THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2010

TABLE OF CONTENTS

Page

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.

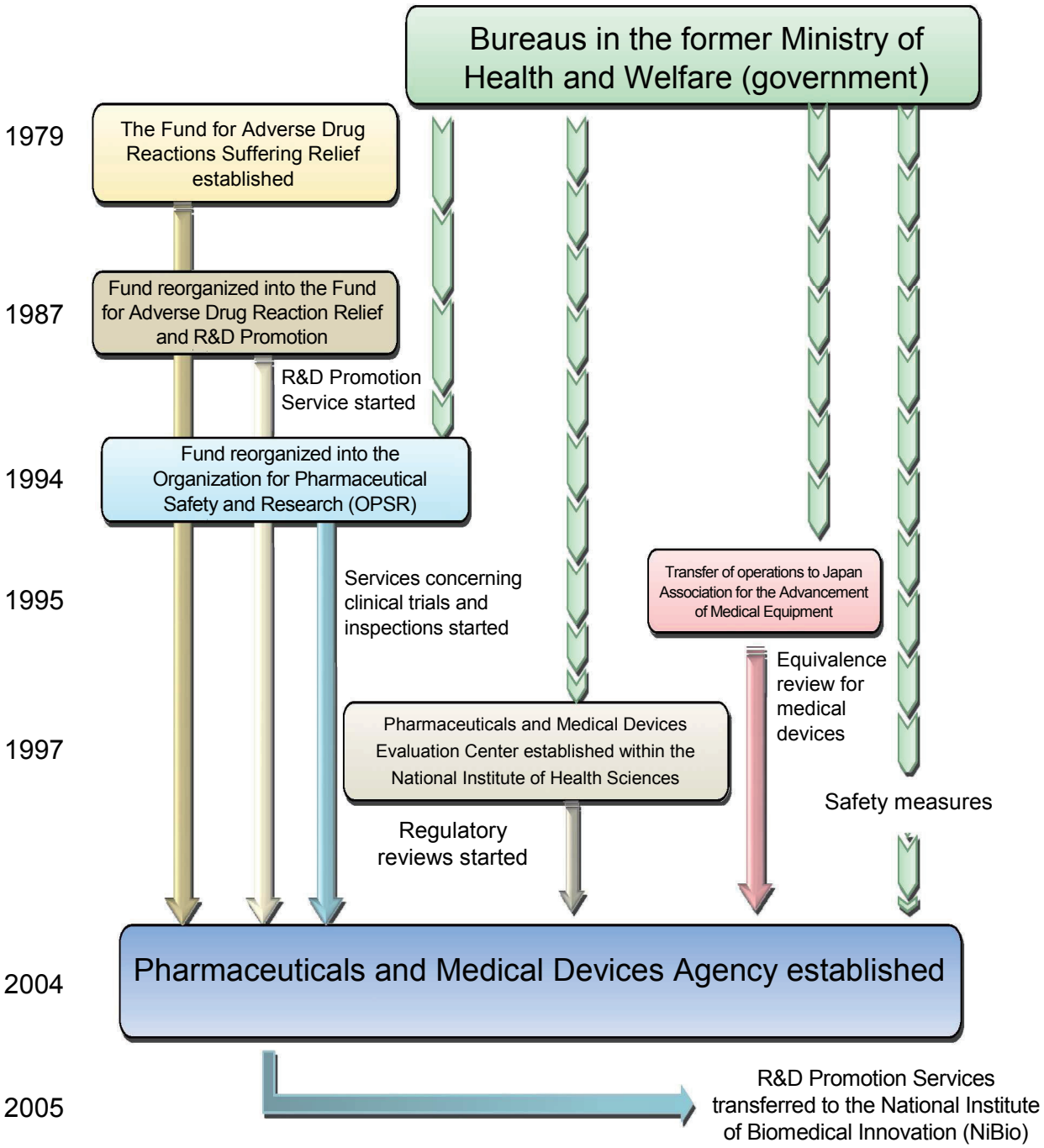
  In the midst of these situations, the Cabinet adopted the Special Service Agency Restructuring Plan in December 2001, in which it was decided that the OPSR should be dissolved and that the Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated 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).

- The objective of PMDA is to contribute to improvement in public health by providing prompt relief services for sufferers of adverse health effects resulting from infections acquired through biological products in addition to adverse drug reactions (Relief for Adverse Health Effects); providing guidance and reviews regarding the quality, efficacy, and safety of drugs and medical devices through a system that is consistent from pre-clinical research to approval (Reviews); and collecting, analyzing, and providing information on post-marketing safety (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).

- In April 2004, PMDA started to provide 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).

- In January 2008, PMDA also 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 (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 reliability standards for application documents (GLP/GCP/GPSP Inspections).

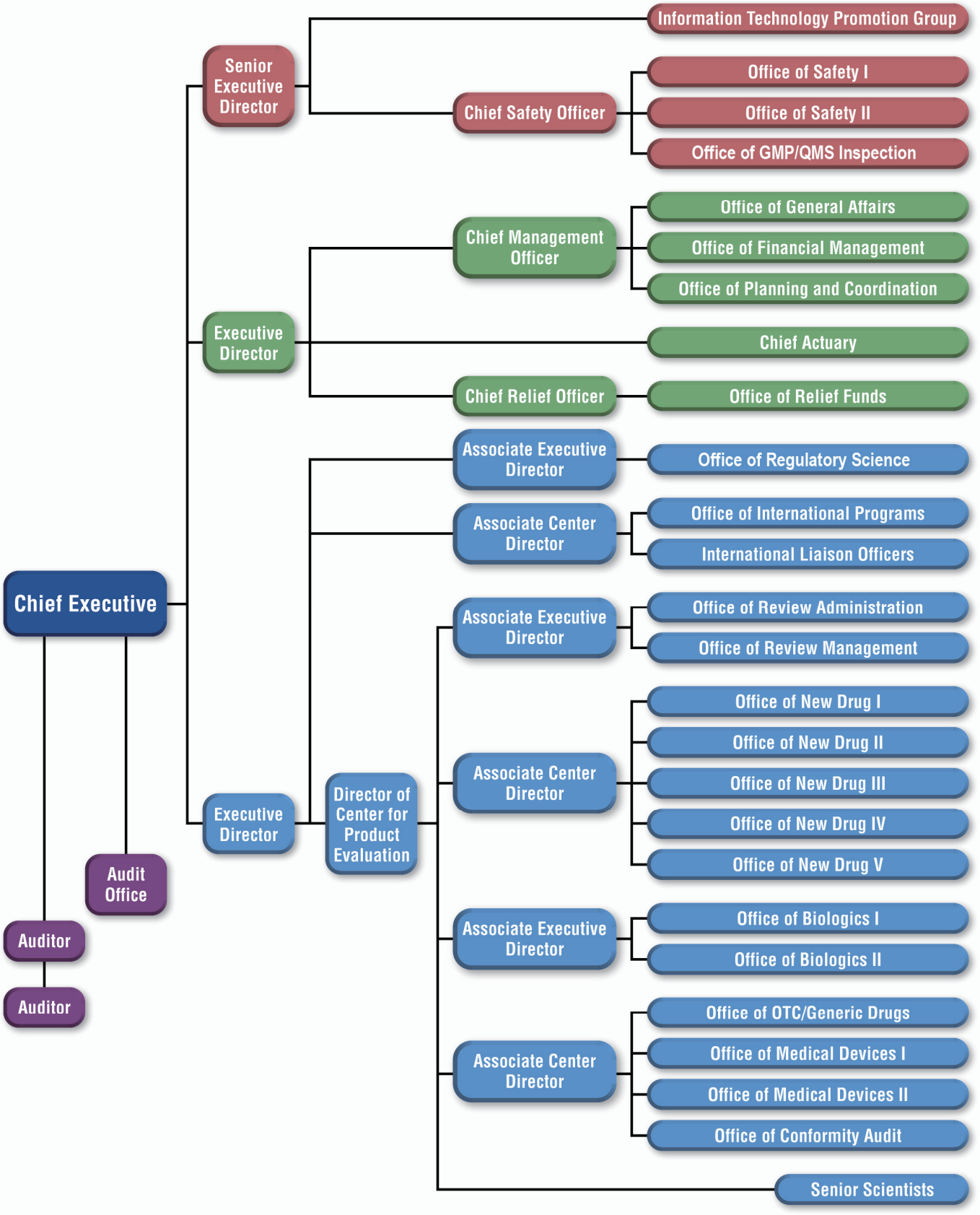
- In addition, on-site and document-based inspections are conducted to determine whether manufacturing facilities and manufacturing control methods for new drugs and medical devices, etc., comply with the requirements of the Ministerial Ordinance on Good Manufacturing Practices/Quality Management System (GMP/QMS), whereby products of appropriate quality can be manufactured (GMP/QMS Inspections).

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).
(v) Research related to developing various standards, such as the Japanese Pharmacopoeia (JP) that is stipulated in the Pharmaceutical Affairs Act (Standards Development-related Research)

Structure of PMDA (FY 2010)



II. OPERATING PERFORMANCE FOR FY 2010

PART 1 Development of Fiscal Year 2010 Plan

1.1. Development and Implementation of Fiscal Year 2010 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 for each fiscal year, submit these plans to the Minister, and announce these plans to the public.

  PMDA developed a plan for FY 2010, submitted it to the Minister of Health, Labour and Welfare at the end of 2009, and implemented its operations in accordance with this plan.

  The FY 2010 plan was developed based on the Second Mid-term Targets and Mid-term Plan as well as the operating performance for FY 2009 evaluated by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW) and opinions from the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications (MIC).

1.2. Results of the Evaluation on Operating Performance for FY 2009

- 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)

  On August 27, 2010, PMDA received the results of evaluation on its performance for FY 2009 from the Evaluation Committee for Incorporated Administrative Agencies of MHLW, which is responsible for conducting evaluations on the Agency's performance. The overall evaluation results consisted of 18 As out of 18 evaluation items.

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

  The "Results of the Evaluation on Operating Performance for FY 2009" was released on the website, and was also reported at the Advisory Council Meeting held on October 21, 2010.

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 FY2008 performance	Results of evaluation FY2009 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	A
		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 (Previous version: Conduct of cross-functional collaboration and surveys on adverse health effects)	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 (Previous version: Conduct of relief services for SMON patients and patients infected with HIV from blood preparations and payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C)	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)	B	A
		11	Expeditious operation and improvement of the system (medical devices)	A	A
		12	Expeditious operation and improvement of the system (inspections)	–	A
			(Previous version: Expeditious operation and improvement of the system (clinical trial consultations))	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 (Previous version: Improvement in quality of review and related services/post-marketing safety measures)	A	A
			(Previous version: Promotion of appropriate clinical trials)	A	–
			(Previous version: Promotion of transparency of review and related services/ post-marketing safety measures)	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 (Previous version: Collection of ADR information)	A	A
		15	Provision of safety information to companies/healthcare professionals and follow-up (Previous version: Provision of safety information to companies and healthcare professionals)	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				
	S	Significantly exceeding the level prescribed in the midterm-plan	0	0
	A	Exceeding the level prescribed in the midterm-plan	19	18
	B	Somewhat exceeding the level prescribed in the midterm-plan	1	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 22, 2010, highlighting the following issues concerning the evaluation results for PMDA:

  (Opinion from the Commission of MIC on the results of the evaluation for FY 2009)

- Regarding PMDA's reviews of drug applications, targets have been set out in the Mid-term Plan, where the total review time including the applicant's time is required to be sequentially shortened starting in FY 2009 in order to resolve the drug lag by FY 2011 and reviewers should be increased substantially toward the target.

  Taking into account these situations, the Commission pointed out last fiscal year that, toward the goal of resolving the drug lag by 2.5 years by FY 2011, in the case of non-achievement of targets for each fiscal year, PMDA should analyze the factors leading to the non-achievement and clearly present improvement measures, and then PMDA's efforts should be strictly evaluated considering the analysis results.

  However, the Committee of MHLW commented in its evaluation results that "the target could not be achieved only for the applicant's time for priority review products" and that "shortening of the applicant's time remained to be addressed," without showing results of factor analysis on non-achievement of the target review times for new drugs (priority review products and standard products) or improvement measures, which did not suggest that the PMDA's efforts were strictly evaluated after sufficient analysis.

  Therefore, in future, in the case of non-achievement of targets, PMDA's efforts should be strictly evaluated based on the results of factor analysis conducted and improvement measures proposed by PMDA, in order to increase the effectiveness of such efforts toward the goal of resolving the drug lag by FY 2011.

- Regarding PMDA's administrative processing time from the filing of a claim for relief benefits to the judgment on approval/rejection, the Mid-term Plan stipulates that PMDA should exercise judgment within 6 months by FY 2013 for more than 60% of the total number of judged cases (regardless of approval/rejection) for each fiscal year.

  In the results of evaluation by the Committee of MHLW, this item was assessed as A (Exceeding the level prescribed in the Mid-term Plan) based on the fact that the rate of claims processed within 8 months was 74.0% against the FY 2009 Annual Plan's target of more than 70% and the number of claims processed within 6 months increased from 355 in FY 2008 to 360 in FY 2009 against the Annual Plan's target of increasing the number compared to the previous fiscal year.

  However, there is a question as to the assessment for this item as exceeding the level prescribed in the Mid-term Plan, even after considering that the final target should be achieved by FY 2013, based on the following facts: that there is still a large discrepancy in comparison to the Mid-term Plan because the ratio of cases processed within 6 months (360) to the total number of judged cases (990) was 36% in FY 2009 against the Mid-term Plan's target of 60%, and that the ratio decreased from 38% to 36% despite the increase of 5 cases compared to FY 2008 (355 cases).

  Therefore, in future, PMDA's efforts should be strictly evaluated and a rationale for the ratings should be detailed after fully examining PMDA's performance against the Mid-term Plan.

1.3. Budget Screening by the Government Revitalization Unit

- The MHLW's internal budget screening and the Government Revitalization Unit (GRU)'s budget screening were conducted in April 2010, GRU's budget screening (repeated screening) was conducted in November 2010, and GRU's regulatory screening was conducted in March 2011.

○ Results of evaluation by the 4th MHLW's internal budget screening (April 22, 2010)

1-(i) Administrative work/projects (reviews and related services: drugs)

- Reform proposal not sufficient (The agency may continue the projects but further consideration is required, e.g., reexamination of implementation method, reduction in subsidy.) 4 evaluators
- Reform proposal appropriate 2 evaluators

1-(ii) Administrative work/projects (reviews and related services: medical devices)

- Reform proposal not sufficient (The agency may continue the projects but further consideration is required, e.g., re-examination of implementation method, reduction in subsidy.) 4 evaluators
- Reform proposal appropriate 2 evaluators

1-(iii) Administrative work/projects (safety measures)

- Reform proposal not sufficient (The agency may continue the projects but further consideration is required, e.g., re-examination of implementation method, reduction in subsidy.) 2 evaluators
- Reform proposal appropriate 4 evaluators

1-(iv) Administrative work/projects (relief services for adverse health effects)

- Reform proposal not sufficient (The projects should be transferred to the central government for implementation after increasing their efficiency.) 1 evaluator
- Reform proposal appropriate 5 evaluators

2 Organization/management system

- Reform proposal not sufficient (Further consideration is required, e.g., in terms of human resources, administrative expenses, surplus assets, organizations.) 4 evaluators
- Reform proposal appropriate 2 evaluators

○ Results of evaluation by the second round of GRU's budget screening (April 27, 2010)

(1) Reviews and related services (drugs/medical devices)

- PMDA should implement the services with an expanded scale.
- PMDA's governance should be drastically reformed/reinforced including the issue of government employee secondment system.

The services should be:

• implemented also by other agencies (including FDA, etc.).	1 evaluator (with an expanded scale: 1 evaluator)
• implemented by the central government, etc.	2 evaluators (with an expanded scale: 2 evaluators)
• implemented by PMDA	13 evaluators (with the current scale: 5 evaluators, with an expanded scale: 8 evaluators)

If reform is needed, it should be:

• increase of self-income	1 evaluator
• reinforcement of governance	13 evaluators
• others	1 evaluator

(2) Safety measures

- PMDA should implement the services with an expanded scale.
- PMDA's governance should be drastically reformed/reinforced.

The services should be:

• implemented by other agencies	2 evaluators (with the current scale: 1 evaluator, with an expanded scale: 1 evaluator)
• implemented by the central government, etc.	2 evaluators (with the current scale: 2 evaluators)
• implemented by PMDA	12 evaluators (with the current scale: 5 evaluators, with an expanded scale: 7 evaluators)

If reform is needed, it should be:

• reinforcement of governance	11 evaluators

○ Results of evaluation by the 3rd round of GRU's budget screening (repeated screening) (November 17, 2010)

(1) Reviews and related services (2) Safety measures

- A part of the results of the 2nd round of budget screening (“PMDA should implement the services with an expanded scale, while implementing drastic reform/reinforcement of governance including the issue of government employee secondment system”) have not been reflected into practice.
  - (i) Not reflected 6 evaluators
  - (ii) Not reflected sufficiently 8 evaluators
  - (iii) Reflected 0 evaluator
- Supplement to the results of the 2nd round of budget screening (focus on the core services, efficient securing of human resources), etc.
  - (i) PMDA should steadily implement the results of evaluation by the 2nd round of budget screening

    2 evaluators
  - (ii) As the supplement to the results of the 2nd round of budget screening (12 evaluators), PMDA should:
    - a. focus on its core services (by reducing academic conference travels, consultations, etc.) 10 evaluators
    - b. reduce general administrative expenses, etc. 5 evaluators
    - c. efficiently secure human resources 12 evaluators
    - d. others 3 evaluators
  - (iii) PMDA should conduct its services in accordance with budgetary request (continue the current practices)

    0 evaluator

○ Results of evaluation by GRU's regulatory screening (March 6, 2011)

A-2 Review procedures of drug and medical device applications for approval

Direction of reform: Ensure further clarification of and increased transparency of review procedures.

Points to consider: Not only review procedures but also the overall process from development to approval of drugs and medical devices should be examined.

- Based on the results of budget screening, the Cabinet adopted the "Basic Policy for Review of Administrative Work/Projects of Incorporated Administrative Agencies" (hereinafter the "Basic Policy") on December 7, 2010. The Basic Policy stipulates reexamination of relief services for adverse health effects/product application reviews and related services/safety measures, reexamination of personnel management and reexamination of organization system for PMDA, as part of the measures that should be taken for each Incorporated Administrative Agency.

- Based on the results of budget screening and the Basic Policy, etc., PMDA plans to promote efforts toward reform of administrative work/projects.

  PMDA established the Advisory Committee for Human Resources/Organization Management of the Pharmaceuticals and Medical Devices Agency in January 2011, and prepared and informed employees of the PMDA Career Paths in March.

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 2010, each office and division formulated their operating plans based on the duties and responsibilities. PMDA has operated through management of the targets set in the operating plans.

- To comprehend the progress of operating plans of each office, from November to December 2010, PMDA conducted interviews with its directors about the actual operating performance up to the end of September 2010 in light of the operating plans.

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 2009, PMDA has been establishing opportunities for the Chief Executive to directly comprehend the progress of operations 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.

- At the Committee on Investment in Information Systems, under the Headquarters of Information Systems Management (headed by the Chief Executive) which was established with the aim of further reinforcing the structure of PMDA's information systems management, PMDA appraised the appropriateness of the investment in the development of new systems and the modification of existing systems from the perspectives of cost-effectiveness and technical difficulties and selected systematic and efficient investment options (two meetings were held during FY 2010).

- 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 2010), during which reports were made on the monthly filing status and monthly cash flow analysis regarding review-related user fees by division, and the declared amount of contributions.

- In the MHLW's and GRU's budget screening, PMDA was instructed to implement the services "with an expanded scale" and the need for further reinforcement of its governance as an agency was pointed out.

- Based on these findings, PMDA established the Advisory Committee for Human Resources/Organization Management of the Pharmaceuticals and Medical Devices Agency that investigates, analyzes and advises on important matters related to human resources/organization management in January 2011, and prepared and informed employees of the PMDA Career Paths in March.

- Since FY 2009, lunch meetings have been held between the Chief Executive and employees of each office twice or three times monthly to promote exchange of views regarding issues that each office face and employees' requests.

