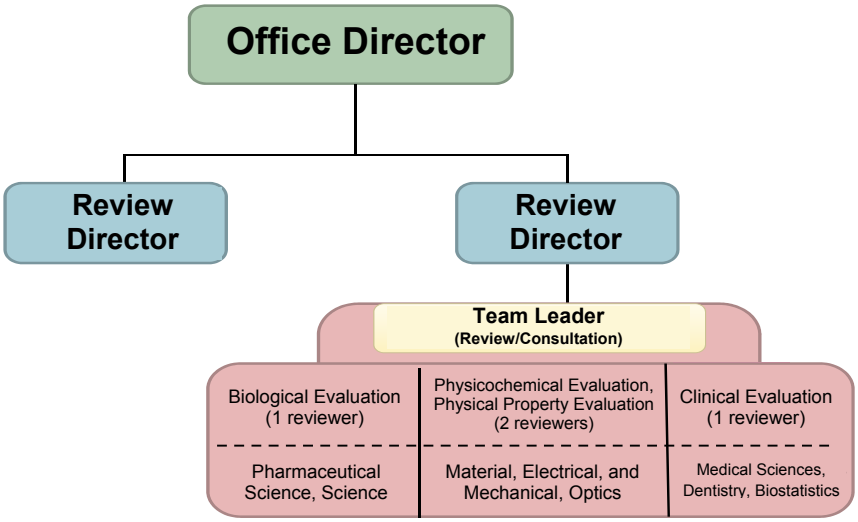
a. System for clinical trial consultations and reviews

Review Performance for FY 2011 (medical devices and in vitro diagnostics)

(i) Number of Expert Discussions conducted: 75 (of which, 57 through document-based discussions and 18 through meetings)
(ii) Applications deliberated at the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 11
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 233 (of which, 214 for medical devices and 19 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 engineering, pharmacology, medicine, dentistry, veterinary medicine, statistics, etc.
  The review team is typically comprised of team leader(s), and reviewers specialized in biological evaluations, physicochemical/physical property evaluations, and clinical evaluations.

Organization Chart for Reviews of New Medical Devices



- PMDA increased the medical device reviewers based on the Action Program to Accelerate Reviews of Medical Devices, and also established the Office of Medical Devices III in November 2011 to reinforce the review system for generic medical devices, thereby enhancing the quality of reviews and reducing review times.

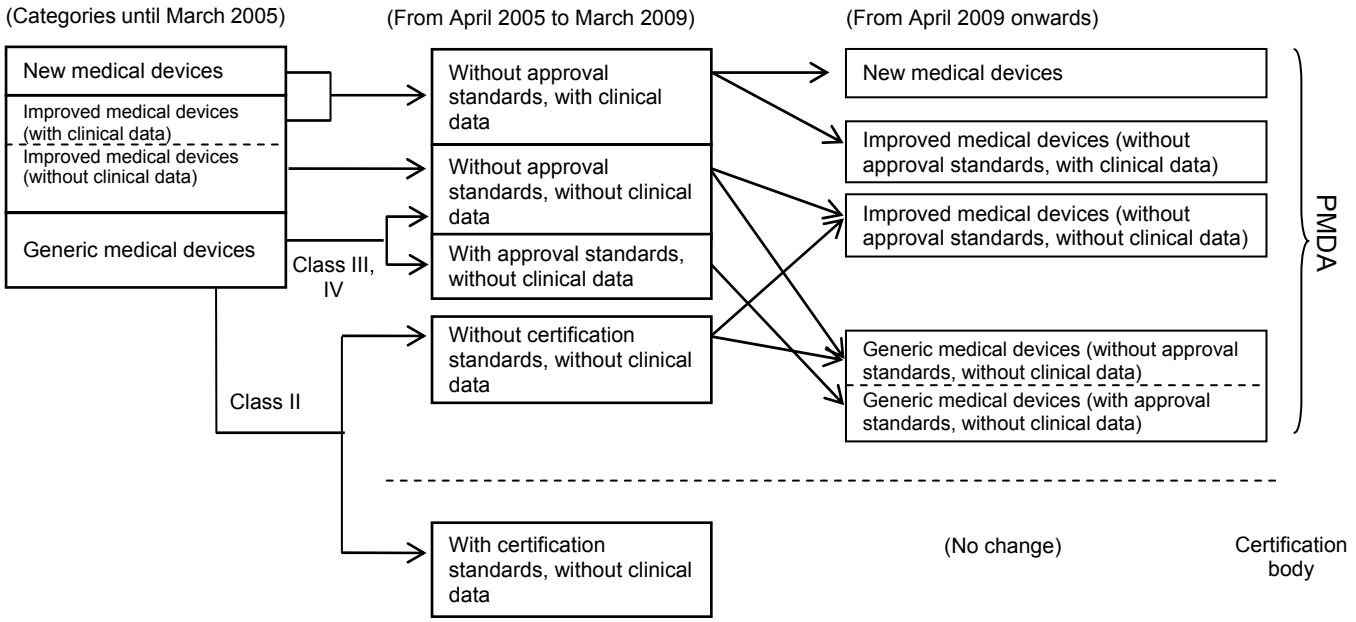
- Reviews of new medical devices were conducted upon establishing a team to each review category as shown below:

Review Categories Covered by the Offices of Medical Devices

Name of 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 from a review team.

- With the enforcement of the Pharmaceutical Affairs Act, as revised in April 2009, the categories of application were reclassified.



Note: Roman numerals, 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. Conduct of 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 1,137 PMDA staff members participated in 338 academic conferences and seminars in Japan.

- Based on the study results provided by the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Needs (chaired by Dr. Soichiro Kitamura, Honorary Director-General of National Cardiovascular Center) as established in October 2006, PMDA conducted clinical trial consultations and reviews. As a result, 6 medical devices and 3 *in vitro* diagnostics were approved.

- For cellular and tissue-based products using state-of-the-art technology such as novel biomarkers and regenerative medicine, advice on product development and regulatory submission is highly desired, as there are only a few precedents for such types of development.

  In order to respond to these needs, PMDA continued to conduct consultations on pharmacogenomics/biomarkers that were started in FY 2009.

c. Introduction of the 3-track review system

- For review teams for generic medical devices, in FY 2011, PMDA introduced the buddy system in which an experienced reviewer and a newcomer are paired to perform a review, in order to enhance the quality of reviews and solve the variability problem. In November 2011, in order to accelerate reviews for generic medical devices, the Office of Medical Devices III was set up as a review office specializing in generic medical devices. Reviews of generic medical devices were thus separated from those for new medical devices and for improved medical devices, and the 3-track review system has been completely put in place.

d. Promotion of digitization in reviews

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

e. Standardization of review

- To provide basic considerations for reviewers of new medical devices, etc. from the viewpoint of clarification of review standards, "Points to Consider in Preparing Applications for New Medical Devices, etc." was published in FY 2008. The document was revised to reflect revisions of related notifications and posted on the website. The revised points to consider were explained to relevant reviewers and has been used 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)" as a revision 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. Also for generic medical devices, PMDA posted the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices" on the website. The Agency presented these guidelines in its workshops to ensure that they are thoroughly acknowledged.

- In order to achieve the target review times as specified in the Mid-term Plan and to conduct reviews and related services promptly and appropriately, 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 office directors of the review division assessed the operational progress on a routine basis. Based on the reports from these office directors, the Director and Associate Center Directors of the Center for Product Evaluation provided necessary guidance at the Review Segment Meeting for Progress Management.

f. Rationalization of application documents for improved medical devices and generic medical devices

- In order to rationalize application documentation for improved medical devices and generic medical devices, PMDA posted guidance documents "Points to Consider in Preparing Data for Applications of Improved Medical Devices" and "Points to Consider in Preparing Data for Applications of Generic Medical Devices" on its website. PMDA also presented these guidance documents in workshops to thoroughly disseminate them.

(ii) Introduction of new review systems

a. Introduction of prior assessment consultation

- 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 continued to offer these consultations in the same scheme in FY 2011.

b. Conduct of short-term review of applications for specified partial changes

- Among 9 product applications filed in FY 2010 and 38 product applications filed in FY 2011 for specified partial changes, 33 received approval. The approved applications, except 1, were reviewed within 2 months of submission (excluding the period for GCP/GLP inspections).

c. Support to 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 three meetings in FY 2011.

  The numbers of standards (established and revised) for approval and certification reported to MHLW in FY 2011 were as follows:

Reported in:	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	Total
Approval standards	6	7	5	2	6	6	32
Certification standards	0	14	86	64	294	84	542
Review guidelines	0	1	2	6	0	0	9

- The number of standards established by MHLW in FY 2011 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	Total
Approval standards	0	17	8	10	-2*	5	3	0	41
Certification standards	363	9	24	0	17	68	274	67	822
Review guidelines	0	0	0	0	3	1	4	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 2011)

Certification standards (67 established), approval standards (0 established), review guidelines (0 established)	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 264 dated July 29, 2011	12 certification standards including the standard for x-ray system, diagnostic, bone absorptiometer, single energy
MHLW Ministerial Announcement No. 69 dated March 1, 2012	11 certification standards including the standard for contrast medium delivery/evaluation kits for barium enema
MHLW Ministerial Announcement No. 69 dated March 1, 2012	41 certification standards including the standard for infrared skin thermometers

- 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 individual products through simple consultations on the scope of changes for which applications for partial changes 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 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 the consultations, etc. based on the notification titled "Partial Revision of 'Points to Consider in Filing Applications for Medical Devices" (PFSB/ELD/OMDE Notification No.1224007 dated December 24, 2010).

d. Equivalence review of generic medical devices

- PMDA continuously conducted the equivalence review of generic medical devices filed in FY 2011 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 to the development of certification standards, etc.

- PMDA supported the development of certification standards by MHLW. A total of 67 certification standards were established in FY 2011.

(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 engineering, pharmaceutical science, 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 and identified factors interfering with shortening of review times, and also made efforts to accelerate reviews, such as by sending reminder notices frequently 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, in order to balance between the quality and promptness of reviews. The buddy pairs are overseen by team leaders who reports to Review Directors, so that the review practices are standardized among review teams. The buddy pairs also supported review of similar products in other review categories that have many products under review. PMDA made such efforts to flexibly operate the buddy system irrespective of review categories with the aim of accelerating reviews.
  (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 HBD (Harmonization by Doing) project which has been performed by both Japan and the US, and had discussions toward the conduct of global clinical trials and the development of common protocols between Japan and the US. In addition, continuously from the previous year, the notification titled "Pilot Scheme of Information Exchange with US Food and Drug Administration (FDA) for Consultations and Reviews for Approval of Medical Devices (No. 3)" (PFSB/ELD/OMDE Notification No. 0616-1 dated June 16, 2011) was issued. In this way, PMDA made efforts to accelerate reviews by exchanging information on reviews and consultation services with the US FDA.

- The status of reviews for medical devices in FY 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	15.7	28.8	13.9	15.1	4.3
Regulatory review time [months]	8.6	5.8	6.0	5.3	2.9
Applicant's time [months]	-	-	7.7	10.7	1.3
Number of approved applications	4	4	3	3	6

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 2011, the median total review time for priority review products was 4.3 months, showing achievement of the target. Meanwhile, the number of approvals increased.

  The median regulatory review time was 2.9 months, and the median applicant's time was 1.3 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 2011, 6 priority review products (all were new medical devices) were approved.

  There were no new requests for designation for priority review as a medical device regarded as having particularly high medical need. The two priority review requests under examination at the end of FY 2010 were 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 [months]	14	14	12	10	7

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

Results

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	15.1	14.4	11.0	16.5	9.7
Regulatory review time [months]	7.7	9.8	6.8	7.1	5.1
Applicant's time [months]	-	-	7.1	8.2	3.4
Number of approved applications	19	12	33	15	27

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 2011, the median total review time for standard review products was 9.7 months, showing achievement of the target. Meanwhile, the number of approvals increased.

  The median regulatory review time was 5.1 months, and the median applicant's time was 3.4 months.

- PMDA reviewed the submitted product applications in the order of receipt of applications, giving full consideration to the target review time.

- The number of product applications under review at the end of FY 2011 was 44 (including 4 orphan medical devices and 1 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	Withdrawn	Under review
On or before Mar 31, 2004	132	54	78	0
FY 2004	56	35 (0)	21 (1)	0 [-1]
FY 2005	7	7	0	0
FY 2006	23	19 (0)	4 (1)	0 [-1]
FY 2007	37	29 (0)	6 (0)	2 [0]
FY 2008	32	28 (2)	2 (0)	2 [-2]
FY 2009	24	17 (5)	3 (2)	4 [-7]
FY 2010	28	21 (18)	2 (2)	5 [-20]
FY 2011	42	10 (10)	1 (1)	31 [31]
Total	381	220 (35)	117 (7)	44 [0]

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 2011 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2010.

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 2011	Number of processed applications	25	12	16	33
	Median total review time	29.0 days	238.0 days	81.5 days	8.0 days

Note 1: The duration shown in each review process are the median of the total review time (the sum of regulatory review time and applicants' times) of the period.
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 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	-	-	17.2	15.5	13.9
Regulatory review time [months]	-	-	10.4	7.6	7.0
Applicant's time [months]	-	-	6.6	7.6	7.2
Number of approved applications	-	-	30	40	55

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 55 improved medical devices (with clinical data) approved in FY 2011, and the median total review time was 13.9 months, showing achievement of the target. The number of approvals steadily increased.

  The median regulatory review time was 7.0 months, and the median applicant's time was 7.2 months.

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

Improved medical devices (with clinical data) Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	34	30 (6)	1 (1)	3 [-7]
FY 2010	34	30 (28)	0 (0)	4 [-28]
FY 2011	26	1 (1)	0 (0)	25 [25]
Total	94	61 (35)	1 (1)	32 [-10]

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 in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2011 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2010.

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 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	-	-	13.2	14.5	13.3
Regulatory review time [months]	-	-	8.5	8.0	5.6
Applicant's time [months]	-	-	3.9	6.2	6.5
Number of approved applications	-	-	158	182	218

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 (without clinical data) approved in FY 2011 was 218, and the median total review time for these applications was 13.3 months, showing non-achievement of the target. The number of approvals steadily increased.

  The median regulatory review time was 5.6 months, and the median applicant's time was 6.5 months.

- For improved medical devices (without clinical data), the target review time was not achieved in FY 2011. However, the old applications filed in past years with prolonged review times have been strenuously processed, thereby substantially reducing the number of product applications under review.

  PMDA intends to further accelerate the process of such remaining product 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	Withdrawn	Under review
FY 2009	137	110 (24)	12 (8)	15 [-32]
FY 2010	165	105 (80)	9 (7)	51 [-87]
FY 2011	177	38 (38)	2 (2)	137 [137]
Total	479	253 (142)	23 (17)	203 [18]

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 in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2011 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2010.

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 2011 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Total review time [months]	-	-	12.9	11.0	5.0
Regulatory review time [months]	-	-	5.9	5.1	2.5
Applicant's time [months]	-	-	3.6	4.7	2.3
Number of approved applications	-	-	1,797	1,391	907

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 generic medical devices approved in FY 2011 was 907. The median total review time was 5.0 months and the median regulatory review time was 2.5 months, both

showing the achievement of the target for the fiscal year, but the median applicant's time was 2.3 months. Aiming at achieving the targets set up in the Action Program, PMDA has shortened the total review time, regulatory review time, and applicant's time for generic medical devices. From FY 2012 onwards, the targets are set at 4.0 months, 3.0 months, and 1.0 month, respectively, and therefore PMDA intends to continuously shorten the total review time, etc., by increasing the number of reviewers, fulfilling training programs, and clarifying review standards.

The number of approvals in FY 2011 was 907, showing a reduction compared to that in FY 2010. Although the number of applications decreased in FY 2011, many products are still under review. Hence, PMDA intends to make efforts to increase the number of approvals and reduce the number of products under review in parallel with shortening of review times.

Review Status of Generic Medical Devices by Fiscal Year of Application

Generic medical devices Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	1,126	977 (86)	53 (24)	96 [-110]
FY 2010	1,020 (-1)	766 (343)	55 (40)	199 [-384]
FY 2011	994	498 (498)	17 (17)	479 [479]
Total	3,140	2,241 (927)	125 (81)	774 [-15]

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: One application, which was withdrawn, was subtracted from the number of applications in FY 2010.
Note 3: The number of approved products includes those approved in other medical device categories.
Note 4: Values in parentheses in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2011 (included in values on their left).
Note 5: Values in brackets indicate difference from the status reported in FY 2010.

(iv) Efficient conduct of clinical trial consultations

a. 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. Conduct of clinical trial consultations and improvement of the system

Number of Consultations

		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations		72	76	110	112 (-1)	141
	(Medical devices)	71	74	104	105 (-1)	136
	(*In vitro* diagnostics)	1	2	6	7	5
Withdrawals		0	2	1	1	4
	(Medical devices)	0	2	1	1	4
	(*In vitro* diagnostics)	0	0	0	0	0
Total (conducted and withdrawn consultations)		72	78	111	113 (-1)	145
	(Medical devices)	71	76	105	106 (-1)	140
	(*In vitro* diagnostics)	1	2	6	7	5

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

		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations		-	-	-	2	3
	(Medical devices)	-	-	-	2	3
	(*In vitro* diagnostics)	-	-	-	0	0
Withdrawals		-	-	-	0	0
	(Medical devices)	-	-	-	0	0
	(*In vitro* diagnostics)	-	-	-	0	0
Total (conducted and withdrawn consultations)		-	-	-	2	3
	(Medical devices)	-	-	-	2	3
	(*In vitro* diagnostics)	-	-	-	0	0

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Conducted consultations	-	-	0	0	0
Withdrawals	-	-	0	0	0
Total (conducted and withdrawn consultations)	-	-	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.
Note 5: One consultation, which was not applicable to the consultation conducted, was subtracted from the number of consultations in FY 2010.

- In FY 2011, PMDA conducted a total of 145 consultations (including 4 withdrawals).

- A total of 142 clinical trial consultations (excluding prior assessment consultations and consultations on pharmacogenomics/biomarkers; including 4 withdrawals) were carried out in FY 2011. 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 2011, 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 2011, the target was achieved in 120 (91.6%) of 131 consultations.

Number of Consultations for Medical Devices by Category in FY 2011

Consultation category	Number of consultations conducted	Withdrawals	Total (Conducted consultations and withdrawals)
Pre-development consultation for medical devices	36	2	38
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	0	0	0
Performance testing consultation for medical devices	11	0	11
Clinical evaluation consultation for medical devices	19	0	19
Exploratory clinical trial consultation for medical devices	1	0	1
Clinical trial consultation for medical devices	28	2	30
Pre-application consultation for medical devices	11	0	11
Application procedure consultation for medical devices	17	0	17
Additional consultation for medical devices	6	0	6
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)	3	0	3
Prior assessment consultation for medical devices (clinical)	0	0	0
Pre-development consultation for *in vitro* diagnostics	0	0	0
Quality consultation for *in vitro* diagnostics	0	0	0
Consultation on conformity with standards for *in vitro* diagnostics	1	0	1
Clinical evaluation consultation for *in vitro* diagnostics	0	0	0
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 preparation of documents for cellular and tissue-based products	0	0	0
Consultation on pharmacogenomics/biomarkers	0	0	0
Total	141	4	145

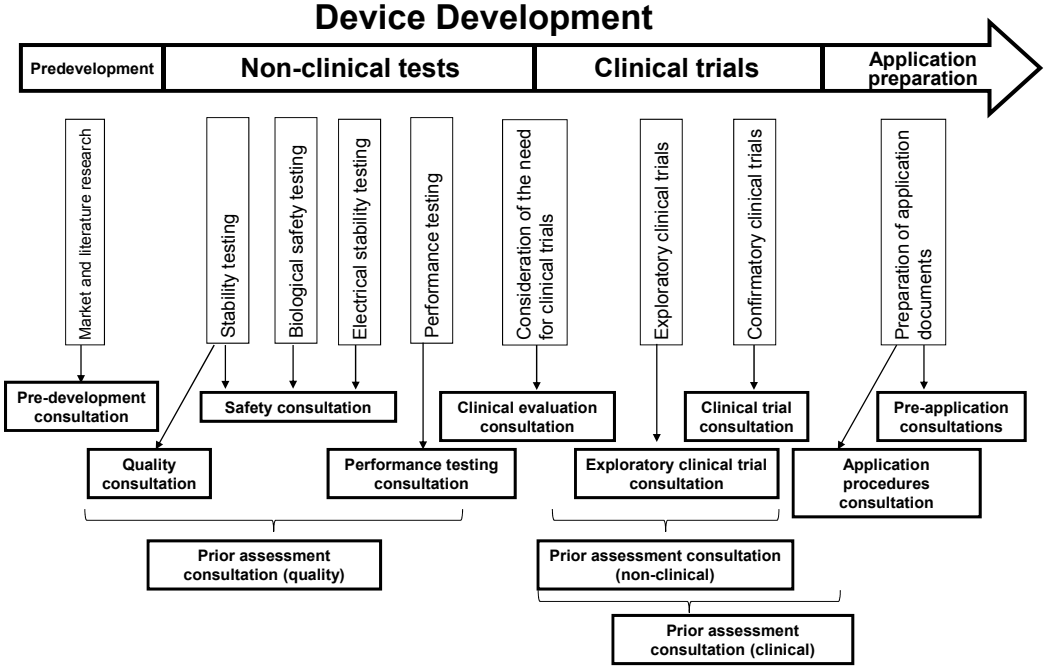
Note: Consultation on preparation of documents for cellular and tissue-based products was provided until June 2011.

d. Expansion of consultation categories

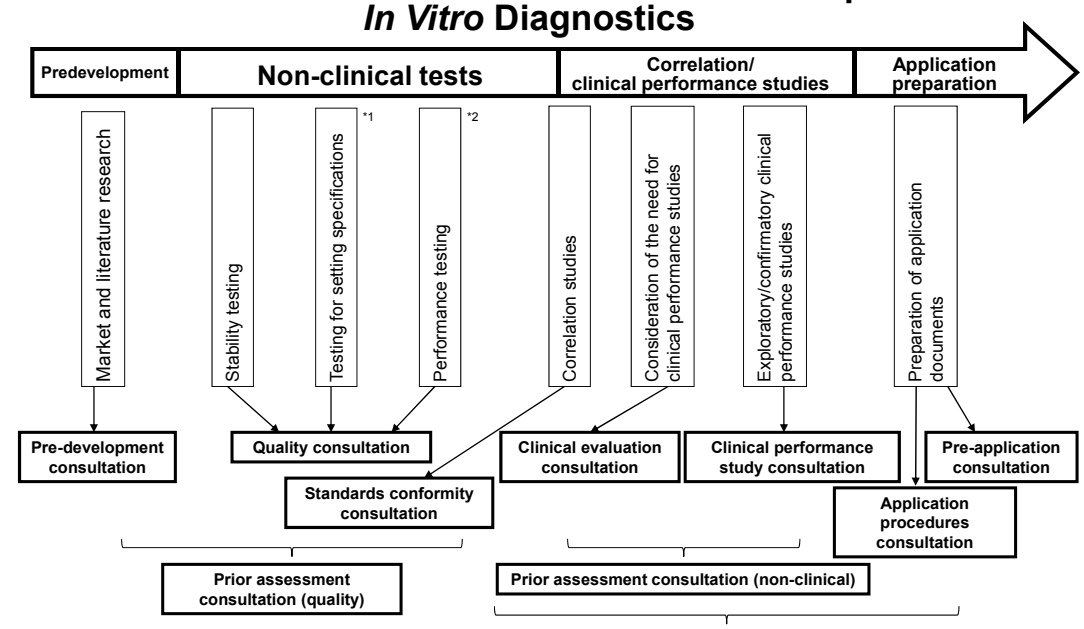
- Since FY 2007, in order to promote product development and speed up reviews by providing detailed advice that meets various needs at each stage, the clinical trial consultations on medical devices and *in vitro* diagnostics have been improved to provide specific advice for each development stage.

- 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 continued to offer these consultations in the same scheme in FY 2011.

Consultations Offered in the Course of Medical Device Development



Consultations Offered in the Course of Development of *In Vitro* Diagnostics



Note 1: Refers to quality control testing, measuring range testing, etc.
Note 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 2011 was 75 (of which, 57 through document-based discussions and 18 through meetings).

- PMDA had discussions with external experts on issues raised in clinical trial consultations and application reviews for cellular and tissue-based products (a total of 8 experts for 4 cases). In addition, through telephone conferences with foreign regulatory authorities such as the European Medicines Agency (EMA) and the US FDA, and participation in international academic conferences, PMDA exchanged opinions on the regulation of cellular and tissue-based products or topics discussed in international harmonization forums, such as ICH.

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

b. Support to the development of national guidelines

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

- PMDA worked with the MHLW to develop the "Guidance for the Evaluation of Emerging Technology Medical Devices (Cell Sheets for Treatment of Periodontal Tissues, Orthopedic Customized Artificial Hip Joint Prosthesis, and Computer-assisted Diagnosis Systems)" (PFSB/ELD/OMDE Notification No. 1207-1 dated December 7, 2011), and promoted the dissemination of the notification.

c. Preliminary reviews on cellular and tissue-based products, 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 to 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 efficiently conducted on-site and document-based inspections and data integrity assessment concerning the studies and data submitted in applications for new drugs and medical devices, to determine whether such data were collected in compliance with the requirements of the Ministerial Ordinance on Good Laboratory Practice (GLP), the Ministerial Ordinance on Good Clinical Practice (GCP), and the data integrity standards for products applications.

- PMDA created the "Checklist for GCP on-site and document-based inspections and data integrity assessment for new drugs" and released it on the PMDA website. The checklist has been put into

operation since July 2011. PMDA conducted 84 GCP on-site inspections (at companies) for new drugs (the number is that of active ingredients) in FY 2011, all of which 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 inspection and data integrity assessment for new drugs. In FY 2011, 76 inspections (75.2%) were conducted by this company-visit, out of the total of 101 inspections (the numbers are those of active ingredients).

b. Introduction of the GCP system inspection

- PMDA compiled the results of "Current situation survey on electronic storage of clinical trial data" collected from pharmaceutical companies and presented them at GCP Workshops. In the GCP Workshops, PMDA provided explanation for questions received in the survey, and posted the explanation on the website to thoroughly inform users of the system.

- As a part of investigation on the GCP system inspection, PMDA reviewed the Electronic Data Capture (EDC) Inspection Check List (draft) based on the above questionnaire survey, and prepared an EDC system sheet (draft). A pilot study using the sheet was started.

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

- With regard to document-based inspections and data integrity assessment for non-clinical tests of medical devices, PMDA issued the "Q&A on Procedures for Document-based Inspections and Data Integrity Assessment of Submitted Data of Non-Clinical Tests for Medical Devices" (PMDA/CPE Notification No. 0830004 of the Center for Product Evaluation, PMDA, dated August 30, 2011)," and also improved the web page of the Office of Conformity Audit by adding downloadable forms for applicants so that document-based compliance assessment can be efficiently conducted.

- In FY 2011, 1,039 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 2011, the number of completed assessment was 109 for new drugs and 2 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 prepared in compliance with the data integrity standards for product applications, etc., but there were no products subject to the data integrity assessment in FY 2011.

Number of GLP/GCP/GPSP Compliance Assessments

		FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Document-based assessments		774	942	1,136	1,319	1,319
	New drugs	234	293	246	251	280
	Medical devices	540	649	890	1,068	1,039
GCP inspections		132	198	175	171	149
	New drugs	122	182	164	158	140
	Generic drugs	9	15	10	10	8
	Medical devices	1	1	1	3	1
Document-based assessment for re-examination		119	83	66	138	111
	New drugs	119	83	66	135	109
	New medical devices	–	–	–	3	2
GPSP inspections (new drugs)		107	79	65	135	109
Document-based assessments for re-evaluation		31	–	–	–	–
GLP inspections		27	43	26	30	32
	Drugs	23	32	18	26	23
	Medical devices	4	11	8	4	9

Note 1: The numbers of document-based assessments (excluding those for medical devices), GCP inspections (excluding those for medical devices), document-based assessments for re-examination (excluding those for medical devices), GPSP inspections, 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 (for medical devices), GCP inspections (for medical devices) and document-based assessments for re-examination (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 2007 and 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)*

b. Building of the inspection system

- PMDA continued to recruit GMP/QMS specialists and the number of inspectors was 45 as of April 1, 2011. At the same time, PMDA has promoted participation of GMP/QMS inspectors in training programs, both in Japan and overseas, including seminars hosted by the Pharmaceutical Inspection Cooperation Scheme (PIC/S), a European-based international organization for GMP inspections.

- The administrative processing status of GMP/QMS inspections in FY 2011 are shown below:

GMP/QMS Inspections Conducted under the Revised Pharmaceutical Affairs Act

	FY 2007				FY 2008			
	Requested	Completed	Withdrawn	In progress	Requested	Completed	Withdrawn	In progress
Drugs*	1,011	893 (233)	55	444	1,158	738 (214)	52	812
In vitro diagnostics	85	84 (1)	0	44	70	78 (1)	3	33
Quasi-drugs	3	0 (0)	0	3	2	3 (0)	0	2
Medical devices	1,006	1,021 (12)	15	348	971	915 (42)	44	360
Total	2,105	1,998 (246)	70	839	2,201	1,734 (257)	99	1,207

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

	FY 2011			
	Requested	Completed	Withdrawn	In progress
Drugs*	1,538	1,283 (185)	31	908
In vitro diagnostics	73	85 (0)	1	6
Quasi-drugs	0	0 (0)	0	2
Medical devices	697	765 (36)	24	57
Total	2,308	2,133 (221)	56	973

** 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 2011 are shown below:

Median Processing Time of GMP/QMS Inspections

	FY 2007		FY 2008		FY 2009	
	Total processing time	PMDA processing time	Total processing time	PMDA processing time	Total processing time	PMDA processing time
Drugs*	170 days	111 days	155 days	100 days	162 days	91 days
In vitro diagnostics	158 days	88 days	117 days	46 days	110 days	56 days
Quasi-drugs	-	-	156 days	29 days	154 days	108 days
Medical devices	157 days	88 days	131 days	59 days	142 days	56 days

	FY 2010		FY 2011	
	Total processing time	PMDA processing time	Total processing time	PMDA processing time
Drugs*	118 days	63 days	147 days	77 days
In vitro diagnostics	117 days	62 days	83 days	38 days
Quasi-drugs	-	-	-	-
Medical devices	145 days	69 days	113 days	21 days

** Excluding in vitro diagnostics.*

- The processing status of inspections of manufacturing facilities conducted in FY 2011 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 2007		FY 2008		FY 2009		FY 2010		FY 2011	
Drugs*	16	(14)	8	(6)	40	(25)	20	(19)	25	(19)
In vitro diagnostics	2	(2)	2	(2)	4	(2)	1	(1)	3	(3)
Medical devices	0	(0)	1	(1)	2	(1)	3	(3)	0	(0)
Total	18	(16)	11	(9)	46	(28)	24	(23)	28	(22)

** 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 2011 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs*	27	13	12	6	12
In vitro diagnostics	1	1	3	2	3
Medical devices	2	0	0	1	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 2011 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2008	FY 2009	FY 2010	FY 2011
Drugs*	44	39	36	44
In vitro diagnostics	1	1	0	0
Quasi-drugs	0	0	1	0
Medical devices	17	17	6	6
Total	62	57	43	50

** Excluding in vitro diagnostics.*

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

- The performance 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

Note: Breakdown of FY 2011: (Europe) France, Belgium, Austria, Germany, Greece
(North, Central and South America) United States, Mexico
(Asia/Oceania) China, India, South Korea, Taiwan, Thailand, Vietnam

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

Note: Breakdown of FY 2011: (Europe) Ireland, United Kingdom, Italy, France
(North, Central and South America) United States (including Puerto Rico), Canada, Mexico, Costa Rica
(Asia) Israel

- The processing status of inspections of manufacturing facilities conducted in FY 2011 at foreign manufacturing sites, as 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs*	387	294	390	230	579
In vitro diagnostics	69	69	40	27	60
Quasi-drugs	57	39	41	26	72
Medical devices	1,682	1,191	910	677	1,187
Total	2,195	1,593	1,381	960	1,898

** 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 2011 is shown below:

Number of For-cause Inspections (Foreign Manufacturing Sites)

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs*	5	2	1	1	1
In vitro diagnostics	0	0	0	0	0
Medical devices	0	1	0	4	1
Total	5	3	1	5	2

** Excluding in vitro diagnostics.*

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

Region	Country	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	Total
Europe	France	4	6	5	6	1	3	25
	Denmark	2	3	2	2	0	0	9
	Ireland	2	2	5	3	2	0	14
	UK	0	4	1	3	0	0	8
	Netherlands	3	1	1	5	0	0	10
	Spain	0	3	1	1	0	0	5
	Italy	0	2	5	3	2	0	12
	Belgium	0	1	2	4	3	1	11
	Austria	1	0	2	2	0	1	6
	Finland	1	0	0	2	0	0	3
	Germany	0	0	3	7	0	3	13
	Sweden	0	0	1	0	0	0	1
	Romania	0	0	1	0	0	0	1
	Slovenia	0	0	2	1	0	0	3
	Portugal	0	0	0	0	3	0	3
	Greece	0	0	0	0	0	1	1
	Turkey	0	0	0	0	1	0	1
	Subtotal	13	22	31	39	12	9	126
North, Central and South America	USA	20	22	14	18	23	6	103
	Canada	0	0	2	2	1	0	5
	Mexico	0	0	1	0	0	1	2
	Bahamas	0	0	0	0	0	0	0
	Argentina	0	0	2	0	0	0	2
	Subtotal	20	22	19	20	24	7	112
Asia	China	0	5	11	25	10	20	71
	India	0	1	12	4	7	4	28
	Singapore	0	2	4	0	0	0	6
	South Korea	1	0	3	9	10	18	41
	Indonesia	1	0	0	0	0	0	1
	Taiwan	0	0	2	6	1	1	10
	Thailand	0	0	0	2	0	1	3
	Vietnam	0	0	0	0	1	1	2
	New Zealand	0	0	0	1	0	0	1
	Subtotal	2	8	32	47	29	45	163
Africa	South Africa	1	0	0	0	0	0	1
	Subtotal	1	0	0	0	0	0	1
Grand Total		36	52	82	106	65	61	402

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 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	Total
Europe	Ireland	3	0	6	0	4	1	14
	UK	0	0	1	0	0	1	2
	Italy	0	0	2	0	2	1	5
	Netherlands	0	0	1	0	1	0	2
	Switzerland	2	0	1	1	0	0	4
	Spain	0	0	1	0	0	0	1
	France	0	1	1	1	1	1	5
	Denmark	0	0	0	1	0	0	1
	Subtotal	5	1	13	3	8	4	34
North, Central and South America	USA	10	10	16	27	19	12	94
	Mexico	0	0	1	0	0	1	2
	Brazil	0	0	0	1	0	0	1
	Canada	0	0	0	0	0	1	1
	Costa Rica	0	0	0	0	0	1	1
	Subtotal	10	10	17	28	19	15	99
Asia	China	0	0	0	3	0	0	3
	South Korea	0	0	0	0	1	0	1
	Singapore	0	0	0	2	0	0	2
	Israel	0	0	0	0	0	1	1
	Subtotal	0	0	0	5	1	1	7
Grand Total		15	11	30	36	28	20	140

Note 1: Not including for-cause inspections at overseas 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 medical devices, regarding 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 as well as 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 medical device training programs including observation of surgery and hands-on use of pacemakers, biological heart valves, and catheters for placing transvascular stents, etc. A hands-on training using orthopedic medical devices was also provided.

  The Agency conducted a training program including research at university laboratories studying medical devices, in order to reinforce the training curriculum.

  A training program (adverse drug reactions 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: special training lectures (39 times) including training in which product development activities at companies are presented and training for respective review part; training on regulations such as the Pharmaceutical Affairs Act (once); and a training course on clinical study design (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 GMP/QMS joint simulated 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 one inspector to one facility 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 eleven employees to three medical institutions to do practical training as pharmacists and in the department of pharmacy services at hospitals.

f. Visits to manufacturing facilities

- PMDA conducted on-site training programs, such as visits to drug manufacturing facilities (3 facilities), medical device manufacturing facilities (4 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 5 universities (Note 2) in FY 2011, in addition to the 6 partner universities (Note 1). In April FY 2011, PMDA accepted one graduate student from Gifu Pharmaceutical University as a pre-doctoral fellow and provided research guidance.

(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)

(Note 2) 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)

- As a part of efforts to promote the diffusion of regulatory science, PMDA made arrangement as needed when there is a request from universities, etc. for PMDA staff to give lectures (FY 2011: 27 universities, 71 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 graduate schools of the partner university, and accepted one student on April 1, 2011.

(iii) Efforts to integrate pharmacogenomics into regulatory activities

a. Support to the development of evaluation guidelines

- In FY 2011, the PMDA Omics Project (POP) team made investigations and discussions toward the start of guidance development regarding the way of collecting samples for genetic testing and procedures for conducting clinical trials that use pharmacogenomics, etc.

- In order to help MHLW to develop product evaluation guidelines, PMDA newly set up six cross-sectional project working groups for standards development within PMDA. The projects is intended to provide scientific decision making basis for reviews of drug and medical device applications, thereby promoting product development, promoting international collaboration on review standards, etc., and accelerating reviews. The new six projects/working groups are the orphan drugs working group, the pediatric drugs working group, the QbD assessment project, the project on innovative statistical strategies for new drug development, the nanomedicine initiative project, and the global clinical study project.

b. Contribution to establishment of internationally harmonized methods

- In FY 2011, in order to examine the appropriate application of biomarkers and pharmacogenomics to drug development and challenges thereof, the PMDA Omics Project (POP) team conducted teleconference, etc. with experts of regulatory agencies in the European Union (EU) and the US to exchange opinions. The team also participated in presentation sessions and panel discussions in international academic conferences, and thus contributed to the processes toward global harmonization.

(iv) Promotion of appropriate clinical trials

- PMDA exchanged opinions with medical institutions, etc., which were subjected to GCP on-site inspection, on GCP or the conduct of clinical trials after completion of the inspection.

- In order to enhance understanding of the proper conduct of clinical trials, PMDA held GCP Workshops in Tokyo and Osaka targeting drug development and regulatory affairs personnel and 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 in document-based compliance assessment or GCP on-site inspections. The workshop materials were posted on PMDA's website with the aim of informing 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Tokyo	1,212	1,338	1,165	1,048	1,086
Osaka	495	543	461	455	418
Total	1,707	1,881	1,626	1,503	1,504

(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 post-marketing safety measures available to foreign users, PMDA has created and released the English version of review reports on its English website. In FY 2011, the Agency created and released the English translations of 5 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 2011, PMDA released 141 review reports (median time from approval to release, 16 days), 90 summaries of product applications (median time from approval to release, 61 days) and 52 re-examination reports (median time from result notification to release, 7 days).

  The percentage of review reports released within one month after approval was 86.5% (53.7% in FY 2010) and the percentage of summaries of product applications released within 3 months after approval was 90% (60.7% in FY 2010).

(Review reports on new medical devices)

- In FY 2011, PMDA released 12 review reports (median time from approval to release, 29 days) and 10 summaries of product applications (median time from approval to release, 101 days).

  The percentage of review reports released within one month after approval was 58.3% (44.4% in FY 2010) and the percentage of summaries of product applications released within 3 months after approval was 50.0% (14.3% in FY 2010).

(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 2011, 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 judgment 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 participated in the MHLW's study group for infrastructure development to internationally exchange information on medical devices, and worked with MHLW to develop a requirement definition document as the basis of infrastructure development. The document was completed at the end of February 2012.

(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 EU/EMA in collaboration with the MHLW.

- PMDA collected information on the review system and post-marketing safety measures from FDA, EMA, etc. while exchanging information with them on operational methods and other issues. Specifically, a bilateral meeting with the FDA was held in June 2011 and with the European Commission (EC)/EMA in September 2011, where views were exchanged actively.

- PMDA dispatched its executives as liaison officers to the US Pharmacopoeia and the EMA, in order to gather information and exchange views.

- PMDA participated in the 6th Heads of Medicines Regulatory Agencies Summit held in Sydney in October 2011, and exchanged opinions on pharmaceutical regulatory affairs with regulators in various countries including the FDA and EMA.

- PMDA concluded a confidentiality arrangement with Australia in September 2011 and with Ireland in October 2011, and developed a framework to share information. In February 2012, PMDA extended the expiration of the confidentiality arrangement with EC/EMA by one year to continuously share information.

- A bilateral meeting with China was held in August 2011 to reinforce the collaborative relationship by reaching an agreement to advance four projects (GCP, GMP, Training, Clinical Development) by the working group in the area of drugs. In addition, the 3rd China-Japan Symposium on Drug

Development was held in China in March 2012 to exchange views on pharmaceutical regulatory systems in both countries and ethnic factors.

- In October 2011, the 4th China-Korea-Japan Director-General Meeting and Working Group on Pharmaceutical Affairs were held in Japan, where the progress status of the research project on ethnic differences coordinated by Japan was reported.

- In November 2011, the APEC Multi-Regional Clinical Trials Tokyo Workshop was co-hosted by PMDA, MHLW, Society for Regulatory Science of Medical Products, and APEC Harmonization Center. The results of the China-Korea-Japan Director-General Meeting on Pharmaceutical Affairs were reported. Case studies of global clinical trials of therapeutic agents for various cancers and other presentations were given, and topics such as the promotion of global clinical trials in Asia were discussed.

b. Strengthening of activities for international harmonization

- In FY 2011, 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, as well as in the Expert Working Group Meetings of PDG*.

  * ICH: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
  * PDG: Pharmacopoeial Discussion Group

- In FY 2011, PMDA continued to actively participate in Steering Committee Meetings and Expert Working Group Meetings of GHTF*, Steering Committee Meetings and Working Group Meetings of HBD*, ISO*, etc. It was determined that GHTF would terminate its activities in 2012. As Japan has held the last chair of GHTF since July 2011, PMDA organized meetings and provided instructions to Expert Working Group Meetings, in addition to conventional activities including preparation of guidance documents in cooperation with related countries. Being grounded in the GHTF activities, IMDRF* was newly established in October 2011. PMDA participated in IMDRF as a steering committee member from the establishment.

  ** GHTF: Global Harmonization Task Force for Medical Devices*
  ** HBD: Harmonization by Doing*
  ** ISO: International Organization for Standardization*
  ** IMDRF: International Medical Device 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 Expert Working Groups

  ICH Meeting in Cincinnati

  ICH Meeting in Seville

Topics discussed in FY 2011

- Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use (S2 [R1])
- Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals (S6 [R1])
- Photosafety Evaluation of Pharmaceuticals (S10)
- Impurities: Guideline for Metal Impurities (Q3D)
- Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (M7)
- Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions (Q4B)
- Development and Manufacture of Drug Substances (Q11)
- Q&A on Quality (Q-IWG)
- Q&A on CTD-Quality Documents (CTD-Q)
- MedDRA Term Selection: Points to Consider (M1 PtC WG)
- Electronic Standards for Transmission of Regulatory Information (M2)
- Electronic Common Technical Document (M8)
- Data Elements and Standards for Drug Dictionaries (M5)
- Data Elements for Transmission of Individual Case Safety Reports (E2B [R3])
- Clinical Safety Data Management: Periodic Safety Update Reports (PSUR) for Marketed Drugs (E2C [R2])
- Q&A on the Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs (E14-IWG)
- Q&A on the Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals (M3 [R2]-IWG)
- Need for Carcinogenicity Studies of Pharmaceuticals (S1A Informal WG)
- Q&A on Structure and Content of Clinical Study Reports (E3 IWG)

* PDG
* 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)
* CIOMS (Council for International Organizations of Medical Sciences) Working Group
* Working Group on Good Laboratory Practice (GLP) of OECD
* WHO INN (international nonproprietary names) meeting
* APEC LSIF RHSC (Life Science Innovation Forum, Regulatory Harmonization Steering Committee)

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

- PMDA held 5 Expert Discussion meetings on drug names and reported 53 Japanese accepted names (JAN) to MHLW. Two consultations on applications for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in April and October 2011.

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.

- PMDA received foreign trainees, including three from Korea Food and Drug Administration (KFDA) and two from Taiwan Food and Drug Administration (TFDA). PMDA also accepted government research teams from China, Taiwan, Russia, Indonesia, and Vietnam and provided explanations regarding Japanese pharmaceutical regulations.

- PMDA held a training seminar for regulators from Asian countries and provided training programs on the services of the Agency, the system and principles of GMP inspections of drugs, 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 of employees in English, and provided a practical business English program (20 members) or an intermediate English program (28 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, 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 post-marketing safety measures to international audiences, PMDA has created and released English translations of the review reports and safety information on its website. In FY 2011, the Agency prepared and published English translations of 5 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.

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 689 clinical trial notifications submitted in FY 2011, 121 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of global clinical trial notifications	38	82	113	134	121

- PMDA intends to take an active approach to global clinical trials. In FY 2011, it carried out 73 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of consultations on global clinical trials	56	51	56	66	73

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

(i) Proper assessment of reports of 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 266,000 reports on adverse drug reactions and approximately 17,000 reports on malfunctions of medical devices submitted to PMDA from within and outside of Japan in FY 2011. 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 in-country measures for 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 adverse reaction reports and malfunction reports 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs	204	151	260	339	185
Medical devices	10	37	62	19	17
Medical safety*	1	4	4	5	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 drugs and medical devices expertise, 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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs	Directions for revision to precautions in package insert	202	141	254	339	185
	Posting articles and cases on PMDSI*	86	20	29	32	41
Medical devices	Directions for revision to precautions in package insert or issuance of notifications on self-check	8	4	4	3	5
	Posting articles on PMDSI	3	2	5	3	4

** 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 2011, PMDA made the following efforts to appropriately collect, organize, and examine the adverse drug reaction reports and medical device malfunction reports submitted by companies and medical institutions:
  a. Upgraded the information management system for adverse drug reactions and the safety measures support system, and built the progress management system for medical institution's reports
  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 198 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 2011, PMDA started to operate a pilot system to verify them.

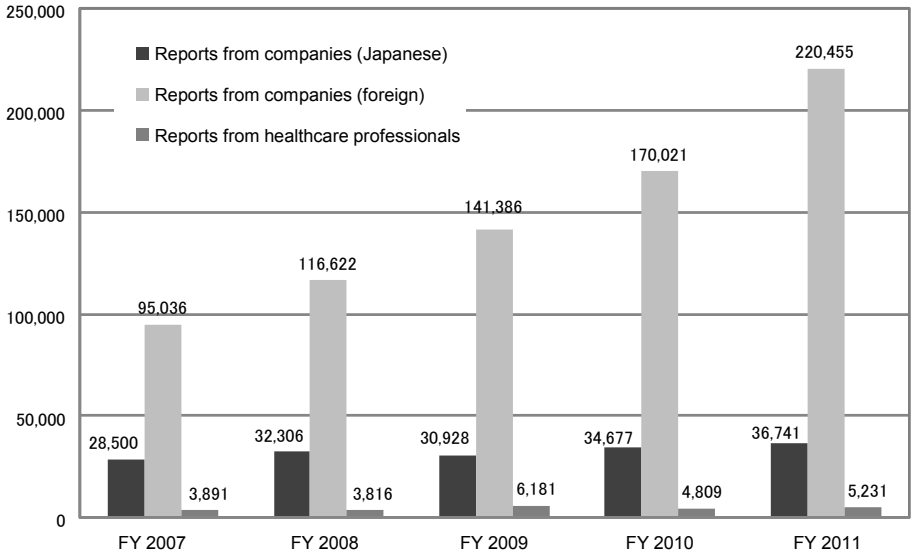
Collection of adverse reaction reports, etc.

1-1) Number of reports relating to drugs

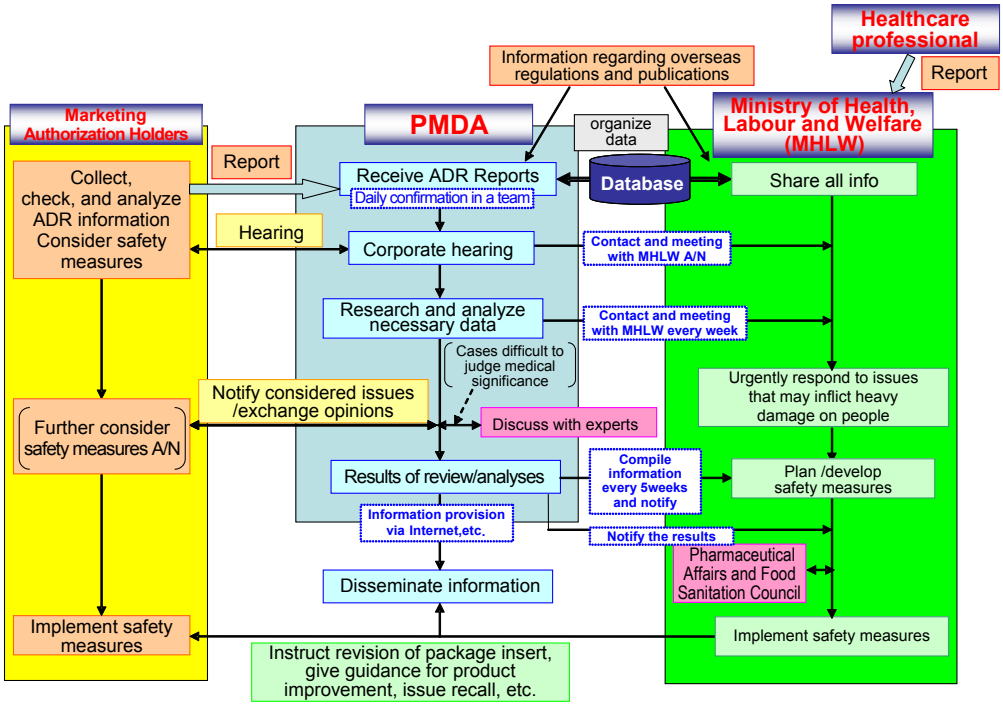
	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Reports from companies	126,181	151,726	175,285	207,772	260,473
(cases of adverse drug reactions, Japanese)	(28,231)	(31,455)	(30,814)	(34,578)	(36,641)
(cases of infections caused by drugs, Japanese)	(269)	(851)	(114)	(99)	(100)
(cases of adverse drug reactions, foreign)	(95,015)	(116,592)	(141,364)	(169,994)	(220,410)
(cases of infections caused by drugs, foreign)	(21)	(30)	(22)	(27)	(45)
(research reports)	(858)	(855)	(933)	(940)	(841)
(foreign safety measure reports)	(695)	(869)	(930)	(1,033)	(1,347)
(periodic infection reports)	(1,092)	(1,074)	(1,108)	(1,101)	(1,089)
Reports from healthcare professionals	3,891	3,816	6,181	4,809	5,231
(i) Safety information reporting system	3,891	3,816	3,721	3,656	3,388
(ii) Three vaccines/influenza*			2,460	1,153	1,843
Total	130,072	155,542	181,466	212,581	265,704

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

Changes in the Numbers of Reports on Adverse Drug Reactions/Infections



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.

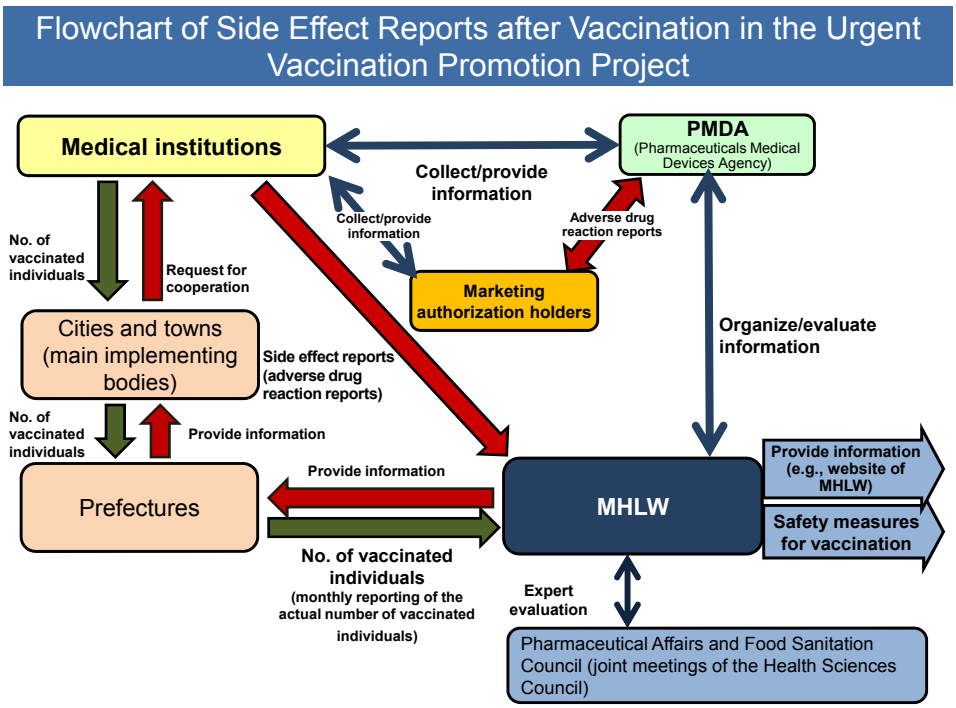
It was decided to handle influenza A (H1N1) as ordinary seasonal influenza from April 1, 2011 onwards, and consequently the Program was completed. However, in accordance with HSB Notification No. 0929-3 from the Health Service Bureau of MHLW and PFSB Notification No. 0929-8, dated September 29, 2011, "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
Influenza Vaccines	2,460	684	558

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	Cervical cancer vaccine	Hib vaccine	Pediatric pneumococcal conjugate vaccine
FY 2010	176	135	158
FY 2011	765	210	310



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 a patient adverse reaction reporting system 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 started 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 2011 is shown in the following table.

	FY 2011
Adverse drug reaction reports from patients	30

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

The necessity of establishment of a system which enables utilization of reports on adverse drug reactions, etc. from medical institutions 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.

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.

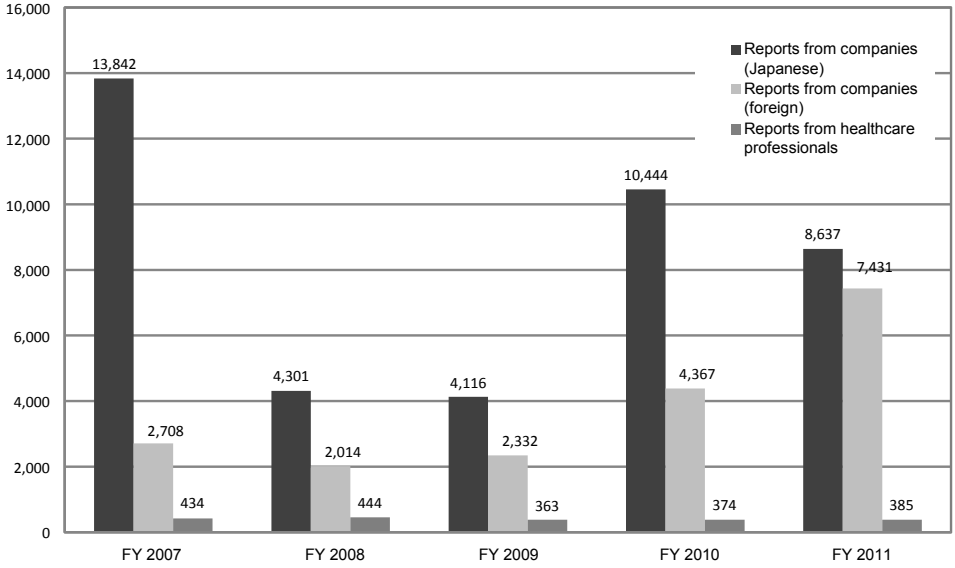
	FY 2010	FY 2011
Number of cases in detailed investigation	75	613

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 2007	FY 2008	FY 2009	FY 2010	FY 2011
Reports from companies	17,142	7,137	7,344	15,874	17,192
(cases of malfunctions of medical devices, Japanese)	(13,842)	(4,301)	(4,114)	(10,444)	(8,637)
(cases of malfunctions of medical devices, foreign)	(2,708)	(2,014)	(2,332)	(4,367)	(7,431)
(cases of infections caused by medical devices, Japanese)	(0)	(0)	(2)	(0)	(0)
(research reports)	(15)	(10)	(6)	(27)	(2)
(foreign safety measure reports)	(525)	(748)	(831)	(978)	(1,060)
(periodic infection reports)	(52)	(64)	(59)	(58)	(62)
Reports from healthcare professionals	434	444	363	374	385
Total	17,576	7,581	7,707	16,248	17,577

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



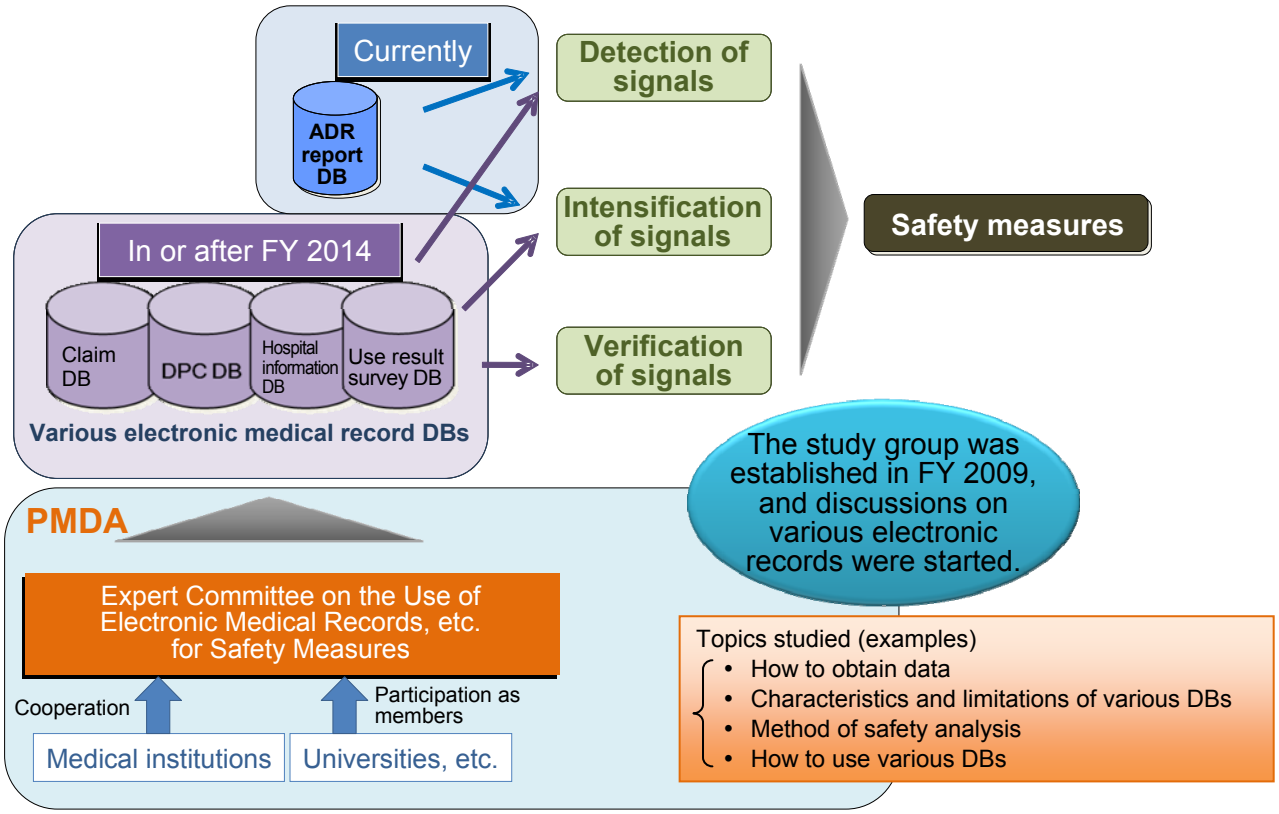
(ii) Sophistication of safety measures

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 2011, the pilot studies were conducted mainly to explore appropriate analytical methods and to evaluate the usability, limitations, etc. of each data source (see the following table).