- Regarding opinion exchange sessions with the pharmaceutical industry, PMDA convened two sessions for new drugs (July and February) and two sessions for drug safety (July and March).

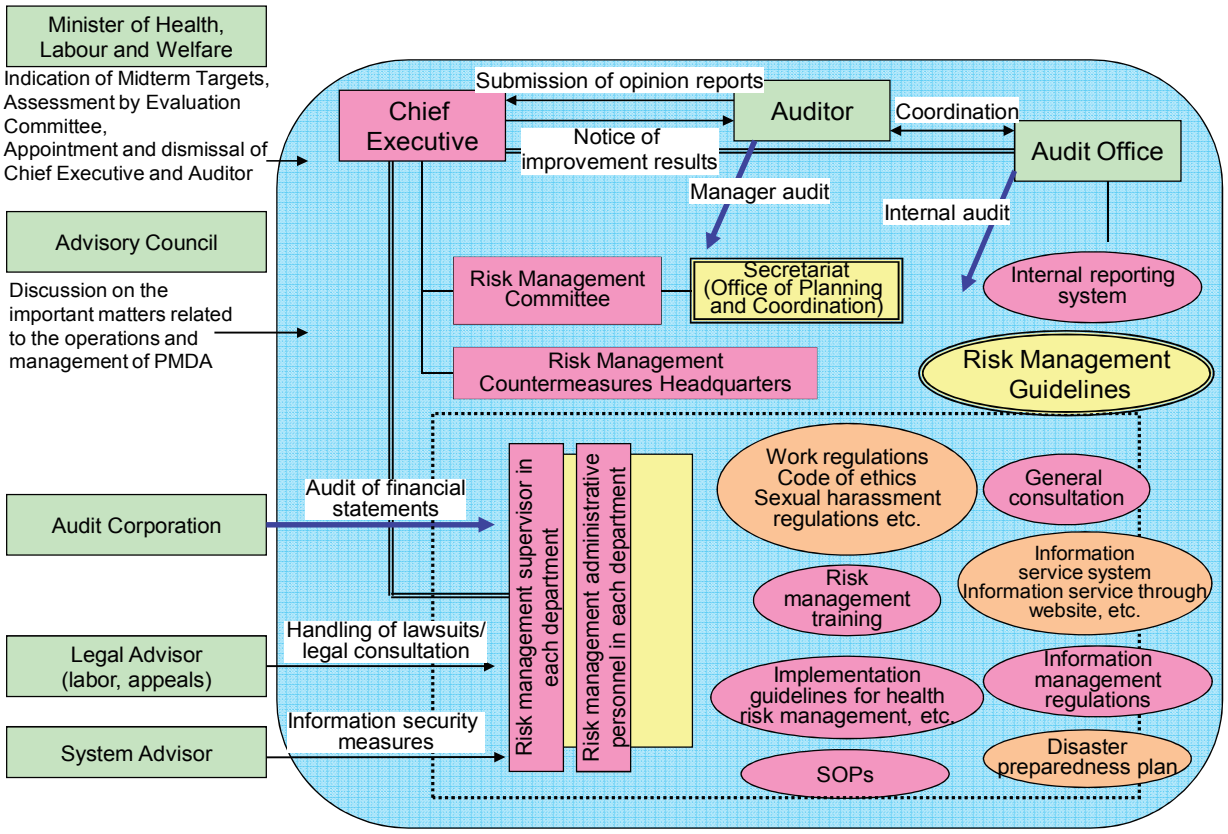
  Further, regarding medical devices and *in vitro* diagnostics, PMDA established a working-level joint task force related to medical devices and *in vitro* diagnostics in February 2007 and convened 3 meetings (May, October and March).

- The Risk Management Committee held 12 meetings in FY 2010 to promote discussion on PMDA's risks among directors, and examined the appropriateness of document and information management by reviewing the operational flow.

  PMDA has also continued the efforts to familiarize the executives and employees with the risk management manual. The Audit Office, which directly reports to the Chief Executive, has continued to conduct internal auditing and management of internal reporting systems.

- In order to respond to disaster risks resulting from fires and earthquakes, PMDA duly informed all executives and employees of the disaster preparedness plan.

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 address as part of its tasks
   - Risks relating to PMDA's operations which might cause or expand serious adverse health effects due to drugs, medical devices, etc. (drug, medical device, quasi-drug, and cosmetic products, as well as agents and devices subject to clinical trials)

- From the viewpoint of systematically promoting PR activities as a whole during the effective period for 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 and is proactively providing information in line with the strategic plan.

- From the viewpoint of promoting international activities as a whole during the effective period of the Second Mid-term Targets in a planned and systematic manner in cooperation with the Ministry of Health, Labour and Welfare, PMDA developed the PMDA International Strategic Plan (February 6, 2009) as a basic policy for its overall international activities and decided to improve services to patients and their families not only in Japan but also in the world and to establish its international positioning by proactively promoting international activities in line with the strategic plan.

- In October 2010, in order to strengthen the system for promoting regulatory science, PMDA newly established the Regulatory Science Research Division in the Office of Regulatory Science as well as dissolved the Standards Division in the Office of GMP/QMS Inspection (formerly Office of Compliance and Standards) and newly established the Division of Standards for Drugs and Division of Standards for Medical Devices in the Office of Review Management.

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 (currently chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University), which are open to the public, consisting 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 (currently chaired by Atsushi Ichikawa, Dean of School of Pharmacy and Pharmaceutical Sciences, Mukogawa Women's University) were also formed to discuss specialized issues relating to operations. The dates of the meetings and specific agendas for FY 2010 are as follows.
  Note: Until the end of June 2010, the Advisory Council and the Committee on Review and Safety Operations were chaired by Masaaki Hirobe, Professor Emeritus, University of Tokyo.

Advisory Council—FY 2010

Agenda for the 1st Meeting (June 23, 2010)
(1) Annual Report for FY 2009
(2) Financial Report for FY 2009
(3) Report on the employment status of personnel from the private sector
(4) Cash contributions, etc., received by commissioned external experts in relation to Expert Discussions
(5) Others

Agenda for the 2nd Meeting (October 21, 2010)
(1) Selection of the Chairperson and the Acting Chairperson
(2) Results of the evaluations of operating performance for FY 2009
(3) Organizational restructuring of PMDA
(4) Employment status of personnel from the private sector
(5) Cash contributions, etc., received by commissioned external experts in relation to Expert Discussions
(6) Others

Agenda for the 3rd Meeting (March 22, 2011)
(1) Fiscal year 2011 plan (draft)
(2) Budget for FY 2011 (draft)
(3) Report on the employment status of personnel from the private sector and revision of the administrative rules on work restrictions for such employees (draft)
(4) Cash contributions and contract money, etc., received by commissioned external experts in relation to Expert Discussions

(5) Restrictions on employment in the private sector for PMDA employees
(6) Others

Committee on Relief Services—FY 2010
Agenda for the 1st Meeting (June 21, 2010)
(1) Annual Report for FY 2009
(2) Fiscal year 2010 plan
(3) Others

Agenda for the 2nd Meeting (December 24, 2010)
(1) Selection of the Chairperson and the Acting Chairperson
(2) Results of the evaluations of operating performance for FY 2009
(3) Achievements for the first half of FY 2010, etc.
(4) Results of the survey on awareness of the Relief System for Adverse Drug Reaction in FY 2010 and future public relations
(5) Implementation of the investigative research for improvements in QOL of patients with hepatitis C through treatment of congenital diseases
(6) Others

Committee on Review and Safety Operations—FY 2010
Agenda for the 1st Meeting (June 8, 2010)
(1) Annual Report for FY 2009
(2) Fiscal year 2010 plan
(3) Report on the employment status of personnel from the private sector
(4) Cash contributions, etc., received by commissioned external experts in relation to Expert Discussions
(5) Others

Agenda for the 2nd Meeting (December 22, 2010)
(1) Selection of the Chairperson and the Acting Chairperson
(2) Results of the evaluations of operating performance for FY 2009
(3) Achievements by the end of October in FY 2010 and issues to be addressed hereafter
(4) Organizational restructuring of PMDA
(5) Budget for FY 2011, etc.
(6) Employment status of personnel from the private sector
(7) Cash contributions, etc., received by commissioned external experts in relation to Expert Discussions
(8) Others

- In order to ensure the transparency of the Advisory Council, Committee on Relief Services, and Committee on Review and Safety Operations, meetings held by these committees are open to the public and the minutes, materials, etc. relating to the meetings are 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.

  (As of March 31, 2011, the number of commissioned experts is 1,024 including external experts commissioned for issues relating to safety measures)

  Furthermore, PMDA invited 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.

  (91 commissioned external experts are present as of March 31, 2011)

  The names of the commissioned external experts on review and safety operations and relief services are listed on the PMDA website.

- Based on the need to secure fairness 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 judgment 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 2010, meetings of the Committee on Information Systems Management and the Committee on Investment in Information Systems, etc. were held. In addition, discussions were made regarding the operational status of each information system, upgrades for the shared LAN system that serves as the common infrastructure system, and improvements in the security of the e-mail system, for which effective measures were taken.

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

- The notifications, etc. issued by the MHLW and PMDA that are relevant to the Agency's operations or that require broad dissemination of information 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. Additionally, PMDA publicized the revised version of the plan in June 2009 and carries out tasks for building appropriate systems based on this Plan.

  In FY 2010, based on this Plan, PMDA reviewed its internal review-related systems and defined the requirements for building the next systems.

  In addition, PMDA decided to optimize the systems related to safety measures and relief services and started creation of requirements definitions as well as research and reviews to reinforce the information management and IT control of PMDA as a whole.

2.2. Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general administrative expense

- By making continuous efforts to improve operations and increase management efficiency, PMDA was expected to balance the FY 2010 budget for general administrative expenses (excluding expenses for office relocation and retirement allowance), which was reduced by about 6% from the FY 2008 budget, plus the following additional general administrative expenses (the expenses incurred starting in FY 2009 that were reduced by about 3% and those incurred starting in FY 2010):

  1) General 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 administrative expenses incurred starting in FY 2009 and FY 2010 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 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 2010, 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 last 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 administrative expenses by 20.6% of its budget size which was subject to more efficient budget control, even excluding the fact that the target number of new employees was not achieved.

2.2.(2) Cost control of operating expenses

- By increasing operational efficiency through promotion of digitization, PMDA was expected to balance the FY 2010 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.), which was reduced by about 2% from the FY 2008 budget, plus the following additional operating expenses (the expenses incurred starting in FY 2009 that were reduced by about 1% and those incurred starting in FY 2010):

  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 and FY 2010 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 2010, PMDA promoted general competitive bidding in relation to operating expenses, as with the case of general 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 6.3% compared with the budget size which was subject to more efficient budget control, even excluding unused budget amounts allocated to expenses for new employees of which target number was not achieved and overseas GMP on-site inspections because the number of inspections was less 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 of that, of all the contracts, the ratio of competitive contract schemes including planning competition and invitation to bids increased by 7.0% in terms of the number of bids and 24.8% in terms of the monetary amount compared to the previous fiscal year.

	FY 2009	FY 2010	Change
General competitive bidding (including planning competition and invitation to bids)	132 bids (58.9%) 1,796 million yen (40.6%)	116 bids (65.9%) 3,310 million yen (65.4%)	-16 bids (7.0%) 1,514 million yen (24.8%)
Non-competitive optional contracts	92 bids (41.1%) 2,630 million yen (59.4%)	60 bids (34.1%) 1,753 million yen (34.6%)	-32 bids (-7.0%) -877 million yen (-24.8%)
Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	67 bids (29.9%) 725 million yen (16.4%)	45 bids (25.6%) 296 million yen (5.8%)	-22 bids (-4.3%) -429 million yen (-10.6%)
Total	224 bids 4,426 million yen	176 bids 5,063 million yen	-48 bids 637 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 inside the Agency including external knowledgeable experts. In the Committee meeting, PMDA underwent a pre-inspection of procurement cases, etc. for which conclusion of a contract is planned in FY 2010, regarding the appropriateness of contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 4 meetings in FY 2010 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 contributions to the adverse drug reaction fund, infections fund, and post-marketing safety measures fund in an integrated fashion. Consequently, 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 four major banks and the Postal Savings Operation Centers (post offices) 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 2010, the collection rates achieved for ADR contributions, infection contributions, and safety measure contributions were 99.6%, 100%, and 99.2%, respectively.

FY 2010 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	716	716	100%	3,984
	Pharmacies	7,111	7,082	99.6%	7
	Total	7,827	7,798	99.6%	3,991
Infection contributions	MAHs	93	93	100%	693
Post-marketing safety measures contributions	MAHs of drugs	627	627	100%	971
	MAHs of medical devices	2,150	2,096	97.5%	212
	MAHs of drugs & medical devices	199	199	100%	1,348
	Pharmacies	7,111	7,082	99.6%	7
	Total	10,087	10,004	99.2%	2,537

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,

  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

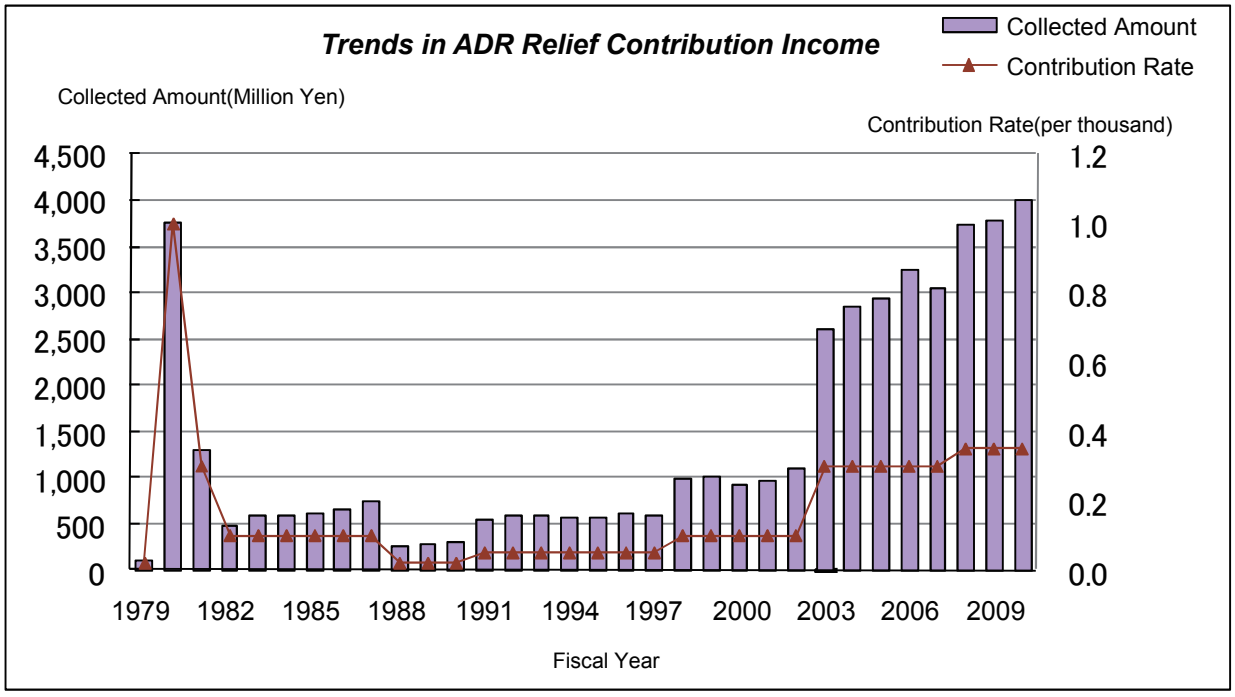
a. Adverse drug reaction fund

- 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 2010, the contribution rate applied to such marketing authorization holders was set at 0.35/1000 and the collected amount was 3,991 million yen.

(Million yen)

Fiscal year	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
MAHs of approved drugs [Number of MAHs]	3,240 [778]	3,049 [762]	3,722 [752]	3,783 [742]	3,984 [716]
MAHs of pharmacy-compounded drugs [Number of MAHs]	9 [8,968]	8 [8,309]	8 [8,015]	8 [7,598]	7 [7,082]
Total amount	3,249	3,057	3,730	3,790	3,991
Contribution rate	0.3/1000	0.3/1000	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

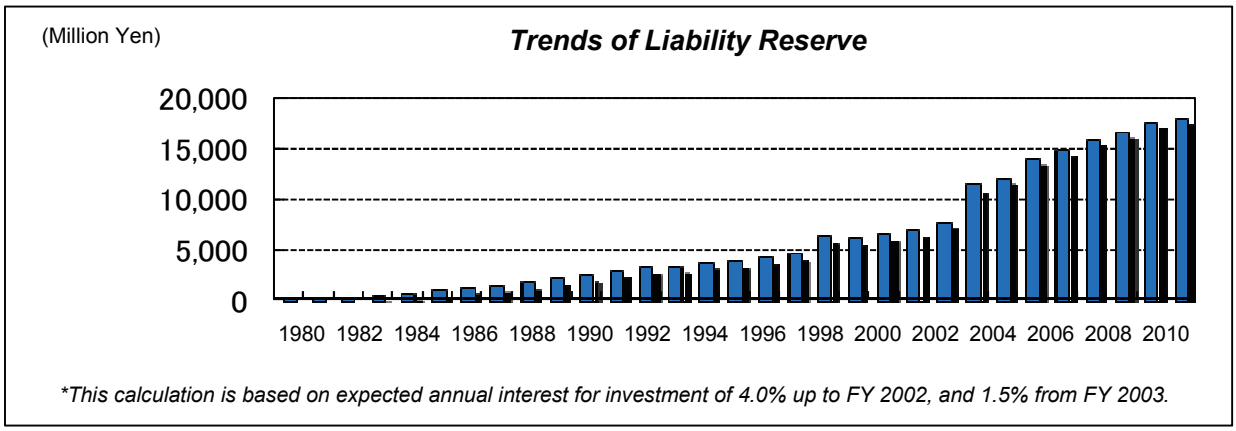
- To fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from marketing authorization holders of approved biological products. In FY 2010, the contribution rate applied to such marketing authorization holders was set at 1/1000 and the collected amount was 693 million yen.

(Million yen)

Fiscal year	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
MAHs of approved biological products [Number of MAHs]	556 [101]	574 [98]	620 [96]	631 [97]	693 [93]
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 2010 was 18,065 million yen.



(ii) Collected contributions for post-marketing safety measures

- To fund services for improvements in 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 2010, 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 2,537 million yen.

(Million yen)

Fiscal year	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
MAHs of drugs/medical devices [Number of MAHs]	1,211 [3,180]	1,219 [3,094]	1,284 [3,053]	2,354 [3,019]	2,530 [2,922]
MAHs of pharmacy-compounded drugs [Number of MAHs]	9 [8,960]	8 [8,297]	8 [8,013]	8 [7,594]	7 [7,082]
Total amount	1,220	1,227	1,292	2,362	2,537
Contribution rate	0.11/1000	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)

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

- The personnel expenses for FY 2010 was reduced by approximately 8.1% (in comparison with personnel expense per person for FY 2005) by taking into account the results of the personnel evaluation and appropriately reflecting the results in pay raises, etc.

- PMDA compared the remuneration system for its staff for FY 2009 with that of national government employees in order to win the understanding of the public on its remuneration standards, and released the results on its website.

Fiscal year	FY 2005 (Base year)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
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
Rate of personnel expense reduction (unit personnel expense per person)		- 2.7 %	- 2.8 %	- 6.0 %	- 8.5 %	- 11.3%
Corrected rate* of personnel expense reduction (unit personnel expense per person)		- 2.7 %	- 3.3 %	- 6.6 %	- 7.0 %	- 8.1%

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

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

- PMDA steadily carried out the measures stipulated in the "Reinforcement of the efforts to reduce unnecessary expenditures (December 22, 2009)" developed in FY 2009.

- At the end of FY 2009, PMDA developed a document titled "Cost-cutting targets toward reduction of unnecessary expenditures in PMDA" which specifies reduction targets, ensured that all staff members were thoroughly informed of the targets to promote autonomous and proactive efforts and, consequently, was able to achieve some results. The major results were a 12% reduction in the duration of overtime work, a 78% reduction in the number of taxi tickets used (a 76% reduction in terms of the monetary amount) and a 9% reduction in utility cost.