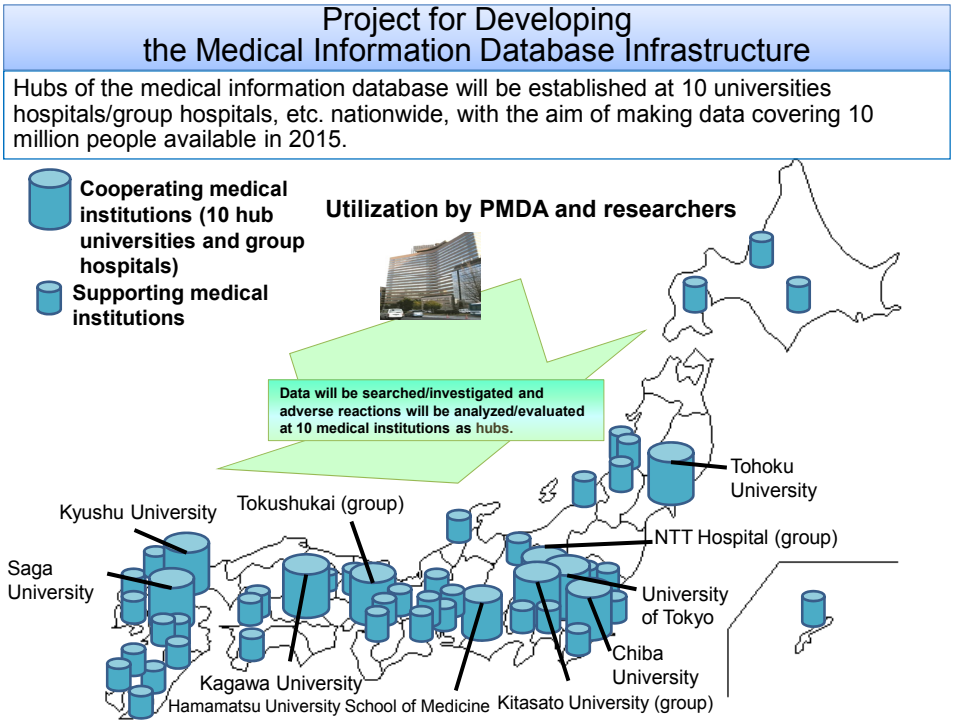
Study for Introducing New Databases (DBs) for Drug Safety Evaluation Process



Data sources	Study started in	Study	Design
Claim data (commercially 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 been already 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 been already 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 been already posted on the Medical Product Information web page. Partly presented in an academic conference)
	FY 2010	Risk analysis of adverse drug reactions (cohort study, nested case-control study)	Risk analyses 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 pharmacoepidemiological method (PSSA†)	Signal detection was performed by using PSSA for a known association between a drug and an adverse reaction (drug-induced parkinsonism associated with antipsychotic agents) (presented in an academic conference) †PSSA: prescription 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 and 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.
DPC (Diagnosis Procedure	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.

Combination) Data	FY 2011	Actual condition of prescription of drugs	Patients who were prescribed any one of the following three drugs/drug groups were identified and analyses of respective drugs/drug groups were performed. 1. Antimicrobial drugs (for pediatrics) 2. Doxorubicin 3. Sorafenib
	FY 2011	Survey on effects of safety measures	Patients who were prescribed sorafenib were identified and analyses were performed for safety measures taken during the follow-up period.
Hospital information data (HIS)	FY 2009-2011	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 criteria for case identification	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. (Presented in academic conference)

- In FY 2011, the "Project for developing the medical information database infrastructure" 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 people 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).

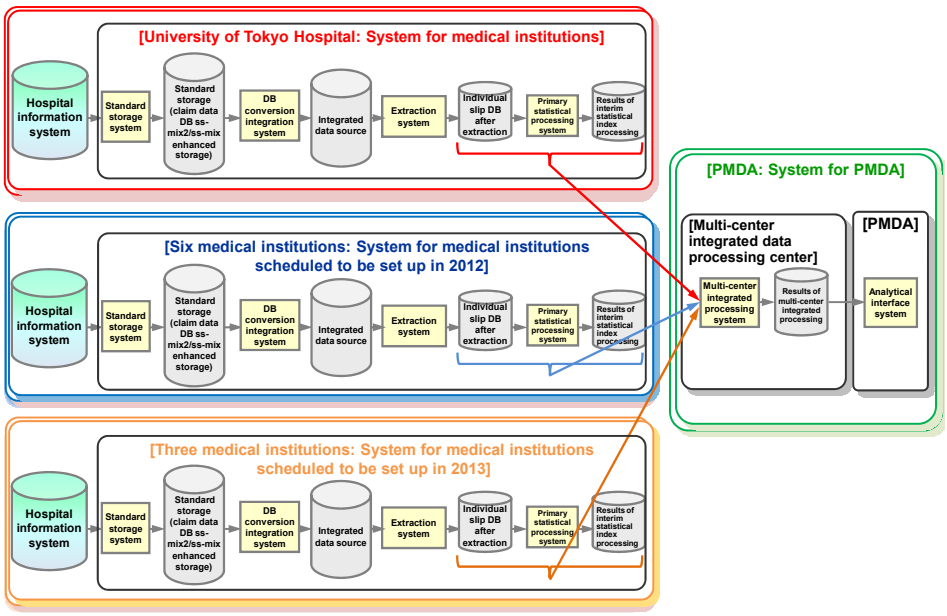


- The establishment of the medical information database is scheduled to be carried forward sequentially from FY 2011 to FY 2013, with the aim of operating the database at 7 cooperating medical institutions in FY 2012 and at 3 medical institutions in FY 2013.

  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, PMDA plans to upgrade existing hospital information systems at 6 other medical institutions, and also complete the development of the planned database system for medical institutions, which is to be installed in the 7 cooperating medical institutions including the University of Tokyo Hospital. 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 System



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 adverse reaction information, 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.

- In FY 2011, PMDA upgraded its system to allow the public to access to adverse reaction reports as compiled in the database. 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 2011, 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 were continuously reviewed from both theoretical and practical aspects, such as justification for threshold values, use of onset dates of adverse drug reactions, quantity of signals, timing of detection, etc. The results of the review were compiled as a report.

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)

- 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 2011, PMDA continued the "Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS)" project based on the protocols that were developed under the industry-government-academia collaboration in the First Mid-term Plan. PMDA developed a web-based entry system and implementation structures at participating medical institutions, and started data collection in June 2010. As of March 28, 2012, 88 patients (57 for IVAD*, 31 for ECMO*) have been enrolled at 12 participating institutions. The number of enrolled patients and other data have been updated on the PMDA's Medical Product Information web page.

IVAD: Implantable ventricular-assist devices

ECMO: Extra-corporeal membrane oxygenation

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.

- PMDA compiled an interim report on data over a follow-up period of three years (26 institutions, 15,792 patients [13,592 patients with PCI, 2,200 patients with CABG]; excluding patients who did not give their consent), which were summarized and analyzed in FY 2010, and posted the report on the Medical Product Information web page in October 2011. In FY 2011, PMDA completed the preparations (contract procedures with 26 institutions, etc.) for data collection over a follow-up period of five years. PMDA started data collection in January 2012, and has completed the collection of data from 8,533 patients at 17 institutions as of February 24, 2012.

- 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 relating to a company's own products

- PMDA investigates adverse drug reactions which has been reported to the regulatory authorities but not informed to companies by medical institutions. The Agency has started operating 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.

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 2011 is shown below:

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Drugs	486	559	619	752	670
Medical devices	260	283	247	171	163
Medical safety	166	172	142	83	59

- 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. One reason for the reduction in the number of consultations on medical devices is considered to be the improvement in knowledge and understanding on the part of companies as a result of consultations on the revision of package inserts that have been provided from FY 2004.

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

- From among the contents of all adverse reaction reports that were submitted by companies in or after April 2004, PMDA has publicly released their fiscal year reported, sex, age, primary disease, suspected drug, adverse event, suspected concomitant drug, and outcome on its Medical Product Information web page, since January 2006. By the end of March 2012, PMDA posted 210,413 reports which had been submitted up to November 2011.

- In addition to the above, in March 2012, PMDA began to expand data items and reports to be released, and all domestic adverse drug reaction reports are to be released 4 months after reporting in principles so that the contents will be more easily utilized by related parties. The newly released reports and added/changed data items are as follows.

  Newly released reports:
  Uncompleted, domestic adverse drug reaction reports from marketing authorization holders, etc.; Reports of cases about which PMDA conducted investigations such as making inquiries, among adverse drug reaction/infection reports from healthcare professionals to the Minister of Health, Labour and Welfare.

  Added/changed data items:
  "fiscal year and quarter of a year reported" "reporting category" "type," "job category of reporter," "investigation status," "height/weight of patient," "suspected drug/brand name," "reason for use," "route of administration," "a single-dose," "start date/end date of administration," "adverse events (onset date)," "action against suspected drug," "presence/absence of recurrence due to re-administration," "other concomitant drug"

- PMDA makes the database of adverse reaction reports publicly available as a line listing format. In FY 2011, the Agency prepared for providing the datasets in the CSV format so that the database can be used for research/studies, including the expanded items/reports for public release (Data have been released from April 2012).

- The time from receiving adverse reaction reports to release was maintained for a 4-month period, showing that the target period for FY 2011 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, sex, age, outcome, generic name, condition of the medical device, and patient adverse event on its Medical Product Information web page, since March 2006. By the end of March 2012, PMDA posted 62,898 reports submitted up to September 2011.

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

- By the end of FY 2011, PMDA posted 12,064 package inserts of prescription drugs on the Medical Product Information web page. Upon the issuance of directions for revision of a package insert by the government, PMDA posted the directions 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 15,584 instructions for use by the end of FY 2011. 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 10,065 package inserts are available on the website as of the end of FY 2011.

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 3,994 package inserts were posted on the website as of the end of FY 2011.

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

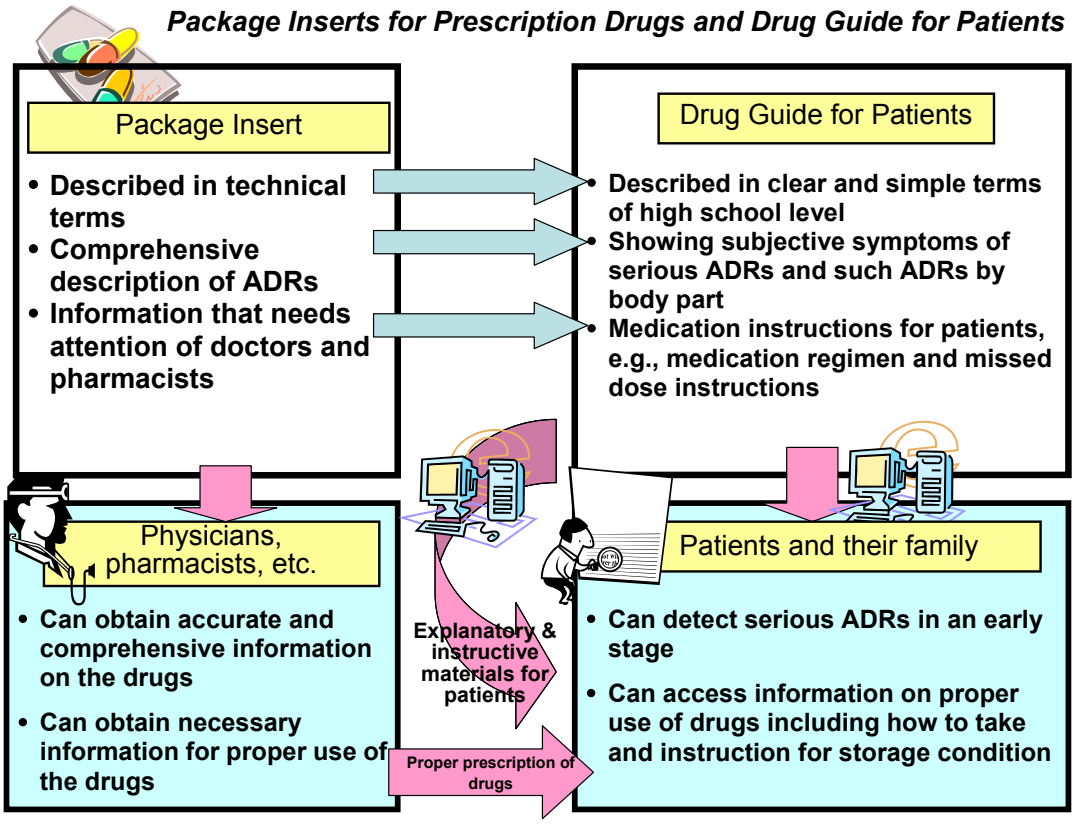
- The manuals for management of individual serious adverse drug reactions prepared by MHLW have been made available on the PMDA website since November 2006. As of the end of FY 2011, manuals for a total of 75 diseases were posted on the website.

  These manuals contain information for patients and their family members, that allows early detection of serious adverse drug reactions based on subjective symptoms, and also contain methods of their diagnosis and management for healthcare professionals.

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 2011, the drug guides for 33 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 363 active ingredients in 1,951 products (1,307 package inserts) were posted by the end of FY 2011.

- 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 (a study supported by the Health and Labour Sciences Research Grant titled "Research on how to provide patients and people with drug safety information").



l. Upgrading Medical Product Information web page

- PMDA has been making efforts to enhance and reinforce the provision of safety information. The Agency distributes important post-marketing safety information, such as revision of precautions in package inserts, to healthcare professionals and relevant people in companies by e-mail upon issuance of such information, and posts various safety information including package inserts, on the Medical Product Information web page: http://www.info.pmda.go.jp/.

- In FY 2011, taking into account opinions given by website users, PMDA upgraded the search system for package inserts of prescription drugs to allow search of those with warning and added the link to the top page.

- PMDA also added functions for easier searching such as non-proprietary names/brand names search, prefix search, etc. to the search engine for information of package inserts of prescription drugs, etc.

- In addition to functional improvements, PMDA improved its website by adding new content, re-designing the existing content, informing maintenance schedules, etc., thereby making the website more user-friendly.

- Besides the above, the information site for the general public was upgraded for more user-friendliness.

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

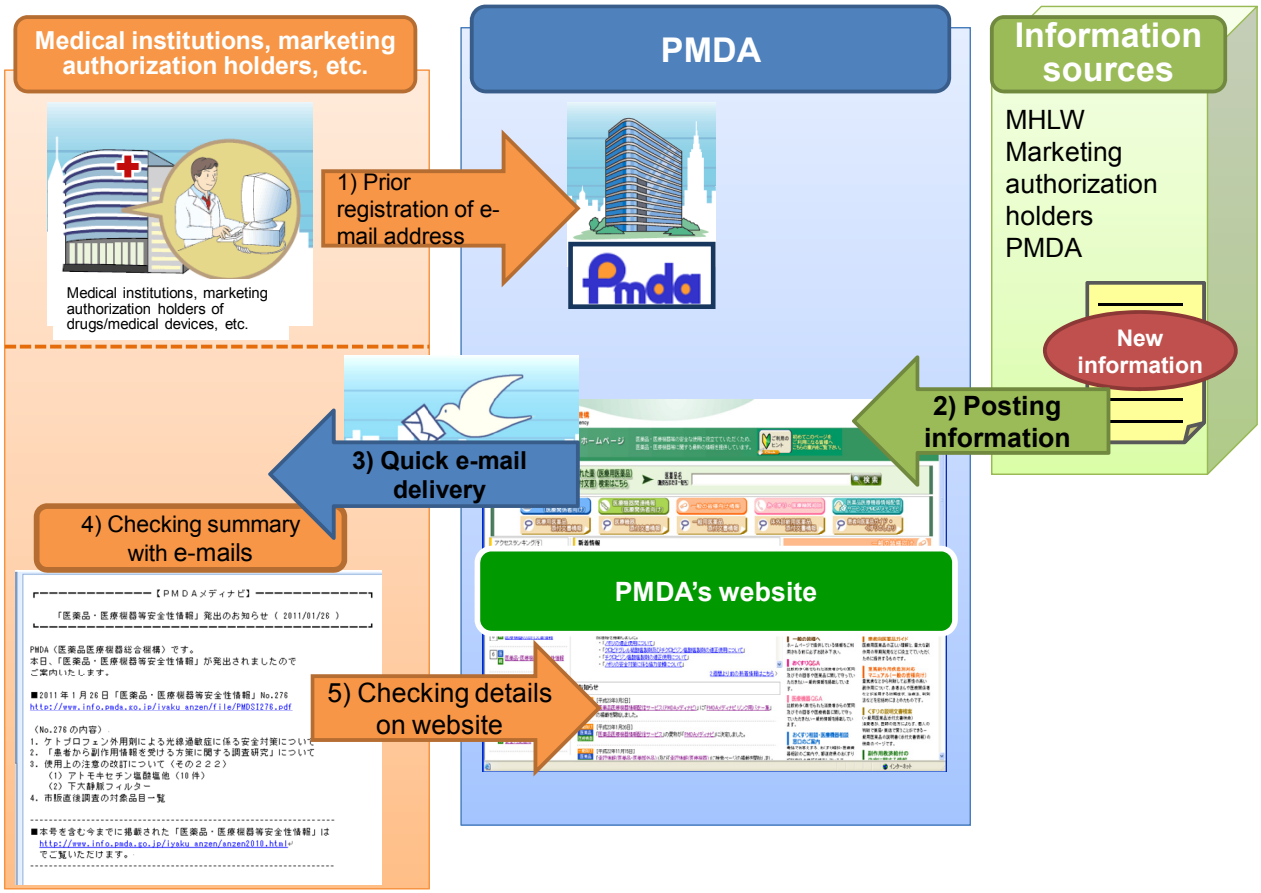
- The "Pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)" which provides safety information such as revisions to package inserts and Class I recalls, is provided via e-mail to healthcare professionals who subscribe to the service. To enhance its public recognition and increase 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 55,372 e-mail addresses were registered as of the end of March 2012 (increased by about 20,000/year in FY 2011). Approximately, 40% of these subscribers were at hospitals and clinics, 20% were pharmacies, 10% were dentist clinics or other medical facilities, and 20% 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 2012, 4,565 subscribers have been registered.

- This is a service which enables users to prepare a customizable drug list on the website. In this service, when users register necessary drugs (My Drugs), a listing 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 urgent safety information is issued for any registered drug.

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



PMDA medi-navi by Content in FY 2011

Contents of e-mails	Number of releases
Recalls (Class I)	42
Pharmaceuticals and Medical Devices Safety Information	12
Drug Safety Update (DSU)	10
Revision of PRECAUTIONS of drugs	12
Revision of PRECAUTIONS of medical devices	5
Notification on self-check (medical devices)	0
PMDA Medical Safety Information	6
Approval information (medical devices)	10
Approval information (prescription drugs)	82
Notifications on drugs, Notifications on medical devices	14
Information on proper use of drugs	29
Information on drug risk under evaluation	15
MHLW notification on medical safety measures	10
Information released by MHLW	3
Others	9
Total	259

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 2011, 5,059 cases associated with drugs and 429 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 5,488 cases for which deliberations were completed by MHLW, the details of the cases were posted on the Medical Product Information web page as shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 5,488 cases	5,059	429
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.	5	0
2) Cases in which measures have already been taken, or are currently under consideration, by the marketing authorization holder etc.	21	24
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.	5,033	405

- 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 2011, the following seven 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.23	April 2011	Precautions in Handling of Insulin Syringes
No.24	June 2011	Precautions in Using Needle-free Valves
No.25	September 2011	Precautions for Magnetic Resonance Imaging (MRI) Scans (Part 1)
No.26	September 2011	Precautions for Magnetic Resonance Imaging (MRI) Scans (Part 2)
No.27	October 2011	Precautions in Handling of Drug Products Attached with Reconstitution Solution
No.28	November 2011	Precautions in Handling of Blood Glucose Meter
No.29	December 2011	Precautions in Handling of Electrocardiogram Monitoring System

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 2011, the number of persons receiving consultations was 8,945 (12,473 calls) for drugs, and 660 (686 calls) for medical devices.

- Regarding generic drugs, requests for consultation have been accepted from not only general consumers but also healthcare professionals such as physicians and pharmacists since May 2007 as consultations on generic drugs. In FY 2011, the number of persons receiving consultations was 453. General consumers accounted for 90.3% of them, whereas physicians/pharmacists accounted for 3.0%.

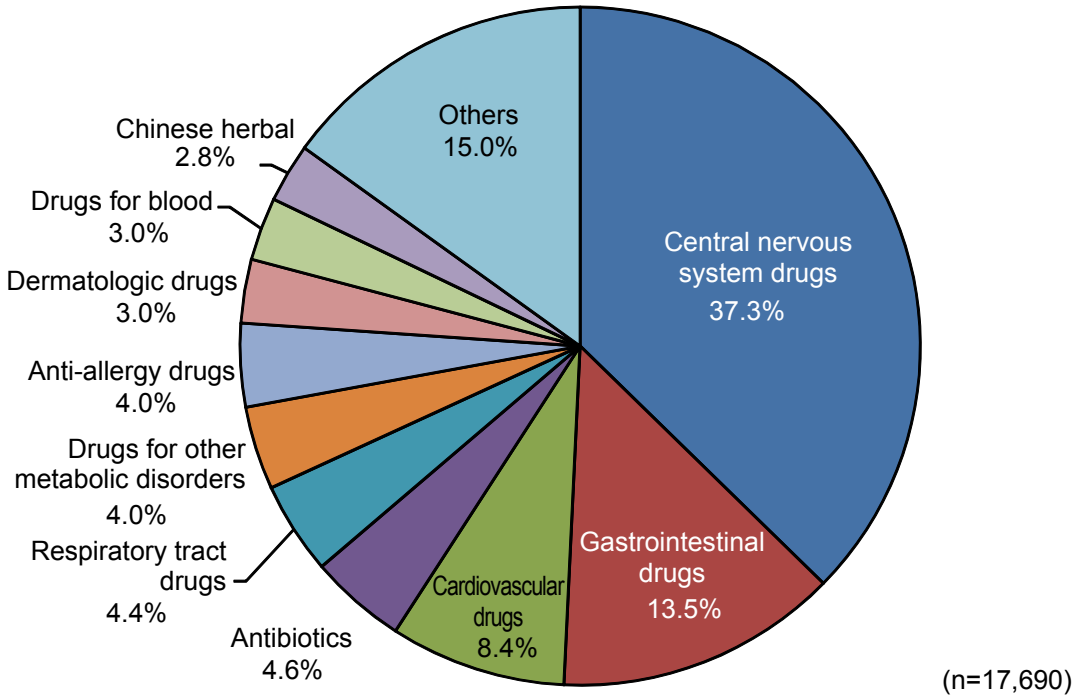
Number of Consultations on Drugs/Medical Devices

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Consultations on drugs	8,696 [35.5 cases/day]	8,479 [34.9 cases/day]	9,316 [38.5 cases/day]	8,846 [36.4 cases/day]	8,945 [36.7 cases/day]
(of which, consultations on generic drugs)	(122)	(143)	(687)	(617)	(453)
Consultations on medical devices	564 [2.3 cases/day]	639 [2.6 cases/day]	558 [2.3 cases/day]	574 [2.4 cases/day]	660 [2.7 cases/day]

Contents of Consultations on Drugs

Contents of consultation	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
(1) Safety	5,731 (45.9%)	6,347 (50.6%)	5,727 (42.4%)	5,553 (45.0%)	5,146 (41.3%)
(2) Indications	1,175 (9.4%)	954 (7.6%)	1,079 (8.0%)	890 (7.2%)	1,147 (9.2%)
(3) Administration and Dosage	1,072 (8.6%)	836 (6.7%)	746 (5.5%)	784 (6.4%)	981 (7.9%)
(4) Interactions	715 (5.7%)	732 (5.8%)	753 (5.6%)	784 (6.4%)	986 (7.9%)
(5) Active Ingredient	236 (1.9%)	214 (1.7%)	251 (1.9%)	181 (1.5%)	199 (1.6%)
Others	3,548 (28.4%)	3,450 (27.5%)	4,960 (36.7%)	4,144 (33.6%)	4,014 (32.1%)
Total	12,477 (100.0%)	12,533 (100.0%)	13,516 (100.0%)	12,336 (100.0%)	12,473 (100.0%)

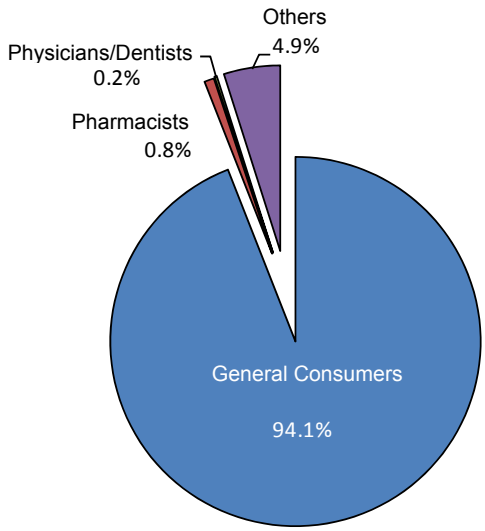
Number of Consultations on Drugs by Therapeutic Category (FY 2011)



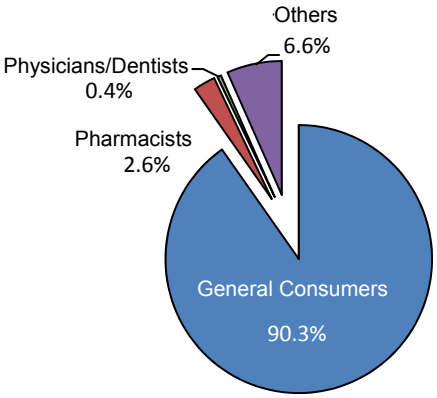
(n=17,690)

Breakdown of Persons Receiving Consultations on Drugs in FY 2011 (by Profession, etc.)