- Furthermore, on the basis of various efforts in FY2010, PMDA released the "Reinforcement of the efforts to reduce unnecessary expenditures" as partially revised, and also developed and released the "Cost-cutting targets for FY 2011."

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. PMDA also receives comments and opinions via its website as well as telephone/facsimile so that it can collect the public's opinions and requests easily.

- 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 2,192 inquiries that PMDA received in FY 2010, 748 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 2010	1,950 (717)	11 (2)	231 (29)	0 (0)	2,192 (748)

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 reviews and post-marketing safety operations

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

- In FY 2004, PMDA established a system where, if an applicant files claims of dissatisfaction, etc., regarding reviews and safety measures, the responsible office director (or 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 2010.

- In addition, PMDA developed a consultation manual to handle complaints, etc., from relevant companies. From among the complaints received from relevant companies, 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 2009, which concerns the operating performance for FY 2009.
- In addition, materials and minutes of the Advisory Council meetings and other meetings were also posted on the website sequentially to release the details of the meetings.
- Newly arriving information and topics, updates of existing contents, etc. were posted on the website in accordance with requests made by relevant offices.
- Taking into account opinions on the convenience from visitors/users of the website, PMDA took measures such as improvement of banners related to the links to the Medical Product Information web page.

2.3.(4) Proactive PR activities

- PMDA intends to improve services to the public by proactively providing information 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.

  In FY 2010, PMDA implemented PR activities by distributing brochures on PMDA's services and relief systems, give-away goods, etc. during the "Drug and Health Week" in cooperation with pharmaceutical associations in 9 prefectures. PMDA also created newsletters (e-mail magazines for prospective employees) and released them on its website. In addition, the Chief Executive himself delivered speeches, etc. in Japan and overseas (23 times in Japan and 5 times overseas).

2.3.(5) Disclosure request for corporate documents

- The status of requests for disclosure of corporate documents based on the Act on Access to Information Held by Incorporated Administrative Agencies is shown below (for the past five years). In FY 2010, the number of requests increased by 73.1% compared to the previous fiscal year. PMDA appropriately processed them in accordance with the relevant laws and regulations.

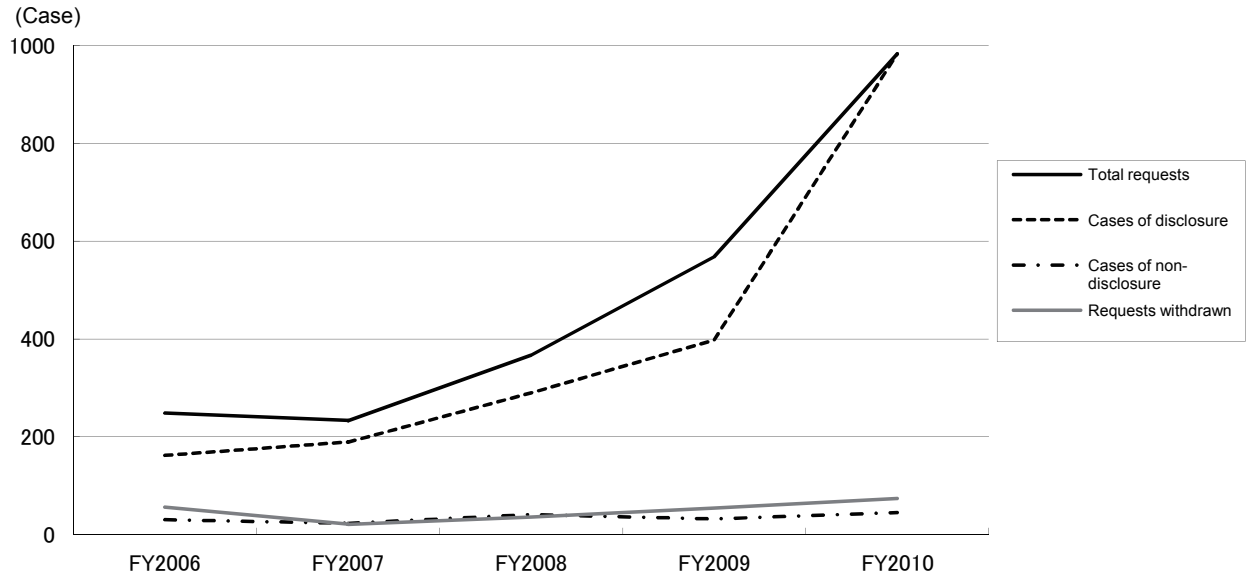
Number of Requests for Disclosure of Corporate Documents

(Unit: Case)

	Total requests	Requests withdrawn	Decisions*					Objections	Carry-over into FY 2011 **
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer about existence/non-existence of the document		
FY 2006	248	56	15	147	9	21	0	6	0
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	75

*: *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 2011 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 Article 10, Paragraph 2 of the Pharmaceutical Affairs Act (hereinafter referred to as "the Act") or the exceptional measure for due dates for decision of disclosure, etc. pursuant to Article 11 of the Act 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 Corporate Documents by Requester

(Unit: Case)

Requester/FY	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Individuals	113	86	99	103	370
Corporate (e.g., drug manufacturers)	132	143	250	426	563
Press	3	4	18	39	50
Total	248	233	367	568	983

Note: The category "Individuals" includes requests made under an individual's name, even if it substantially represents a corporation.

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

(Unit: Case)

Operational category/FY	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Examples
Product application review	90	115	263	377	475	Marketing notification for products not subject to approval
GLP/GCP/GMP/ QMS, etc. inspections	117	74	52	102	427	Notification of the results of GCP inspections
Post-marketing safety	40	44	52	89	78	ADR reports
Others	1	0	0	0	3	
Total	248	233	367	568	983	

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 2011
			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	1

Note: There was no request for disclosure of personal information in or before FY 2006.

Number of Requests for Disclosure of Personal Information by Requester

(Unit: Case)

Requester/FY	FY 2007	FY 2008	FY 2009	FY 2010
Identical person	1	3	1	1
Legal representative (person with parental authority, etc.)	2	0	0	2
Others	0	2	0	0
Total	3	5	1	3

Number of Requests for Disclosure of Personal Information by Operational Category of the Corporate Documents

(Unit: Case)

Operational category/FY	FY 2007	FY 2008	FY 2009	FY 2010	Examples
Adverse health effects relief	3	5	0	3	Request for judgment, etc.
Product application review	0	0	1	0	Clinical trial notification, etc.
Total	3	5	1	3	

Note: The numbers include requests that were decided not to be disclosed.

2.3.(7) Auditing and related matters

- PMDA undergoes audits conducted by an external accounting firm in accordance with the general rules for incorporated administrative agencies and through the Agency's Auditor. 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 2010, PMDA conducted internal audits on the management status of information system, the management status of goods, 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 2009, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2010 on its website.

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

- PMDA publicly announced the Plan for the Review of Optional Contracts, etc., on its website in June 2010.

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, and to manage a personnel evaluation system which enhances the morale of employees so that the results of the evaluation and the attainment of individual goals are properly reflected in remuneration, pay raise, and promotion.

- For this reason, PMDA appropriately reflected the results of personnel evaluation during the period from April 2009 to March 2010 in pay raise, etc. in July 2010. In order to ensure the proper implementation of this personnel evaluation system, PMDA provided briefing sessions for all employees, and took up the personnel evaluation system as a subject of the training course for the new recruits to inform them of the system.

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 scientific technology for developing drugs and medical devices.

- Under such circumstances, it is necessary for PMDA to make capacity building satisfactory 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. Consequently, employees can attend programs systematically. In FY 2010, PMDA continued to systematically provide these training courses.

Furthermore, in order to provide efficient and effective training tailored to the capabilities and qualifications of individual employees, PMDA actively deployed external institutions and experts, striving to reinforce training. 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 introduced below, were implemented.

1) General Training Course

(i) New recruit training between April and May 2010. 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) English training to improve the communication skills of employees in English. PMDA also conducted a TOEIC examination 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) 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 (6 facilities), medical device manufacturing facilities (3 facilities), and IRB of medical institutions (including practical training, workshops, etc.)

2) Specialized Training Course

(i) Dispatch of a total of 99 employees (76 in Japan, 23 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(24 sessions), special training programs on regulatory science to nurture employees from a broad perspective through interactions with various knowledgeable experts (11 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 (12 sessions)

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

(iv) Dispatch of the 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) Training actually using medical devices such as pacemakers, biological heart valves, and catheters for transvascular placement of stents, with cooperation of AMDD member companies. Also, PMDA conducted training on orthopedic medical devices.

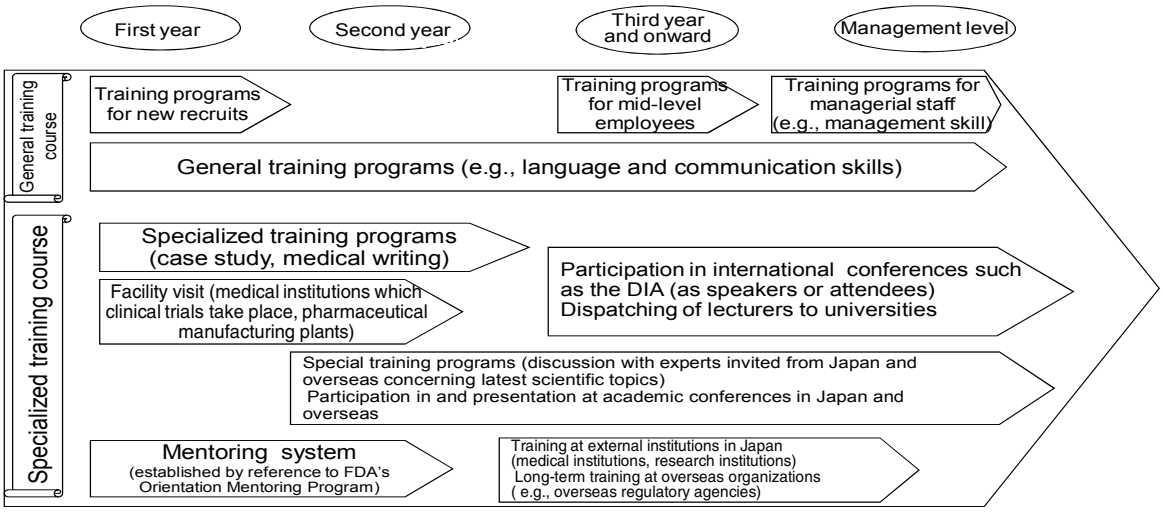
(vi) Dispatch of employees to ICPE meetings, ISMP workshops to reinforce basic skills related to safety measures as well as trainings on the method of conducting pharmacoepidemiological studies using medical databases

(vii) Dispatch of six employees to three medical institutions for practical training of pharmacists conducted at hospitals to learn the actual clinical practice

(viii) Dispatch of one employee to an accounting training course sponsored by the Accounting Center, Ministry of Finance to improve administrative processing skills. Also, 6 employees attended a grade 2 or 3 bookkeeping course.

Training and Human Resource Development

PMDA's training programs were fundamentally revised by reference to FDA's training program and put into practice stepwise from the latter half of FY 2007.



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.

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 expeditiously and properly.

- 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. Consequently, PMDA is required to recruit capable people in areas where more manpower is needed, based on the recruitment plan for each job category. PMDA held information sessions on career opportunities, conducted open recruitment of regular technical employees 4 times in FY 2010 by making use of its website as well as job information websites, and decided to recruit new employees, formally or informally, as shown below.

Employment through Open Recruitment in FY 2010 (as of April 1, 2011)

1) Technical employees (4 public recruitments)

Number of applicants	1,066
Number of employments	45
Number of prospective employees	40

2) Administrative employees (2 public recruitments)

Number of applicants	302
Number of employments	9

Recruitment Activities (FY 2010)

- Schedule of PMDA information sessions
  - May to June: Two sessions in Tokyo and one session in Osaka (total participants, 224 persons)
  - September to October: Two sessions in Tokyo, two sessions in Osaka and one session each in Sendai, Nagoya and Fukuoka (total participants, 397 persons)
  - November to December: Two sessions in Tokyo, two sessions in Osaka and one session in Fukuoka (total participants, 270 persons)
  - February: Two sessions in Tokyo and one session in Osaka (total participants, 191 persons)
- 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
  - Advertising via booth displays at academic conferences, etc. (e.g., distribution of brochures and display of posters at the 27th Live Demonstration in Kokura)
- 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 2012 (NIKKEI NAVI 2012, My NAVI 2012, RIKUNABI 2012)
  - Website presenting job information for those seeking a career change (NIKKEI Career Net. For 1 month from September 17, for 1 month from November 26 and for 1 month from February 4)
  - Number of distributed/subscribed direct mails: 50,772
- Recruitment advertising via academic journals
  - "Japan Medical Journal", "Japanese Journal of Pharmaceutical Health Care and Sciences", the Pharmaceutical Society of Japan (FARUMASHIA), "Journal of Japan Society of Mechanical Engineers", Proceedings of Lectures at the Annual Meetings of the Japanese Federation of Statistical Science Associations, Computational Statistics Seminar Textbook, the NIKKEI (featuring advertisements of grad hiring)

Numbers of the PMDA Staff

	April 1, 2004	April 1, 2005	April 1, 2006	April 1, 2007	April 1, 2008	April 1, 2009	April 1, 2010	At the end of the effective period for the Second Mid-term Plan (end of FY 2013)
Total	256	291	319	341	426	521	605	751
Review Department	154	178	197	206	277	350	389	
Safety Department	29	43	49	57	65	82	123	

Note 1: The "Total" includes 6 executives (including one part-time auditor), except for that of April 1, 2006, which includes 5 executives.

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, Offices of New Drug I to V, Offices of Biologics I and II, Office of OTC/Generic Drugs, Offices of Medical Devices I and II, and Office of Conformity Audit, and Senior Specialists.

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

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

- PMDA is careful to conduct appropriate personnel management so that 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 conducts appropriate personnel management by prescribing, in the work regulations, the submission of a written oath for newly-employed staff members, personnel allocation, restrictions regarding employment after resignation, and work restrictions for employees whose family members work in the pharmaceutical industry. PMDA also strives to keep 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 January 2010 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 confirmed 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 entry/exit control system for each office to reinforce the internal security control system.

- Specifically, by introducing a security access control system where access to each office is limited only to PMDA staff members through using unique ID cards and by recording the history of when each staff member enters each office, outsiders are not able to enter the rooms unaccompanied.

  In May 2010, PMDA set up non-stop floors at which elevators do not stop if the users (executives and employees, etc.) have no ID card, to reinforce security.

- In order to ensure further strict access control, PMDA has also prescribed restrictions on the entry/exit control, and has made maximum efforts to thoroughly inform its staff members of these restrictions through the intranet and during new recruit training.

2.4.(2) Security measures for information systems

- Based on the FY 2010 plan, PMDA strived to ensure the security of the information relating to 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 expand the use of secure e-mails to the audio transcription processes of records of face-to-face consultations, PMDA revised relevant rules and improved security so that the use of secure e-mails could be available for these services.

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

	Number of registered companies	Number of issued certificates
Outside PMDA	47	487
Within PMDA		661

Note: The numbers of registered companies and issued certificates as of the end of March 2011

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"), and to operate these Relief Systems appropriately, 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 middle of the following month.
  Information on Cases of Approval/Rejection is available at:
  http://pmda.go.jp/kenkouhigai/help/information2.html

- 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.

- From the viewpoint of making the administration of the system more transparent, PMDA disclosed the operating performance for the first half of FY 2010 on its website.

(ii) Improvement of brochures, etc.

- To make operations more efficient by reducing the amount of time required for administrative processing of incomplete claim forms and supporting documents, and PMDA carried out the following:

a) PMDA reviewed the descriptions of the brochure entitled "Do You Know about Relief Systems?", which gives a clear explanation of the Relief Systems. 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 2010, the Agency newly prepared the instructions for lung disorder and blood cell disorders, and also reviewed those for relief benefits for infections and skin lesions. Also, these revised instructions were posted on the website.

c) PMDA made efforts to improve the convenience for requestors 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 a notice that explains items frequently resulting in incomplete claim forms, 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 2010

(i) In June 2010, PMDA posted the explanatory slide "What is the Relief System for Sufferers from Adverse Drug Reactions?" on its website so that it can be utilized when there are lectures, briefing sessions, etc. on the Relief System at universities and hospitals.

(ii) On December 6, 2010, PMDA held the 30th anniversary symposium of the Relief System for Sufferers from Adverse Drug Reactions in Tokyo, which was attended by approximately 380 participants.

Contents (overview)

- What is the Relief System for Sufferers from Adverse Drug Reactions? (explanation of the outline)

[Part 1 "How the Relief System was established"]

- Lecture by persons affected by SMON and thalidomide which triggered the establishment of the System
- Lecture by a government official involved in the establishment of the System

[Part 2 "Today's Relief System" (current situation and challenges)]

- Lecture by the beneficiaries of the Relief System and their family
- Lecture on the current situation and challenges of the System by members of the Committee on Relief Services
- Discussion to promote the dissemination of the System titled "For a Better Understanding of the System"

The questionnaire survey conducted among the participants showed that 91% of them answered, "Very comprehensible" or "Comprehensible."

Activities conducted by direct visits

(i) Academic conferences

PMDA conducted the following publicity activities at academic conferences:

◆ Publicity efforts by using PMDA's exhibition booth

- Annual Meeting of the Japan Society of Transfusion Medicine and Cell Therapy

◆Provision of educational lectures/presentations

- Annual Meeting of the Japan Society of Transfusion Medicine and Cell Therapy (educational lecture)
- Annual Meeting of the Japan Society for Health Care Management (presentation)
- Annual Meeting of the Japanese Society of Drug Informatics (presentation)

◆Distribution of brochures

- Annual Meeting of the Japanese Society of Internal Medicine
- Annual Meeting of the Japanese Ophthalmological Society
- Annual Meeting of the Japanese Dermatological Association

(19 academic conferences in total)

(ii) Training workshops

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

- Regulatory affairs workshop jointly conducted by 9 special wards of Tokyo
- Training course for the Care Section of the Tokyo Hospital Pharmacists Association
- Training workshop for the Drug Consultation Research Group of the Pharmaceutical Manufacturers' Association of Tokyo
- Training workshop for PMS experts held by the Pharmaceutical Manufacturers' Association of Tokyo
- Training course for experts of pharmaceutical affairs, special course, 1st basic research workshop "Education on Drug-induced Suffering"
- Workshops for vaccination specialists (at 7 locations in Japan)
- Practical training courses of the Medical Safety Support Center (in Tokyo and Osaka)
- Workshop of Fukui Association of Medical Technologists
- Meeting of chairpersons of the Committees on Blood Transfusion Therapy in Shizuoka

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

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

◆Pharmaceutical associations

- Prefectural pharmaceutical associations (in 6 prefectures)
- Municipal pharmaceutical associations (in 5 municipalities)
- Hospital pharmaceutical associations (in 1 hospital)
- School pharmaceutical associations (in 1 school)

◆Associations of Medical Social Workers

- Prefectural Associations of Medical Social Workers (in 3 prefectures)

◆Government bodies

- Medicine Division, Health and Medical Department, Osaka Prefectural Government

(iv) Others

- At the 24th 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 12th Forum on Eradication of Drug-induced Sufferings (Sapporo), 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 acknowledge 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.

- General public Survey period: July to August 2010; Released on: December 24, 2010
- Healthcare professionals Survey period: November 2010; Released on: February 22, 2011

Results of the survey on awareness in FY 2010 were as follows:

General public

FY 2010 "Relief System for Sufferers from Adverse Drug Reactions"

Definitely aware (5.1%) Indefinitely aware (13.8%) Total: 18.9%

(References)

FY 2009 “Relief System for Adverse Health Effects”

Definitely aware (5.3%) Indefinitely aware (33.8%) Total: 39.1%

FY 2009 “Relief System for Sufferers from Adverse Drug Reactions”

Definitely aware (6.3%) Indefinitely aware (24.0%) Total: 30.3%

Healthcare professionals

FY 2010 “Relief System for Sufferers from Adverse Drug Reactions”

Definitely aware (53.1%) Indefinitely aware (27.9%) Total: 80.9%

(By job category)

	Definitely aware:	Indefinitely aware:	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%

(*References)*

FY 2009 “Relief System for Adverse Health Effects”

Definitely aware (37.2%) Indefinitely aware (42.8%) Total: 80.0%

FY 2009 “Relief System for Sufferers from Adverse Drug Reactions”

Definitely aware (42.8%) Indefinitely aware (32.0%) Total: 74.8%

(By job category)

	Definitely aware:	Indefinitely aware:	Total:
• Physicians	(41.3%)	(40.7%)	82.0%
• Pharmacists	(79.9%)	(16.1%)	96.0%
• Nurses	(12.3%)	(36.7%)	49.0%
• Dentists	(27.7%)	(39.9%)	67.6%

Note: In the FY 2010 survey, the awareness of 5 relief systems including “Relief System for Sufferers from Adverse Drug Reactions” and “Relief System for Infections Acquired through Biological Products” was inquired about directly. On the other hand, in the FY 2009 survey, the awareness of “Relief System for Adverse Health Effects” was inquired about first, and the responders who were aware (definitely or indefinitely aware) of the System were asked about their awareness of 2 relief systems, “Relief System for Sufferers from Adverse Drug Reactions” and “Relief System for Infections Acquired through Biological Products.”

(iii) PMDA conducted nationwide publicity activities for the Relief Systems from February to March 2011 (part of activities were continued in and after April).
- Newspaper advertisement
- Transportation advertisement (stickers inside train cars, train channel, large-size posters for display in stations)
- Internet advertisement (banner ads)
- Advertisement in professional journals (medical journals, free papers for general practitioners, free papers for distribution to drug stores)
- Video advertisement through in-house television systems at hospitals
- Distribution of and request for displaying publicity posters, etc. (dispensing pharmacies, drug stores)
- Distribution of brochures on the Relief System through attachment to free papers for physicians
- Utilization of PMDA website

(iv) PMDA posted a poster on the Relief System for Adverse Health Effects 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) PMDA conducted publicity activities using the brochure titled “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 103,000 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, colleges of nursing/schools of nursing/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.

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

(viii) 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.

(ix) 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,” and distributed it to relevant organizations, etc.

(x) 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.

(xi) 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.

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

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

(xiv) PMDA placed an article titled “The Relief System for Sufferers from Adverse Drug Reactions and Diseases Infected from Biological Products” in the "Pharmaceuticals and Medical Devices Safety Information No. 273" (issued in October 2010).

(xv) 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 Japanese Society of Hospital Pharmacists).

Brochure titled “Do You Know about Relief Systems?”

Large-size poster displayed in a station

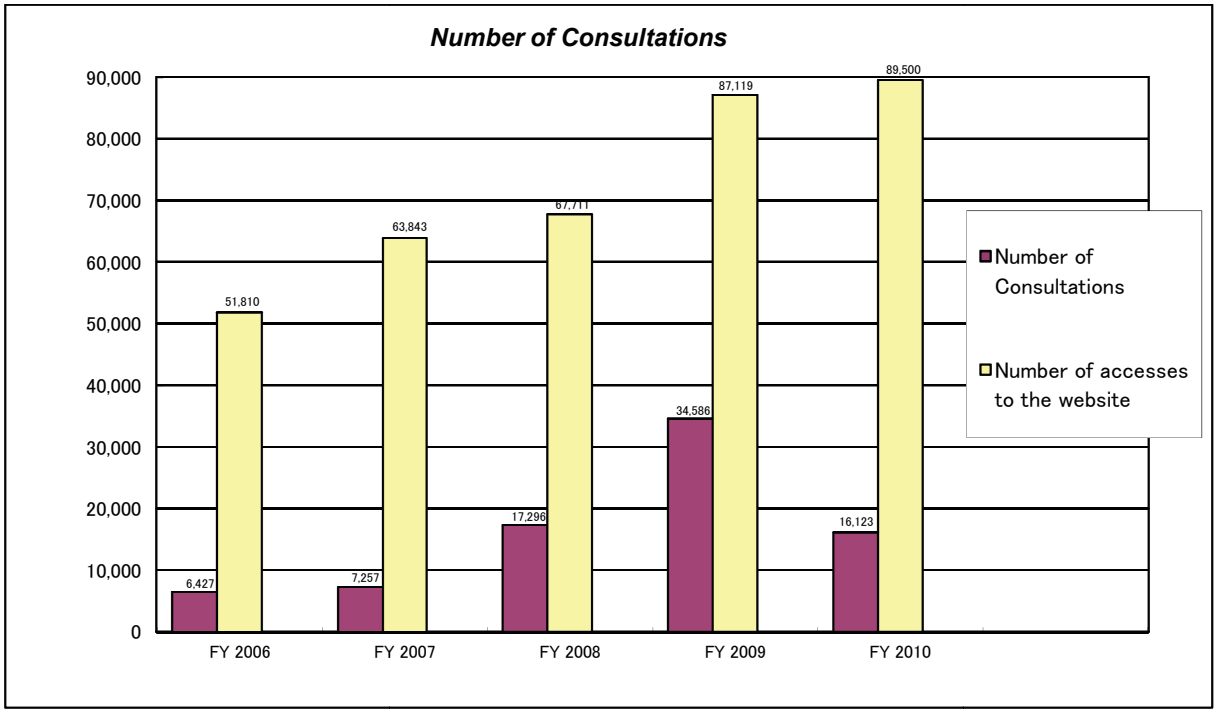
3.1.(3) Efficient management of the consultation service

- In FY 2010, the number of accesses to the website was 89,500, with a ratio of 103% compared with the previous fiscal year.

- In FY 2010, the number of consultations was 16,123, with a ratio of 47% compared with the previous fiscal year (34,586 consultations).This is because the number of consultations provided in FY 2009 included a significant number of inquiries and complaints on particular products from users who called PMDA by referring to the descriptions of the “Relief System for Adverse Drug Reactions” or “PMDA's toll-free number” on the outer boxes of OTC drugs, though those inquiries/complaints should have been directed to the manufacturers. To improve this situation, PMDA introduced the pre-recorded voice guidance system on September 25, 2009 to inform callers that the 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. Accordingly, the apparent number of consultations decreased because consultations that were actually handled by PMDA were counted.

- 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 2006	FY 2007	FY 2008	FY 2009	FY 2010	Compared with FY 2009
Number of consultations	6,427	7,257	17,296	34,586	16,123	47%
Number of accesses to the website	51,810	63,843	67,711	87,109	89,500	103%



Toll-free number: 0120-149-931
e-mail for relief system consultation: kyufu@pmda.go.jp

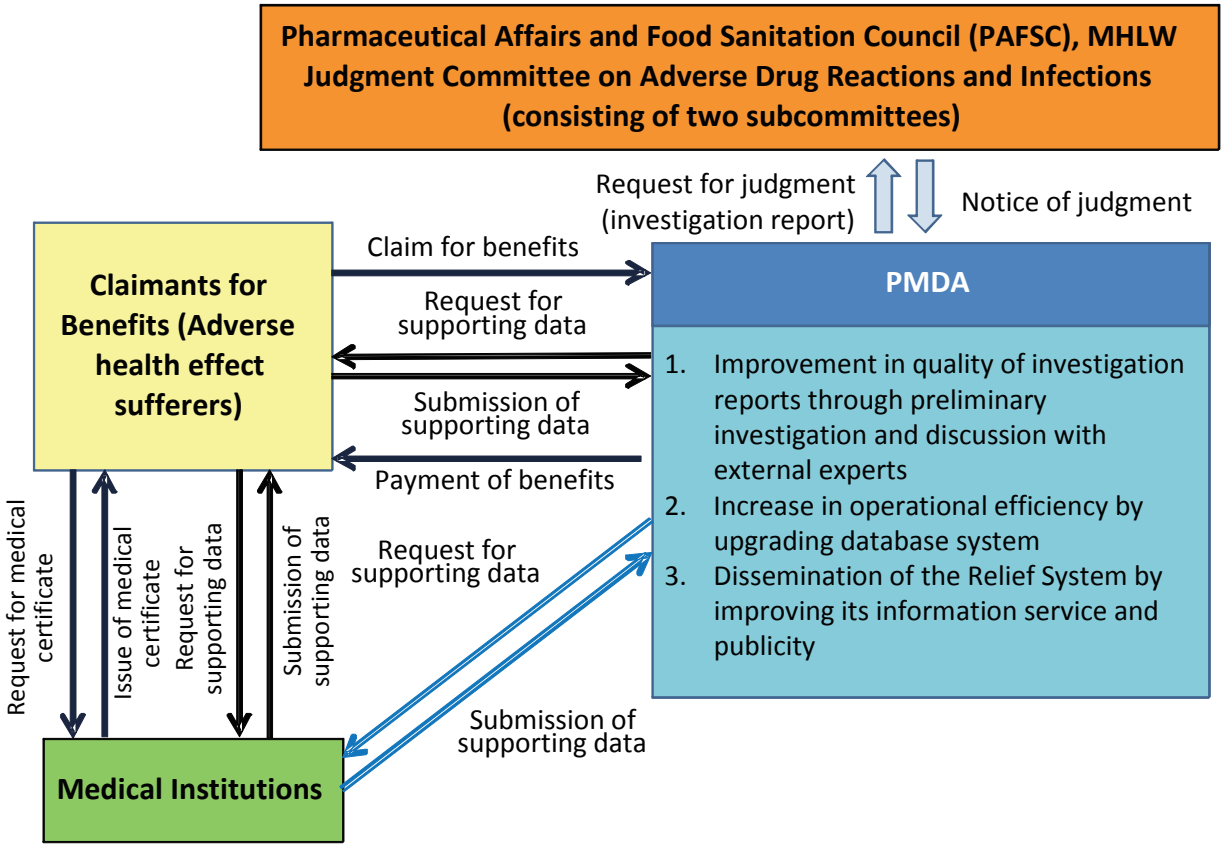
3.1.(4) Integrated management of information through databases

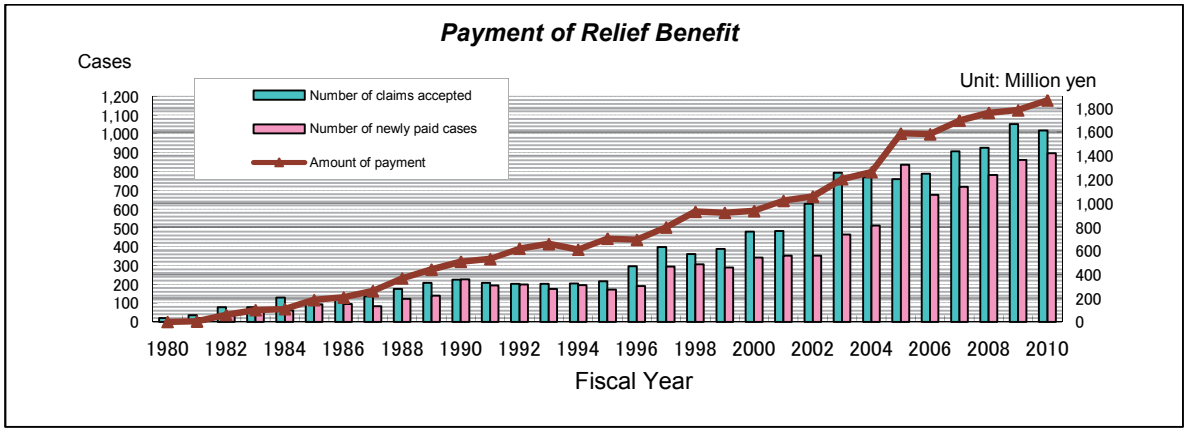
- To make operations more efficient and swift, PMDA upgraded the following systems:
  (i) System of Relief Fund Services
    - Added codes and indicators for “drug products partially applicable to the relief benefits” among drug products not applicable to the relief benefits
    - Added a function to enter the overview of cases in dispute
  (ii) Integration and Analysis System for Databases on Relief Benefits Services
    - Expanded the search function to identify previous similar cases in order to make more effective use of information accumulated in the system to date
    - Improved the progress management for cases having administrative processing time within 6 months set as a goal.

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





FY 2010

- Relief services for adverse drug reactions→Number of claims: 1,018　Number of cases of approval/rejection: 1,021 (of which 897 were judged approved)
- Relief services for infections→Number of claims: 6　Number of cases of approval/rejection: 7 (of which 6 were judged approved)

In accordance with the Second Mid-term Plan, PMDA plans to exercise judgment of approval/rejection of claims within 6 months for 60% or more of the total number of judged cases in each fiscal year. In FY 2010, PMDA planned to increase the number of claims judged within 6 months by 10% compared with FY 2009, while ensuring that 70% or more of claims are judged within 8 months of the standard administrative processing time. As a result, the number of claims judged within 8 months was 765, with a percentage of 74.9%. The number of claims judged within 6 months was 434, resulting in an increase of 20.6% compared with that in FY 2009 (360). The percentage of claims judged within 6 months was 42.5%.

(i) Relief Service for Adverse Drug Reactions

PMDA implements 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. Actual performance of Relief Service for Adverse Drug Reactions

The actual performance for FY 2010 is shown below.

(Cases)

Fiscal Year			FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of claims			788	908	926	1,052	1,018
Number of judged cases			845	855	919	990	1,021
		Approved	676	718	782	861	897
		Rejected	169	135	136	127	122
		Withdrawn	0	2	1	2	2
	Within 8 months	Number of cases	552	634	683	733	765
		Achievement rate*1	65.3%	74.2%	74.3%	74.0%	74.9%
	Within 6 months	Number of cases	344	367	355	360	434
		Achievement rate*2	40.7%	42.9%	38.6%	36.4%	42.5%
Cases in progress*3			624	677	684	746	743
Median processing time			6.6 months	6.4 months	6.5 months	6.8 months	6.4 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 2010 by type of benefit are shown below.

(Cases)

Fiscal Year		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of claims		788	908	926	1,052	1,018
Types of benefits	Medical expenses	643	730	769	902	854
	Medical allowances	694	786	824	943	911
	Disability pensions	60	70	79	71	74
	Pensions for raising handicapped children	14	10	7	11	4
	Bereaved family pensions	31	33	26	36	46
	Lump-sum benefits for bereaved families	51	72	49	50	54
	Funeral expenses	88	105	78	83	100

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

c. Judgment status by type of benefit

The status of judgments made in FY 2010 by type of benefit is shown below.

(Thousand yen)

Types	FY 2006		FY 2007		FY 2008	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	572	67,502	603	67,603	659	75,339
Medical allowances	624	60,034	651	62,668	711	62,055
Disability pensions	35	692,446	42	730,007	27	747,362
Pensions for raising handicapped children	6	30,131	7	35,760	7	40,127
Bereaved family pensions	22	493,010	20	501,454	22	523,455
Lump-sum benefits for bereaved families	34	229,446	39	286,373	47	335,977
Funeral expenses	53	10,386	63	12,661	72	14,391
Total	1,346	1,582,956	1,425	1,696,525	1,545	1,798,706

Types	FY 2009		FY 2010	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	763	86,666	803	87,475
Medical allowances	813	70,963	837	71,142
Disability pensions	26	804,251	38	853,854
Pensions for raising handicapped children	7	50,804	5	44,210
Bereaved family pensions	18	545,843	31	583,501
Lump-sum benefits for bereaved families	30	215,342	29	214,081
Funeral expenses	46	9,914	63	12,927
Total	1,703	1,783,783	1,806	1,867,190

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

Note 2: Since the figures of payment amount 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 implements 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. Actual performance of relief for infections

The actual performance for FY 2010 is shown below.

Fiscal Year		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of claims		6	9	13	6	6
Number of judged cases		7	5	11	10	7
	Approved	7	3	6	8	6
	Rejected	0	2	5	2	1
	Withdrawn	0	0	0	0	0
Cases in progress*		1	5	7	3	2
Achievement rate**		100.0%	100.0%	100.0%	100.0%	85.7%
Median processing time		3.8 months	3.8 months	5.2 months	5.4 months	6.9 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 2010 by type of benefit are shown below.

(Cases)

Fiscal Year		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of claims		6	9	13	6	6
Types of benefits	Medical expenses	5	7	11	5	5
	Medical allowances	5	8	13	6	5
	Disability pensions	0	1	0	0	1
	Pensions for raising handicapped children	0	0	0	0	0
	Bereaved family pensions	1	0	0	0	0
	Lump-sum benefits for bereaved families	0	0	1	0	1
	Funeral expenses	1	0	1	0	1

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

c. Judgment status by type of benefit

The status of judgments made in FY 2010 by type of benefit is shown below.

(Thousand yen)

Types of benefits	FY 2006		FY 2007		FY 2008		FY 2009		FY 2010	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	6	473	3	102	5	204	6	375	5	425
Medical allowances	6	497	3	352	6	386	8	567	5	384
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	1	1,387	–	2,378	–	2,378	–	2,378	–	2,378
Lump-sum benefits for bereaved families	–	–	–	–	1	7,135	–	–	1	7,160
Funeral expenses	1	199	–	–	1	199	–	–	1	193
Total	14	2,556	6	2,833	13	10,302	14	3,320	12	10,540

Note: Since the figures of payment amount 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 12 liaison meeting sessions between the Office of Relief Funds and Office of Safety II to promote information sharing.

- 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.

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

- As it may be 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 implements health and welfare services for sufferers from adverse health effects as below in accordance with the Act on the Pharmaceuticals and Medical Devices Agency:

Investigative Research for Improvements in Quality of Life of Sufferers of Severe 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 Severe 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 severe 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 2010, the data on the operating performance for FY 2009 were organized at a meeting of the above-mentioned Research Team held on October 29, and also its results were sent to the members of the Committee on Relief Services and other concerned parties.

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 (66 volunteers in FY 2010).

Investigative Research Team

Leader:	Atsushi Ozawa	Professor, Faculty of Human Life Design, Toyo University
	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

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, injuries, 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 implementation 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 FY 2009.

Consultation services by experts who are qualified for welfare were started in January 2010, for the purpose of providing advice, etc. on mental care and on the use of welfare services to persons suffering from health damage caused by adverse drug reactions or infections acquired through biological products and their families. In FY 2010, 37 consultations were performed.

Distribution of the Benefit Recipient Card:

For beneficiaries of the Relief System for Adverse Health Effects, a service in which a handy, credit-card size certificate is issued upon request was started in January 2010. 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 2010, the card was issued to 504 persons.

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.

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 (187 volunteers in FY 2010).