Consultations on drugs (n=8,945)

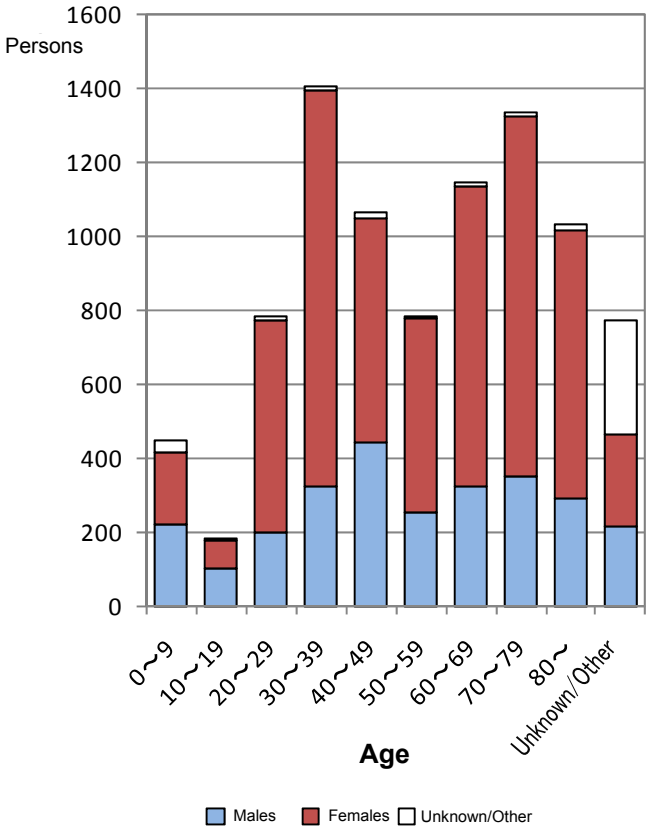


Consultations on generic drugs (n=453)

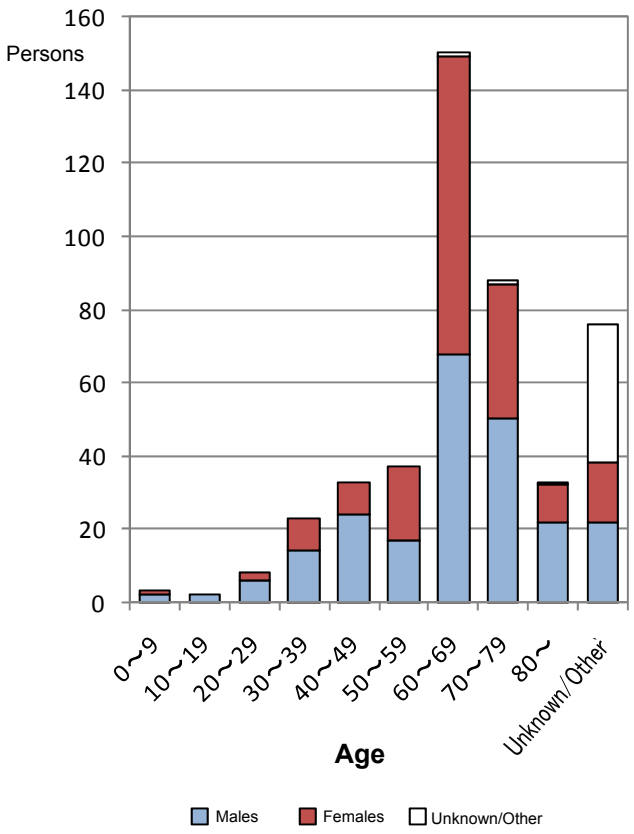


Breakdown of Persons Receiving Consultations on Drugs in FY 2011 (by Age and Gender)

Consultations on drugs (n=8,945)



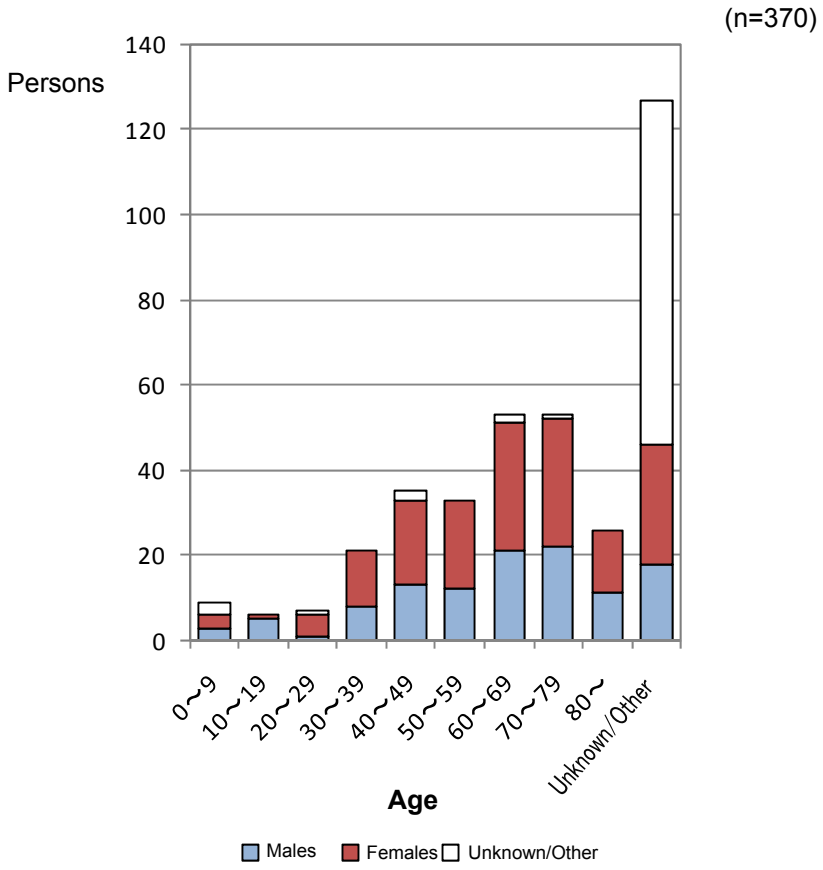
Consultations on generic drugs (n=453)



Contents of consultations on medical devices

Contents of consultation	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
(1) Safety	91 (11.0%)	96 (10.6%)	74 (12.0%)	78 (12.5%)	85 (12.4%)
(2) Indications	85 (10.3%)	90 (10.0%)	59 (9.6%)	61 (9.8%)	69 (10.1%)
(3) Performance	37 (4.5%)	46 (5.1%)	27 (4.4%)	17 (2.7%)	24 (3.5%)
(4) Directions for use	12 (1.5%)	17 (1.9%)	15 (2.4%)	12 (1.9%)	10 (1.5%)
Others	599 (72.7%)	653 (72.4%)	441 (71.6%)	454 (73.0%)	498 (72.5%)
Total	824 (100.0%)	902 (100.0%)	616 (100.0%)	622 (100.0%)	686 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2011 (by Age and Gender)*



** Summary results from a total of 370 persons consisting of general consumers and consultants of consumer affairs centers*

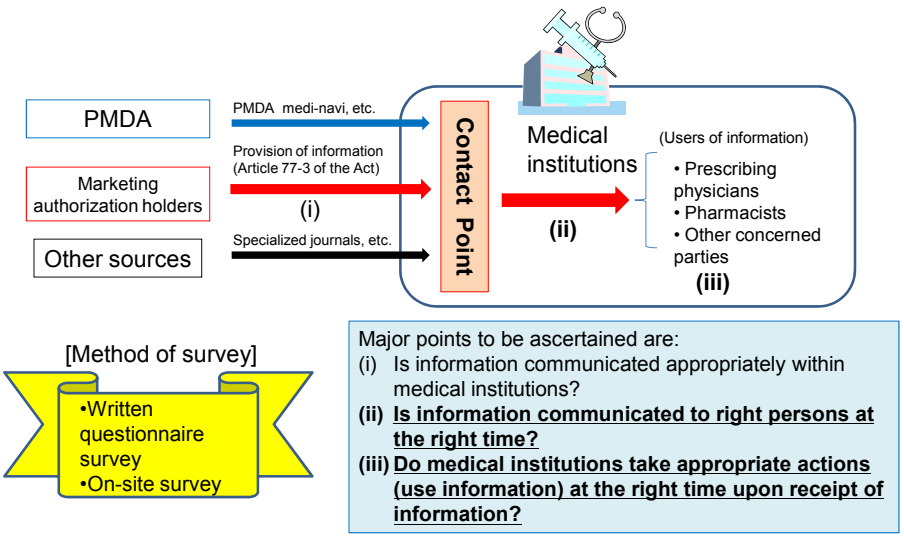
r. Status of communication and use of transmitted safety information within medical institutions

- 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.

  In FY 2010, PMDA conducted a mail-in questionnaire survey among hospitals (8,679 institutions) nationwide, and posted the results of the survey on the PMDA's Information web page. In FY 2011, PMDA conducted a survey among hospitals (8,640 institutions) nationwide

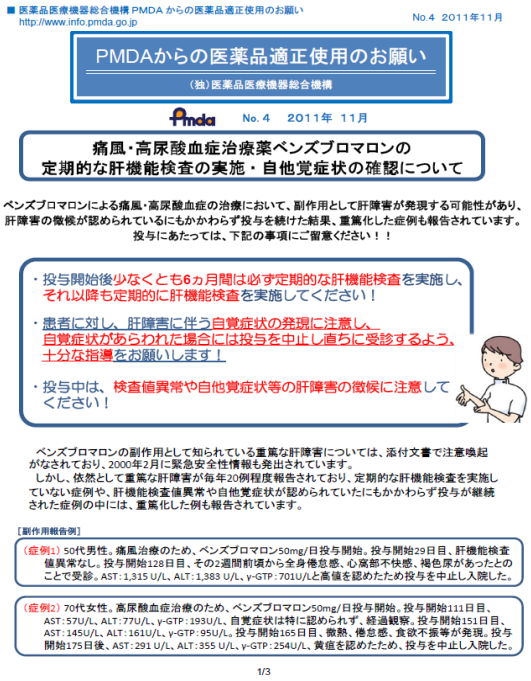
with changed survey items. The results of the survey will be released as soon as they are finalized and used to promote proper communication and use of information in medical institutions.

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 2011, the Agency provided information on five active ingredients (Champix tablets and benzbromarone, etc). For Champix tablets, PMDA also prepared and provided the information for patients.



■ 医薬品医療機器総合機構 PMDA からの医薬品適正使用のお願い
http://www.info.pmda.go.jp
No.4 2011年11月

PMDAからの医薬品適正使用のお願い
(独)医薬品医療機器総合機構

No. 4 2011年 11月

痛風・高尿酸血症治療薬ベンズブロマロンの
定期的な肝機能検査の実施・自他覚症状の確認について

ベンズブロマロンによる痛風・高尿酸血症の治療において、副作用として肝障害が発現する可能性があり、肝障害の徴候が認められているにもかかわらず投与を続けた結果、重篤化した症例も報告されています。
投与にあたっては、下記の事項にご留意ください！！

・投与開始後少なくとも6ヵ月間は必ず定期的な肝機能検査を実施し、それ以降も定期的に肝機能検査を実施してください！
・患者に対し、肝障害に伴う自覚症状の発現に注意し、自覚症状があらわれた場合には投与を中止し直ちに受診するよう、十分な指導をお願いします！
・投与中は、検査値異常や自他覚症状等の肝障害の徴候に注意してください！

ベンズブロマロンの副作用として知られている重篤な肝障害については、添付文書で注意喚起がなされており、2000年2月に緊急安全性情報も発出されています。
しかし、依然として重篤な肝障害が毎年20例程度報告されており、定期的な肝機能検査を実施していない症例や、肝機能検査値異常や自他覚症状が認められていたにもかかわらず投与が継続された症例の中には、重篤化した例も報告されています。

【副作用報告例】

(症例1) 50代男性。痛風治療のため、ベンズブロマロン50mg/日投与開始。投与開始29日目、肝機能検査値異常なし。投与開始128日目、その2週間前頃から全身倦怠感、心窩部不快感、褐色尿があったとのことで受診。AST:1,315 U/L、ALT:1,383 U/L、γ-GTP:701U/Lと高値を認めたため投与を中止し入院した。

(症例2) 70代女性。高尿酸血症治療のため、ベンズブロマロン50mg/日投与開始。投与開始111日目、AST:57U/L、ALT:77U/L、γ-GTP:193U/L、自覚症状は特に認められず、経過観察。投与開始151日目、AST:145U/L、ALT:161U/L、γ-GTP:95U/L。投与開始165日目、微熱、倦怠感、食欲不振等が発現。投与開始175日後、AST:291 U/L、ALT:355 U/L、γ-GTP:254U/L、黄疸を認めたため、投与を中止し入院した。

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■ 医薬品医療機器総合機構 PMDA からの医薬品適正使用のお願い
http://www.info.pmda.go.jp
No.1 2011年10月

PMDAからの医薬品適正使用のお願い
(独)医薬品医療機器総合機構

No.1 2011年 10月

禁煙補助薬チャンピックス錠を服用中の方へ

チャンピックス錠を服用中の方は
自動車の運転などの危険を伴う
機械の操作をしないでください！

危ない!!

チャンピックス錠を服用している方で、運転中に突然意識がなくなり、自動車事故に至った事例が報告されております。

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(Request for Proper Use of Drugs to patients)

Number of Information Documents Released on the Medical Product Information Web Page as of the End of March 2012

Posted information	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Package inserts*1					
Prescription drugs	13,090	13,287	13,050	12,256	12,064
Medical devices	5,462	8,164	11,213	13,979	15,584
OTC drugs	7,437	8,356	9,513	9,884	10,136
In vitro diagnostics		2,237	3,301	3,984	3,994
Drug Guide for Patients*1	270 active ingredients (1,567 products)	294 active ingredients (1,958 products)	312 active ingredients (1,920 products)	330 active ingredients (2,311 products)	363 active ingredients (1,951 products)
Safety information issued by MHLW • Directions for revision of package inserts • Pharmaceuticals and Medical Devices Safety Information • Press release	323	350	376	409	438
Urgent safety information (by pharmaceutical companies)*2	24	24	24	24	24
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])	41	51	61	71	81
Notification of safety measures for medical devices					
Notification on self-check	45	47	49	50	50
Notification of revisions of labeling	28	30	32	33	41
Other related notification	54	57	66	74	83
Information about case reports on suspected ADR	84,094	110,879	142,084	175,360	210,412
Information about case reports on suspected malfunction	34,226	42,405	46,551	51,169	62,898
Notification related to preventive measures for medical accidents	26	44	56	68	77
PMDA Medical Safety Information	3	9	15	22	29
Manuals for management of individual serious adverse drug reactions	25	38	63	63	75
Information on approved new drugs • Review reports, summaries of product applications	308 active ingredients (642 products)	373 active ingredients (763 products)	445 active ingredients (895 products)	513 active ingredients (1,034 products)	592 active ingredients (1,189 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	2,777	3,448	1,979	1,977	2,299
Pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)					
E-mails issued*4	87	107	188	203	259
Subscribers	11,965	20,707	27,410	35,719	55,372
Number of site visitors*5	497 million	642 million	754 million	873 million	949 million

**1 Added or deleted as necessary*

**2 The total number of urgent safety information (yellow letter) and safety information (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 2011: New Drugs