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	Head of Department of Pediatrics, Nara Medical University
	Akira Terashima	Professor, Faculty of Child Studies, Urawa University

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

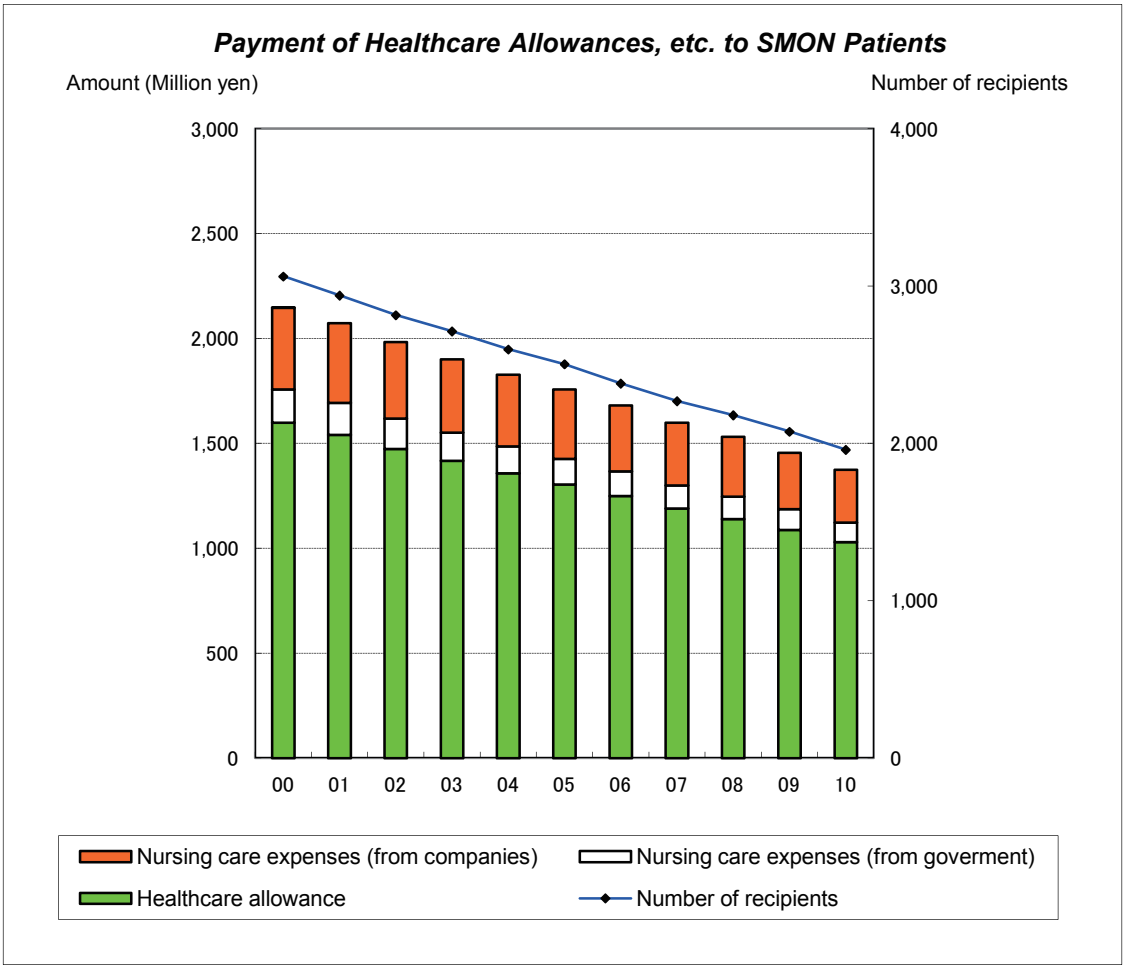
PMDA appropriately provided healthcare allowances, etc. to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

(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 2010, the number of patients receiving such allowances was 1,960, and the total amount paid was 1,376 million yen.

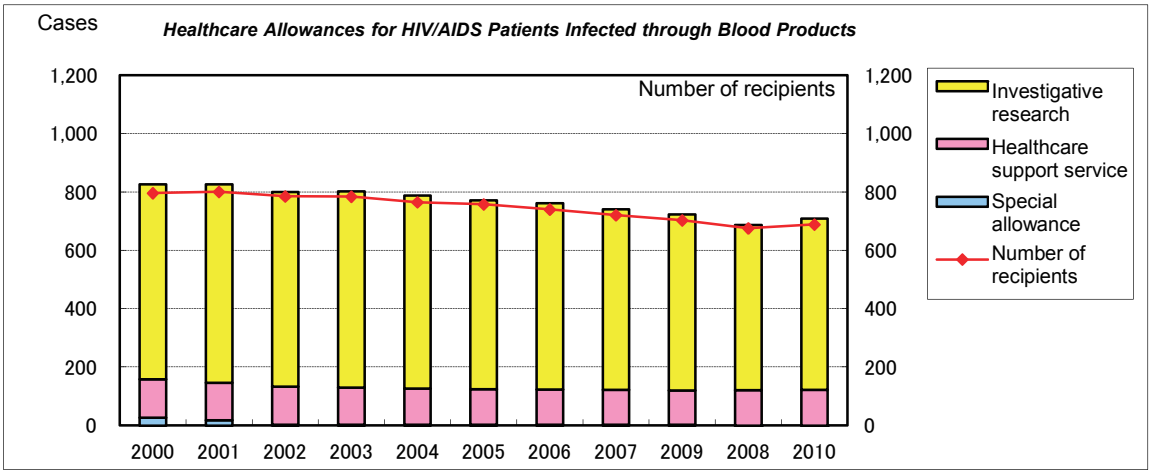
Fiscal Year		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of recipients		2,381	2,269	2,180	2,075	1,960
Amount paid (thousand yen)		1,683,500	1,601,134	1,531,745	1,457,724	1,375,622
Break down	Healthcare allowances	1,251,622	1,191,245	1,140,517	1,089,491	1,031,376
	Allowance for nursing care expenses (from companies)	315,027	299,108	284,981	268,749	250,946
	Allowance for nursing care expenses (from government)	116,850	110,781	106,247	99,485	93,300

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



(ii) AIDS-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 2010, 562 HIV-positive patients received allowances relating to the investigative research, 116 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 680, and the total amount paid was 522 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 2006		FY 2007		FY 2008	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	618	334,653	603	327,857	586	320,122
Healthcare support services	120	210,000	117	224,796	121	211,800
Special allowance	3	8,678	3	8,084	2	6,300
Total	741	553,331	723	560,737	709	538,222

Fiscal Year	FY 2009		FY 2010	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	566	313,676	562	309,355
Healthcare support services	120	210,600	116	206,100
Special allowance	2	6,300	2	6,300
Total	688	530,576	680	521,755

3.1.(9) Appropriate Implementation 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 305, with 6,293 million yen as the total amount paid in FY 2010.

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

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 settings 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, so that drugs and medical devices can fulfill their purpose over a longer period of time. Therefore, 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 2010 plan.

3.2.(1) Faster 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 intends to take various measures with the aim of resolving the lag of 2.5 years between approval of new drugs in the US and approval in Japan, by FY 2011.

(i) Implementation of appropriate and prompt reviews

a. Implementation structure for clinical trial consultations and reviews

- The review system for drugs and medical devices has 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 kinds of measures, further improvements in the system were made.

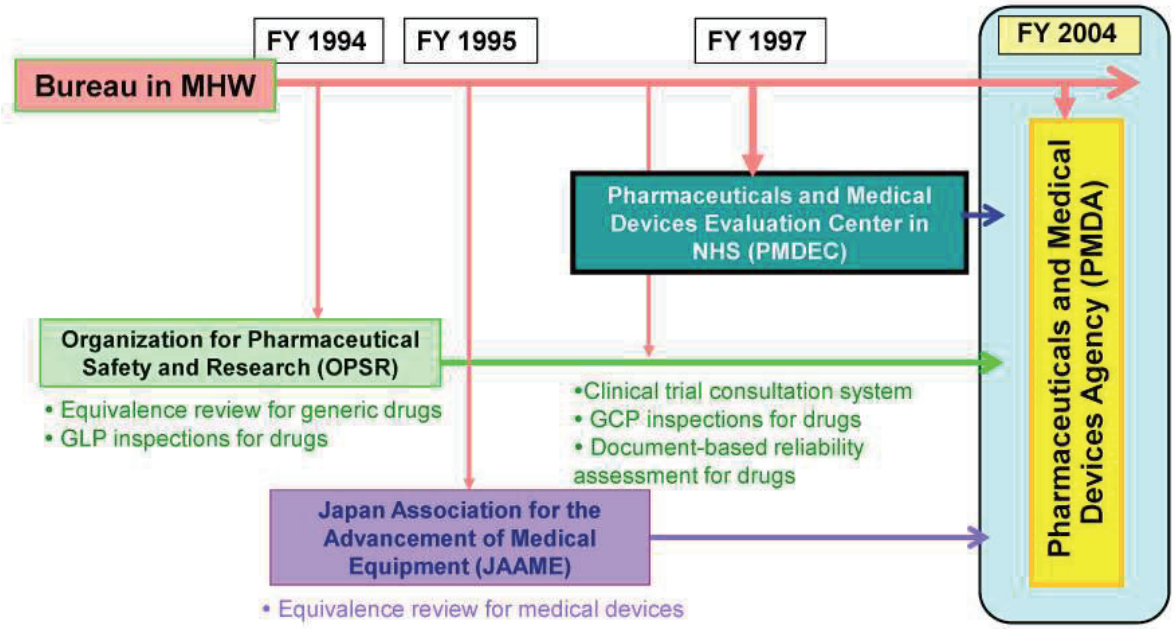
  1) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the “Pharmaceuticals and Medical Devices Agency (PMDA)” was established through the integration of three separate organizations that were responsible for reviews and related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

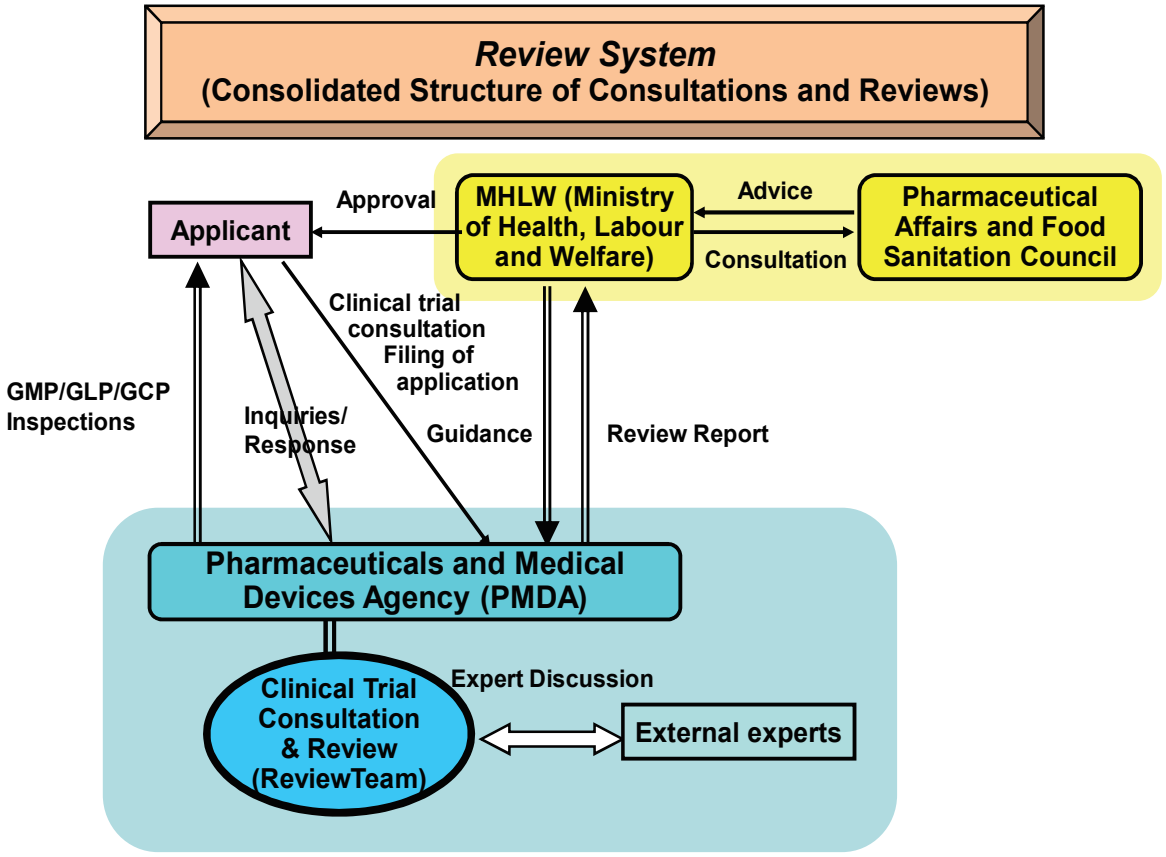
  2) Substantial increase in the number of its staff including reviewers.

  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.

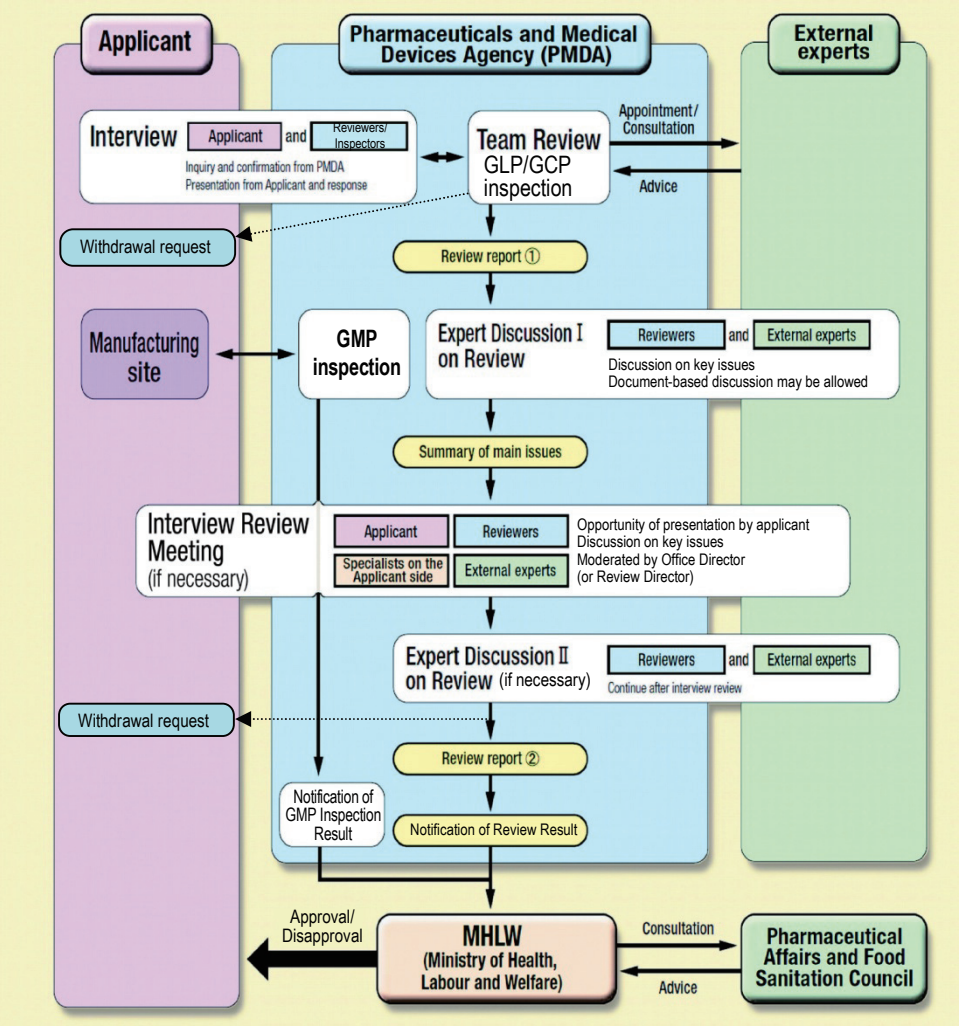
  4) Reinforcement of the functions for reviewing medical devices, as well as enhancement of reviews of biological and biotechnology-derived products.

Transition of approval review system on drugs and medical devices





Flowchart of review process



Actual Results of Reviews in FY 2010

Reviews:

Drugs

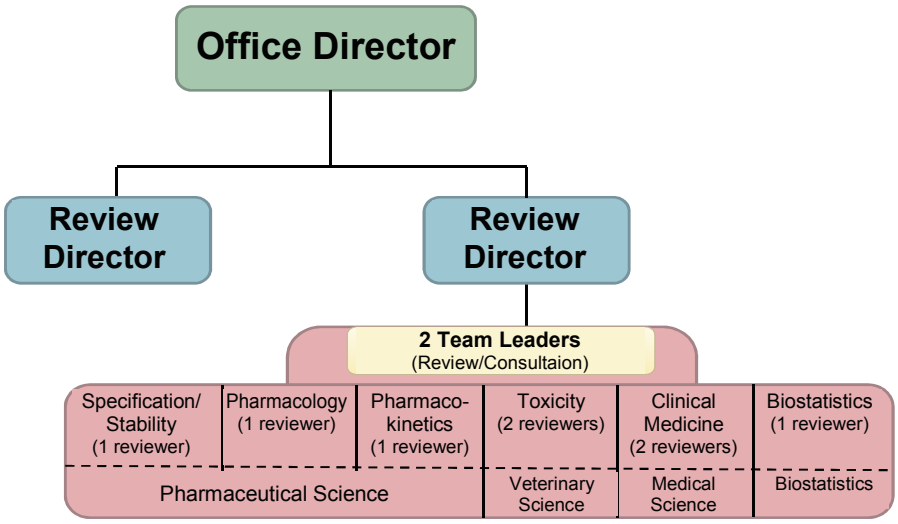
(i) Number of Expert Discussions conducted:
175 (of which, 124 through document-based discussions, 51 through meetings)

(ii) Applications deliberated at the Drug Committees (under PAFSC): 69
Applications reported to the Drug Committees (under PAFSC): 45

- Reviews of new drugs were conducted by review teams consisting of experts under the guidance of an office director and a review director. In most cases, the team members had academic degrees in pharmaceutical science, medicine, veterinary medicine, biostatistics, or other specialized courses. The review team is fundamentally 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

Structure of a Review Team for New Drugs



- In order to enhance the review system, PMDA increased the number of reviewers of the categories where many new drug applications were filed and likely to remain pending.
- Reviews of new drug applications are assigned to the offices and teams based on their review category, which consists of specific therapeutic categories. The review categories are as follows:

Review Categories Handled by the Offices of New Drugs

Name of office	Review Category	
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
	Cell- 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 Chief Reviewer and the Deputy Chief Reviewer in charge, who were appointed from a review team.

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 2010, 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 had 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 make improvements in the progress as needed. 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, which was established in the review division in FY 2008, to control the progress of reviews, was constantly convened in FY 2010. 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, countermeasures and future approaches were examined, and the detailed review status of new drugs and other products under review were informed (11 meetings were held in FY 2010).

  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 Information Sharing between an Applicant and Pharmaceuticals and Medical Devices Agency during the Review Process for New Drugs” (dated March 19, 2009) and 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 reviews 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 and has been used at reviews, etc.

d. Implementation of consultations and reviews based on medical care needs

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

  Note: A total of 806 PMDA staff members participated in 266 academic conferences and seminars held in and outside of Japan.

- In order to contribute to the promotion of development of unapproved drugs and off-label use drugs by pharmaceutical companies regarding drugs and indications approved in Europe and the U.S. but not yet 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 will continuously support this Committee, and deal with clinical trial consultations and reviews based on the results of the investigations.

- For cell- 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 development.

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

e. Consistency among contents of clinical trial consultations and reviews

- In order to ensure that the contents of clinical trial consultations and reviews are consistent, 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 relevant review teams.

f. Appropriate implementation of re-examinations and re-evaluations

- 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.

  Regarding already-approved drugs that are specified by the Minister of Health, Labour and Welfare, re-evaluations of the drug efficacy and safety, in the light of the current standards of medical/pharmaceutical sciences, are conducted based on the data submitted by marketing authorization holders. In addition, the re-evaluations of quality are conducted to examine whether the quality is appropriate in terms of the dissolution of solid oral dosage forms, based on the data submitted by these marketing authorization holders. Once the quality has been assured, appropriate dissolution specifications are to be established to ensure that the quality of solid oral dosage forms is maintained at a certain level.

- In FY 2010, 115 products underwent re-examinations, no product underwent re-evaluation for drug efficacy, and 53 products underwent re-evaluation for quality.

Implementation Status of Re-examinations/Re-evaluations

		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Products that underwent re-examination		152	95	235	164	115
Re-evaluation	Products that underwent re-evaluation for drug efficacy	0	0	0	0	0
	Products that underwent re-evaluation for quality	70	434	89	12	53

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 in MHLW, Regional Bureau of Health and Welfare, prefectural governments, pharmaceutical companies, etc, 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) and (ix) are 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 official licenses, 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 approval registration list.

- In FY 2010, PMDA reviewed the structure and procurement method of the new application/review system in order to achieve the Mid-term Targets and the Mid-term Plan. At the same time, PMDA conducted the following system development projects to promptly and efficiently perform reviews and inspections. Also, in order to ensure the support for the new application/review system and the other individual systems and maintain the stable operation by replacing existing hardware and software with reliable ones fulfilling the current technological level, PMDA procured a set of rental devices.

  1) Addition of a function to DEVICE System in order to assist the achievement of the Action Program to Accelerate Reviews of Medical Devices

     - PMDA added this function to improve the convenience of the DEVICE System for further enhancement of the efficiency of the operations related to review of medical device applications.

  2) Conversion of documents for regulatory approval for drugs etc. into electronic media

     - PMDA converted past documents for regulatory approval, which are referred to at the time of application review, into electronic media and developed a database in which the documents can be searched and accessed, for acceleration and enhancement of application review.