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Apr. 22, 2011	1	Lipacreon Granules 300 mg Sachet Lipacreon Capsules 150 mg (Abbott Japan Co., Ltd.)	Approval Approval	Pancrelipase	Drugs with a new active ingredient indicated for the replacement of pancreatic digestive enzymes in pancreatic exocrine insufficiency.
1	Apr. 22, 2011	2	Mircera Injection Syringe 25 μg Mircera Injection Syringe 50 μg Mircera Injection Syringe 75 μg Mircera Injection Syringe 100 μg Mircera Injection Syringe 150 μg Mircera Injection Syringe 200 μg Mircera Injection Syringe 250 μg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval Approval Approval Approval	Epoetin beta pegol (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of renal anemia.
1	Apr. 22, 2011	3	Thymoglobuline for Intravenous Infusion 25 mg (Genzyme Japan K.K.)	Change	Anti-human thymocyte immunoglobulin, rabbit	A drug with a new additional indication and a new dosage for the treatment of acute rejection after renal transplantation. [Expedited review]
1	May 20, 2011	4	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.) Sol-Melcort for Injection 40 Sol-Melcort for Injection 125 Sol-Melcort for Injection 500 Sol-Melcort for Injection 1,000 (Fuji Pharma Co., Ltd.)	Change Change Change Change Change Change Change Change	Methylprednisolone sodium succinate	Drugs with a new additional indication and a new dosage for the treatment of nephrotic syndrome. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
1	Jul. 1, 2011	5	Nexium Capsules 10 mg (AstraZeneca K.K.)	Approval	Esomeprazole magnesium hydrate	A drug with a new active ingredient indicated for the treatment of gastric ulcer, duodenal ulcer, anastomotic ulcer, reflux esophagitis, non-erosive reflux disease and Zollinger-Ellison syndrome, prevention of recurrence of gastric ulcer or duodenal ulcer in patients treated with nonsteroidal antiinflammatory drugs, and aid to eradication of *Helicobacter pylori* in patients with gastric ulcer, duodenal ulcer, gastric MALT lymphoma, idiopathic thrombocytopenic purpura, and stomach after endoscopic treatment for early gastric cancer.
			Nexium Capsules 20 mg (AstraZeneca K.K.)	Approval	Esomeprazole magnesium hydrate	A drug with a new active ingredient indicated for the treatment of gastric ulcer, duodenal ulcer, anastomotic ulcer, reflux esophagitis and Zollinger-Ellison syndrome, prevention of recurrence of gastric ulcer or duodenal ulcer in patients treated with nonsteroidal antiinflammatory drugs, and aid to eradication of *Helicobacter pylori* in patients with gastric ulcer, duodenal ulcer, gastric MALT lymphoma, idiopathic thrombocytopenic purpura, and stomach after endoscopic treatment for early gastric cancer.
1	Jul. 1, 2011	6	Pegasys S.C. 90 μg Copegus Tablets 200 mg (Chugai Pharmaceutical Co., Ltd.)	Change Change	Peginterferon alfa-2a (genetical recombination) Ribavirin	Drugs with a new additional indication for the improvement of viremia in patients with compensated cirrhosis C. A new dosage of Pegasis S.C. 90 μg has also been approved. [Priority review]
1	Jul. 1, 2011	7	Ditripentat-Cal Injection 1000 mg Zinc-Tripentat Injection 1055 mg (Nihon Medi-Physics Co., Ltd.)	Approval Approval	Pentetate calcium trisodium Pentetate zinc trisodium	Drugs with a new active ingredient indicated for the reduction of internal contamination with transuranium elements (plutonium, americium, and curium). [Expedited review]
1	Aug. 17, 2011	8	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new dosage indicated for the treatment of Crohn's disease. [Orphan drug]
1	Sep. 16, 2011	9	Endoxan Tablets 50 mg (Shionogi & Co., Ltd.)	Change	Cyclophosphamide hydrate	A drug with a new additional indication and a new dosage for the treatment of nephrotic syndrome (for use only in patients who have not sufficiently responded to adequate treatment with corticosteroids). [Public knowledge-based application after PAFSC's preliminary assessment]
1	Sep. 16, 2011	10	Cellcept Capsule 250 (Chugai Pharmaceutical Co., Ltd.)	Change	Mycophenolate mofetil	A drug with a new additional pediatric dosage indicated for the prevention of rejection in renal transplantation. [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
1	Sep. 26, 2011	11	Proemend for Intravenous Infusion 150 mg (Ono Pharmaceutical Co., Ltd.)	Approval	Fosaprepitant meglumine	A drug with a new active ingredient indicated for the treatment of gastrointestinal symptoms (nausea and vomiting) associated with administration of antineoplastic drugs (cisplatin, etc.) (including delayed phase).
1	Sep. 26, 2011	12	Pegasys S.C. 180 µg Pegasys S.C. 90 µg (Chugai Pharmaceutical Co., Ltd.)	Change Change	Peginterferon alfa-2a (genetical recombination)	Drugs with a new additional indication and a new dosage for the improvement of viremia in patients with chronic active hepatitis B. [Priority review]
1	Nov. 25, 2011	13	Beselna Cream 5% (Mochida Pharmaceutical Co., Ltd.)	Change	Imiquimod	A drug with a new additional indication and a new dosage for the treatment of actinic keratosis (limited to the face or baldness).
1	Dec. 22, 2011	14	Kytril Fine Granule 0.4% Kytril Tablet 1 mg Kytril Tablet 2 mg Kytril Injection 1 mg Kytril Injection 3 mg Kytril Intravenous Bag 3 mg/50 mL Kytril Intravenous Bag 3 mg/100 mL (Chugai Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change	Granisetron hydrochloride	Drugs with a new additional indication for the treatment of gastrointestinal symptoms (nausea and vomiting) associated with radiation. [Public knowledge-based application after PAFSC's preliminary assessment]
1	Dec. 22, 2011	15	Certican Tablets 0.25 mg Certican Tablets 0.5 mg Certican Tablets 0.75 mg (Novartis Pharma K.K.)	Change Change Change	Everolimus	Drugs with a new additional indication and a new dosage for the inhibition of rejection in renal transplantation.
1	Dec. 22, 2011	16	(1) Pegintron Powder for Injection 50 µg/0.5 mL Pegintron Powder for Injection 100 µg/0.5 mL Pegintron Powder for Injection 150 µg/0.5 mL (2) Rebetol Capsules 200 mg (MSD K.K.)	Change Change Change Change	(1) Peginterferon alfa-2b (genetical recombination) (2) Ribavirin	Drugs with a new additional indication and a new dosage for the improvement of viremia in patients with compensated cirrhosis C by concomitant use. [Priority review]
1	Mar. 30, 2012	17	Kiklin Capsules 250 mg (Astellas Pharma Inc.)	Approval	Bixalomer	A drug with a new active ingredient indicated for the improvement of hyperphosphatemia in patients with chronic renal failure under dialysis.
2	Apr. 22, 2011	18	Mirapex-LA Tablets 0.375 mg Mirapex-LA Tablets 1.5 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval	Pramipexole hydrochloride hydrate	Drugs in new dosage forms and with new dosages indicated for the treatment of Parkinson's disease.
2	Apr. 22, 2011	19	Exelon Patch 4.5 mg Exelon Patch 9 mg Exelon Patch 13.5 mg Exelon Patch 18 mg (Novartis Pharma K.K.) Rivastach Patch 4.5 mg Rivastach Patch 9 mg Rivastach Patch 13.5 mg Rivastach Patch 18 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval Approval Approval Approval Approval	Rivastigmine	Drugs with a new active ingredient indicated for inhibition of progression of symptoms of dementia in mild and moderate Alzheimer's dementia.
2	Apr. 22, 2011	20	Lixiana Tablets 15 mg Lixiana Tablets 30 mg (Daiichi Sankyo Company, Limited)	Approval Approval	Edoxaban tosilate hydrate	Drugs with a new active ingredient indicated for prevention of venous thromboembolism in patients undergoing orthopedic surgery of lower limbs including total knee arthroplasty, total hip arthroplasty and hip fracture surgery.
2	May 20, 2011	21	Novastan HI Inj. 10 mg/2 mL (Mitsubishi Tanabe Pharma Corporation) Slonnon HI Injection 10 mg/2 mL (Daiichi Sankyo Company, Limited)	Change Change	Argatroban hydrate	Drugs with new additional indications and new dosages for the prevention of perfusion blood coagulation during blood extracorporeal circulation (hemodialysis) in patients with heparin-induced thrombocytopenia (HIT) type II and in addition for the prevention of blood coagulation during percutaneous coronary intervention in HIT type II patients (including the patients who have the risk for HIT). [Orphan drug]
2	May 20, 2011	22	Vasolan for Intravenous Injection 5 mg (Eisai Co., Ltd.)	Change	Verapamil hydrochloride	A drug with a new additional dosage indicated for the treatment of tachyarrhythmia in pediatric patients (paroxysmal supraventricular tachycardia, paroxysmal atrial fibrillation, paroxysmal atrial flutter). [Public knowledge-based application after PAFSC's preliminary assessment]
2	May 20, 2011	23	Vasolan Tablets 40 mg (Eisai Co., Ltd.)	Change	Verapamil hydrochloride	A drug with a new additional indication and a new dosage for the treatment of tachyarrhythmia in pediatric patients (atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia). [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	May 20, 2011	24	Maintate Tablets 2.5 Maintate Tablets 5 Maintate Tablets 0.625 (Mitsubishi Tanabe Pharma Corporation)	Change Change Change	Bisoprolol fumarate	Drugs with a new additional indication and new dosages for the treatment of chronic heart failure secondary to ischemic heart disease or dilated cardiomyopathy in patients receiving basic treatment with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists, diuretics, digitalis preparations, etc. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 16, 2011	25	Depakene Tablets 100 Depakene Tablets 200 Depakene Fine Granules 20% Depakene Fine Granules 40% Depakene-R Tablets 100 Depakene-R Tablets 200 Depakene Syrup 5% (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change Change Change Change Change	Sodium valproate	Drugs with a new additional indication and a new dosage for prevention of migraine attack. [Public knowledge-based application after PAFSC's preliminary assessment]
2	Jun. 16, 2011	26	Selenica-R Granules 40% Selenica-R Tab.200 mg Selenica-R Tab.400 mg (Kowa Company, Ltd.)	Change Change Change	Sodium valproate	Drugs with a new additional indication and a new dosage for prevention of migraine attack.
2	Jul. 1, 2011	27	Corebeta for Intravenous 12.5 mg (Ono Pharmaceutical Co., Ltd.)	Approval	Landiolol hydrochloride	A drug with a new indication, a new dosage, and an additional dosage form indicated for the improvement of visualization of coronary arteries at high heart rate in coronary angiography by computed tomography.
2	Dec. 22, 2011	28	Plavix 25 mg Tablets Plavix 75 mg Tablets (Sanofi-Aventis K.K.)	Change Change	Clopidogrel sulfate	Drugs with new additional indications for the treatment of the following ischemic heart disease for which percutaneous coronary intervention (PCI) is applied: stable angina and old myocardial infarction.
2	Jan. 18, 2012	29	Azilva Tablets 20 mg Azilva Tablets 40 mg (Takeda Pharmaceutical Company Limited)	Approval Approval	Azilsartan	Drugs with a new active ingredient indicated for the treatment of hypertension.
2	Jan. 18, 2012	30	Xarelto Tablets 15 mg Xarelto Tablets 10 mg (Bayer Yakuhin, Ltd.)	Approval Approval	Rivaroxaban	Drugs with a new active ingredient indicated for the prevention of ischemic stroke and systemic embolism in patients with nonvalvular atrial fibrillation.
2	Mar. 30, 2012	31	Apokyn Subcutaneous Injection 30 mg (Kyowa Hakko Kirin Co., Ltd.)	Approval	Apomorphine hydrochloride hydrate	A drug with a new active ingredient indicated for the treatment of "off" episodes associated with Parkinson's disease (when levodopa-containing products that are frequently administered and other anti-Parkinson drugs at increased doses are not sufficiently effective). [Orphan drug]
3-1	Apr. 22, 2011	32	Lexapro Tablets 10 mg (Mochida Pharmaceutical Co., Ltd.)	Approval	Escitalopram oxalate	A drug with a new active ingredient indicated for the treatment of depression.
3-1	Jul. 1, 2011	33	Fostoin 750mg for injection (Nobelpharma Co., Ltd.)	Approval	Fosphenytoin sodium hydrate	A drug with a new active ingredient indicated for: 1. treatment of status epilepticus 2. prevention of seizures occurring in connection with neurosurgery, and/or consciousness disorder (head trauma, etc.) 3. temporary substitution of oral phenytoin therapy in epilepsy patients.
3-1	Jul. 1, 2011	34	Lamictal Tablets 25 mg Lamictal Tablets 100 mg (GlaxoSmithKline K.K.)	Change Change	Lamotrigine	Drugs with a new additional indication and a new dosage for the prevention of recurrence/relapse of mood episodes in patients with bipolar disorder.
3-1	Jul. 1, 2011	35	Gabapen Tablets 200 mg Gabapen Tablets 300 mg Gabapen Tablets 400 mg Gabapen Syrop 5% (Pfizer Japan Inc.)	Change Change Change Approval	Gabapentine	Drugs with a new additional pediatric dosage and an additional dosage form indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Sep. 26, 2011	36	Venoglobulin IH 5% I.V. 0.5 g/10 mL Venoglobulin IH 5% I.V. 1 g/20 mL Venoglobulin IH 5% I.V. 2.5 g/50 mL Venoglobulin IH 5% I.V. 5 g/100 mL (Benesis Corporation)	Change Change Change Change	Polyethylene glycol treated human normal immunoglobulin	Drugs with a new additional indication for the treatment of generalized myasthenia gravis (for use only in patients who have not sufficiently responded to steroids or other immunosuppressants). [Orphan drug]
3-1	Sep. 26, 2011	37	Imusera Capsules 0.5 mg (Mitsubishi Tanabe Pharma Corporation) Gilenya Capsules 0.5 mg (Novartis Pharma K.K.)	Approval Approval	Fingolimod hydrochloride	Drugs with a new active ingredient indicated for the prevention of relapse and for delaying the accumulation of physical disability in multiple sclerosis. [Orphan drug]
3-1	Nov. 25, 2011	38	Modiodal Tablets 100 mg (Alfresa Pharma Corporation)	Change	Modafinil	A drug with a new additional indication for the treatment of excessive daytime sleepiness in patients with obstructive sleep apnea syndrome who receive treatment of airway obstruction with continuous positive airway pressure (CPAP) therapy, etc.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Jan. 18, 2012	39	Lunesta Tablets 1 mg Lunesta Tablets 2 mg Lunesta Tablets 3 mg (Eisai Co., Ltd.)	Approval Approval Approval	Eszopiclone	Drugs with a new active ingredient indicated for the treatment of insomnia.
3-1	Jan. 18, 2012	40	Regnite Tablets 300 mg (Astellas Pharma Inc.)	Approval	Gabapentin enacarbil	A drug with a new active ingredient indicated for the treatment of moderate to severe idiopathic restless legs syndrome.
3-1	Jan. 18, 2012	41	[1] Abilify Tablets 3 mg Abilify Tablets 6 mg Abilify Tablets 12 mg Abilify Powder 1% Abilify Oral Solution 0.1% [2] Abilify OD Tablets 3 mg Abilify OD Tablets 6 mg Abilify OD Tablets 12 mg Abilify OD Tablets 24 mg (Otsuka Pharmaceutical Co., Ltd.)	Change Change Change Change Change Approval Approval Approval Approval	Aripiprazole	Drugs with a new additional indication and a new dosage in new dosage forms for the improvement of manic symptoms in patients with bipolar disorder.
3-1	Feb. 22, 2012	42	Zyprexa Tablets 2.5 mg Zyprexa Tablets 5 mg Zyprexa Tablets 10 mg Zyprexa Fine Granule 1% Zyprexa Zydis Tablets 5 mg Zyprexa Zydis Tablets 10 mg (Eli Lilly Japan K.K.)	Change Change Change Change Change Change	Olanzapine	Drugs with a new additional indication and a new dosage for the improvement of depressive symptoms in patients with bipolar disorder.
3-1	Feb. 22, 2012	43	Cymbalta Capsules 20 mg Cymbalta Capsules 30 mg (Shionogi & Co., Ltd.)	Change Change	Duloxetine hydrochloride	Drugs with a new additional indication for the treatment of pain associated with diabetic neuropathy.
3-2	Jan. 18, 2012	44	Aiphagan Ophthalmic Solution 0.1% (Senju Pharmaceutical Co., Ltd.)	Approval	Brimonidine tartrate	A drug with a new active ingredient indicated for the treatment of glaucoma and ocular hypertension when other glaucoma drugs are not sufficiently effective or cannot be used.
3-2	Jan. 18, 2012	45	Emla Cream (Sato Pharmaceutical Co., Ltd.)	Approval	Lidocaine/propitocaine	A new combination drug with a new active ingredient indicated for the relief of pain in skin laser radiation therapy.
3-2	Jan. 18, 2012	46	OxyFast Injection 10 mg OxyFast Injection 50 mg (Shionogi & Co., Ltd.)	Approval Approval	Oxycodone hydrochloride hydrate	Drugs with a new route of administration indicated for analgesia in various types of cancer with moderate to severe pain.
3-2	Apr. 22, 2011	47	Suprane Liquid for Inhalation (Baxter Limited)	Approval	Desflurane	A drug with a new active ingredient indicated for the maintenance of general anesthesia.
3-2	Apr. 22, 2011	48	Tramcet Combination Tablets (Janssen Pharmaceutical K.K.)	Approval	Tramadol hydrochloride/ acetaminophen	A new combination drug indicated for analgesia of chronic non-cancer pain and pain after tooth extraction which are not managed by treatments with non-opioid analgesics.
3-2	Apr. 22, 2011	49	Popscaine 0.5% Inj. 50 mg/10 mL Popscaine 0.5% Inj. syringe 50 mg/10 mL Popscaine 0.25% Inj. 25 mg/10 mL Popscaine 0.25% Inj. syringe 25 mg/10 mL (Maruishi Pharmaceutical Co., Ltd.)	Approval Approval Change Change	Levobupivacaine hydrochloride	Drugs with a new route of administration, a new additional indication and new dosages indicated for conduction anesthesia.
4	Apr. 22, 2011	50	Finibax 0.25 g IV Solution Finibax 0.25 g IV Solution Kit (Shionogi & Co., Ltd.)	Change Change	Doripenem hydrate	Drugs with a new dosage that enables high-dose (1 g three times daily) use.
4	May 20, 2011	51	Rifadin Capsules 150 mg (Daiichi Sankyo Company, Limited) Rifampicin Capsules 150 mg "Sandoz" (Sandoz K.K.)	Change Change	Rifampicin	Drugs with a new additional indication and a new dosage for the treatment of nontuberculous mycobacteriosis including *Mycobacterium avium* complex (MAC) infection. [Public knowledge-based application after PAFSC's preliminary assessment]
4	May 20, 2011	52	Foscarvir Infusion Solution 24 mg/mL (AstraZeneca K.K.)	Change	Foscarnet sodium hydrate	A drug with new additional indications and a new dosage for the treatment of cytomegalovirus viremia and cytomegalovirus infection in patients undergoing hematopoietic stem cell transplantation.
4	May 20, 2011	53	Esanbutol Tablets 125 mg Esanbutol Tablets 250 mg (Sandoz K.K.) Ebutol 125 mg Tablets Ebutol 250 mg Tablets (Kaken Pharmaceutical Co., Ltd.)	Change Change Change Change	Ethambutol hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of nontuberculous mycobacteriosis including *Mycobacterium avium* complex (MAC) 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	Jul. 1, 2011	54	Cubicin IV 350 mg (MSD K.K.)	Approval	Daptomycin	A drug with a new active ingredient indicated for the treatment of sepsis, infective endocarditis, deep skin infection, secondary infection of trauma, burn, and surgical wounds, and secondary infection of erosion and ulcer caused by daptomycin-sensitive methicillin-resistant *Staphylococcus aureus* (MRSA).
4	Jul. 1, 2011	55	Zithromac Tablets 250 mg (Pfizer Japan Inc.) Zithromac Intravenous Use 500 mg (Pfizer Japan Inc.)	Change Approval	Azithromycin hydrate	A drug with a new additional indication for *Legionella pneumophila* as applicable microorganism. A drug with a new route of administration indicated for the treatment of pneumonia.
4	Aug. 17, 2011	56	Gracevit Tablets 50 mg Gracevit Fine Granules 10% (Daiichi Sankyo Company, Limited)	Change Change	Sitafloxacin hydrate	Drugs with a new dosage indicated for the treatment of pharyngitis and laryngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, secondary infection of chronic respiratory disease, cystitis, pyelonephritis, urethritis, cervicitis, otitis media, sinusitis, periodontal inflammation, pericoronitis, and jaw inflammation.
4	Sep. 26, 2011	57	Telavic 250 mg Tablet (Mitsubishi Tanabe Pharma Corporation)	Approval	Telaprevir	A drug with a new active ingredient indicated for the improvement of viremia in serogroup 1 (genotype I [1a] or II [1b]) chronic hepatitis C in: (1) untreated patients with high blood HCV RNA; or (2) patients who did not respond to, or in whom the symptom relapsed with, interferon monotherapy or interferon-ribavirin combination therapy. [Priority review]
4	Sep. 26, 2011	58	Itrizole Oral Solution 1% (Janssen Pharmaceutical K.K.)	Change	Itraconazole	A drug with new indications for (1) the treatment of fungal infection, (2) the treatment of febrile neutropenia with suspected fungal infection, and (3) the prevention of deep mycosis in patients with hematologic malignancy or hematopoietic stem cell transplantation in whom neutropenia is anticipated.
4	Nov. 25, 2011	59	Diflucan Intravenous Solution 50 mg Diflucan Intravenous Solution 100 mg Diflucan Intravenous Solution 200 mg Diflucan Capsules 50 mg Diflucan Capsules 100 mg (Pfizer Japan Inc.)	Change Change Change Change Change	Fluconazole	Drugs with a new additional pediatric dosage and a new additional indication for the prevention of deep mycosis in patients with hematopoietic stem cell transplantation. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Dec. 22, 2011	60	Claforan Injection 0.5 g Claforan Injection 1 g (Sanofi-Aventis K.K.) Cefotax Injection 0.5 g Cefotax Injection 1 g (Sanofi-Aventis Nichi-Iko K.K.)	Change Change Change Change	Cefotaxime sodium	Drugs with a new dosage for the treatment of pediatric purulent meningitis. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Jan. 18, 2012	61	Samtirel Oral Suspension 15% (GlaxoSmithKline K.K.)	Approval	Atovaquone	A drug with a new active ingredient indicated for the treatment and prevention of Pneumocystis pneumonia. [Priority review]
4	Jan. 18, 2012	62	Cancidas for Intravenous Drip Infusion 50 mg Cancidas for Intravenous Drip Infusion 70 mg (MSD K.K.)	Approval Approval	Caspofungin acetate	Drugs with a new active ingredient indicated for the treatment of febrile neutropenia suspected of a fungal infection and fungal infections due to *Candida* or *Aspergillus* (esophageal candidiasis, invasive candidiasis, aspergillosis).
4	Feb. 22, 2012	63	Sawacillin Fine Granules 10% Sawacillin Capsules 125 Sawacillin Capsules 250 Sawacillin Tablets 250 (Astellas Pharma Inc.) Pasetocin Fine Granules 10% Pasetocin Capsules 125 Pasetocin Capsules 250 Pasetocin Tablets 250 (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change Change Change Change Change Change	Amoxicillin hydrate	Drugs with a revised maximum dosage for pediatric patients indicated for the treatment of infections except *Helicobacter pylori* infection. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Feb. 22, 2012	64	Penicillin G Potassium 200000 Units for Injection Penicillin G Potassium 1000000 Units for Injection (Meiji Seika Pharma Co., Ltd.)	Change Change	Benzylpenicillin potassium	Drugs with a new route of administration and a new dosage for a new additional indication for the treatment of syphilis. [Public knowledge-based application after PAFSC's preliminary assessment]
4	Mar. 21, 2012	65	Flagyl Oral Tablet 250 mg Flagyl Vaginal Tablet 250 mg (Shionogi & Co., Ltd.)	Change Change	Metronidazole	Drugs with a new indication and new dosages for the treatment of bacterial vaginosis. [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
5	May 20, 2011	66	Anti-D Globulin for I.M. Injection 1000 "Nichiyaku" (Nihon Pharmaceutical Co., Ltd.)	Change	Dry anti-Rho(D) immune human globulin	A drug with a new indication and a new dosage for the prevention of sensitization to the D(Rho) factor in women who are D(Rho) negative and are not already sensitized to the D(Rho) factor, to be used at around 28 weeks of pregnancy or in the case of possible sensitization such as after delivery, miscarriage, artificial abortion, ectopic pregnancy, testing/procedure during pregnancy (e.g., amniocentesis, external cephalic version) or abdominal bruise. [Public knowledge-based application after PAFSC's preliminary assessment]
5	May 20, 2011	67	Anti-D Human Immunoglobulin I.M. 1000-Benesis (Benesis Corporation)	Change	Dry anti-Rho(D) immune human globulin	A drug with a new indication and a new dosage for the prevention of sensitization to the D(Rho) factor in women who are D(Rho) negative and are not already sensitized to the D(Rho) factor, to be used at around 28 weeks of pregnancy or in the case of possible sensitization such as after delivery, miscarriage, artificial abortion, ectopic pregnancy, testing/procedure during pregnancy (e.g., amniocentesis, external cephalic version) or abdominal bruise. [Public knowledge-based application after PAFSC's preliminary assessment]
5	May 20, 2011	68	Gonalef for Subcutaneous Injection 150 (Merck Serono Co., Ltd.)	Change	Follitropin alfa (genetical recombination)	A drug with a new additional indication and a new dosage for induction of ovulation in patients with anovulation and infrequent ovulation associated with hypothalamic-pituitary dysfunction or polycystic ovarian syndrome.
5	May 20, 2011	69	Leuplin for Injection 1.88 Leuplin for Injection 3.75 (Takeda Pharmaceutical Company Limited)	Change Change	Leuprorelin acetate	Drugs with a new additional dosage indicated for the treatment of central precocious puberty. [Public knowledge-based application after PAFSC's preliminary assessment]
5	Jul. 1, 2011	70	Betanis Tablet 25 mg Betanis Tablet 50 mg (Astellas Pharma Inc.)	Approval Approval	Mirabegron	Drugs with a new active ingredient indicated for the treatment of urinary urgency, urinary frequency, and urge urinary incontinence associated with overactive bladder.
5	Nov. 25, 2011	71	L'estrogel 0.06% (Shiseido Company, Limited)	Change	Estradiol	A drug with a new dosage. This drug is indicated for the treatment of vasomotor symptoms (hot flush and sweating) associated with menopausal disorder and ovarian deficiency symptoms.
5	Mar. 30, 2012	72	Minirinmelt OD Tablets 120 μg Minirinmelt OD Tablets 240 μg (Ferring Pharmaceuticals Co., Ltd.)	Approval Approval	Desmopressin acetate hydrate	Drugs with a new route of administration indicated for the treatment of nocturnal enuresis associated with decreased urine osmolality or urinary specific gravity.
6-1	May 20, 2011	73	Imuran Tablets 50 mg (GlaxoSmithKline K.K.) Azanin Tablets 50 mg (Mitsubishi Tanabe Pharma Corporation)	Change Change	Azathioprine	Drugs with new additional indications and a new dosage for the treatment of the following treatment-resistant rheumatic diseases: systemic vasculitis (e.g., microscopic polyangiitis, Wegener granulomatosis, polyarteritis nodosa, Churg-Strauss syndrome, aortitis syndrome), systemic lupus erythematosus (SLE), polymyositis, dermatomyositis, pachyderma, mixed connective tissue disease and refractory rheumatic disease. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Jul. 1, 2011	74	Allelock Granule 0.5% (Kyowa Hakko Kirin Co., Ltd.)	Approval	Olopatadine hydrochloride	A drug with an additional dosage form of granules and with a new additional pediatric dosage indicated for the treatment of allergic rhinitis, urticaria, and itching associated with skin disease (eczema/dermatitis and pruritus cutaneous).
6-1	Jul. 1, 2011	75	Simponi Subcutaneous Injection 50 mg Syringe (Janssen Pharmaceutical K.K.)	Approval	Golimumab (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	Jul. 1, 2011	76	Onbrez Inhalation Capsules 150 μg (Novartis Pharma K.K.)	Approval	Indacaterol maleate	A drug with a new active ingredient indicated for the alleviation of various symptoms due to airway obstructive impairment in chronic obstructive pulmonary diseases (chronic bronchitis and emphysema).
6-1	Jul. 1, 2011	77	Humira 40 mg for S.C. Injection Syringe 0.8 mL Humira 20 mg for S.C. Injection Syringe 0.4 mL (Abbott Japan Co., Ltd.)	Change Approval	Adalimumab (genetical recombination)	Drugs with a new additional indication, a new dosage, and an additional dosage form for the treatment of polyarticular-course juvenile idiopathic arthritis (for use only in patients who have not sufficiently responded to conventional treatments).
6-1	Aug. 17, 2011	78	Patanol EX Ophthalmic Solution 0.2% (Alcon Japan Ltd.)	Approval	Olopatadine hydrochloride	A drug with a new dosage and an additional dosage form indicated for the treatment of allergic conjunctivitis.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Sep. 26, 2011	79	Ilaris for S.C. Injection 150 mg (Novartis Pharma K.K.)	Approval	Canakinumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of cryopyrin-associated periodic syndrome. [Orphan drug]
6-1	Sep. 26, 2011	80	Mucosta Ophthalmic Solution UD 2% (Otsuka Pharmaceutical Co., Ltd.)	Approval	Rebamipide	A drug with a new route of administration indicated for the treatment of dry eye.
6-1	Dec. 22, 2011	81	Celecox Tablets 100 mg Celecox Tablets 200 mg (Astellas Pharma Inc.)	Change Change	Celecoxib	Drugs with a new additional indication and a new dosage for the relief of inflammation and pain after operation, trauma, and tooth extraction.
6-1	Dec. 22, 2011	82	Onon Drysyrup 10% (Ono Pharmaceutical Co., Ltd.)	Change	Pranlukast hydrate	A drug with a new additional indication for the treatment of allergic rhinitis in pediatric patients.
6-1	Mar. 21, 2012	83	Enbrel 25 mg for S.C. Injection Enbrel 25 mg Syringe 0.5 mL for S.C. Injection Enbrel 10 mg for S.C. Injection Enbrel 50 mg Syringe 1.0 mL for S.C. Injection (Pfizer Japan Inc.)	Change	Etanercept (genetical recombination)	Drugs with a new additional indication for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not sufficiently responded to conventional treatments.
6-1	Mar. 30, 2012	84	Pulmozyme Inhalation Solution 2.5 mg (Chugai Pharmaceutical Co., Ltd.)	Approval	Dornase alfa (genetical recombination)	A drug with a new active ingredient indicated for the improvement of lung function in patients with cystic fibrosis. [Orphan drug]
6-2	Apr. 22, 2011	85	Glubes Combination Tab. (Kissei Pharmaceutical Co., Ltd.)	Approval	Mitiglinide calcium hydrate/voglibose	A new combination drug indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of mitiglinide calcium hydrate with voglibose is deemed appropriate).
6-2	May 20, 2011	86	Januvia Tablets 25 mg Januvia Tablets 50 mg Januvia Tablets 100 mg (MSD K.K.) Glactiv Tablets 25 mg Glactiv Tablets 50 mg Glactiv Tablets 100 mg (Ono Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change	Sitagliptin phosphate hydrate	Drugs with a new additional indication for the treatment of type 2 diabetes mellitus in patients who have not responded sufficiently to alpha-glucosidase inhibitors along with diet and exercise therapies.
6-2	May 20, 2011	87	Forteo for S.C. Injection Kit 600 μg (Eli Lilly Japan K.K.)	Change	Teriparatide (genetical recombination)	A drug with a new dosage with a revised treatment period from "up to 18 months" to "up to 24 months" indicated for the treatment of osteoporosis with an increased risk for fracture.
6-2	Jul. 1, 2011	88	Liovel Combination Tablets LD Liovel Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Alogliptin benzoate/pioglitazone hydrochloride	New combination drugs indicated for the treatment of type 2 diabetes mellitus.
6-2	Jul. 1, 2011	89	Trazenta Tablets 5 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Linagliptin	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to diet and exercise therapies alone).
6-2	Jul. 1, 2011	90	Recalbon Tablets 50 mg (Ono Pharmaceutical Co., Ltd.) Bonoteo Tablets 50 mg (Astellas Pharma Inc.)	Approval Approval	Minodronic acid hydrate	Drugs with a new dosage and an additional dosage form indicated for the treatment of osteoporosis.
6-2	Sep. 16, 2011	91	Levemir Penfill Levemir FlexPen Levemir InnoLet (Novo Nordisk Pharma Ltd.)	Approval Approval Approval	Insulin detemir (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated. This application applies only to the change in manufacturing method of the drug substance, and thus formulation, manufacturing method, indications and dosage and administration of the product are the same as the approved product.
6-2	Sep. 16, 2011	92	Glactiv Tablets 25 mg Glactiv Tablets 50 mg Glactiv Tablets 100 mg (Ono Pharmaceutical Co., Ltd.) Januvia Tablets 25 mg Januvia Tablets 50 mg Januvia Tablets 100 mg (MSD K.K.)	Change Change Change Change Change Change	Sitagliptin phosphate hydrate	Drugs with a new additional indication for the treatment of type 2 diabetes mellitus in patients who have not responded sufficiently to insulin along with diet and exercise therapies.
6-2	Sep. 26, 2011	93	Teribone Inj. 56.5 μg (Asahi Kasei Pharma Corporation)	Approval	Teriparatide acetate	A drug with a new route of administration, a new indication, and a new dosage indicated for the treatment of osteoporosis with high risk of fracture.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Nov. 25, 2011	94	Metopirone Capsules 250 mg (Novartis Pharma K.K.)	Change	Metyrapone	A drug with a new additional indication and a new dosage for the treatment of Cushing's syndrome. [Public knowledge-based application after PAFSC's preliminary assessment]
6-2	Jan. 18, 2012	95	Bonalon Bag for I.V. Infusion 900 μg (Teijin Pharma Limited)	Approval	Alendronate sodium hydrate	A drug with a new dosage in a new additional dosage form indicated for the treatment of osteoporosis (not in the reexamination period).
6-2	Mar. 30, 2012	96	Brazaves Capsules 100 mg (Actelion Pharmaceuticals Japan Ltd.)	Approval	Miglustat	A drug with a new active ingredient indicated for the treatment of Niemann-Pick disease Type C. [Orphan drug]
6-2	Mar. 30, 2012	97	Bydureon for Subcutaneous Injection 2 mg (Eli Lilly Japan K.K.)	Approval	Exenatide	A drug with a new additional indication and a new dosage in a new dosage form for the treatment of type 2 diabetes mellitus.
Blood products	Jun. 16, 2011	98	NovoSeven for Injection 1.2 mg NovoSeven for Injection 4.8 mg NovoSeven HI for Intravenous Injection 1 mg NovoSeven HI for Intravenous Injection 2 mg NovoSeven HI for Intravenous Injection 5 mg (Novo Nordisk Pharma Ltd.)	Change Change Change Change Change	Eptacog alfa (activated) (genetical recombination)	Drugs with a new additional indication and a new dosage for inhibition of bleeding tendency in patients with Glanzmann thrombasthenia with alloantibodies against platelet, and with past or present refractoriness to platelet transfusions. [Public knowledge-based application after PAFSC's preliminary assessment]
Blood products	Sep. 26, 2011	99	TachoSil Tissue Sealing Sheet (CSL Behring K.K.)	Approval	Human fibrinogen/thrombin fraction	A new combination drug indicated for the adhesion and closure of wounds in tissues at surgery in the fields of hepatic surgery, pulmonary surgery, cardiovascular surgery, obstetrics and gynecology, and urologic surgery.
Oncology drugs	Apr. 22, 2011	100	Halaven Injection 1 mg (Eisai Co., Ltd.)	Approval	Eribulin mesylate	A drug with a new active ingredient indicated for the treatment of inoperable or recurrent breast cancer. [Priority review]
Oncology drugs	Jun. 16, 2011	101	Sprycel Tablets 20 mg Sprycel Tablets 50 mg (Bristol-Myers K.K.)	Change Change	Dasatinib hydrate	Drugs with a new additional indication and a new dosage for the treatment of chronic myelocytic leukemia.
Oncology drugs	Jul. 1, 2011	102	Tarceva Tablets 25 mg Tarceba Tablets 100 mg (Chugai Pharmaceutical Co., Ltd.)	Change Change	Erlotinib hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of unresectable pancreatic cancer.
Oncology drugs	Jul. 1, 2011	103	Zolinza Capsules 100 mg (MSD K.K.)	Approval	Vorinostat	A drug with a new active ingredient indicated for the treatment of cutaneous T-cell lymphoma.
Oncology drugs	Sep. 16, 2011	104	Velcade Injection 3 mg (Janssen Pharmaceutical K.K.)	Change	Bortezomib	A drug with a new indication and a new dosage for the treatment of multiple myeloma. [Orphan drug]
Oncology drugs	Sep. 16, 2011	105	Predonine Tablets 5 mg (Shionogi & Co., Ltd.) Prednisolone Tablets 1 mg (Asahi Kasei) Prednisolone Tablets 5 mg (Asahi Kasei) (Asahi Kasei Pharma Corporation) Prednisolone Tablets 5 mg "Takeda" Prednisolone Powder 1% "Takeda" (Takeda Pharmaceutical Company Limited)	Change Change Change Change Change	Prednisolone	Drugs with a new indication for the treatment of multiple myeloma. [Expedited review]
Oncology drugs	Sep. 26, 2011	106	Faslodex Intramuscular Injection 250 mg (AstraZeneca K.K.)	Approval	Fulvestrant	A drug with a new active ingredient indicated for the treatment of postmenopausal breast cancer.
Oncology drugs	Sep. 26, 2011	107	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of unresectable or recurrent breast cancer.
Oncology drugs	Nov. 25, 2011	108	Paraplatin Injection 50 mg Paraplatin Injection 150 mg Paraplatin Injection 450 mg (Bristol-Myers K.K.)	Change Change Change	Carboplatin	Drugs with a new additional indication and new dosages for the treatment of breast cancer. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Nov. 25, 2011	109	Sandostatin LAR for I.M. Injection 10 mg Sandostatin LAR for I.M. Injection 20 mg Sandostatin LAR for I.M. Injection 30 mg (Novartis Pharma K.K.)	Change Change Change	Octreotide acetate	Drugs with a new additional indication and a new dosage for the treatment of gastrointestinal neuroendocrine 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	Nov. 25, 2011	110	Elplat for Injection 50 mg Elplat for Injection 100 mg Elplat I.V. Infusion Solution 50 mg Elplat I.V. Infusion Solution 100 mg (Yakult Honsha Co., Ltd.)	Change Change Change Change	Oxaliplatin	Drugs with a new dosage for post-operative adjuvant chemotherapy for colon cancer.
Oncology drugs	Nov. 25, 2011	111	Herceptin Intravenous Infusion 60 Herceptin Intravenous Infusion 150 (Chugai Pharmaceutical Co., Ltd.)	Change Change	Trastuzumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of breast cancer with HER2 overexpression. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Nov. 25, 2011	112	Iressa Tablets 250 (AstraZeneca K.K.)	Change	Gefitinib	A drug with a revised indication for the treatment of unresectable advanced or recurrent non-small cell lung cancer in patients with EGFR gene mutation.
Oncology drugs	Dec. 22, 2011	113	Afinitor Tablets 5 mg (Novartis Pharma K.K.)	Change	Everolimus	A drug with a new additional indication and a new dosage for the treatment of pancreatic neuroendocrine tumor.
Oncology drugs	Jan. 18, 2012	114	Ranmark Subcutaneous Injection 120 mg (Daiichi Sankyo Company, Limited)	Approval	Denosumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of bone lesions due to multiple myeloma and bone lesions due to bone metastasis of solid tumor.
Oncology drugs	Feb. 22, 2012	115	Vepesid Capsules 25 mg Vepesid Capsules 50 mg (Bristol-Myers K.K.) Lastet S Cap. 25 mg Lastet S Cap. 50 mg (Nippon Kayaku Co., Ltd.)	Change Change Change Change	Etoposide	Drugs with a new additional indication and a new dosage for the treatment of ovarian cancer which has progressed after cancer chemotherapy. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 22, 2012	116	Randa Inj. 10 mg/20 mL Randa Inj. 25 mg/50 mL Randa Inj. 50 mg/100 mL (Nippon Kayaku Co., Ltd.) Briplatin Injection 10 mg Briplatin Injection 25 mg Briplatin Injection 50 mg (Bristol-Myers K.K.) Cisplatin Injection 10 mg 'Nichi-iko' Cisplatin Injection 25 mg 'Nichi-iko' Cisplatin Injection 50 mg 'Nichi-iko' (Nichi-Iko Pharmaceutical Co., Ltd.) Cisplatin for I.V. Infusion 10 mg 'Maruko' Cisplatin for I.V. Infusion 25 mg 'Maruko' Cisplatin for I.V. Infusion 50 mg 'Maruko' (Nichi-Iko Pharmaceutical Co., Ltd.) Platosin Injection 10 Platosin Injection 25 Platosin Injection 50 (Pfizer Japan Inc.)	Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change	Cisplatin	Drugs with a new additional indication and a new dosage for the treatment of biliary tract cancer. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 22, 2012	117	Glivec Tablets 100 mg (Novartis Pharma K.K.)	Change	Imatinib mesilate	A drug with new additional indications and a new dosage for the treatment of FIP1L1-PDGFRα-positive hypereosinophilic syndrome or chronic eosinophilic leukemia. [Public knowledge-based application after PAFSC's preliminary assessment] [Orphan drug]
Oncology drugs	Mar. 21, 2012	118	Ifomide for Injection 1 g (Shionogi & Co., Ltd.)	Change	Ifosfamide	A drug with a new additional indication and a new dosage for the treatment of malignant lymphoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 21, 2012	119	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.) Paclitaxel Intravenous Infusion 30 mg 'Sandoz' Paclitaxel Intravenous Infusion 100 mg 'Sandoz' (Sandoz K.K.)	Change Change Change Change Change Change Change Change Change	Paclitaxel	Drugs with new additional indications and new dosages for the treatment of relapsed or metastatic head and neck cancer, relapsed or metastatic esophagus cancer, angiosarcoma, advanced or relapsed cervical cancer. A new dosage for once-weekly administration for ovarian cancer has also been added. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Mar. 30, 2012	120	Poteligeo Injection 20 mg (Kyowa Hakko Kirin Co., Ltd.)	Approval	Mogamulizumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of recurrent or relapsed CCR4-positive adult T-cell leukemia/lymphoma. [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	Mar. 30, 2012	121	Xalkori Capsules 200 mg Xalkori Capsules 250 mg (Pfizer Japan Inc.)	Approval	Crizotinib	Drugs with a new active ingredient indicated for the treatment of unresectable advanced/relapsed ALK fusion gene-positive non-small-cell lung cancer. [Orphan drug]
Biologicals	Jul. 1, 2011	122	Rotarix Oral Solution (GlaxoSmithKline K.K.)	Approval	Live attenuated human rotavirus vaccine, oral	A drug with a new active ingredient indicated for the prevention of gastroenteritis due to rotavirus.
Biologicals	Jul. 1, 2011	123	Gardasil Aqueous Suspension for Intramuscular Injection Gardasil Aqueous Suspension for Intramuscular Injection Syringe (MSD K.K.)	Approval Approval	Recombinant adsorbed quadrivalent human papillomavirus virus-like particle vaccine (yeast origin)	Drugs with a new active ingredient indicated for the prevention of cervical cancer and its precursor lesions, vulvar intraepithelial neoplasia, vaginal intraepithelial neoplasia, and condyloma acuminatum caused by infection with human papillomavirus types 6, 11, 16 and 18.
Biologicals	Aug. 8, 2011	124	Influenza HA Vaccine "Kaketsuken" TF Influenza HA Vaccine "Kaketsuken" Influ "Kaketsuken" Syringe (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change Change Change	Influenza HA Vaccine	Drugs with a new pediatric dosage indicated for the prevention of influenza. [Expedited review]
Biologicals	Aug. 8, 2011	125	Influenza HA Vaccine "Biken" Flubik HA Flubik HA Syringe (The Research Foundation for Microbial Diseases of Osaka University)	Change Change Change	Influenza HA Vaccine	Drugs with a new pediatric dosage indicated for the prevention of influenza. [Expedited review]
Biologicals	Aug. 8, 2011	126	Influenza HA Vaccine "Seiken" Flu-Syringe “Seiken” (Denka Seiken Co., Ltd.)	Change Change	Influenza HA Vaccine	Drugs with a new pediatric dosage indicated for the prevention of influenza. [Expedited review]
Biologicals	Aug. 8, 2011	127	Influenza HA Vaccine "Kitasatodaiichisankyo" Influenza HA Vaccine "S Hokken" Influenza HA Vaccine "Kitasatodaiichisankyo" Syringe (Kitasato Daiichi Sankyo Vaccine Co., Ltd.)	Change Change Change	Influenza HA Vaccine	Drugs with a new pediatric dosage indicated for the prevention of influenza. [Expedited review]
Biologicals	Jan. 18, 2012	128	RotaTeq Oral Solution (MSD K.K.)	Approval	Live attenuated rotavirus vaccine, oral, pentavalent	A drug with a new active ingredient indicated for the prevention of gastroenteritis due to rotavirus.
In vivo diagnosis	Feb. 22, 2012	129	Diagnogreen for Injection 25 mg (Daiichi Sankyo Company, Limited)	Change	Indocyanine green	A drug with a new additional indication and a new dosage for the use of cerebral angiography (by fluorescence measurement in infrared-ray irradiation) in neurosurgical operation. [Public knowledge-based application after PAFSC's preliminary assessment]
Radio-pharmaceuticals	May 20, 2011	130	MyoMIBG-I123 Injection (Fujifilm RI Pharma Co., Ltd.)	Change	3-iodobenzylguanidine (^{123}I) injection	A drug with a new additional indication and a new dosage for diagnosis of melanocytoma in tumor scintigraphy. [Public knowledge-based application after PAFSC's preliminary assessment]

Table 2. Products Approved in FY 2011: 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
1	Aug. 31, 2011 Total review time: 518 days Regulatory review time: 209 days	Feb. 11, 1991 Clinical evaluation report	1	Baerveldt Glaucoma Implant (AMO Japan K.K..)	New	Medical products 4 Intraocular drain	An artificial aqueous drainage device implanted to decrease intraocular pressure in patients with refractory glaucoma who have not responded to conventional therapy. It drains aqueous humor from the anterior or posterior chamber to the episclera to decrease intraocular pressure. It consists of a silicone plate and a tube and has holes for suturing the device to the sclera. It is available in straight tube type and pars plana insertion type. A clinical evaluation report summarizing the results of literature search on overseas clinical studies and experiences of this product was submitted to evaluate its safety and efficacy in decreasing intraocular pressure. [Priority review]
1	Nov. 24, 2011 Total review time: 594 days Regulatory review time: 191 days	– Foreign clinical study results	2	ICL (STAAR Japan Inc.)	Change	Instrument & apparatus 72 Phakic posterior chamber intraocular lens	A phakic posterior chamber intraocular lens. The existing product is a myopia correction model which is intended for vision correction of myopia. Application for a partial change to add "vision correction for eyes with refractive error (myopic astigmatism)" as an intended use by addition of the astigmatism correction model. In the astigmatism correction model, the placement position of the lens and the postoperative rotation of the lens affect the efficacy, and therefore a clinical study was conducted to evaluate the efficacy and safety by using the astigmatism correction model. (A partial change in the reexamination period)
1	Dec. 20, 2011 Total review time: 418 days Regulatory review time: 238 days	Mar. 13, 2003 Clinical evaluation report	3	Alcon Express Glaucoma Filtration Device (Alcon Japan Ltd.)	New	Medical products 4 Intraocular drain	A stainless-steel glaucoma filtration device intended to create an aqueous humor outflow pathway between the anterior chamber and extraocular segment and to lower the intraocular pressure by puncture and placement from the limbus into the anterior chamber under the scleral flap. A clinical evaluation report summarizing the results of literature search on the foreign clinical studies for subconjunctival placement and the survey results of literature regarding the experience of this product was submitted to evaluate the safety and efficacy for intraocular pressure lowering.
1	Mar. 19, 2012 Total review time: 537 days Regulatory review time: 270 days	– Domestic clinical study results	4	Breath-O Correct (Universal View Co., Ltd.)	New	Instrument & apparatus 72 Orthokeratology contact lens	An orthokeratology contact lens with a special shape added to the inner lens surface that is intended to reshape the corneal surface by wearing it during sleep and to correct and maintain the unaided vision during daytime after removal of the lens. A clinical study was conducted to evaluate the efficacy of the correction precision, etc. and the safety for corneal disorder, etc. (The original product is in a reexamination period)
1	Mar. 29, 2012 Total review time: 66 days Regulatory review time: 30 days	– No clinical study results	5	ICL (STAAR Japan Inc.)	Change	Instrument & apparatus 72 Phakic posterior chamber intraocular lens	An intraocular lens to be implanted in the posterior chamber of the phakic eye (in front of the human crystalline lens) to correct refractive errors in the eye (myopia or myopic astigmatism). Addition of a manufacturing site. (A partial change in the reexamination period)
3-1	Jun. 3, 2011 Total review time: 49 days Regulatory review time: 14 days	Jul. 2, 2008 No clinical study results	6	PROMUS Drug-Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with everolimus coating used for dilating and holding a stenotic site of the coronary artery in symptomatic ischemic heart disease. Changes of manufacturing site. (A partial change in the reexamination period)
3-1	Jun. 3, 2011 Total review time: 49 days Regulatory review time: 14 days	Jul. 2, 2008 No clinical study results	7	XIENCE V Drug Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with everolimus coating used for dilating and holding a stenotic site of the coronary artery in symptomatic ischemic heart disease. Changes of manufacturing site. (A partial change in the reexamination period)
3-1	Jan. 24, 2012 Total review time: 543 days Regulatory review time: 133 days	– Global clinical trial results	8	Zilver PTX Drug-Eluting Peripheral Stent (Cook Japan Inc.)	New	Instrument & apparatus 7 Drug-eluting stent for femoral artery	A stent system consisting of a self-expanding nitinol stent to be inserted and placed at the site of a lesion to maintain the inner cavity of a stenosis site of the femoropopliteal artery and a delivery system to deliver the stent to the site of the lesion. The outer surface of the stent tube is coated directly with paclitaxel to prevent restenosis of the treated site due to neointimal proliferation. A clinical study was conducted to evaluate the efficacy and safety of this product in the treatment of symptomatic vascular diseases in the above-knee femoropopliteal artery.
3-1	Jan. 24, 2012 Total review time: 375 days Regulatory review time: 129 days	– Global clinical trial results	9	Zilver Flex Vascular Stent for SFA (Cook Japan Inc.)	New	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nitinol stent to be inserted and placed at the site of a lesion to maintain the inner cavity of a stenosis site of the femoropopliteal artery and a delivery system to deliver the stent to the site of the lesion. A clinical study was conducted to evaluate the efficacy and safety of this product for bail-out use at the time of failure in intervention therapy for the treatment of symptomatic vascular diseases in the above-knee femoropopliteal artery.