  3) Improvement of the database system on excipients used in already-approved drug products

     - PMDA built the support system for research of excipients that are used in already-approved drug products in FY 2009 to improve the efficiency of the research, and then initial data were entered in the system.

  4) Replacement of equipment for review support system for drugs, etc.

     - To execute reviews, inspections, and management of user fees, PMDA newly procured servers and other equipment for replacement as well as established the environment for up-grading and enhancement of servers and integration of equipment.

5) Leasing of equipment for the new application/review system for drugs, etc.

- In order to promote the optimization and rationalization of reviews for drugs, etc., PMDA integrated servers for the review systems.

6) Addition of new functions to the new application/review system

- PMDA added functions to the new application/review system so as to allow correct and rapid verification of the completion of inspections, especially for the management of inspection lists.

7) Conversion of final decision documents for regulatory approval for medical devices etc. into electronic media

- PMDA outsourced conversion of paper-based materials, such as final decision documents for regulatory approval for medical devices, etc., into electronic image data that were good quality and could be stored for a long time. This project intends to promote sharing of information with MHLW and to facilitate extensive utilization of data for ensuring the efficiency and acceleration of reviews.

8) 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, PMDA established a method of submission of reports through the Web application platform for medical devices that was intended for use in coordination with the new application/review system.

9) Addition of a function to the clinical trial database system

- In response to the expiration of the maintenance period for servers, etc., a function was added to the clinical trial database system to promote the efficiency of operations and to reduce the work load, which enabled PMDA to further enhance the research relating to the receipt of clinical trial notifications.

10) Improvement of the facsimile function, etc. for the review support system for drugs, etc.

- In order to promote the optimization of reviews for drugs, etc., PMDA upgraded the facsimile function, etc.

11) Addition of a function to and improvement of the new drug database system

- PMDA updated the system to allow integrated management of information on pre-consultation meetings, questions on re-examination/re-evaluation, etc. on the same system and to reduce operations of entry and modification of existing review-related information.

12) 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 submitted documents 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.

13) IT literacy training

- In order to utilize electronic documents more efficiently, an IT literacy training (Microsoft Access 2007, Excel 2007) was carried out through e-learning in which trainees learn at the personal computer on their own desk.

h. Improvement of environment for eCTD

- The eCTD viewer system was improved through procurement via general competitive bidding process, by which the review-related function for eCTD implemented in FY 2008 was improved, and the review environment by eCTD was enhanced. In accordance with the notification as revised in FY 2010, the efficiency of operations was promoted by improving functions of a cost free validation tool that allows applicants to check the format by themselves before eCTD submission, which reduced unnecessary findings at the time of reception of applications in the eCTD format.

- In accordance with the direction notified by the National Information Security Center to recommend up-grading from Internet Explorer (IE) 6 to IE 8, the eCTD viewer system was improved and validated so that the system would operate on IE 8, through the procurement via general competitive bidding process.

i. Development of Japanese Pharmacopoeia

- In FY 2010, the Japanese Pharmacopoeia Draft Committee held a total of 83 meetings, and posted information on the PMDA website to seek public comments regarding 451 official monographs (106 new articles, 330 amendments, 15 deletions), 15 general tests (15 amendments), 28 ultraviolet-visible reference spectra, 38 infrared reference spectra, 14 reference information (4 new information, 10 amendments), amendments to other General Notices, and full revision of the General Rules for Preparations as a draft of the 16th edition of the Japanese Pharmacopoeia (JP) (published as a Ministerial Announcement in March, 2011).

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
New monographs	102	90	1	106	-	106
Amendments	276	171	1	122	2	330

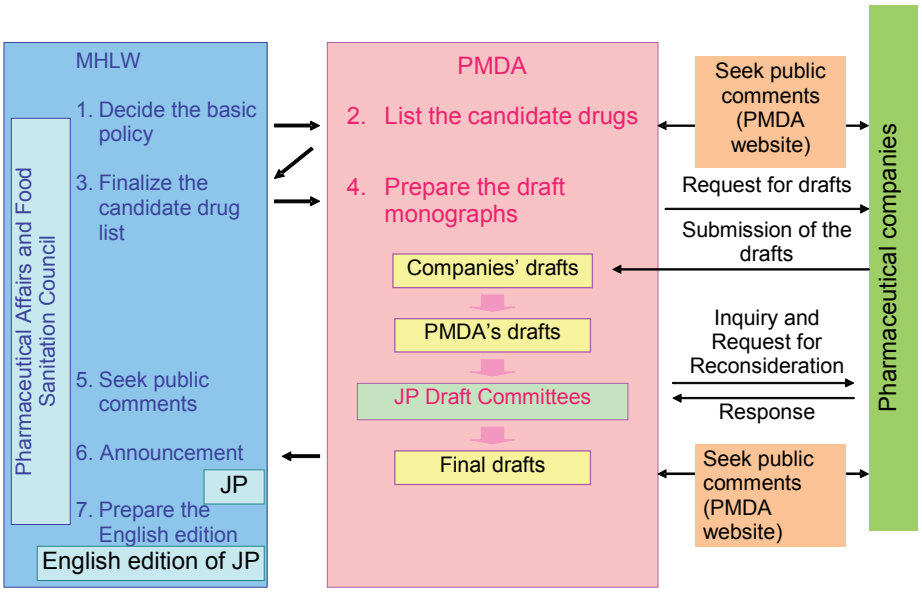
Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for General Notices, General Rules for Preparations, General Rules for Crude Drugs, General Tests, Processes, and Apparatus, and General Information. PMDA usually provides those drafts to MHLW 6 months before the normal publication timing. In FY 2010, PMDA reported the draft of the 16th edition (published as a Ministerial Announcement in March 2011) to MHLW in August 2010.

Ministerial Announcement on the Japanese Pharmacopoeia (JP) by MHLW

	15th edition of the JP	1st supplement to the 15th edition of the JP	Partial revision	2nd supplement to the 15th edition of the JP	Partial revision	16th edition of the JP
Month and year announced	March 2006	September 2007	March 2009	September 2009	July 2010	March 2011
New monographs	102	90	1	106	0	106
Listed monographs	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 the PMDA 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. (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 has offered prior assessment consultations as a pilot scheme since FY 2009 and continued in FY 2010 (Category 2, 1 product; Category 3-1, 1 product; Category 4, 2 products; Category 5, 1 product; Category 6-1, 1 product; Category 6-2, 1 product; Oncology drugs, 1 product; Biological products, 1 product).

  Based on the results of the pilot scheme, while exchanging opinions with the industry at the clinical trial consultation working group meetings, PMDA created a new category of prior assessment consultation that covers a part of phase III studies (phase II/III studies). Also, PMDA accepted requests for consultations for the first half of FY 2011 in accordance with "Way of Acceptance of Request Forms for Prior Assessment Consultations for Drugs " (PMDA/CPE Notification No. 0120001 of the Center for Product Evaluation, PMDA, dated January 20, 2011), which stipulates that requests for consultations are to be accepted twice a year.

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 three review teams in FY 2009, were increased and placed in nine review teams in FY 2010, 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 PMDA were reviewed by 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 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 2010 is shown below:

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

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

Targets

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

**PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Median Total Review Time for New Drugs (Priority Review Products)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	13.7	12.3 (19.4)	15.4 (19.1)	11.9 (24.5)	9.2 (12.6)
Regulatory review time [months]	6.4	4.9 (7.7)	7.3 (8.3)	(3.6) (6.7)	4.9 (6.8)
Applicant's time [months]	6.0	6.5 (12.0)	6.8 (11.4)	6.4 (15.9)	3.4 (7.6)
Number of approved applications	20	20	24	15	20

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

	FY 2010
Total review time [months]	12.0 (13.2)
Regulatory review time [months]	5.3 (7.9)
Applicant's time [months]	6.0 (7.9)
Number of approved applications	13

Note 1: For FY 2010, products submitted for public knowledge-based applications in relation to the Study Group on Unapproved and Off-label Drugs of High Medical Need are included as priority review products.

Note 2: 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 2010 in the Supplementary Information for details.

Note 3: Values in parentheses are reference values (80th percentile).

- 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 20 applications were approved in FY 2010 in this category (including 7 public knowledge-based applications in relation to the Study Group on Unapproved and Off-label Drugs of High Medical Need). In FY 2010, 8 applications requesting priority reviews of drugs regarded as having particularly high medical need were submitted.

  Of the 8 products for which priority reviews were requested, 3 applications were judged to be "applicable" as priority review products, and 2 were "not applicable," and 3 are currently under consideration.

- The median total review time for priority review products in FY 2010 was 9.2 months, the median regulatory review time was 4.9 months, and the median applicant's time was 3.4 months, all showing the achievement of the target.

  Among approved applications in FY 2010, priority review products accounted for 18%, and the percentage was higher than that in FY 2009 (14%).

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

Targets

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

**PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Median Total Review Time for New Drugs (Standard Review Products)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	20.3	20.7 (29.5)	22.0 (27.6)	19.2 (24.8)	14.7 (22.7)
Regulatory review time [months]	12.8	12.9 (17.7)	11.3 (18.5)	10.5 (15.3)	7.6 (10.9)
Applicant's time [months]	6.9	7.9 (11.2)	7.4 (14.1)	6.7 (10.7)	6.4 (12.2)
Number of approved applications	29	53	53	92	92

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 2010 in the Supplementary Information for details.

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

- In FY 2010, the median total review time for standard review products was shortened to 14.7 months, compared with 19.2 months in FY 2009. The median regulatory review time was shortened to 7.6 months in FY 2010 from 10.5 months in FY 2009, showing a reduction of 2.9 months, and the median applicant's time was also shortened to 6.4 months in FY 2010 from 6.7 months in FY 2009, showing a reduction of 0.3 months.

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

- PMDA has asked applicants to withdraw their applications that were considered to be difficult to approve due to a lack of response from the applicants to inquiries made by PMDA. Of the applications submitted in or before March 2004, 136 were processed through approvals or withdrawals by FY 2010.

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

	From application to first consultation	From first consultation to inquiries about important matters	From inquiries about important matters to Expert Discussion	From Expert Discussion to approval
FY 2010	1.8 months (2.2 months) 52 applications	0.5 months (0.9 months) 51 applications	2.1 months (4.7 months) 91 applications	2.6 months (3.6 months) 90 applications

Note 1: Values in parentheses are reference values (80th percentile).
Note 2: Values are of applications filed in or after April 2004.
Note 3: Because 2 applications were approved without Expert Discussion, the number of approved applications in this table is different from the 92 approvals for standard review products in FY 2010.

- The number of applications under review at the end of FY 2010 was 130 (including 11 applications for orphan drugs; 14 public knowledge-based applications for unapproved drugs; 7 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	Withdrawn	Under review
On or before Mar 31, 2004	140	108 (2)	28 (0)	4 [-2]
FY 2004	87	78	9	0
FY 2005	57	50 (1)	7 (0)	0 [-1]
FY 2006	102	92 (2)	9 (0)	1 [-2]
FY 2007	92	78 (7)	14 (4)	0 [-11]
FY 2008	81	76 (30)	3 (0)	2 [-30]
FY 2009	106 (1)	69 (56)	14 (11)	23 [-67]
FY 2010	118	16 (16)	2 (2)	100 [100]
Total	783	567 (114)	86 (17)	130 [-13]

Note 1: The number of applications in FY 2009 includes 3 additional applications (2 applications were changed to new drugs from other category during the review, and 1 application was later changed to be included in "Applications"), and 2 deleted applications (2 separate applications for a single active ingredient were integrated into 1 application, and there were 2 such dual applications).

Note 2: Values in parentheses in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2010 (included in values on their left).

Note 3: Values in brackets indicate difference from the status reported in FY 2009.

Number of Applications Processed and Time Spent by Review Process

	Review process	1. From receipt of applications to first consultation	2. From first consultation to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2010	Number of processed applications	63	66	102	112
	Median total review time	63.0 days	193.5 days	28.0 days	65.5 days

Note 1: The duration shown in each review process are the median of the total review time (the sum of reviewers' and applicants' time clocks) of the period.

Note 2: Values are of applications filed in or after April 2004.

(iv) Efficient implementation of clinical trial consultations

a. Implementation of priority consultations

- In FY 2010, 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 3 priority consultations related to the designated ingredients.

b. Acceleration of the procedure for clinical trial consultations

- As for the acceleration of clinical trial consultations, requests for schedule arrangement had been accepted after clarifying the number of clinical trial consultations using a temporary request form for consultations and posting notices of the available dates for consultations (in a calendar format) on the website. However, aiming at shortening the duration from consultation request to the date of consultation in the perspective of efficient implementation of clinical trial

consultations, the use of temporary request form and the calendar format was abolished for requests for consultation starting October 2010 to improve the efficiency in the management of request activities of applicants as well as receipt operations of PMDA staff. As a result, the time was shortened by approximately 1 month. 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 Clinical Trial Consultations (CTCs)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC	288	281	315	370	390
Withdrawals	7	21	23	23	44
Total (Conducted consultations and withdrawals)	295	302	338	393	434

Number of Prior Assessment Consultations for Drugs Conducted

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC	-	-	-	33	30
Withdrawals	-	-	-	0	0
Total (Conducted consultations and withdrawals)	-	-	-	33	30

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC	-	-	-	1	1
Withdrawals	-	-	-	0	0
Total (Conducted consultations and withdrawals)	-	-	-	1	1

Note 1: Prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers have been conducted since FY 2009.

Note 2: The numbers of prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers were counted on the basis of delivery dates of consultation documents to PMDA.

Note 3: Prior assessment consultations for drugs are conducted for the categories of quality, non-clinical: toxicity, non-clinical: pharmacology, non-clinical: pharmacokinetics, phase I study and phase II study.

- To achieve the target of meeting all the demands for clinical trial consultations 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 2010, PMDA provided a total of 434 consultations (including 44 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 70% of all consultations conducted. In FY 2010, the meeting records were finalized for 330 out of 346 consultations (95.4%) within 30 business days from the consultation.

- 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 Clinical Trial Consultations for Drugs by Review Category in FY 2010

Review category	Actual results												Total
	4	5	6	7	8	9	10	11	12	1	2	3	
Category 1 (Gastrointestinal drugs, etc.)	3	3	2	8	1	2	3	2	3	1	2	3	33
Category 6-2 (Hormone drugs)	4	2	2	3	4	8	2	4	5	2	4	2	42
Category 2 (Cardiovascular drugs)	2	3	3	8	5	2	3	7	3	3	4	2	45
Category 5 (Drugs for the urogenital system, etc.)	2	2	0	1	0	6	0	1	1	0	0	1	14
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	0	1	0	1
In vivo diagnostics	0	0	1	1	1	0	0	0	0	0	0	0	3
Category 3-1 (Central nervous system drugs, etc.)	4	1	2	4	4	1	1	2	5	7	5	4	40
Category 3-2 (Anesthetic drugs, etc.)	6	2	3	0	1	1	1	5	3	2	4	1	29
Category 4 (Antibacterial agents, etc.)	2	2	1	1	5	5	4	1	3	1	3	3	31
Category 6-1 (Respiratory tract drugs, etc.)	2	3	3	3	5	2	2	5	5	0	2	13	45
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Oncology drugs	9	3	2	6	3	5	7	6	7	3	4	7	62
Blood products	2	2	1	1	2	1	0	3	0	0	0	0	12
Bio-CMC	1	1	1	2	0	4	0	1	0	0	1	2	13
Biological products	1	0	2	1	1	1	2	3	2	1	1	1	16
Cell- and tissue-based products	0	0	0	0	0	0	0	1	0	0	0	2	3
[Re-listed] Prior assessment (pre-NDA review) for drugs	0	0	0	4	7	3	1	4	4	5	1	1	30
Pharmacogenomics/biomarkers	0	0	0	0	0	0	0	0	0	0	0	1	1
GLP/GCP compliance (for priority review)	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	38	24	23	39	32	38	25	41	37	20	31	42	390
Withdrawals	2	3	3	2	2	3	5	6	7	2	6	3	44
Grand Total	40	27	26	41	34	41	30	47	44	22	37	45	434

Note 1: A consultation covering several categories was counted in terms of its main category.
Note 2: Prior assessment consultations for drugs are conducted for the categories of quality, non-clinical: toxicity, non-clinical: pharmacology, non-clinical: pharmacokinetics, phase I study and phase II study.
Note 3: The numbers of prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers were counted on the basis of delivery dates of consultation documents to PMDA.
Note 4: Consultations on pharmacogenomics/biomarkers were conducted by the Omics Project Team.
Note 5: Consultations on GLP/GCP compliance were all conducted by the Office of Conformity Audit, regardless of category.

(v) Promotion of evaluation of new technologies

a. Use of external experts

- As PMDA is required to raise the scientific level of its guidance and review mainly on 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 relating to scientifically significant matters at occasions such as Expert Discussions for reviews and post-marketing safety measures.

(As of March 31, 2011, the number of commissioned experts is 1,024 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2010 was 175 (of which, 124 through document-based discussions; 51 through meetings).

- In order to examine the appropriate application of biomarkers and pharmacogenomics to drug development and challenges thereof, PMDA has conducted teleconference, etc. with experts of regulatory agencies in the EU and the US to promote information sharing.

b. Support to the development of national guidelines

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

- In order to study the effects of genetic factors of individual patients on the safety and efficacy of drugs so that the drugs can be administered to each patient in more appropriate conditions, there are expectations for the application of pharmacogenomics and biomarkers to drug development. However, there are many issues to be discussed because these technologies represent the state-of-the-art field. PMDA established the PMDA Omics Project (POP) that collected information from a scientific standpoint in relation to the application of biomarkers, etc. to the drug development, while working toward developing specific guidelines in cooperation with MHLW. In FY 2010, PMDA periodically held internal meetings and unofficial meetings with companies, etc. to exchange opinions on pharmacogenomics, biomarkers, etc.

c. Preliminary reviews on cell- and tissue-based products, gene therapy products, Cartagena Act, etc.

- PMDA conducts preliminary reviews on cell- and tissue-based products and gene therapy products before clinical trials as to whether the quality and safety conform to the guidelines.

Number of Applications for Preliminary Reviews and Number of Completed Applications

	FY 2006		FY 2007		FY 2008		FY 2009		FY 2010	
	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
Cell- and tissue-based products	1	0	2	2	1	0	2	2	0	1
Gene therapy products	1	0	0	2	1	0	0	2	1	1

- With regard to the use of genetically modified living organisms, preliminary reviews are conducted as to whether 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)” are made. PMDA set the target regulatory review time to be 6 months for approval of first-class use and 3 months for confirmation of second-class use, with the goal of achieving 50% (median) of applications for each class.

Review under the Cartagena Act (Median Regulatory Review Time)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
No. of preliminary reviews for first-class use Median review time	0 -	1 -	0 -	0 -	0 -
No. of preliminary reviews for second-class use Median review time	12 -	8 -	24 -	11 2.5 months	13 2.5 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. Improvement of the consultation system for drugs using the latest technologies

- For cell- and tissue-based product 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 development.

  In order to respond to these needs, PMDA started consultations on pharmacogenomics/biomarkers in FY 2009 and continued to conduct such consultations upon request.

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

- PMDA supported the consultation meetings on pharmaceutical regulatory affairs for the Super Special Consortia for development of state-of-the-art medicine. PMDA lent their support to the 4th meeting held on August 27, 2010 and the study meetings by category of the Super Special Consortia held on March 1 and 23, 2011.

  In addition, PMDA promptly deals with clinical trial consultations, etc. concerning topics addressed by the Super Special Consortia.

Over-the-counter drugs and generic drugs

- PMDA takes various measures to promote self-medication and wide use of generic drugs in public.

(i) Implementation of appropriate and prompt reviews

a. Implementation of consultations and reviews based on medical care needs

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

  Note: A total of 806 PMDA staff members participated in 266 domestic and international academic conferences and seminars.

b. Promotion of digitization in reviews

- See (i)-g [New drugs]

c. Development of Japanese Pharmacopoeia

- See (i)-i [New drugs]

d. 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, PMDA has not only discussed how to deal with individual products but also collected opinions from experts regarding desirable review methods as a whole. While taking into account these opinions, PMDA has been considering the enhancement and strengthening of the review system. PMDA has also made efforts to improve the expertise of reviewers through measures such as having reviewers actively participate in Expert Discussions and exchange opinions on reviews of Chinese herbal medicine products 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 generic drug applications, etc. submitted on or after April 1, 2004, and has conducted reviews toward achievement of these targets.