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	Feb. 8, 2012 Total review time: 103 days Regulatory review time: 88 days	Sep. 30, 2011 No clinical study results	10	Endeavor Sprint Coronary Stent System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with zotarolimus coating used for dilating and maintaining the stenotic site of the coronary artery in symptomatic ischemic heart diseases. An application for a partial change to alter specifications of zotarolimus drug substance, shelf life, etc. (A partial change in the reexamination period)
3-1	Feb. 8, 2012 Total review time: 330 days Regulatory review time: 252 days	Nov. 22, 2011 Global clinical trial results	11	Promus Element Stent System (Boston Scientific Japan K.K.)	New	Instrument & apparatus 7 Coronary stent	A product consisting of a drug-eluting stent coated with everolimus used for dilating and holding a stenotic site of the coronary artery in ischemic heart disease. Platinum chromium alloy is used as a raw material for the stent, and the stent strut design was changed from the original product. A clinical study was conducted to confirm the efficacy and safety for the treatment of coronary stenotic sites when using this product. (The original product is in a reexamination period)
3-2	May. 19, 2011 Total review time: 286 days Regulatory review time: 142 days	Aug. 11, 2004 No clinical study results	12	Merci Retriever (Century Medical, Inc.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A wire device with helical loops at the distal end used for thrombectomy. Patients in acute phase of cerebral infarction who are ineligible for intravenous infusion of tissue plasminogen activator (t-PA) or who fail intravenous infusion of t-PA to restore blood flow are candidates for treatment. Application for a partial change to add V2.0 Soft and V3.0 Soft of Merci Retriever and an insertion tool for V2.0 Soft. (A partial change in the reexamination period)
3-2	Jun. 9, 2011 Total review time: 479 days Regulatory review time: 150 days	Dec. 28, 2007 (Types 1 - 3) Sep. 21, 2009 (Type 4) Foreign clinical study results	13	Penumbra System (Medico's Hirata Inc.)	New	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A device used for thrombectomy. Patients in acute phase of cerebral infarction who are ineligible for intravenous infusion of tissue plasminogen activator (t-PA) or who fail intravenous infusion of t-PA to restore blood flow are candidates for treatment. It is a product to aspirate the thrombus by connecting a reperfusion catheter and an aspiration pump (Penumbra aspiration pump) via an aspiration tubing. A clinical study was conducted to evaluate its efficacy and safety in thrombectomy for cerebral infarction.
3-2	Jun. 13, 2011 Total review time: 138 days Regulatory review time: 92 days	Jul. 21, 2005 No clinical study results	14	ONYX Liquid Embolic System LD (Ev3 K.K.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthesis for embolization in vessels of the central circulation system to be used as an embolic material in cases where preoperative embolization is necessary in surgical resection of cerebral arteriovenous malformation that cannot be managed by treatment with other means than surgery. This product consists of a vial containing Onyx solution, a vial containing dimethyl sulfoxide (DMSO), and syringes. Application for a partial change to modify descriptions concerning the stopper thickness of vials containing Onyx solution and DMSO. (A partial change in the reexamination period)
3-2	Dec. 20, 2011 Total review time: 554 days Regulatory review time: 338 days	- Domestic clinical study results	15	Matsudaito (Sanyo Chemical Industries, Ltd.)	New	Medical products 4 Non-absorbable topical hemostatic material for central circulatory system	A non-absorbable topical hemostatic material consisting of a viscous liquid made of polyether-based fluorine-containing urethane prepolymer filled in syringe and accessory sheets and spatula. It is used for auxiliary hemostasis at the site of artificial anastomosis associated with thoracic aorta replacement or branching artery arch replacement in which hemostasis cannot be achieved by usual surgical procedures including ligation. Clinical studies were conducted to evaluate the efficacy and safety of the hemostatic effect of this product at sites of vascular anastomosis in thoracic aorta replacement.
3-2	Mar. 29, 2012 Total review time: 262 days Regulatory review time: 196 days	Aug. 11, 2004 No clinical study results	16	Merci Retriever (Century Medical, Inc.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A wire device with helical loops at the distal end used for thrombectomy. Patients in acute phase of cerebral infarction who are ineligible for intravenous infusion of tissue plasminogen activator (t-PA) or who fail intravenous infusion of t-PA to restore blood flow are candidates for this treatment. An application for a partial change to add an insertion tool improved for easily pushing out the main body of this device from the insertion tool. (A partial change in the reexamination period)
4	Nov. 24, 2011 Total review time: 79 days Regulatory review time: 40 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. An application for a partial change to alter the shape of the battery connector part. (A partial change in the reexamination period)
4	Feb. 8, 2012 Total review time: 65 days Regulatory review time: 25 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 used to improve circulation until heart transplantation in patients with severe heart failure for whom heart transplantation is indicated. Change of manufacturing site. (A partial change in 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	Feb. 14, 2012 Total review time: 54 days Regulatory review time: 39 days	– No clinical study results	19	DuraHeart Left Ventricular Assist System (Terumo Corporation)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device used to improve circulation until heart transplantation in patients with severe heart failure for whom heart transplantation is indicated. An application for a partial change to add an emergency controller which can cancel the alarm during a magnetic levitation error due to cable disconnection or another cause. (A partial change in the reexamination period)
4	Feb. 29, 2012 Total review time: 176 days Regulatory review time: 136 days	– No clinical study results	20	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device used to improve circulation until heart transplantation in patients with severe heart failure for whom heart transplantation is indicated. An application for a partial change to add a type in which the inside of the artificial blood vessel of the outflow graft is coated with the same material as the inflow cannula for reducing the amount of fluid drained from the thoracic cavity drain. (A partial change in the reexamination period)
4	Mar. 29, 2012 Total review time: 538 days Regulatory review time: 341 days	– Foreign clinical study results	21	Medtronic Advisa MRI (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker used to treat bradycardia. The design concept allows MRI examination to patients implanted with the device; it is the first MRI-compatible pacemaker in Japan. The device has the identical pacing function with the approved product "Medtronic Advisa DR." It is used in combination with "CapSure FIX MRI leads" as implantable pacemaker leads. A clinical study using the previous product was conducted to confirm the safety of MRI examination to patients implanted with the device.
4	Mar. 29, 2012 Total review time: 538 days Regulatory review time: 341 days	Feb. 8, 2011 Foreign clinical study results	22	CapSureFix MRI Lead (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 7 Endocardial implantable pacemaker leads	Implantable pacemaker leads used by connecting them to an implantable cardiac pacemaker. The design concept allows MRI examination to patients implanted with the device when used in combination with "Medtronic Advisa MRI." A clinical study was conducted to confirm the safety of MRI examinations to patients implanted with the device.
5	Aug. 31, 2011 Total review time: 257 days Regulatory review time: 154 days	Jul. 26, 2007 Domestic and foreign clinical study results	23	CryoSeal Disposable kit (Asahi Kasei Kuraray Medical Co., Ltd.)	New	Instrument & apparatus 7 Blood component separation kit	A device to be used to prepare a biological tissue adhesive of autologous plasma origin in a sterilized closed circuit for patients whose blood was donated for preserved blood type autotransfusion. This product is to be used with "CryoSeal CS-1." Biological tissue adhesives prepared with this product are used in the adhesion and closure of tissues (in the case of leakage of blood, body fluid, or internal gas from sutured or bonded tissues). Clinical studies were conducted to evaluate efficacy and safety concerning the adhesion and closure of tissues by biological tissue adhesives prepared using this product.
5	Aug. 31, 2011 Total review time: 257 days Regulatory review time: 154 days	Jul. 26, 2007 Domestic and foreign clinical study results	24	CryoSeal CS-1 (Asahi Kasei Kuraray Medical Co., Ltd.)	New	Instrument & apparatus 7 Apparatus for blood component separation	A device to be used to prepare a biological tissue adhesive of autologous plasma origin in a sterilized closed circuit for patients whose blood was donated for preserved blood type autotransfusion. This product is to be used with "CryoSeal Disposable Kit." Biological tissue adhesives prepared with this product are used in the adhesion and closure of tissues (in the case of leakage of blood, body fluid, or internal gas from sutured or bonded tissues). Clinical studies were conducted to evaluate efficacy and safety concerning the adhesion and closure of tissues by biological tissue adhesives prepared using this product.
5	Dec. 20, 2011 Total review time: 390 days Regulatory review time: 164 days	- Clinical evaluation report	25	Fetal Shunt (Hakko Co., Ltd.)	New	Instrument & apparatus 51 Shunt for fetal pleural effusion	A shunt tube to be placed in the fetal pleural cavity under ultrasonic guidance and a delivery system for the purpose of continuously draining fetal pleural effusion into the maternal amniotic cavity. A clinical evaluation report summarizing the results of literature research on the efficacy and safety of fetal thoraco-amniotic shunt and results of clinical research in Japan was submitted. [Orphan device]
6-2	May. 19, 2011 Total review time: 90 days Regulatory review time: 65 days	Oct. 10, 2003 No clinical study results	26	V.A.C.ATS Therapy System (KCI K.K.)	Change	Medical products 4 Negative pressure wound therapy system	A therapy system used for protection of wounds, maintaining a healing environment, and promoting and shortening the time of wound healing in patients with intractable traumatic wounds or dehisced wounds, post-operative open wounds or skin defective wounds, and post-operative wounds after dismemberment of extremities due to diabetes, etc. Application for a partial change to add manufacturing and sterilization facilities. (A partial change in 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
6-2	Jun. 3, 2011 Total review time: 308 days Regulatory review time: 190 days	Jul. 7, 2004 Foreign clinical study results	27	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 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. This application for a partial change is to add an indication for painful spinal compression fracture of up to three levels due to multiple myeloma or metastatic bone tumor to an already approved indication for acute compression fracture of one vertebral body due to primary osteoporosis. A clinical study was conducted to evaluate the efficacy and safety of this product for the additional indication. (A partial change in the reexamination period)
6-2	Jun. 3, 2011 Total review time: 308 days Regulatory review time: 190 days	Jul. 9, 2004 Foreign clinical study results	28	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 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 Bone Cement HV-R. This application for a partial change is to add an indication for painful spinal compression fracture of up to three levels due to multiple myeloma or metastatic bone tumor to an already approved indication for acute compression fracture of one vertebral body due to primary osteoporosis. A clinical study was conducted to evaluate the efficacy and safety of this product for the additional indication. (A partial change in the reexamination period)
6-2	Jul. 21, 2011 Total review time: 659 days Regulatory review time: 309 days	Dec. 7, 2007 Clinical evaluation report	29	VertaPlex Bone Cement (Stryker Japan K.K.)	New	Medical products 4 Orthopedic bone cement	An orthopedic bone cement to mitigate pain that is used in percutaneous vertebroplasty in patients with malignant spinal tumor such as painful metastatic bone tumor and myeloma who have not responded to conventional therapy. This product was developed with the aim of attaining a working time longer than that of the original product "Stryker Bone Cement for Exclusive Use in the Spine" (22100BZX01112000) by containing a homopolymer component without the styrene group and decreasing a catalyst. A clinical evaluation report summarizing a literature search on the results of domestic general clinical studies including previous products and the clinical results of bone cement that is used in percutaneous vertebroplasty in Japan and overseas was submitted to evaluate its efficacy and safety.
6-2	Jul. 21, 2011 Total review time: 13 days Regulatory review time: 13 days	Aug. 8, 2006 No clinical study results	30	X-STOP PEEK Implant (Medtronic Sofamor Danek Co., Ltd.)	Change	Medical products 4 Single-use interspinous implant device	An implant to be placed between target spinous processes in order to hold the lumbar spine in flexion and prevent it from going into extension for relief of lower back pain and leg pain in patients with lumbar spinal stenosis. Application for a partial change to correct the column for operation methods. (A partial change during the reexamination period)
8	Aug. 26, 2011 Total review time: 169 days Regulatory review time: 141 days	Apr. 29, 2005 No clinical study results	31	da Vinci Surgical System (Johnson & Johnson K.K.)	Change	Instrument & apparatus 12 Surgical robot, operation unit	A device to assist a surgeon in controlling endoscopic instruments attached to three arms of the patient cart with master-slave control in order to cut, coagulate and suture the tissue by manipulating the master controller on the surgeon console. Addition of a manufacturing site. (A partial change during the reexamination period)
8	Dec. 27, 2011 Total review time: 292 days Regulatory review time: 208 days	Apr. 29, 2005 No clinical study results	32	EndoWrist Instrument (Johnson & Johnson K.K.)	Change	Instrument & apparatus 25 Reusable active endotherapy device	An endoscopic instrument to be connected to "da Vinci Surgical System" to follow the movement of surgeon's hands and wrists by manipulating the master controller intended to work mechanically including grasping, suturing, ligation etc. under endoscopic visualization. Addition of a manufacturing site. (A partial change in the reexamination period)
8	Dec. 27, 2011 Total review time: 111 days Regulatory review time: 86 days	Apr. 29, 2005 No clinical study results	33	EndoWrist Bipolar Instrument (Johnson & Johnson K.K.)	Change	Instrument & apparatus 25 Reusable active endotherapy device using radio frequency	An endoscopic instrument to be connected to "da Vinci Surgical System" to follow the movement of surgeon's hands and wrists by manipulating the master controller intended to work mechanically including grasping, suturing etc. and to cut and coagulate the tissue by using radiofrequency electrosurgery current under endoscopic visualization. Addition of a manufacturing site. (A partial change in the reexamination period)

Table 3. Products Approved in FY 2011: 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	Jul. 13, 2011 Total review time: 351 days Regulatory review time: 134 days	May 3, 2011 Foreign clinical study results	1	Alcon AcrySof IQ Toric Single-Piece (Alcon Japan Ltd.)	Change	Instrument & apparatus 72 Posterior chamber lens	A posterior chamber lens to be inserted into an aphakic eye after cataract surgery, with corneal astigmatism-correcting function. This product is the only approved posterior chamber lens for astigmatism correction. The existing product is models with cylinder power of 1.50D, 2.25D, and 3.00D. This application is an application for a partial change to add the models with cylinder power of 3.75D, 4.50D, 5.25D, and 6.00D to deal with severe astigmatic eyes. A clinical study was conducted to confirm the efficacy and safety for correction of severe astigmatism.
1	Aug. 26, 2011 Total review time: 227 days Regulatory review time: 140 days	Jan. 4, 2008 Domestic clinical study results	2	Avaira (CooperVision Japan, Inc.)	New	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Reusable colored contact lenses for correcting visual acuity. The silicone hydrogel lens is indicated for daily wear and replaced in two-week intervals. There is no novelty in the lens design, but the use of cross-linking agent and ultraviolet absorbing agent and the blend ratio of monomer among raw materials have novelty, and therefore a clinical study was conducted to confirm the efficacy and safety for wearing the lens for vision correction.
1	Nov. 14, 2011 Total review time: 1102 days Regulatory review time: 176 days	– Domestic clinical study results	3	HOYA iSii (HOYA Corporation)	New	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal posterior chamber lens to be inserted into an aphakic eye after cataract surgery, with multifocal function consisting of three zones for distant, near, and distant visions in a concentric pattern on the optic surface. A clinical study was conducted to evaluate the efficacy and safety of the intraocular lens, focusing on the efficacy of the multifocal mechanism.
1	Nov. 14, 2011 Total review time: 1095 days Regulatory review time: 169 days	– Domestic clinical study results	4	AF-1 iSii (HOYA Corporation)	New	Instrument & apparatus 72 Posterior chamber lens with an injector	A posterior chamber lens with an injector, for which "HOYA iSii" is preloaded in an injector. A clinical study was conducted to evaluate the efficacy and safety of the intraocular lens, focusing on the efficacy of the multifocal mechanism.
1	Nov. 18, 2011 Total review time: 326 days Regulatory review time: 207 days	Mar. 19, 2003 Clinical evaluation report	5	O_2 Optix (Ciba Vision Corporation)	Change	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	A silicon hydrogel contact lens that can be worn continuously for up to 1 month. An application for a partial change to add the intended use "for treatment accompanied with vision correction capability for eyes with corneal diseases" to the conventional use "for visual acuity." A clinical evaluation report summarizing the results of a literature research on use-results of this product and other contact lenses used for treatment in Japan and overseas was submitted to evaluate the efficacy and safety in therapeutic use.
1	Feb. 23, 2012 Total review time: 1704 days Regulatory review time: 383 days	Oct. 12, 2000 Domestic clinical study results	6	Mechanical Microkeratome M2 (Moria Japan K.K.)	New	Instrument & apparatus 34 Mechanical keratome	A medical blade (mechanical keratome) for lamellar resection of the cornea in LASIK (laser in situ keratomileusis). A flap is made by putting negative pressure around the sclera to stabilize the cornea and resecting the corneal surface layer with the self-propelled blade. A clinical study was conducted to evaluate the efficacy in terms of the precision, quality, etc. of the flap, and the safety for the cornea, etc.
1	Feb. 28, 2012 Total review time: 1169 days Regulatory review time: 497 days	Apr. 11, 2006 (hardware) Aug. 17, 2006 (software) Foreign clinical study results	7	HiRes Auria Sound Processor (Nihon Bionics Co., Ltd.)	Change	Medical products 4 Cochlear implant	A cochlear implant for recovering sound perception by electrical stimulation in patients with bilateral severe hearing loss who have not responded sufficiently to wearing hearing aids. This application is an application for a partial change to add a sound processor and the HiRes 120 sound processing strategy. A clinical study was conducted to evaluate the efficacy and safety of HiRes 120.
1	Mar. 19, 2012 Total review time: 493 days Regulatory review time: 220 days	– Domestic clinical study results	8	Avansee 1P (Kowa Company, Ltd.)	New	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. A one-piece lens for which the optic and haptic are made from the same material. As the raw material has novelty, a clinical study was conducted to evaluate the efficacy for vision correction and the safety for the eye.
2	Dec. 6, 2011 Total review time: 832 days Regulatory review time: 222 days	Jan. 15, 2004 Domestic clinical study results	9	Geistlich Bio-Oss (Geistlich Pharma AG)	New	Medical products 4 Nonabsorbable material for bone regeneration	A nonabsorbable bone substitute that uses bovine bones originating from Australia as raw material and is prepared in the form of granules by heating and drying. It is used with a membrane for filling up bone defects when Guided Tissue Regeneration (GTR) is performed for vertical bone defects and defects in bones with class II root bifurcation lesions that are destroyed by periodontal disease. A clinical study was conducted to evaluate the efficacy and safety with the objective of bone improvement by conducting combination therapy of this product which is a bone substitute for bone regeneration and a dental collagen membrane for vertical bone defects and root bifurcation lesions caused by periodontitis.

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
2	Jan. 13, 2012 Total review time: 840 days Regulatory review time: 341 days	Jul. 22, 2005 Clinical evaluation report	10	Cerasorb M (Hakuho Corporation)	New	Medical products 4 Absorbable dental bone reconstruction implant material	An absorbable dental bone reconstruction implant material made from beta tricalcium phosphate (β-TCP) with a phase purity of higher than 99% in compliance with ASTM F 1088 and a granular product to be used as a substitute for bone for alveolar bone defects as a dental bone substitute (excluding indications on the assumption of placement of an implant). A clinical evaluation report was submitted to evaluate the clinical efficacy and safety of the product as a dental bone substitute.
3-1	May 23, 2011 Total review time: 879 days Regulatory review time: 457 days	May 5, 2005 (change of the time limit for removal) Nov. 18, 2007 (addition of a type) Foreign clinical study results	11	Inferior Vena Cava Filter Set (Cook Japan Inc.)	Change	Instrument & apparatus 51 Inferior vena cava filter	A permanent thrombus-capturing filter to be placed in the inferior vena cava to capture thrombi occurring in veins in the lower limb or pelvis for the prevention of pulmonary artery embolism or the prevention of its recurrence. If removal of this product is required for some reason, the product can be removed by using the dedicated loop system for removal. An application for a partial change was filed to add a type of delivery system and change the time limit for removal from within 10 days to an indefinite period. A clinical study was conducted to confirm the feasibility of removal after long-term placement.
3-1	Jul. 7, 2011 Total review time: 251 days Regulatory review time: 216 days	– Clinical evaluation report	12	Kaneka PTCA Catheter CO-R5 (Kaneka Corporation)	New	Instrument & apparatus 51 Balloon-dilating coronary perfusion catheter for angioplasty	A balloon catheter to be used for dilating stenotic sites in percutaneous transluminal coronary angioplasty (PTCA) or temporary sealing of blood vessel perforations caused during PTCA. With multiple holes made on the proximal and distal sides of the balloon, it enables perfusion from the proximal to distal side during expansion of the balloon. A clinical evaluation report was submitted to confirm the efficacy and safety of the use of the catheter for sealing of blood vessel perforations.
3-1	Aug. 2, 2011 Total review time: 368 days Regulatory review time: 209 days	Sep. 14, 2010 Clinical evaluation report	13	Integrity Coronary Stent System (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 7 Coronary stent	A stent set for percutaneous coronary stent placement to be inserted and placed at the site of a lesion to maintain the vascular lumen. The approved product is formed by lining up the rings with crowns, whereas this product is formed by wrapping a wire that has crowns. A clinical evaluation report was submitted to confirm that this product can be used similarly to the approved product.
3-1	Sep. 5, 2011 Total review time: 418 days Regulatory review time: 243 days	Apr. 22, 2011 Foreign clinical study results	14	Taxus Element Stent System (Boston Scientific Japan K.K.)	New	Instrument & apparatus 7 Coronary stent	A product consisting of a drug-eluting stent coated with paclitaxel and a delivery catheter to inhibit neointimal proliferation. The stent strut design of this product is changed and platinum chromium is used as a raw material for the stent to enhance the deliverability. The use of semisynthetic paclitaxel was also added. A clinical study was conducted to confirm the efficacy and safety for the treatment of coronary stenotic sites by using this product.
3-1	Feb. 21, 2012 Total review time: 424 days Regulatory review time: 118 days	May 19, 2011 Foreign clinical study results	15	ExoSeal (Johnson & Johnson K.K.)	New	Medical products 4 Absorbable topical hemostatic material	An absorbable topical hemostatic material to be used for hemostasis at the femoral artery puncture site in patients who have undergone percutaneous catheterization. The product consists of a polyglycolic acid plug which is a bioabsorbable material and a delivery system to place the plug. This product is intended for hemostasis by placement of the plug on the side of the vascular wall tissue. A clinical study was conducted to confirm the efficacy and safety of this product for hemostasis at the femoral artery puncture site.
3-2	Sep. 16, 2011 Total review time: 421 days Regulatory review time: 215 days	Dec. 16, 2010 Foreign clinical study results	16	ENDURANT Stent Graft System (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 7 Aortic stent graft	The product consists of a stent graft and a delivery system used for endovascular treatment of lower abdominal aortic aneurysm of the renal artery. Compared to the approved product "TALENT Abdominal Stent Graft System," a tip-capture system was introduced and also the low profile delivery system was adapted in order to enhance the control capability for positioning the stent graft. A clinical study was conducted to confirm the efficacy and safety of this product for the treatment of aortic aneurysm.
3-2	Mar. 29, 2012 Total review time: 359 days Regulatory review time: 117 days	Apr. 1, 2011 Foreign clinical study results	17	VALIANT Thoracic Stent Graft System (Medtronic Japan Co., Ltd.)	New	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. Compared to the approved product "TALENT Thoracic Stent Graft System" (Approval No. 22100BZX00355000), improvements such as improvement of the stent graft design and introduction of a tip-capture system to the distal side of the delivery system (enhancement of the control capability for positioning the stent graft) were performed. A clinical study was conducted to evaluate the efficacy and safety of this product in the treatment of descending thoracic aortic aneurysm.

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4	Apr. 13, 2011 Total review time: 285 days Regulatory review time: 164 days	– Foreign clinical study results	18	Fortify ST Pre (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 12 Automatic implantable defibrillator	An implantable defibrillator with the function of bradycardia pacing. The four variations of conectors are as follows: single-chamber types (VR) (IS-1/DF-1 or DF4 connector) and dual-chamber types (DR) (IS-1/DF-1 or IS-1/DF4 connector). Improvements compared with approved defibrillators are as follows: (1) downsizing, (2) addition of thoracic impedance measurement function, (3) addition of ATP treatment in the VF zone, (4) addition of pacing rate alert, (5) addition of low-frequency attenuation filter and (6) setting of the maximum defibrillation energy to be 40J. The device automatically adjusts pulse amplitude, when the patient's ventricular and atrial thresholds change. The efficacy and safety of the function was evaluated by the results of clinical studies for the different defibrillator, because another device with the identical function was under review at the time to compile this application.
4	Apr. 13, 2011 Total review time: 285 days Regulatory review time: 164 days	– Foreign clinical study results	19	Unify (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with defibrillator function. The two variations of connector are as follows: IS-1/DF4 connectors. Improvements from approved defibrillators are as follows: (1) downsizing, (2) addition of thoracic impedance measurement function, (3) addition of ATP treatment in the VF zone, (4) addition of pacing rate alert, (5) addition of low-frequency attenuation filter, and (6) setting of the maximum defibrillation energy to be 40J. The device automatically adjusts pulse amplitude, when the patient's ventricular and atrial thresholds change. The efficacy and safety of the function was evaluated by the results of clinical studies for the different defibrillator, because another device with the identical function was under review at the time to compile this application.
4	Jul. 5, 2011 Total review time: 333 days Regulatory review time: 137 days	May 3, 2010 Foreign clinical study results	20	SJM FD-OCT Imaging System (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 12 OCT diagnostic imaging instrument	The OCT diagnostic imaging instrument is intended for intravascular tomographic imaging. The device is for exclusive use with the catheter "SJM OCT Imaging Catheter". A clinical study was conducted to evaluate the observation capability and the intrinsic safety for target patients.
4	Jul. 5, 2011 Total review time: 333 days Regulatory review time: 137 days	May 3, 2010 Foreign clinical study results	21	SJM OCT Imaging Catheter (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 51 Intravascular optical tomographic catheter	The catheter is intended for intravascular tomographic imaging. The device is for exclusive use with "SJM FD-OCT Imaging System." A clinical study was conducted to evaluate the observation capability and the intrinsic safety for target patients.
4	Aug. 19, 2011 Total review time: 479 days Regulatory review time: 187 days	Nov. 26, 2010 Foreign clinical study results	22	Evia DR-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual-chamber implantable cardiac pacemaker with the remote monitoring function. In the application for a partial change, the following functions are added: a capture control function for the right atrium, a ventricular pacing suppression function and a rate stabilization function. The setting range of parameters is also expanded. A clinical study was conducted to evaluate the efficacy and safety of the capture control function for the right atrium and ventricular pacing suppression function.
4	Aug. 19, 2011 Total review time: 280 days Regulatory review time: 204 days	Nov. 26, 2010 Foreign clinical study results	23	Evia DR (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual-chamber implantable cardiac pacemaker. In the application for a partial change, the following functions are added: a capture control function for the right atrium, a ventricular pacing suppression function and a rate stabilization function. The setting range of parameters is also expanded. A clinical study was conducted to evaluate the efficacy and safety of the capture control function for the right atrium and the ventricular pacing suppression function.
4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	May 12, 2009 Foreign clinical study results	24	Evia DR-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual-chamber implantable cardiac pacemaker with the remote monitoring function. By using the home monitoring function of the device, the information collected by the device is provided to healthcare professionals via a component "Cardio Messenger." In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to evaluate the usefulness of the home monitoring function.
4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	May 12, 2009 Foreign clinical study results	25	Evia SR-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	A single-chamber implantable cardiac pacemaker with the remote monitoring function. By using the home monitoring function of the device, the information collected by the device is provided to healthcare professionals via a component "Cardio Messenger." In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to evaluate the usefulness of the home monitoring function.