- In order to carry out review operations of generic drugs, etc. promptly and accurately, PMDA developed the “Procedures for Review of Generic Drugs,” “Procedures for Review of OTC Drugs,” “Procedures for Review of Insecticides/Rodenticides,” and “Procedures for Review of Quasi-drugs” as well as 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 2010).

- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2010 are as follows:

Targets

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

** By FY 2011, PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Number of Approved Generic Drugs, etc. and Median Regulatory Review Time

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Generic drugs	2,152	3,278	1,980	3,271	2,633
Of which: Number of approved applications filed in or after April 2004	2,029	3,228	1,960	3,245	2,590
Median review time (for the applications filed in or after April 2004)	4.0 months	4.5 months	5.3 months	7.5 months	6.9 months
OTC drugs	1,030	1,329	1,821	2,171	1,008
Of which: Number of approved applications filed in or after April 2004	923	1,309	1,807	2,166	1,007
Median review time (for the applications filed in or after April 2004)	6.3 months	4.0 months	3.5 months	4.6 months	4.0 months
Quasi-drugs	2,287	2,236	2,340	2,221	1,976
Of which: Number of approved applications filed in or after April 2004	2,275	2,230	2,339	2,220	1,976
Median review time (for the applications filed in or after April 2004)	5.5 months	5.2 months	5.0 months	4.8 months	5.2 months
Total	5,469	6,843	6,141	7,663	5,617
Of which: Number of approved applications filed in or after April 2004	5,227	6,767	6,106	7,631	5,573

Note 1: The medians for OTC drugs and quasi-drugs in FY 2007, FY 2008, FY 2009, and FY 2010 were calculated excluding data for 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 2006	2,631	2,152	173	2,465
	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
OTC drugs	FY 2006	1,236	1,030	181	2,232
	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	1,761
	FY 2010	1,092	1,008	133	1,712
Quasi-drugs	FY 2006	2,503	2,287	96	1,615
	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	1,824
	FY 2010	2,297	1,976	135	2,010

Note: Values in the Withdrawal etc. column include the number of products switched to other review categories during the review.

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

OTC drugs

New 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 2010	1	0	0	0	1	25	5	10	0	5	6	77	3	953	1,086
Approved in FY 2010	0	0	2	0	0	1	12	1	0	0	0	36	0	801	853

Category of application	Insecticides	Total
Filed in FY 2010	6	6
Approved in FY 2010	7	7

Former category of application	1	2	3	4-1	4-2	OTC test agents	Total
Approved in FY 2010	1	7	8	21	111	0	148

Quasi-drugs

Category of application	1,3	2	Total
Filed in FY 2010	96	2,201	2,297
Approved in FY 2010	34	1,942	1,976

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

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

Note 3: Each application belongs to the category for which it was filed.

Note 4: Each approval belongs to the category in which it was granted.

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 2010 were 6.9 months for generic drugs (target: 10 months), 4.0 months for OTC drugs (target: 8 months), and 5.2 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 2006	FY 2007	FY 2008	FY 2009	FY 2010
Generic drugs	628	1,135	601	1,004	1,040

- For generic drugs, PMDA conducted 1,040 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 implementation of clinical trial consultations

a. Improvement of pre-application consultations for generic drugs

- With regard to pre-application consultations for generic drugs, the Second Mid-term Plan stipulates that PMDA will establish a new consultation system within FY 2013 that is different from the existing simple consultation. In FY 2010, PMDA proceeded with the preparation of the consultation to be introduced on a trial basis in FY 2011, by examining the needs for content of consultations, consultation time, etc. through the Federation of Pharmaceutical Manufacturers' Associations of JAPAN.

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

- As pre-application consultations for OTC drugs, PMDA started to provide pre-application consultations for Switch OTC drugs, consultations on key points of clinical trial protocols, and consultations on the appropriateness of development of OTC drugs on a trial basis in June 2010. In addition, PMDA conducted questionnaire surveys, etc. among pharmaceutical companies that received these consultation services. PMDA intends to improve the consultation system by referring to the results of questionnaire surveys, and the opinions of industry associations, etc.

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

	FY 2010
Conducted consultations	23
Withdrawals	0
Total (conducted and withdrawn consultations)	23

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 Category in FY 2010

Consultation category	Conducted consultations	Withdrawals	Total (conducted and withdrawn consultations)
Pre-application consultations for Switch OTC drugs	0	0	0
Consultations on key points of clinical trial protocols	2	0	2
Consultations on appropriateness of development of OTC drugs	21	0	21
Total	23	0	23

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

- In FY 2010, for pre-application consultations for quasi-drugs, PMDA exchanged opinions with the Japan Cosmetic Industry Association (JCIA) regarding issues such as how to identify their demands for such consultations in future. PMDA intends to continue to exchange opinions with the JCIA, including opinions on the need for the consultation system.

Medical devices

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

(i) Implementation of appropriate and prompt reviews

a. Implementation structure for clinical trial consultations and reviews

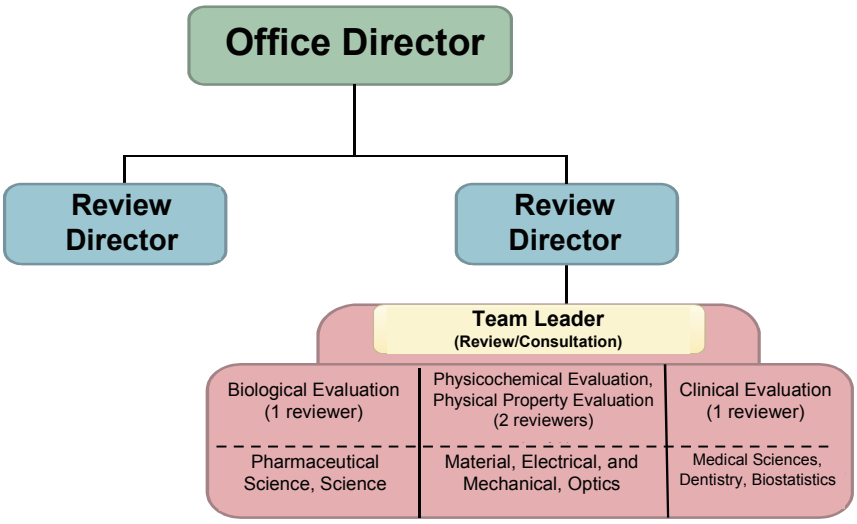
Actual Results of Reviews in FY 2010

Reviews:
Medical devices and *in vitro* diagnostics
(i) Number of Expert Discussions conducted: 51 (of which, 40 through document-based discussions and 11 through meetings)
(ii) Applications deliberated at the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 7
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 62 (of which, 39 for medical devices and 23 for *in vitro* diagnostics)

- Under the guidance of office directors and review directors, reviews of new medical devices were conducted in principle by review teams consisting of experts who have academic degrees in engineering, pharmacology, medicine, dentistry, veterinary medicine, statistics, etc. The review team is fundamentally comprised of team leader(s), and reviewers specialized in biological evaluations, physicochemical/physical property evaluations, and clinical evaluations.

Organization Chart for Reviews

Structure of a Review Team for New Medical Devices



- PMDA increased the medical device reviewers based on the “Action Program to Accelerate Reviews of Medical Devices,” and also reorganized the Office of Medical Devices into two offices: Office of Medical Devices I and Office of Medical Devices II in August 2009. Moreover, in July 2010, the Agency reinforced the review system by dividing Review Category 6, in which many products are filed for approval, into two categories.

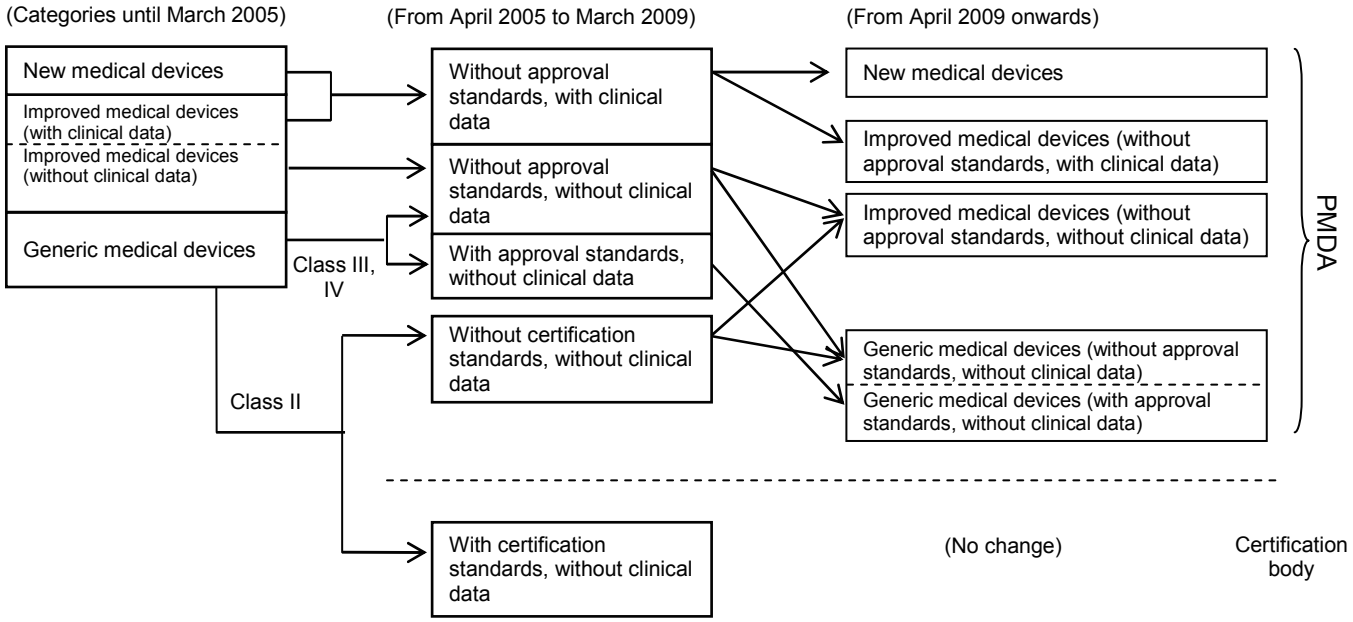
  In addition, in order to intensively process “product applications with prolonged time after filing of application,” which lead to overall poor performance for the time clock, the Agency created an application processing team with time limitation from August 2010 to March 2011, and processed such applications.

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

Review Categories Handled by the Office of Medical Devices

Name of office	Review Category	
Office of Medical Devices I	Category 3-1	Mainly for intervention devices in cerebral, cardiovascular, respiratory, and psychoneurologic (materials) areas
	Category 3-2	Mainly for non-intervention devices in cerebral, cardiovascular, respiratory, and psychoneurologic (materials) areas
	Category 4	Mainly for cerebral, cardiovascular, respiratory, psychoneurologic (mechanical) 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 Chief Reviewer and the Deputy Chief Reviewer 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 categories 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. Implementation of consultations and reviews based on medical care needs

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

  ** A total of 806 PMDA staff members participated in 266 academic conferences and seminars in and outside of Japan.*

- Efforts were made based on the results of the examination 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)" established in October 2006, and clinical trial consultations and reviews were carried out taking into account these examination results.

- For cell- and tissue-based products that are developed with state-of-the-art technology such as biomarkers 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 development.

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

c. Efforts to introduce the 3-track review system

- In order to implement the 3-track review system (which includes a track each for new medical devices, improved medical devices, and generic medical devices) from FY 2011 sequentially, PMDA introduced the 2-track review system (which includes a track for new medical devices/improved medical devices and a track for generic medical devices) in all categories in FY 2010.

d. Promotion of digitization in reviews

- See (i)-g [New drugs]

e. Standardization of review

- To provide basic considerations for reviewers, from the viewpoint of clarification of review standards, "Points to Consider in Preparing Applications for New Medical Devices, etc." prepared in FY 2008 was explained to relevant reviewers and has been used for reviews, etc.

- For new medical devices, PMDA revised the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices and improved medical device)," which was prepared in FY 2009, and released as "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices)" in February 2011 to ensure that the guidelines were thoroughly explained to the reviewers. For generic medical devices, PMDA prepared the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices" in FY 2009, and made efforts to ensure that the guidelines were thoroughly explained to the reviewers.

- With regard to the progress of reviews, etc., 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 had 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 for improvements in progress.

  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

- PMDA released guidance documents "Points to Consider in Preparing Applications for Generic Medical Devices" in March 2009 for generic medical devices and "Points to Consider in Preparing Applications for Improved Medical Devices" in January 2011 for improved medical devices. These guidance documents were explained to relevant reviewers and have been used for reviews, etc.

(ii) Introduction of new review systems

a. Introduction of prior assessment consultations

- To preliminarily evaluate the quality, efficacy and safety of drugs from the clinical trial consultation stage, PMDA started prior assessment consultations as a pilot scheme in October 2010.

b. Implementation of the short-term review system for approvals for specified partial changes

- Among 13 product applications filed in FY 2009 and 47 product applications filed in FY 2010, 48 were approved within 2 months of regulatory review time (excluding the period for GCP/GLP inspections).

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

- In order to support MHLW in developing approval standards for medical devices, the Committee on Medical Device Approval Standards held six meetings in FY 2010.

  The numbers of standards (established and revised) for approval and certification reported to MHLW in FY 2010 were as follows:

Reported in:	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
Approval standards	6	7	5	2	6	26
Certification standards	0	14	86	64	294	458
Review guidelines	0	1	2	6	0	9

- The number of standards established by MHLW in FY 2010 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	Total
Approval standards	0	17	8	10	-2*	5	3	41
Certification standards	363	9	24	0	17	68	274	755
Review guidelines	0	0	0	0	3	1	4	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 2010)

Medical device certification standards (274 established), medical device approval standards (3 established), review guidelines (4 established)	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 207 dated April 30, 2010	4 certification standards including the standard for stationary diagnostic X-ray generators
MHLW Ministerial Announcement No. 261 dated June 30, 2010	Standard for nuclear medicine workstations, etc.
MHLW Ministerial Announcement No. 354 dated September 27, 2010	80 certification standards including the standard for electronic stethoscopes
MHLW Ministerial Announcement No. 97 dated March 31, 2011	186 certification standards including the standard for nuclear medicine diagnostic ring-type SPECT system
PFSB Notification No. 0331-27 dated March 31, 2011	Approval standard for catheter introducers
PFSB Notification No. 0331-30 dated March 31, 2011	Approval standard for shunts for treatment of hydrocephalus
PFSB Notification No. 0331-33 dated March 31, 2011	Approval standard for catheters for temporary vascular access
PFSB/ELD/OMDE Notification No.0730-1 dated July 30, 2010	Review guideline for compression hip screws (CHS) for internal fixation
PFSB/ELD/OMDE Notification No.0730-4 dated July 30, 2010	Review guideline for cables for internal fixation
PFSB/ELD/OMDE Notification No.0730-7 dated July 30, 2010	Review guideline for pins for internal fixation
PFSB/ELD/OMDE Notification No.0730-10 dated July 30, 2010	Review guideline for screws/plates for internal fixation

- PMDA provides the latest information on how each certification standard and approval standard is interrelated with JIS, ISO/IEC as their components, MHLW Notifications, and Japanese Medical Device Nomenclature (JMDN), etc., on the website dedicated to the information service on standards for medical devices. In addition, PMDA continued to provide information on the status of establishments/revisions of JIS standards for medical devices (related to revisions of certification standards, etc.), and also has been continuously providing information to overseas users with the English version of the website regarding medical devices. The information on the website has been updated periodically, at least twice a month.

- PMDA provided advice on individual products through simple consultations in order to clarify the scope of changes for which applications for partial changes are not required, and minor change notifications are required, based on “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 notifications, etc. issued by MHLW.

- PMDA considered issues such as clarification of the scope of one product, at the working group of the working-level joint task force comprised of MHLW, PMDA, and the industry, and rendered assistance in the issuance of the notification of the partial revision of the guidance document “Points to Consider in Filing Applications for Medical Devices” (PFSB/ELD/OMDE Notification No.1224007 dated December 24, 2010).

d. Introduction of the equivalence review method for generic medical devices

- PMDA introduced the equivalence review method for the generic medical devices filed in FY 2010 based on “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 274 certification standards were established in FY 2010.

(iii) Efforts to solve the device lag

- The targets for total review time, regulatory review time, and applicant’s time for medical devices 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 new medical devices (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]) for which application was made.

- To ensure consistency among review teams and to review new medical device applications promptly and appropriately, PMDA developed SOPs relating to various operations, which describe reviews and related procedures for each category 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.

- The status of reviews for medical devices in FY 2010 is shown below:

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

Targets

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

** PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

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

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	14.2	15.7	28.8	13.9	15.1
Regulatory review time [months]	5.7	8.6	5.8	6.0	5.3
Applicant's time [months]	-	-	-	7.7	10.7
Number of approved applications	1	4	4	3	3

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.

- Reviews of 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) were conducted on a priority basis as priority review products. In FY 2010, 3 products (all were new medical devices) were approved.

  There were three requests for designation for priority review as a medical device regarded as having particularly high medical need. One of the three requests for priority review was withdrawn, and the remaining two requests are currently under consideration.

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

Targets

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

** PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

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

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	15.7	15.1	14.4	11.0	16.5
Regulatory review time [months]	3.2	7.7	9.8	6.8	7.1
Applicant's time [months]	-	-	-	7.1	8.2
Number of approved applications	14	19	12	33	15

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 2010, the median total review time for priority review products was 15.1 months, showing achievement of the target.

  The median regulatory review time was 5.3 months, and the median applicant's time was 10.7 months.

- In FY 2010, the median total review time for standard review products was 16.5 months, showing achievement of the target.

  The median regulatory review time was 7.1 months, and the median applicant's time was 8.2 months.

- For the submitted applications, PMDA processed reviews taking the target review time sufficiently into consideration.

- PMDA has called for withdrawal of applications that were considered to be difficult to approve due to a lack of response from applicants to inquiries made by PMDA. The Agency processed 132 applications, which were submitted in or before March 2004, through approvals or withdrawals by FY 2010 and completed processing all these applications.

- The number of product applications under review at the end of FY 2010 was 44 (including 2 orphan medical devices and 2 priority review products excluding orphan medical devices).

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 (0)	78(3)	0 [-3]
FY 2004	56	35 (0)	20(2)	1 [-2]
FY 2005	7	7	0	0
FY 2006	23	19 (1)	3(0)	1 [-1]
FY 2007	37	29 (1)	6(2)	2 [-3]
FY 2008	32	26 (5)	2(2)	4 [-7]
FY 2009	24	12 (7)	1(0)	11 [-7]
FY 2010	28	3 (3)	0 (0)	25 [25]
Total	339	185 (17)	110 (9)	44 [2]

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 2010 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2009.

Number of Applications Processed and Time Spent in Each Review Process

	Review process	1. From receipt of applications to first consultation	2. From first consultation to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2010	Number of processed applications	14	10	10	18
	Median total review time	38.0 days	311.0 days	149.0 days	33.0 days

Note 1: The duration shown in each review process are the median of the total review time (the sum of reviewers' and applicants' time clocks) 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 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 (medical devices for which clinical trial results are required).

Targets

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

** PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Review Times for Improved Medical Devices (with Clinical Data)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	-	-	-	17.2	15.5
Regulatory review time [months]	-	-	-	10.4	7.6
Applicant's time [months]	-	-	-	6.6	7.6
Number of approved applications	—	—	—	30	40

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 40 improved medical devices (with clinical data) approved in FY 2010, and the median total review time was 15.5 months, showing achievement of the target.

  The median regulatory review time was 7.6 months, and the median applicant's time was 7.6 months.

- The review status of improved medical devices (with clinical data) is as follows:

Review Status of Improved Medical Devices (with Clinical Data) Applications Filed in FY 2010

Improved medical devices (with clinical data) Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	34	24 (23)	0 (0)	10 [-23]
FY 2010	34	2 (2)	0 (0)	32 [32]
Total	68	26 (25)	0 (0)	42 [9]

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 2010 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2009.

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

- Improved medical devices (without clinical data) refer to 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 (medical devices for which clinical trial results are not required).

Targets

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

** PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Review Times for Improved Medical Devices (without Clinical Data)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	-	-	-	13.2	14.5
Regulatory review time [months]	-	-	-	8.5	8.0
Applicant's time [months]	-	-	-	3.9	6.2
Number of approved applications	-	-	-	158	182

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 2010 was 182, and the median total review time for these applications was 14.5 months, showing non-achievement of the target.

  The median regulatory review time was 8.0 months, and the median applicant's time was 6.2 months.

- The review status of improved medical devices (without clinical data) is as follows:

Review Status of Improved Medical Devices (without Clinical Data) Applications Filed in FY 2010

Improved medical devices (without clinical data) Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	137	86 (64)	4 (4)	47 [-68]
FY 2010	165	25 (25)	2 (2)	138 [138]
Total	302	111 (89)	6 (6)	185 [70]

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 2010 (included in values on their left).
Note 4: Values in brackets indicate difference from the status reported in FY 2009.

e. Review times for generic medical devices

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

Targets

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

** PMDA is aiming to achieve the targets determined in the table for 50% (median) of applications filed.*

Approval Status and Review Times for Generic Medical Devices

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total review time [months]	-	-	-	12.9	11.0
Regulatory review time [months]	-	-	-	5.9	5.1
Applicant's time [months]	-	-	-	3.6	4.7
Number of approved applications	-	-	-	1,797	1,391

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 2010 was 1,391, and the median total review time was 11.0 months, showing non-achievement of the target.

  The median regulatory review time was 5.1 months, and the median applicant's time was 4.7 months.

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

Review Status of Generic Medical Devices Applications Filed in FY 2010

Generic medical devices Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	1,126 (-1)	891 (440)	29 (19)	206 [-459]
FY 2010	1,021	423 (423)	15 (15)	583 [583]
Total	2,147	1,314 (863)	44 (34)	789 [124]

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 not for a medical device, was subtracted from the number of applications in FY 2009.
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 2010 (included in values on their left).
Note 5: Values in brackets indicate difference from the status reported in FY 2009.

- For improved medical devices (without clinical data) and generic medical devices, the target for total review time could not be achieved.

  The target for FY 2010 could not be achieved probably because the applications processed in this fiscal year included many older applications filed in past years. An analysis of the cause of prolonged review of such applications revealed that it resulted from waiting time for responses due to insufficient data, etc. and repeated inquiries and responses. Moreover, there seemed to be chronic prolongation of waiting time for reviews due to insufficient reviewers. Therefore, in FY 2011, PMDA will further increase reviewers and introduce the 3-track review system for enhancement of its review system. PMDA also plans to examine measures for resolving the cause of review prolongation at the meeting of the Action Program Review Committee, etc. while seeking cooperation of the industry.

  Meanwhile, the total number of approvals in both categories was 1,334, showing an increase compared with 1,275 corresponding approvals in FY 2009. The median total review time for generic medical devices was 8.9 months, the median regulatory review time was 3.9 months, and the median applicant's time was 3.5 months (excluding applications for transition of licensed products to a new category due to the change in regulations as an exceptional measure).

(iv) Efficient implementation of clinical trial consultations

a. Implementation of priority consultations

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

b. Acceleration of the procedure for clinical trial consultations

- To accelerate clinical trial consultations, PMDA has shortened times such as the duration from request for clinical trial consultation to consultation or to the first meeting of a priority consultation by establishment of the procedures and appropriate improvements in operation.

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

Number of Clinical Trial Consultations for Medical Devices

		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC		42	72	76	110	113
	(Medical devices)	39	71	74	104	106
	(*In vitro* diagnostics)	3	1	2	6	7
Withdrawals		0	0	2	1	1
	(Medical devices)	0	0	2	1	1
	(*In vitro* diagnostics)	0	0	0	0	0
Total (Conducted consultations and withdrawals)		42	72	78	111	114
	(Medical devices)	39	71	76	105	107
	(*In vitro* diagnostics)	3	1	2	6	7

Number of Prior Assessment Consultations for Medical Devices and Prior Assessment Consultations for In Vitro Diagnostics Conducted

		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC		-	-	-	-	2
	(Medical devices)	-	-	-	-	2
	(*In vitro* diagnostics)	-	-	-	-	0
Withdrawals		-	-	-	-	0
	(Medical devices)	-	-	-	-	0
	(*In vitro* diagnostics)	-	-	-	-	0
Total (Conducted consultations and withdrawals)		-	-	-	-	2
	(Medical devices)	-	-	-	-	2
	(*In vitro* diagnostics)	-	-	-	-	0

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Conducted CTC	-	-	-	0	0
Withdrawals	-	-	-	0	0
Total (Conducted consultations and withdrawals)	-	-	-	0	0

Note 1: The values are based on the numbers of submitted written requests for arrangement of CTC schedule for each fiscal year.

Note 2: Consultations on pharmacogenomics/biomarkers have been conducted since FY 2009.

Note 3: Prior assessment consultations for medical devices and prior assessment consultations for in vitro diagnostics have been conducted since FY 2010.

Note 4: 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 5: Prior assessment consultations for medical devices and prior assessment consultations for in vitro diagnostics are conducted for the categories of quality, non-clinical and clinical.

- A total of 114 clinical trial consultations (including 1 withdrawn consultation) were carried out. Basically, PMDA responded to all of the consultations requested. The goal is to be able to deal with all consultations requested, after developing the yearly capability to process 200 consultations by FY 2013.

- PMDA aimed to complete the process from a consultation to finalization of meeting records within 30 business days for 60% of all consultations conducted. In FY 2010, the meeting records were finalized for 86 out of 113 consultations (76.1%) within 30 business days from the consultation.

Number of Clinical Trial Consultations for Medical Devices by Category in FY 2010

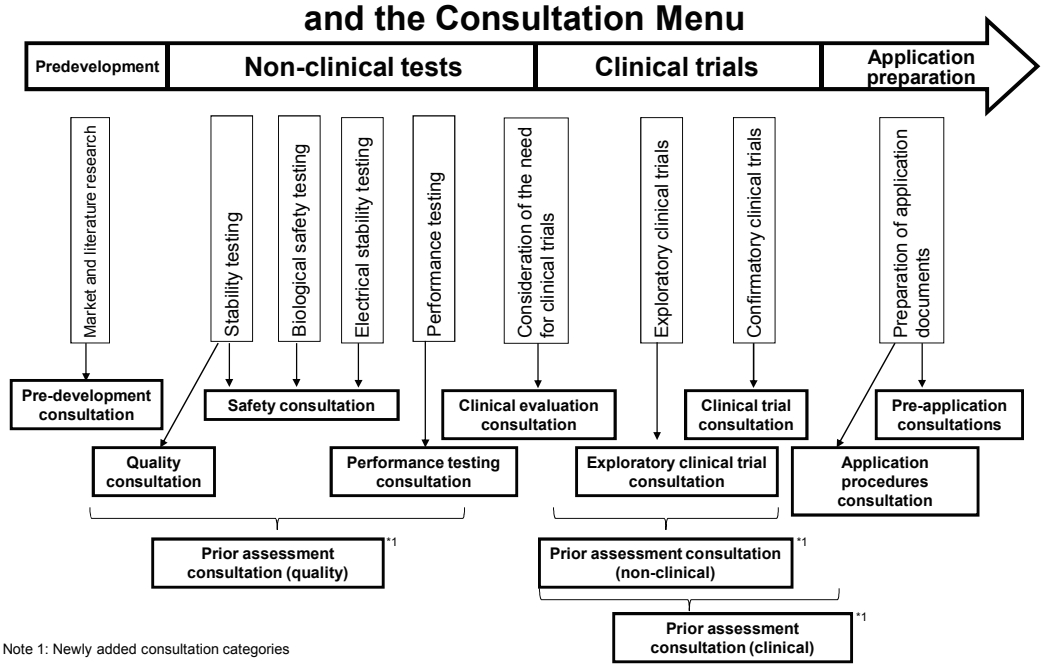
Consultation category	Number of clinical trial consultations conducted	Withdrawals	Total (Conducted consultations and withdrawals)
Pre-development consultation for medical devices	26	0	26
Safety consultation for medical devices (excluding biological medical devices)	4	1	5
Quality consultation for medical devices (excluding biological medical devices)	4	0	4
Safety consultation for biological medical devices	0	0	0
Quality consultation for biological medical devices	1	0	1
Performance testing consultation for medical devices	1	0	1
Clinical evaluation consultation for medical devices	11	0	11
Exploratory clinical trial consultation for medical devices	0	0	0
Clinical trial consultation for medical devices	20	0	20
Pre-application consultation for medical devices	19	0	19
Application procedure consultation for medical devices	16	0	16
Additional consultation for medical devices	2	0	2
Consultation on GLP/GCP compliance for medical devices	0	0	0
Prior assessment consultation for medical devices (quality)	0	0	0
Prior assessment consultation for medical devices (non-clinical)	2	0	2
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 GLP/GCP compliance for *in vitro* diagnostics	0	0	0
Clinical evaluation consultation for *in vitro* diagnostics	0	0	0
Clinical performance study consultation for *in vitro* diagnostics	3	0	3
Pre-application consultation for *in vitro* diagnostics	4	0	4
Application procedure consultation for *in vitro* diagnostics	0	0	0
Additional consultation for *in vitro* diagnostics	0	0	0
Prior assessment consultation for *in vitro* diagnostics (quality)	0	0	0
Prior assessment consultation for *in vitro* diagnostics (non-clinical)	0	0	0
Prior assessment consultation for *in vitro* diagnostics (clinical)	0	0	0
Consultation on preparation of documents for cell- and tissue-based products	0	0	0
Consultation on pharmacogenomics/biomarkers	0	0	0
Total	113	1	114

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.

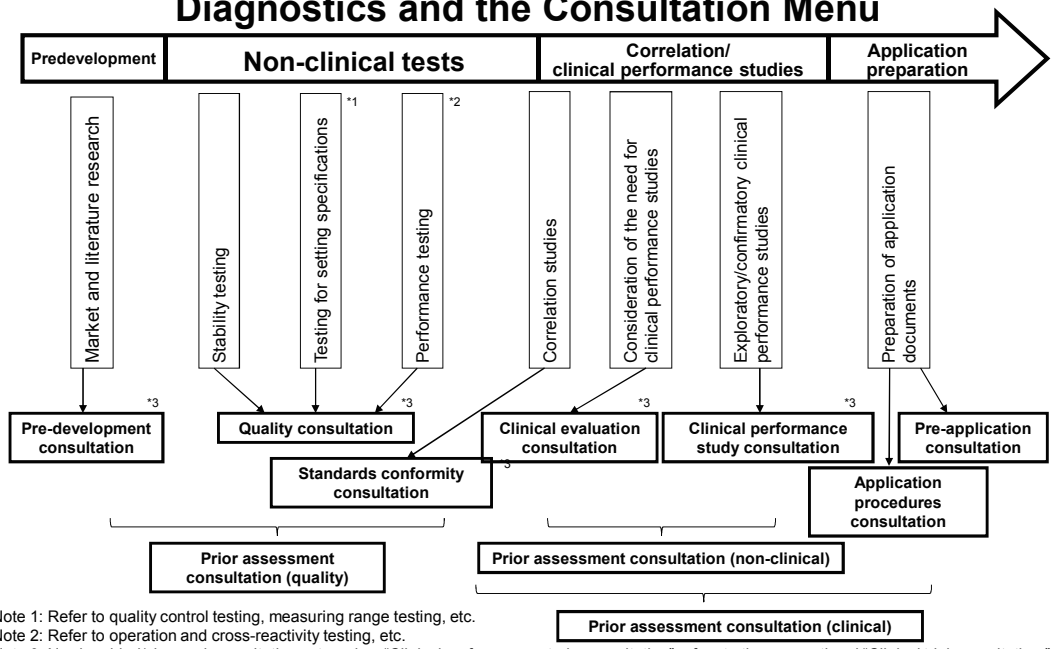
- In FY 2010, PMDA introduced additional consultation categories for *in vitro* diagnostics and started operations with the expanded consultation category. PMDA also started prior assessment consultations as a pilot scheme in October 2010.

Relationship between the Development of Medical Devices and the Consultation Menu



Note 1: Newly added consultation categories

Relationship between the Development of *In Vitro* Diagnostics and the Consultation Menu



Note 1: Refer to quality control testing, measuring range testing, etc.
Note 2: Refer to operation and cross-reactivity testing, etc.
Note 3: Newly added/changed consultation categories. "Clinical performance study consultation" refers to the conventional "Clinical trial consultation."

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. Use of external experts

- See (v)-a [New drugs]

b. Support to the development of national guidelines

- See (v)-b [New drugs]

- PMDA cooperated with the MHLW to develop "Points to Consider for the Assessment of Next-generation Medical Devices (articular cartilage regeneration, neurological function repair equipment and custom-made implants of orthopedic bone fixation materials) (PFSB/ELD/OMDE Notification No. 1215-1 dated December 15, 2010)," and also tried to thoroughly disseminate the notification. PMDA also assisted the MHLW in the development of points to consider for the assessment of regenerative medical techniques (periodontal membrane), implantable materials (custom-made joint prosthesis), computer-assisted diagnosis systems and personalized medical diagnostic devices (DNA chips).

c. Preliminary reviews on cell- and tissue-based products, gene therapy products, Cartagena Act, etc.

- See (v)-c [New drugs]

d. Improvement of the consultation system for medical devices using the latest technologies

- There is a very high need for advice on product development and regulatory submission for cell- and tissue-based products that are developed with state-of-the-art technology such as

regenerative medicine, or for development using new biomarkers, as there are only a few precedents for such types of development.

In order to respond to these needs, PMDA started consultations on pharmacogenomics/biomarkers in FY 2009 and continued to conduct such consultations upon request.

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

- See (v)-e [New drugs]

Inspections

- With regard to drugs and medical devices, PMDA has conducted a full range of inspections and take measures to promote proper conduct of tests and clinical trials related to product applications for approval, secure the reliability of application documents, and properly maintain and manage the manufacturing process and the quality management system.

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

- PMDA conducted efficient document-based and on-site inspections and data integrity assessment concerning the studies and data included in the submitted 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.

- Although a standard administrative processing time for GLP/GCP/GPSP inspections has not been set, PMDA worked hard to make sure that the review time for relevant products was not affected.

a. Promotion of document-based inspection on sites

- As part of document-based inspections/data integrity assessment for new drugs, PMDA introduced a method in FY 2009 whereby its staff members visit companies and conduct document-based inspection. In FY 2010, 92 inspections (85.2%) were conducted based on this method out of 108 inspections (on the basis of the number of active ingredients).

b. Introduction of the GCP system inspection

- PMDA conducted pilot inspections based on an EDC system check list (draft) which was prepared as a part of the GCP system inspection, and also conducted a questionnaire survey on the EDC system check list (draft).

c. Improvement of the efficiency of GLP/GCP/GPSP inspections for medical devices

- In order to improve the efficiency of document-based inspections/data integrity assessment for non-clinical tests of medical devices, "Procedures for Implementing Document-based Inspections/Data Integrity Assessment of Submitted Data of Non-Clinical Tests of Medical Devices" (PMDA Notification No. 0730027 of the Chief Executive, PMDA, dated July 30, 2010) and conducted inspections in accordance with this notification.

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

- PMDA has conducted 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 2010, the number of completed assessments was 135 for new drugs and 3 for new medical devices.

- PMDA has conducted 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.

  In FY 2010, there were no products subject to data integrity assessment relating to re-evaluation of oral prescription drugs (re-evaluations for quality).

Numbers of Conducted GLP/GCP/GPSP Inspections and Data Integrity Assessment

		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Document-based inspections/data integrity assessment		426	774	942	1,136	1,319
	New drugs	251	234	293	246	251
	Medical devices	175	540	649	890	1,068
GCP inspections		149	132	198	175	171
	New drugs	137	122	182	164	158
	Generic drugs	12	9	15	10	10
	Medical devices	0	1	1	1	3
Document-based inspections/data integrity assessment for re-examination		123	119	83	66	138
	New drugs	123	119	83	66	135
	New medical devices	—	—	—	—	3
GPSP inspections (new drugs)		103	107	79	65	135
Data integrity assessment for re-evaluation		145	31	—	—	—
GLP inspections		31	27	43	26	30
	Drugs	23	23	32	18	26
	Medical devices	8	4	11	8	4

Note 1: The numbers of document-based inspections/data integrity assessment (excluding medical devices), GCP inspections (excluding medical devices), document-based inspections/data integrity assessment for re-examination (excluding medical devices), GPSP inspections, data integrity assessment for re-evaluation and GLP inspections represent numbers of products for which inspection was completed. The numbers of document-based inspections/data integrity assessment (medical devices), GCP inspections (medical devices) and document-based inspections/data integrity assessment for re-examination (medical devices) represent numbers of products for which inspection and review was completed.

Note 2: In the row of GPSP inspections, numbers of GPMSP inspections are shown up to FY 2008 and numbers of GPMSP inspections or GPSP inspections are shown from FY 2009.

(iii) Efficient implementation of GMP/QMS inspections

a. Consideration of efficient 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 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 43 as of April 1, 2010. At the same time, PMDA has promoted training for GMP/QMS inspectors, 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 times of GMP/QMS inspections in FY 2010 are shown below:

GMP/QMS Inspections Conducted under the Revised Pharmaceutical Affairs Act

	FY 2006				FY 2007			
	Requested	Completed	Withdrawn	In progress	Requested	Completed	Withdrawn	In progress
Drugs*	1,039	783 (180)	24	381	1,011	893 (233)	55	444
In vitro diagnostics	63	32 (4)	1	43	85	84 (1)	0	44
Quasi-drugs	0	5 (0)	0	0	3	0 (0)	0	3
Medical devices	638	300 (20)	29	378	1,006	1,021 (12)	15	348
Total	1,740	1,120 (204)	54	802	2,105	1,998 (246)	70	839

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

	FY 2010			
	Requested	Completed	Withdrawn	In progress
Drugs*	1,159	1,324 (131)	120	684
In vitro diagnostics	66	81 (0)	2	19
Quasi-drugs	1	0 (0)	1	2
Medical devices	896	944 (54)	40	149
Total	2,122	2,349 (185)	163	854

** Excluding in vitro diagnostics.*

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

- The administrative processing times of GMP/QMS inspections in FY 2010 are shown below:

Median Processing Time of GMP/QMS Inspections under the Revised Pharmaceutical Affairs Act

	FY 2006		FY 2007		FY 2008	
	Total processing time	PMDA processing time	Total processing time	PMDA processing time	Total processing time	PMDA processing time
Drugs*	161 days	117 days	170 days	111 days	155 days	100 days
In vitro diagnostics	149 days	100 days	158 days	88 days	117 days	46 days
Quasi-drugs	142 days	72 days	-	-	156 days	29 days
Medical devices	161 days	110 days	157 days	88 days	131 days	59 days
	FY 2009		FY 2010			
	Total processing time	PMDA processing time	Total processing time	PMDA processing time		
Drugs*	162 days	91 days	118 days	63 days		
In vitro diagnostics	110 days	56 days	117 days	62 days		
Quasi-drugs	154 days	108 days	-	-		
Medical devices	142 days	56 days	145 days	69 days		

** Excluding in vitro diagnostics.*

- The processing status of inspections of manufacturing facilities conducted in FY 2010 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 2006		FY 2007		FY 2008		FY 2009		FY 2010	
Drugs*	30	(23)	16	(14)	8	(6)	40	(25)	20	(19)
In vitro diagnostics	6	(6)	2	(2)	2	(2)	4	(2)	1	(1)
Medical devices	1	(0)	0	(0)	1	(1)	2	(1)	3	(3)
Total	37	(29)	18	(16)	11	(9)	46	(28)	24	(23)

** 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 2010 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs*	11	27	13	12	6
In vitro diagnostics	0	1	1	3	2
Medical devices	0	2	0	0	1

** Excluding in vitro diagnostics.*

• PMDA conducts simple consultations on GMP/QMS inspections. The number of simple consultations on GMP/QMS inspections conducted in FY 2010 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2007	FY 2008	FY 2009	FY 2010
Drugs*	28	44	39	36
In vitro diagnostics	3	1	1	0
Quasi-drugs	0