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4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	May 12, 2009 Foreign clinical study results	26	Lumax 540 HF-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	A CRT-D with the remote monitoring function. By using the home monitoring function of the device, the information collected by the device are provided to healthcare professionals via a component "Cardio Messenger." In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to evaluate the usefulness of the home monitoring function.
4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	May 12, 2009 Foreign clinical study results	27	Lumax 540 DR-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 12 Dual-chamber automatic implantable defibrillator	A dual-chamber pacing ICD with the remote monitoring function. By using the home monitoring function of the device, the information collected by the device is provided to healthcare professionals via the component "Cardio Messenger." In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to verify the usefulness of the home monitoring function.
4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	May 12, 2009 Foreign clinical study results	28	Lumax 540 VR-T (Biotronik Japan, Inc.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	A single-chamber pacing ICD with the remote monitoring function. By using the home monitoring function of the device, the information collected by the device are provided to healthcare professionals via a component "Cardio Messenger." In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to evaluate the usefulness of the home monitoring function.
4	Sep. 12, 2011 Total review time: 346 days Regulatory review time: 177 days	Apr. 16, 2009 Foreign clinical study results	29	Cardio Messenger(Biotronik Japan, Inc.)	Change	Instrument & apparatus 21 Telemetry data transmitter	A device to receive information of patients from implanted pacemaker, ICD, etc, with the remote monitoring function and to transmit them to healthcare professionals by wireless communication. In the application for a partial change, the usefulness of the home monitoring function is professed in the "intended use; indication." A clinical study was conducted to evaluate the usefulness of the home monitoring function.
4	Sep. 22, 2011 Total review time: 328 days Regulatory review time: 94 days	Nov. 26, 2010 Foreign clinical study results	30	Entovis DR-T (Nihon Kohden Corporation)	Change	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual-chamber implantable cardiac pacemaker with the remote monitoring function. In the application for a partial change, the following functions are added: a capture control function for the right atrium, ventricular pacing suppression function and a rate stabilization function. The setting range of parameters is also expanded. A clinical study was conducted to evaluate the efficacy and safety of the capture control function for the right atrium and the ventricular pacing suppression function.
4	Oct. 5, 2011 Total review time: 559 days Regulatory review time: 224 days	Aug. 11, 2006 Foreign clinical study results	31	NaviStar ThermoCool (Johnson & Johnson K.K.)	Change	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter with the irrigation function used for radiofrequency catheter ablation and electrophysiological study. In the application for a partial change, the use for atrial fibrillation and ventricular tachycardia were added to the indication. Clinical studies were conducted to evaluate the efficacy and safety of the use for atrial fibrillation and ventricular tachycardia.
4	Oct. 20, 2011 Total review time: 360 days Regulatory review time: 209 days	Mar. 27, 2009 Clinical evaluation report	32	Activa RC (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 12 Electrical brain stimulation device for tremor	An electrical stimulation device to reduce tremors associated with Parkinson's disease, essential tremor, etc. that do not sufficiently respond to drug therapy. The device stimulates the deep brain unilaterally or bilaterally. It is designed based on the intrinsic concept of the approved product "Itrel II (Approval No. 21100BZY00563000)" with changing to a dual-channel type, adding an electrical charge function, multi-program function, and constant current mode stimulation function, increasing the maximum pulse rate, etc. The clinical efficacy and safety of the multi-program function, the increased maximum pulse rate and constant current mode are evaluated with a clinical evaluation report.
4	Oct. 20, 2011 Total review time: 360 days Regulatory review time: 212 days	Jan. 26, 2011 Clinical evaluation report	33	Activa SC (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 12 Electrical brain stimulation device for tremor	An electrical stimulation device to reduce tremors associated with Parkinson's disease, essential tremor, etc. that do not sufficiently respond to drug therapy. The device stimulates the deep brain unilaterally or bilaterally. It is designed based on the intrinsic concept of the approved product "Itrel II (Approval No. 21100BZY00563000)" with adding a multi-program function and constant current mode stimulation function, increasing the maximum pulse rate, etc. The clinical efficacy and safety of the multi-program function, the increased maximum pulse rate and constant current mode are evaluated with a clinical evaluation report.

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4	Dec. 12, 2011 Total review time: 605 days Regulatory review time: 204 days	Dec. 21, 2011 Foreign clinical study results	34	NaviStar ThermoCool SF (Johnson & Johnson K.K.)	New	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter with the irrigation function used for radiofrequency catheter ablation and electrophysiological study. The device was developed based on the approved product "NaviStar ThermoCool (Approval No. 22000BZX01645000)", and the catheter tip electrode design and the irrigation flow rate were changed. Clinical studies were conducted to evaluate the efficacy and safety of the use for atrial fibrillation and ventricular tachycardia.
4	Jan. 17, 2012 Total review time: 823 days Regulatory review time: 365 days	Aug. 3, 2005 Foreign clinical study results	35	Select Secure Lead (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 7 Endocardial implantable pacemaker leads	A screw-in bipolar transvenous lead. The diameter of device is made smaller than usual leads by modifications such as removal of the lumen for stylet insertion; it aims to combine with "Medtronic Deflectable Catheter" that can be bent at the distal part of the catheter and to be located in cardiac chamber. A clinical study was conducted to evaluate the efficacy and the safety to place the device with "Medtronic Deflectable Catheter" through the comparison with lead placement using the conventional stylet.
4	Jan. 17, 2012 Total review time: 823 days Regulatory review time: 365 days	Oct. 25, 2006 Foreign clinical study results	36	Medtronic Deflectable Catheter (Medtronic Japan Co., Ltd.)	New	Instrument & apparatus 51 Cardiac catheter introducer kit	A guiding catheter and accessories to be used to pass leads for implantable cardiac pacemakers through the atrium or ventricle. It is used together with "Select Secure Lead." A clinical study was conducted to evaluate the efficacy and the safety to place "Select Secure Lead" with the device through the comparison with lead placement using the conventional stylet.
4	Feb. 2, 2012 Total review time: 349 days Regulatory review time: 192 days	– Foreign clinical study results	37	Promote Quadra (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with defibrillator function and accessories to improve cardiac failure symptoms with regular and weak electrical stimulation to bilateral ventricular myocardium. The device conducts cardiac resynchronization therapy that synchronizes the ventricular contraction. The design concept is similar to that of the approved product "Promote Accel RF (Approval No.: 22200BZX00962000)", but the connector is changed from IS-1 (2 poles) to IS4 (4 poles) and the left ventricular pacing polarity is added. A clinical study was conducted to evaluate the efficacy and safety associated with an increase in pacing polarity (e.g. stability of 4-pole lead) .
4	Feb. 2, 2012 Total review time: 349 days Regulatory review time: 192 days	– Foreign clinical study results	38	Unify Quadra (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with defibrillator function and accessories to improve cardiac failure symptoms with regular and weak electrical stimulation to bilateral ventricular myocardium. The device conducts cardiac resynchronization therapy that synchronizes the ventricular contraction. The design concept is similar to that of the approved product "Unify (Approval No. 22300BZX00210000)", but the connector is changed from IS-1 (2 poles) to IS4 (4 poles) and the left ventricular pacing polarity is added. A clinical study was conducted to evaluate the efficacy and safety associated with an increase in pacing polarity (e.g. stability of 4-pole lead).
4	Feb. 2, 2012 Total review time: 349 days Regulatory review time: 182 days	Nov. 29, 2011 Foreign clinical study results	39	Quartet (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A left ventricular lead and accessories to improve cardiac failure symptoms with regular and weak electrical stimulation to bilateral ventricular myocardium. The device is connected with a biventricular pacing pulse generator with defibrillator function when performing cardiac resynchronization therapy. The device has 4 poles and allows to select the more options for pacing polarity than the approved left ventricular leads, which have 2 poles. A clinical study was conducted to evaluate the efficacy and safety associated with an increase in pacing polarity (e.g. stability of 4-pole lead).
4	Feb. 13, 2012 Total review time: 770 days Regulatory review time: 310 days	– Domestic clinical study results	40	Intracardiac Defibrillation Multi-catheter (Japan Lifeline Co., Ltd.)	New	Instrument & apparatus 51 Cardiac catheter-type electrode	A cardiac catheter electrode used for cardiac electrophysiological examination. Moreover, the device is connected with "Intracardiac Defibrillator" and used for defibrillation when atrial fibrillation, atrial flutter, or atrial tachycardia occurs during percutaneous catheter ablation or cardiac electrophysiological examination. A clinical study was conducted to evaluate the efficacy and safety of the defibrillation using the device.
4	Feb. 13, 2012 Total review time: 770 days Regulatory review time: 276 days	– Domestic clinical study results	41	Intracardiac Defibrillator (Japan Lifeline Co., Ltd.)	New	Instrument & apparatus 12 Manual defibrillator	This is a generator for electric defibrillation connected with "Intracardiac Defibrillation Multi-catheter" when atrial fibrillation, atrial flutter, or atrial tachycardia occurs during percutaneous catheter ablation or cardiac electrophysiological examination. A clinical study was conducted to evaluate the efficacy and safety of the defibrillation using the device.

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4	Feb. 23, 2012 Total review time: 423 days Regulatory review time: 234 days	Oct. 2, 2009 Foreign clinical study results	42	Blazer Prime XP Ablation Catheter (Boston Scientific Japan K.K.)	New	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter to apply radiofrequency current to the target site of arrhythmia identified electrophysiologically, in order to treat persistent or recurrent type I atrial flutter. The shaft part was improved in order to enhance the delivery capability. A clinical study was conducted to evaluate the efficacy and safety to use the device for persistent or recurrent type I atrial flutter.
5	Apr. 18, 2011 Total review time: 755 days Regulatory review time: 404 days	Dec. 1, 2006 Foreign clinical study results	43	AMS GreenLight HPS Console (American Medical Systems, Inc.)	New	Instrument & apparatus 31 Double-frequency neodymium-YAG laser	A surgical device for resection of the prostate gland with 532 nm double-frequency neodymium-YAG laser under cystoscopy for the treatment of benign prostate hypertrophy/hyperplasia. Improvements from the approved product are the use of the oscillation wavelength of 532 nm and change of the maximum output power to 120 W. A clinical study was conducted to confirm the efficacy and safety of this product for benign prostate hypertrophy/hyperplasia.
5	Apr. 18, 2011 Total review time: 755 days Regulatory review time: 404 days	Dec. 1, 2006 Foreign clinical study results	44	AMS GreenLight HPS Fiber (American Medical Systems, Inc.)	New	Instrument & apparatus 31 Single-use probe for laser guidance	A side-firing fiber to be used in combination with the surgical device "AMS GreenLight HPS Console" to resect the prostate gland with 532 nm double-frequency neodymium-YAG laser under cystoscopy for the treatment of benign prostate hypertrophy/hyperplasia. A clinical study was conducted to confirm the efficacy and safety of this product for benign prostate hypertrophy/hyperplasia.
5	Jul. 7, 2011 Total review time: 645 days Regulatory review time: 225 days	Sep. 30, 2004 Clinical evaluation report	45	WallFlex Colonic Stent (Boston Scientific Japan K.K.)	New	Instrument & apparatus 7 Colonic stent	A colonic stent to be used for colonic strictures produced by malignant neoplasm to relieve large bowel obstruction prior to operation, also to be used for the palliative treatment for patients who cannot be managed by palliative surgical treatment or are not expected to achieve improvement with other treatments. A clinical evaluation report was submitted to evaluate the efficacy and safety for the use of this product for preoperative relief of bowel obstruction or as palliative treatment.
5	Nov. 14, 2011 Total review time: 693 days Regulatory review time: 363 days	– Clinical evaluation report	46	Niti-S Gastroduodenal Stent (Century Medical, Inc.)	New	Instrument & apparatus 7 Gastroduodenal stent	A gastroduodenal stent to be used to maintain patency at stenotic sites in patients with unresectable malignant gastroduodenal stenosis who are not expected to achieve improvement with surgical treatment or other treatment methods. A clinical evaluation report summarizing the results of literature research on clinical data on gastroduodenal stent placement was submitted to evaluate the efficacy and safety.
5	Mar. 26, 2012 Total review time: 536 days Regulatory review time: 331 days	May 8, 2006 Clinical evaluation report	47	Given Patency Capsule Endoscope (Given Imaging K.K.)	New	Instrument & apparatus 25 Capsule electronic endoscope system	A product to take and provide images of the small-intestinal mucosa for diagnosis of small-intestinal diseases. The approved product "Given Capsule Endoscope (Approval No. 22100BZX00363000) has been improved with the addition of Agile J Patency Capsule (AJP), which is used to assess appropriateness of the patency of the digestive tract prior to the use of a capsule endoscope in patients who have or are suspected of having stenosis or narrowing of the digestive tract. A clinical evaluation report summarizing literature information, etc. on occurrence of retention of capsule endoscopes after assessment of patency by AJP was submitted to evaluate the accuracy of assessment of patency with AJP.
6-1	Apr. 28, 2011 Total review time: 388 days Regulatory review time: 195 days	– Domestic clinical study results	48	Aquala Liner (Japan Medical Materials Corporation)	New	Medical products 4 Artificial hip joint, acetabular component	An ultra-high-molecular-weight polyethylene liner for an artificial hip joint. This product is photoinduced graft-polymerized with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer on the bearing surface in addition to cross-link processing, in order to improve the wear resistance of the bearing surface while inheriting the design of the approved products. A clinical study was conducted to confirm the efficacy and safety of the liner for which the bearing surface was modified with the novel raw material.
6-2	Jun. 14, 2011 Total review time: 1174 days Regulatory review time: 788 days	– Domestic clinical study results	49	Osmix (Kuraray Medical Inc.)	New	Medical products 4 Artificial bone implant	An artificial bone implant in paste form for which silane-coating hydroxyapatite particles and polymerizable monomers are mixed. This product is designed to start polymerization when discharged from the dedicated injector. It is injected into the affected site in paste form to compensate for bone defects after reconstruction of bone fracture of non-loaded region and for bone defects after removals of bone tumor/necrosis bone. A clinical study was conducted to confirm the efficacy and safety of the use of the novel raw material.

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6-2	Jun. 14, 2011 Total review time: 287 days Regulatory review time: 172 days	Jun. 27, 2001 Aug. 8, 2003 Domestic clinical study results	50	TwinFix AB Anchor (Smith & Nephew Endoscopy KK)	New	Medical products 4 Absorbable ligament anchor	An absorbable suture anchor to be used to repair the binding of soft tissues such as ruptured tendons, ligament, and muscles to bones. The product is only indicated for repair of rotator cuff tear in the shoulder. The improvement from the approved nonabsorbable product is the use of absorbable poly-L-lactic acid as raw material for the anchor. A clinical study was conducted to evaluate the efficacy and safety of this product which is an absorbable screw-type anchor.
6-2	Dec. 1, 2011 Total review time: 975 days Regulatory review time: 674 days	Nov. 20, 2001 Clinical evaluation report	51	Lacto Screw Suture Anchor (Biomet Japan, Inc.)	New	Medical products 4 Absorbable ligament anchor	A resorbable screw-type suture anchor made of polylactic/polyglycolic acid copolymer used to attach ligaments or tendons to bones with a suture. The device is to be used in patients who require repair due to damage of soft tissues in regions adjacent to the shoulder joint such as the articular labrum, and soft tissues of the elbow and hand joints. A clinical evaluation report summarizing literatures on clinical data using this device and other screw-type anchor made from the same raw material, was submitted to evaluate the efficacy and safety.
6-2	Dec. 1, 2011 Total review time: 945 days Regulatory review time: 868 days	Jul. 19, 2006 Clinical evaluation report	52	AllThread Screw L15 (Biomet Japan, Inc.)	New	Medical products 4 Absorbable ligament anchor	A resorbable screw-type suture anchor made of polylactic/polyglycolic acid copolymer used to attach ligaments or tendons to bones with a suture. The device is to be used in patients who require repair due to damage of soft tissues in regions adjacent to the shoulder joint, and soft tissues of the elbow and hand joints. A clinical evaluation report summarizing literatures on clinical data using other screw-type anchor made from the same raw material as this device, was submitted to evaluate the efficacy and safety.
6-2	Feb. 17, 2012 Total review time: 1803 days Regulatory review time: 805 days	May 1, 2000 Domestic clinical study results	53	Arthrex Bio-FASTak Suture Anchor (Kobayashi Medical Co., Ltd.)	New	Medical products 4 Absorbable screw for internal fixation	An absorbable screw-type suture anchor made of poly DL-lactic acid to be used to fix soft tissues to bones in shoulder joints. A clinical study was conducted to evaluate the efficacy and safety for the treatment of shoulder joint instability in order to evaluate whether tissues such as ligaments in shoulder joints can be repaired.
Biologics	Apr. 8, 2011 Total review time: 952 days Regulatory review time: 315 days	Nov. 15, 2007 Foreign clinical study results	54	SJM Epic Stented Tissue Valve (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Porcine cardiac valve	A biological prosthetic cardiac valve with stent derived from pig aortic valve that is intended to substitute for the function of aortic valves or mitral valves with a disease, damage, or dysfunction. This product is treated for anticalcification and uses bovine pericardial membrane at the stent part for the protection of the valve leaflet. A clinical study was conducted to confirm the efficacy and safety of this product.
Biologics	Mar. 8, 2012 Total review time: 416 days Regulatory review time: 122 days	Apr. 20, 2011 Foreign clinical study results	55	SJM Trifecta Valve (St. Jude Medical Japan Co., Ltd.)	New	Instrument & apparatus 7 Bovine pericardial valve	A bovine pericardial valve to be used to substitute for the function of aortic valves with a disease, damage, or dysfunction. This product is to be implanted into the supra annular position. It is treated for anticalcification. Pig pericardial membrane is used at the outflow of the stent for the protection of the valve leaflet. A clinical study was conducted to confirm the clinical safety and efficacy of this product.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs, etc., Directed by MHLW in FY 2011

Post-marketing safety measures implemented by MHLW in FY 2011

	Drugs	Medical devices
Revision of PRECAUTIONS directed	185	6
Information published in the Pharmaceuticals and Medical Devices Safety Information	47	5

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

Revision of PRECAUTIONS for Drugs Directed by MHLW in FY 2011

Date	Drug name
Apr. 20, 2011	1. Fludarabine phosphate 2. Miriplatin hydrate 3. Olopatadine hydrochloride (oral dosage form) 4. Ketotifen fumarate (oral dosage form) 5. Iodine addition products of the ethylesters of the fatty acids obtained from poppyseed oil (MIRIPLA suspension vehicle) 6. Alprazolam 7. Pramipexole hydrochloride hydrate 8. Aliskiren fumarate 9. Infliximab (genetical recombination) 10. Pemetrexed sodium hydrate 11. Micafungin sodium 12. Darunavir ethanolate (300 mg) 13. Darunavir ethanolate (400 mg) 14. Ribavirin (tablets) 15. Peginterferon alfa-2a (genetical recombination) 16. Peginterferon alfa-2b (genetical recombination) 17. Over-the-counter drugs Ketotifen fumarate (oral dosage form)
May 31, 2011	1. Sitagliptin phosphate hydrate 2. Metformin hydrochloride 3. Cisplatin (intra-arterial injection) 4. Sorafenib tosilate 5. Freeze-dried live attenuated measles vaccine Freeze-dried live attenuated measles, rubella combined vaccine 6. Cortisone acetate Dexamethasone (oral dosage form) Dexamethasone metasulfobenzoate sodium (injectable dosage form) Dexamethasone sodium phosphate (injectable dosage form) Triamcinolone Triamcinolone acetonide (injectable dosage form for intraarticular/intramuscular/intradermal) Hydrocortisone sodium phosphate Fludrocortisone acetate Prednisolone (oral dosage form) Prednisolone sodium succinate Prednisolone sodium phosphate Betamethasone Betamethasone acetate/betamethasone sodium phosphate Betamethasone sodium phosphate (injectable dosage form, enema) 7. Dexamethasone palmitate 8. Hydrocortisone 9. Hydrocortisone sodium succinate Methylprednisolone Methylprednisolone sodium succinate Methylprednisolone acetate 10. Betamethasone/d-chlorpheniramine maleate 11. Mitotane 12. Linezolid 13. Freeze-dried, cell culture-derived Japanese encephalitis vaccine (inactivated) (ENCEVAC) 14. Freeze-dried, cell culture-derived Japanese encephalitis vaccine (inactivated) (JEBIK V) 15. Inulin

Date	Drug name
Jun. 24, 2011	1. Pioglitazone hydrochloride 2. Pioglitazone hydrochloride/glimepiride Pioglitazone hydrochloride/metformin hydrochloride 3. Ergotamine tartrate/anhydrous caffeine/isopropylantipyrine
Jul. 5, 2011	1. Oxaliplatin 2. Sunitinib malate 3. Lenalidomide hydrate 4. Pneumococcal polysaccharide conjugate vaccine (adsorbed) 5. Recombinant adsorbed hepatitis B vaccine (yeast-derived) (Bimmugen) 6. Varenicline tartrate 7. Gabapentin 8. Terbutaline sulfate 9. Bevacizumab (genetical recombination) 10. Fexofenadine hydrochloride 11. Recombinant adsorbed hepatitis B vaccine (yeast-derived) (HEPTAVAX) 12. Tocilizumab (genetical recombination)
Aug. 9, 2011	Modafinil Doxorubicin hydrochloride (non-ribosom preparation) Thalidomide ShakuyakuKanzoto (for ethical use) Influenza HA vaccine Esmolol hydrochloride Bosentan hydrate Clomifene citrate Methotrexate Azithromycin hydrate (tablet 250 mg, 600 mg, capsule for pediatric, fine granule for pediatric, injectable dosage form) Azithromycin hydrate (dry syrup for adults) Clarithromycin Lansoprazole/amoxicillin hydrate/clarithromycin Ofloxacin (oral dosage form) Levofloxacin hydrate (oral dosage form) (low-dose) Levofloxacin hydrate (oral dosage form) (high-dose) Levofloxacin hydrate (injectable dosage form) Maraviroc Sulfamethoxazole/trimethoprim Eptacog alfa (activated) (genetical recombination) ShakuyakuKanzoto (OTC)
Aug. 12, 2011	Dabigatran etexilate methanesulfonate
Sep. 28, 2011	Voriconazole Gadoxetate sodium Gadodiamide hydrate Gadoteridol Meglumine gadoterate Gadopentetate dimeglumine Carbamazepine Dabigatran etexilate methanesulfonate Fondaparinux sodium Clopidogrel sulfate Sodium hyaluronate crosslinked polymer/sodium hyaluronate crosslinked polymer crosslinked with vinylsulfone

Date	Drug name
	Capecitabine Garenoxacin mesilate hydrate
Oct. 25, 2011	Atomoxetine hydrochloride Ritodrine hydrochloride (injectable dosage form) Temozolomide Anastrozole Dasatinib hydrate Varenicline tartrate
Nov. 8, 2011	Zoledronic acid hydrate Pamidronate disodium hydrate Alendronate sodium hydrate (oral dosage form) Etidronate disodium Sodium risedronate hydrate Alendronate sodium hydrate (injectable dosage form) Minodronic acid hydrate
Nov. 29, 2011	Epoprostenol sodium Solifenacin succinate Nitrazepam Fluticasone furoate Fluticasone propionate (nasal solution) Acetazolamide Acetazolamide sodium Isoniazid Isoniazid sodium methanesulfonate hydrate Remifentanil hydrochloride
Jan. 10, 2012	Galsulfase (genetical recombination) Daikenchuto Aripiprazole Haloperidol (injectable dosage form) Chloramphenicol (preparation for vaginal application) Enoxaparin sodium Acarbose Voglibose Mitiglinide calcium hydrate/voglibose Miglitol Tacrolimus hydrate (oral dosage form, injectable dosage form) Lenalidomide hydrate Saireito Sitafloxacin hydrate Lopinavir/ritonavir Daikenchuto (OTC)
Feb. 14, 2012	Leflunomide Montelukast sodium Monobasic sodium phosphate monohydrate/anhydrous dibasic sodium phosphate Extract from inflamed cutaneous tissue of rabbits inoculated with vaccinia virus (oral dosage form) Extract from inflamed cutaneous tissue of rabbits inoculated with vaccinia virus (injectable dosage form) [1] FK powder [2] HM powder

Date	Drug name
	[3] KM powder [4] NIM combination powder [5] OM powder mix Deferasirox Ritonavir
Mar. 19, 2012	Triclofos sodium Chloral hydrate (oral dosage form, enema) Chloral hydrate (suppository, kit for enema) Acetaminophen Tramadol hydrochloride/acetaminophen Isopropylantipyrine/acetaminophen/allylisopropylacetylurea/anhydrous caffeine Salicylamide/acetaminophen/anhydrous caffeine/chlorpheniramine maleate Salicylamide/acetaminophen/anhydrous caffeine/promethazine methylenedisalicylate Cibenzoline succinate (oral dosage form) Cibenzoline succinate (injectable dosage form) Diprophylline/dihydrocodeine phosphate/dl-methylephedrine hydrochloride/diphenhydramine salicylate/acetaminophen/bromovalerylurea Pioglitazone hydrochloride/metformin hydrochloride Metformin hydrochloride (preparations with “Dosage and Administration” of maximum daily dosage of 750 mg) Buformin hydrochloride Metformin hydrochloride (preparations with “Dosage and Administration” of maximum daily dosage of 2,250 mg) Fingolimod hydrochloride Triazolam Tramadol hydrochloride Tramadol hydrochloride/acetaminophen Paliperidone Risperidone Blonanserin Furosemide Metenolone enanthate Metenolone acetate Mirabegron Pyridoxal phosphate hydrate (injectable dosage form) (preparations containing benzyl alcohol as an excipient) Pyridoxine hydrochloride (injectable dosage form) Ribavirin (capsules) Interferon beta (Products for administration in combination with ribavirin) Iopamidol Products containing acetaminophen (OTC)

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 5. Revision of PRECAUTIONS for Medical Devices Directed in FY 2011

Date	Title
May 25, 2011	Revision of Package Inserts of Subcutaneous Port and Catheter
Jul. 20, 2011	Revision of PRECAUTIONS for Intraocular Lens
Jul. 20, 2011	Revision of PRECAUTIONS for Coronary Stent
Oct. 31, 2011	Handling of Applications for Partial Change for Automated External Defibrillators and Directions for Revision of PRECAUTIONS for Use of Automated External Defibrillators in Preschool-age Children and for Use of Body Surface Defibrillation Electrodes in Adults
Nov. 17, 2011	Revision of Package Inserts for Blood Glucose Meters, etc.
Feb. 29, 2012	Revision of PRECAUTIONS for Radiation Therapy Equipment

Note: Detailed information is available at the PMDA's Medical Product Information web page.

Table 6. FY 2011 Pharmaceuticals and Medical Devices Safety Information (No. 279-289)

Date	No.	Contents
May 25, 2011	279	1. Project of Japan Drug Information Institute in Pregnancy 2. Safety Measures Related to Lenalidomide Hydrate 3. Important Safety Information [1] Aripiprazole [2] Freeze-dried live Attenuated Mumps Vaccine [3] Anti-human Thymocyte Immunoglobulin, Rabbit [4] Tacrolimus Hydrate (oral dosage form, injectable dosage form) [5] Tolvaptan [6] Pioglitazone Hydrochloride, Pioglitazone Hydrochloride/Glimepiride, Pioglitazone Hydrochloride/Metformin Hydrochloride 4. Revision of Precautions (No. 225) Sanilvudine (and 32 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Jun. 29, 2011	280	1. Safety Measures for Pediatric Pneumococcal Conjugate Vaccine and Haemophilus Influenzae Type b (Hib) Vaccine 2. Manuals for Management of Individual Serious Adverse Drug Reactions 3. Important Safety Information [1] Olopatadine Hydrochloride (oral dosage form) [2] Fludarabine Phosphate [3] Miriplatin Hydrate, Iodine Addition Products of the Ethylesters of the Fatty Acids Obtained from Poppyseed oil (MIRIPLA suspension vehicle) 4. Revision of Precautions (No. 226) Ketotifen Fumarate (oral dosage form) (and 12 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Jul. 27, 2011	281	1. Revision of Package Inserts of Subcutaneous Port and Catheter 2. Important Safety Information [1] Freeze-dried Live Attenuated Measles Vaccine; Freeze-dried Live Attenuated Measles, Rubella Combined Vaccine [2] Cisplatin (intra-arterial injection) [3] Sitagliptin Phosphate Hydrate [4] Sorafenib Tosilate [5] Metformin Hydrochloride (products with “Dosage and Administration” of maximum daily dosage of 2,250 mg) 3. Revision of Precautions (No. 227) Cortisone Acetate (and 9 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Aug. 30, 2011	282	1. Revision of Contraindications for the Use of Coronary Stent 2. Revision of Contraindications for the Use of Intraocular Lens 3. Important Safety Information [1] Oxaliplatin [2] Recombinant Adsorbed Hepatitis B Vaccine (yeast-derived) (Bimmugen) [3] Sunitinib Malate [4] Pneumococcal Polysaccharide Conjugate Vaccine (adsorbed) [5] Varenicline Tartrate [6] Lenalidomide Hydrate 4. Revision of Precautions (No. 228) Pioglitazone Hydrochloride (and 8 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Sep. 28, 2011	283	1. Safety Measures against Bladder Cancer Associated with Diabetes Medication “Pioglitazone Hydrochloride-Containing Products” 2. Important Safety Information

Date	No.	Contents
		[1] Influenza HA vaccine [2] Thalidomide [3] Doxorubicin Hydrochloride (non-liposome preparation) [4] Dabigatran Etexilate Methanesulfonate 3. Revision of Precautions (No. 229) Modafinil (and 16 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 26, 2011	284	1. Safety Measures against Disturbed Consciousness Associated with the Use of Smoking Cessation Aid CHAMPIX Tablets 2. The Guidelines for Provision of Dear Healthcare Professional Letters of Emergent/Rapid Safety Communications 3. Summary of Report on Adverse Reactions to the Influenza A (H1N1) Vaccine in the 2010 Season 4. Important Safety Information [1] Voriconazole 5. Revision of Precautions (No. 230) Gadoxetate Sodium (and 11 others) 6. List of Products Subject to Early Post-marketing Phase Vigilance
Nov. 30, 2011	285	1. Safety Measures against Nephrogenic Systemic Fibrosis Associated with Gadolinium Contrast Media 2. Carbamazepine-induced Serious Drug Eruption and Genetic Polymorphism 3. Important Safety Information [1] Anastrozole [2] Temozolomide [3] Ritodrine Hydrochloride (injectable dosage form) 4. Revision of Precautions (No. 231) Atomoxetine Hydrochloride (and 6 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 27, 2011	286	1. Cases of Non-payment under the Relief System for Sufferers from Adverse Drug Reactions and Proper Use of Drugs 2. Important Safety Information [1] Epoprostenol Sodium 3. Revision of Precautions (No. 232) Solifenacin Succinate (and 7 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jan. 25, 2012	287	1. Lamotrigine-induced Severe Drug Eruption and Compliance with Dosage and Administration 2. Fatal Fire Accidents Involving Patients during Use of Long-term Oxygen Therapy 3. List of Products Subject to Early Post-marketing Phase Vigilance (Correction of Products subject to Early Post-marketing Phase Vigilance)
Feb. 1, 2012	288	1. Systemic Allergy Associated with the Use of Quasi-drugs/Cosmetics 2. Important Safety Information [1] Daikenchuto 3. Revision of Precautions (No. 233) Galsulfase (Genetical recombination) (and 13 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance (Correction of Products subject to Early Post-marketing Phase Vigilance)
Mar. 30, 2012	289	1. Reactivation of Hepatitis B Virus Associated with Antineoplastic Agent Everolimus 2. Use of the "PMDA medi-navi" and "My Drug List for Safety Update" 3. Important Safety Information [1] Montelukast Sodium [2] Monobasic Sodium Phosphate Monohydrate/Dibasic Sodium Phosphate

Date	No.	Contents
		Anhydrous 4. Revision of Precautions (No. 234) (1) Leflunomide (and 5 others) (2) Radiation Therapy Equipment 5. List of Products Subject to Early Post-marketing Phase Vigilance (Correction 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 2011 PMDA Medical Safety Information

No.	Month and year published	Title
23	April 2011	Precautions in Handling of Insulin Syringes
24	June 2011	Precautions in Using Needle-free Valves
25	September 2011	Precautions for Magnetic Resonance Imaging (MRI) Scans (Part 1)
26	September 2011	Precautions for Magnetic Resonance Imaging (MRI) Scans (Part 2)
27	October 2011	Precautions in Handling of Drug Products Attached with Reconstitution Solution
28	November 2011	Precautions in Handling of Blood Glucose Meter
29	December 2011	Precautions in Handling of Electrocardiogram Monitoring System

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, 2011)

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 (1) 1-a	
		Document		111,500	111,500
				Article 16 (1) 1-b	
Change/Addition of classification		On-site		97,400	97,400
				Article 16 (1) 2-a	
		Document		55,300	55,300
				Article 16 (1) 2-b	
Renewal of existing license		On-site		97,400	97,400
				Article 16 (1) 3-a	
		Document		55,300	55,300
				Article 16 (1) 3-b	
Assessment for foreign manufacturers accreditation of drugs					
New accreditation		On-site		133,300 + travel expenses	133,300 + travel expenses
				Article 16 (2) 1-a	
		Document		58,100	58,100
				Article 16 (2) 1-b	
Change/Addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 2-a	
		Document		39,700	39,700
				Article 16 (2) 2-b	
Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 3-a	
		Document		39,700	39,700
				Article 16 (2) 3-b	
Review for approval of drugs (new approval)					
New drugs 1 (non-orphan drugs)		First application products	23,788,100	6,559,600	30,347,700
			Article 17 (1) 1-a (1)	Article 17 (2) 1-a	
		Line extension products	2,464,000	1,639,800	4,103,800
			Article 17 (1) 1-a (3)	Article 17 (2) 1-c	
New drugs 1 (orphan drugs)		First application products	19,934,100	3,286,000	23,220,100
			Article 17 (1) 1-a (2)	Article 17 (2) 1-b	
		Line extension products	2,061,500	818,100	2,879,600
			Article 17 (1) 1-a (4)	Article 17 (2) 1-d	
New drugs 2 (non-orphan drugs)		First application products	11,353,100	2,463,200	13,816,300
			Article 17 (1) 1-a (5)	Article 17 (2) 1-e	
		Line extension products	1,174,300	615,900	1,790,200
			Article 17 (1) 1-a (6)	Article 17 (2) 1-f	
New drugs 2 (orphan drugs)		First application products	9,345,700	1,232,500	10,578,200
			Article 17 (1) 1-a (7)	Article 17 (2) 1-g	
		Line extension products	1,004,100	310,100	1,314,200
			Article 17 (1) 1-a (8)	Article 17 (2) 1-h	
Generic prescription drugs (with inspections)			412,100	214,000	626,100
			Article 17 (1) 1-a (9)	Article 17 (2) 1-i	
OTC drugs	Switch to OTC status, etc.	First application products	1,291,600		1,291,600
			Article 17 (1) 1-a (10)		
		Line extension products	1,291,600		1,291,600
			Article 17 (1) 1-a (10)		
	Others		110,300		110,300
			Article 17 (1) 1-a (11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17 (1) 1-a (14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17 (1) 1-a (13)		
		Addition of series	60,300		60,300
			Article 17 (1) 1-a (12)		
Quasi-drugs/Cosmetics			63,500		63,500
			Article 17 (1) 1-b, c		
New application for change or replacement of brand name			35,600		35,600
			Article 17 (1) 1-e		

Classification				User fees		
				Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)						
New drugs 1 (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
	Others			205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
New drugs 1 (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
				Article 17 (1) 2-a (4)	Article 17 (2) 2-d	
			Line extension products	875,600	310,100	1,185,700
				Article 17 (1) 2-a (5)	Article 17 (2) 2-e	
	Others			132,700	109,800	242,500
				Article 17 (1) 2-a (6)	Article 17 (2) 2-f	
New drugs 2 (non-orphan drugs)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
	Others			205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
New drugs 2 (orphan drugs)	Changes in indications, etc.		First application products	8,434,300	1,232,500	9,666,800
				Article 17 (1) 2-a (4)	Article 17 (2) 2-d	
			Line extension products	875,600	310,100	1,185,700
				Article 17 (1) 2-a (5)	Article 17 (2) 2-e	
	Others			132,700	109,800	242,500
				Article 17 (1) 2-a (6)	Article 17 (2) 2-f	
Generic drugs (with inspection)	Changes in indications, etc.		First application products	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Line extension products	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
	Changes based on guidelines			35,600		35,600
				Article 17 (1) 2-a (7)		
	Others			205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	10,190,500		10,190,500
				Article 17 (1) 2-a (1)		
			Line extension products	1,057,400		1,057,400
				Article 17 (1) 2-a (2)		
	Changes based on guidelines			35,600		35,600
				Article 17 (1) 2-a (7)		
	Others			56,400		56,400
				Article 17 (1) 2-a (8)		
In vitro diagnostics (without approval standards)				295,800		295,800
				Article 17 (1) 2-a (11)		
In vitro diagnostics (with approval standards)			Basic	143,500		143,500
				Article 17 (1) 2-a (10)		
			Addition of series	31,900		31,900
				Article 17 (1) 2-a (9)		
Quasi-drugs/Cosmetics				35,600		35,600
				Article 17 (1) 2-b, c		

Classification					User fees		
					Review	Inspection	Total
GMP inspection of drugs							
Approval, partial change and manufacture for export		New drugs		In Japan		739,800 Article 17 (4) 1-b (1)	739,800
				Outside Japan		933,500 + travel expenses Article 17 (4) 1-b (2)	933,500 + travel expenses
		Biological drugs/Radiopharmaceuticals		In Japan		666,100 Article 17 (4) 1-a (1)	666,100
				Outside Japan		844,400 + travel expenses Article 17 (4) 1-a (2)	844,400 + travel expenses
		Sterilized drugs/Sterilized quasi-drugs		In Japan		201,300 Article 17 (4) 1-c (1)	201,300
				Outside Japan		229,800 + travel expenses Article 17 (4) 1-c (2)	229,800 + travel expenses
		Other drugs/quasi-drugs		In Japan		141,200 Article 17 (4) 1-d (1)	141,200
				Outside Japan		155,400 + travel expenses Article 17 (4) 1-d (2)	155,400 + travel expenses
		Package, labeling, storage, external testing, etc.		In Japan		63,800 Article 17 (4) 2-a, Article 17 (5) 1-a	63,800
				Outside Japan		84,800 + travel expenses Article 17 (4) 2-b, Article 17 (5) 1-b	84,800 + travel expenses
Renewal of the above		Biological drugs/ Radiopharmaceuticals	Basic	In Japan		436,000 Article 17 (4) 3-a (1)	436,000
				Outside Japan		554,200 + travel expenses Article 17 (4) 3-a (2)	554,200 + travel expenses
			Addition of products	In Japan		30,500 Article 17 (4) 3-a (1)	30,500
				Outside Japan		30,500 Article 17 (4) 3-a (2)	30,500
		Sterilized drugs/ Sterilized quasi-drugs	Basic	In Japan		380,000 Article 17 (4) 3-b (1)	380,000
				Outside Japan		480,000 + travel expenses Article 17 (4) 3-b (2)	480,000 + travel expenses
			Addition of products	In Japan		12,400 Article 17 (4) 3-b (1)	12,400
				Outside Japan		12,400 Article 17 (4) 3-b (2)	12,400
		Other drugs/ quasi-drugs	Basic	In Japan		336,500 Article 17 (4) 3-c (1)	336,500
				Outside Japan		409,400 + travel expenses Article 17 (4) 3-c (2)	409,400 + travel expenses
			Addition of products	In Japan		9,600 Article 17 (4) 3-c (1)	9,600
				Outside Japan		9,600 Article 17 (4) 3-c (2)	9,600
		Package, labeling, storage, external testing, etc.	Basic	In Japan		258,500 Article 17 (4) 3-d (1), Article 17 (5) 2-a	258,500
				Outside Japan		338,100 + travel expenses Article 17 (4) 3-d (2), Article 17 (5) 2-b	338,100 + travel expenses
			Addition of products	In Japan		6,700 Article 17 (4) 3-d (1), Article 17 (5) 2-a	6,700
				Outside Japan		6,700 Article 17 (4) 3-d (2), Article 17 (5) 2-b	6,700

Classification				User fees		
				Review	Inspection	Total
GLP inspection of drugs						
	GLP	In Japan			2,062,400	2,062,400
					Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
		Outside Japan			2,282,600 + travel expenses	2,282,600 + travel expenses
					Article 17 (3) 1-b, Article 17 (9) 2-a (2)	
GCP inspection of drugs						
	New GCP	First application products	In Japan		2,723,200	2,723,200
					Article 17 (3) 2-a	
			Outside Japan		3,011,900 + travel expenses	3,011,900 + travel expenses
					Article 17 (3) 2-b	
		Line extension products	In Japan		720,800	720,800
					Article 17 (3) 2-c	
			Outside Japan		751,800 + travel expenses	751,800 + travel expenses
					Article 17 (3) 2-d	
	GCP inspection of generic drugs		In Japan		645,200	645,200
					Article 17 (3) 2-e	
			Outside Japan		950,200 + travel expenses	950,200 + travel expenses
					Article 17 (3) 2-f	
Re-examination of drugs						
	Re-examination	First application products		806,600	2,673,700	3,480,300
				Article 17 (8) 1-a	Article 17 (9) 1-a	
		Line extension products		271,500	892,100	1,163,600
				Article 17 (8) 1-b	Article 17 (9) 1-b	
	GPSP	First application products	In Japan		2,193,300	2,193,300
					Article 17 (9) 2-b (1)	
			Outside Japan		2,409,600 + travel expenses	2,409,600 + travel expenses
					Article 17 (9) 2-b (2)	
		Line extension products	In Japan		752,600	752,600
					Article 17 (9) 2-b (3)	
			Outside Japan		772,300 + travel expenses	772,300 + travel expenses
					Article 17 (9) 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 (1) 1-a	
			Document		111,500	111,500
					Article 16 (1) 1-b	
Change/Addition of classification			On-site		97,400	97,400
					Article 16 (1) 2-a	
			Document		55,300	55,300
					Article 16 (1) 2-b	
Renewal of existing license			On-site		97,400	97,400
					Article 16 (1) 3-a	
			Document		55,300	55,300
					Article 16 (1) 3-b	
Assessment for foreign manufacturers accreditation of medical devices						
New accreditation			On-site		133,300 + travel expenses	133,300 + travel expenses
					Article 16 (2) 1-a	
			Document		58,100	58,100
					Article 16 (2) 1-b	
Change/Addition of classification			On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16 (2) 2-a	
			Document		39,700	39,700
					Article 16 (2) 2-b	
Renewal of existing accreditation			On-site		64,600 + travel expenses	64,600 + travel expenses
					Article 16 (2) 3-a	
			Document		39,700	39,700
					Article 16 (2) 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 (1) 1-d (1)	Article 17 (2) 1-j	
			Improved medical devices	6,213,000	664,500	6,877,500
				Article 17 (1) 1-d (2)	Article 17 (2) 1-j	
		Class Ⅲ	New medical devices	6,213,000	664,500	6,877,500
				Article 17 (1) 1-d (3)	Article 17 (2) 1-j	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17 (1) 1-d (4)	Article 17 (2) 1-j	
		Class Ⅱ	New medical devices	6,213,000	664,500	6,877,500
				Article 17 (1) 1-d (3)	Article 17 (2) 1-j	
			Improved medical devices	3,721,200	664,500	4,385,700
				Article 17 (1) 1-d (4)	Article 17 (2) 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 (1) 1-d (7)	Article 17 (2) 1-l	
			Generic medical devices	1,767,700	68,500	1,836,200
				Article 17 (1) 1-d (8)	Article 17 (2) 1-l	
		Class Ⅲ	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17 (1) 1-d (9)	Article 17 (2) 1-l	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17 (1) 1-d (9)	Article 17 (2) 1-l	
		Class Ⅱ	Improved medical devices	1,409,900	68,500	1,478,400
				Article 17 (1) 1-d (9)	Article 17 (2) 1-l	
			Generic medical devices	1,409,900	68,500	1,478,400
				Article 17 (1) 1-d (9)	Article 17 (2) 1-l	
Medical devices (with approval standards, without clinical data)		Class Ⅳ		429,200	68,500	497,700
				Article 17 (1) 1-d (5)	Article 17 (2) 1-k	
		Class Ⅲ		344,100	68,500	412,600
				Article 17 (1) 1-d (6)	Article 17 (2) 1-k	
		Class Ⅱ		344,100	68,500	412,600
				Article 17 (1) 1-d (6)	Article 17 (2) 1-k	
Change of brand name				35,600		35,600
				Article 17 (1) 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 (1) 2-d (1)	Article 17 (2) 2-g	
			Improved medical devices	3,109,900	664,500	3,774,400
				Article 17 (1) 2-d (2)	Article 17 (2) 2-g	
		Class Ⅲ	New medical devices	3,109,900	664,500	3,774,400
				Article 17 (1) 2-d (3)	Article 17 (2) 2-g	
			Improved medical devices	1,872,400	664,500	2,536,900
				Article 17 (1) 2-d (4)	Article 17 (2) 2-g	
		Class Ⅱ	New medical devices	3,109,900	664,500	3,774,400
				Article 17 (1) 2-d (3)	Article 17 (2) 2-g	
			Improved medical devices	1,872,400	664,500	2,536,900
				Article 17 (1) 2-d (4)	Article 17 (2) 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 (1) 2-d (7)	Article 17 (2) 2-i	
			Generic medical devices	884,200	37,100	921,300
				Article 17 (1) 2-d (8)	Article 17 (2) 2-i	
		Class Ⅲ	Improved medical devices	709,500	37,100	746,600
				Article 17 (1) 2-d (9)	Article 17 (2) 2-i	
			Generic medical devices	709,500	37,100	746,600
				Article 17 (1) 2-d (9)	Article 17 (2) 2-i	
		Class Ⅱ	Improved medical devices	709,500	37,100	746,600
				Article 17 (1) 2-d (9)	Article 17 (2) 2-i	
			Generic medical devices	709,500	37,100	746,600
				Article 17 (1) 2-d (9)	Article 17 (2) 2-i	
	Medical devices (with approval standards, without clinical data)	Class Ⅳ		217,600	37,100	254,700
				Article 17 (1) 2-d (5)	Article 17 (2) 2-h	
		Class Ⅲ		173,600	37,100	210,700
				Article 17 (1) 2-d (6)	Article 17 (2) 2-h	
		Class Ⅱ		173,600	37,100	210,700
				Article 17 (1) 2-d (6)	Article 17 (2) 2-h	

Classification					User fees		
					Review	Inspection	Total
QMS inspection of medical devices							
	Approval, partial change and manufacture for export	New medical devices		In Japan		739,800	739,800
						Article 17 (4) 1-b (1)	
				Outside Japan		933,500 + travel expenses	933,500 + travel expenses
						Article 17 (4) 1-b (2)	
		Biological medical devices, specially controlled medical devices (class Ⅳ), etc.		In Japan		666,100	666,100
						Article 17 (4) 1-a (1)	
				Outside Japan		844,400 + travel expenses	844,400 + travel expenses
						Article 17 (4) 1-a (2)	
		Sterilized medical devices		In Japan		201,300	201,300
						Article 17 (4) 1-c (1)	
				Outside Japan		229,800 + travel expenses	229,800 + travel expenses
						Article 17 (4) 1-c (2)	
		Other medical devices		In Japan		141,200	141,200
						Article 17 (4) 1-d (1)	
				Outside Japan		155,400 + travel expenses	155,400 + travel expenses
						Article 17 (4) 1-d (2)	
		Package, labeling, storage, external testing, etc.		In Japan		63,800	63,800
						Article 17 (4) 2-a, Article 17 (5) 1-a	
				Outside Japan		84,800 + travel expenses	84,800 + travel expenses
						Article 17 (4) 2-b, Article 17 (5) 1-b	
	Renewal of the above	Biological medical devices, specially controlled medical devices (class Ⅳ), etc.	Basic	In Japan		436,000	436,000
						Article 17 (4) 3-a (1)	
				Outside Japan		554,200 + travel expenses	554,200 + travel expenses
						Article 17 (4) 3-a (2)	
			Addition of products	In Japan		30,500	30,500
						Article 17 (4) 3-a (1)	
				Outside Japan		30,500	30,500
						Article 17 (4) 3-a (2)	
		Sterilized medical devices	Basic	In Japan		380,000	380,000
						Article 17 (4) 3-b (1)	
				Outside Japan		480,000 + travel expenses	480,000 + travel expenses
						Article 17 (4) 3-b (2)	
			Addition of products	In Japan		12,400	12,400
						Article 17 (4) 3-b (1)	
				Outside Japan		12,400	12,400
						Article 17 (4) 3-b (2)	
		Other medical devices	Basic	In Japan		336,500	336,500
						Article 17 (4) 3-c (1)	
				Outside Japan		409,400 + travel expenses	409,400 + travel expenses
						Article 17 (4) 3-c (2)	
			Addition of products	In Japan		9,600	9,600
						Article 17 (4) 3-c (1)	
				Outside Japan		9,600	9,600
						Article 17 (4) 3-c (2)	
		Package, labeling, storage, external testing, etc.	Basic	In Japan		258,500	258,500
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Outside Japan		338,100 + travel expenses	338,100 + travel expenses
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
			Addition of products	In Japan		6,700	6,700
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Outside Japan		6,700	6,700
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
GLP inspection of medical devices							
	GLP			In Japan		2,062,400	2,062,400
						Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
				Outside Japan		2,282,600 + travel expenses	2,282,600 + travel expenses
						Article 17 (3) 1-b, Article 17 (9) 2-a (2)	
GCP inspection of medical devices							
	GCP			In Japan		635,300	635,300
						Article 17 (3) 3-a	
				Outside Japan		918,400 + travel expenses	918,400 + travel expenses
						Article 17 (3) 3-b	
Re-examination of medical devices							
	New medical devices				502,600	624,600	1,127,200
					Article 17 (8) 2-a	Article 17 (9) 1-c	
	Medical devices other than new ones				51,600	624,600	676,200
					Article 17 (8) 2-b	Article 17 (9) 1-c	
	GPSP			In Japan		610,700	610,700
						Article 17 (9) 2-b (5)	
				Outside Japan		949,000 + travel expenses	949,000 + travel expenses
						Article 17 (9) 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	139,800 yen per consultation	Payment by the date of consultation application after arrangement of the consultation date
	Consultation on bioequivalence testing, etc. for drugs	556,000 yen per consultation	
	Safety consultation for drugs	1,782,800 yen per consultation	
	Quality consultation for drugs	1,478,300 yen per consultation	
	Consultation before start of phase I study for drugs (non-orphan drugs)	4,239,400 yen per consultation	
	Consultation before start of phase I study for drugs (orphan drugs)	3,186,100 yen per consultation	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	1,623,000 yen per consultation	
	Consultation before start of early phase II study for drugs (orphan drugs)	1,222,500 yen per consultation	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	3,028,400 yen per consultation	
	Consultation before start of late phase II study for drugs (orphan drugs)	2,274,200 yen per consultation	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	6,011,500 yen per consultation	
	Consultation after completion of phase II study for drugs (orphan drugs)	4,515,700 yen per consultation	
	Pre-application consultation for drugs (non-orphan drugs)	6,011,400 yen per consultation	
	Pre-application consultation for drugs (orphan drugs)	4,513,000 yen per consultation	
	Consultation on protocols of clinical trials for reevaluation and re-examination of drugs	3,320,600 yen per consultation	
	Consultation at completion of clinical trials for reevaluation and re-examination of drugs	3,319,400 yen per consultation	
	Additional consultation for drugs (non-orphan drugs)	2,675,600 yen per consultation	
	Additional consultation for drugs (orphan drugs)	2,010,400 yen per consultation	
	Consultation on GLP/GCP compliance for drugs (non-orphan drugs)	2,875,500 yen per consultation	
	Consultation on GLP/GCP compliance for drugs (orphan drugs)	2,157,200 yen per consultation	
	Prior assessment consultation for drugs (quality)	3,049,300 yen per consultation	
	Prior assessment consultation for drugs (non-clinical: toxicity)	2,061,100 yen per consultation	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	2,061,100 yen per consultation	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	2,061,100 yen per consultation	
	Prior assessment consultation for drugs (phase I study)	3,484,700 yen per consultation	
	Prior assessment consultation for drugs (phase II study)	4,497,400 yen per consultation	
	Prior assessment consultation for drugs (phase II/III study)	6,985,700 yen per consultation	
	Consultation on drug product eligibility for priority review	823,300 yen per consultation	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	168,700 yen per consultation	
	Consultation on pharmacogenomics/biomarkers	3,028,400 yen per consultation	
	Consultation on R&D strategy for drugs	1,498,800 yen per consultation	
	Consultation on R&D strategy for drugs (Universities/research institutes and venture companies meeting requirements specified separately*)	149,800 yen per consultation	
	Consultations on bioequivalence of generic drugs	997,500 yen per consultation	
	Quality consultation for generic drugs	491,800 yen per consultation	
	Pre-application consultation for switch OTC drugs	1,501,100 yen per consultation	
	Consultation on key points of clinical trial protocols for OTC drugs	502,500 yen per consultation	
	Consultation on appropriateness of development of new OTC drugs	199,100 yen per consultation	
Devices and *in vitro* diagnostics	Pre-development consultation for medical devices	135,200 yen per consultation	
	Safety consultation for medical devices (excluding biological medical devices)	822,100 yen per consultation	
	Safety consultation for biological medical devices	910,100 yen per consultation	
	Quality consultation for medical devices (excluding biological medical devices)	775,400 yen per consultation	
	Quality consultation for biological medical devices	921,400 yen per consultation	
	Performance testing consultation for medical devices	845,900 yen per consultation	
	Clinical evaluation consultation for medical devices	1,026,600 yen per consultation	
	Exploratory clinical trial consultation for medical devices	1,105,300 yen per consultation	
	Clinical trial consultation for medical devices	2,413,000 yen per consultation	
	Pre-application consultation for medical devices	2,413,000 yen per consultation	
	Application procedure consultation for medical devices	135,200 yen per consultation	
	Additional consultation for medical devices	1,130,100 yen per consultation	
	Consultation on GLP/GCP compliance for medical devices	772,900 yen per consultation	
	Prior assessment consultation for medical devices (quality)	2,982,300 yen per consultation	
	Prior assessment consultation for medical devices (non-clinical)	2,982,300 yen per consultation	
	Prior assessment consultation for medical devices (clinical)	4,490,800 yen per consultation	
	Consultation on R&D strategy for medical devices	849,700 yen per consultation	
	Consultation on R&D strategy for medical devices (Universities/research institutes and venture companies meeting requirements specified separately*)	84,900 yen per consultation	
	Pre-development consultation for *in vitro* diagnostics	139,900 yen per consultation	
	Quality consultation for *in vitro* diagnostics	345,500 yen per consultation	
	Consultation on conformity with standards for *in vitro* diagnostics	442,800 yen per consultation	
	Clinical evaluation consultation for *in vitro* diagnostics	675,400 yen per consultation	
	Clinical performance study consultation for *in vitro* diagnostics	1,594,700 yen per consultation	
	Pre-application consultation for *in vitro* diagnostics	1,594,700 yen per consultation	
	Application procedure consultation for *in vitro* diagnostics	135,200 yen per consultation	
	Additional consultation for *in vitro* diagnostics	927,500 yen per consultation	
	Prior assessment consultation for *in vitro* diagnostics (quality)	2,982,300 yen per consultation	
	Prior assessment consultation for *in vitro* diagnostics (non-clinical)	2,982,300 yen per consultation	
	Prior assessment consultation for *in vitro* diagnostics (clinical)	4,490,800 yen per consultation	
	Consultation on preparation of documents for gene therapy products	223,500 yen per consultation	
Simple consultations	Generic drugs	21,000 yen per consultation	
	OTC drugs	21,000 yen per consultation	
	Quasi-drugs (including pesticides and rodenticides)	21,000 yen per consultation	
	Medical devices or *in vitro* diagnostics	34,300 yen per consultation	
	Preparation of new drug applications	21,000 yen per consultation	
	GMP/QMS inspection	24,700 yen per consultation	

		User fees	Timing of payment
Assessment for designation of priority consultation products			
Assessment for designation of drugs for priority consultation		818,800 yen per application	Request to PMDA after advanced payment
Assessment for designation of medical devices or *in vitro* diagnostics for priority consultation		818,800 yen per application	
GLP inspection of test facilities			
All test items (for drugs and medical devices)		3,023,800 yen per facility	Request to PMDA after advanced payment
All test items (for drugs or medical devices)	In Japan	2,062,400 yen per facility	
	Outside Japan	2,282,600 yen + travel expenses per facility	
Limited test items		995,200 yen per facility	
Additional compliance accreditation		932,600 yen per facility	
Confirmation of certification on drugs, etc.			
GMP certification on investigational products (with on-site inspection)		739,800 yen per product of one facility	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)		15,100 yen per product of one facility	
Certification of drug products		15,100 yen per product	
Other certifications (including GMP/QMS certifications)		8,400 yen per matter of one product	
Use of document storage rooms			
		3,000 yen per day per room	Payment upon invoice sent from PMDA after the end of the use period

* To be eligible, universities/research institutes or venture companies should meet all of the following requirements in principle:
For universities/research institutes
・Having not received 90 million yen or more (in the case of drugs) or 50 million yen or more (in the case of medical devices) from the government, to proceed with the research on the seed-stage resource
・Having not received research expenses from a pharmaceutical company/medical device company under a joint research agreement, etc., toward practical application of the seed-stage resource
For venture companies
・Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less)
・Any other corporation does not hold 1/2 or more of the total number of shares or investments
・Two or more other corporations do not hold 2/3 or more of the total number of shares or investments
・For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue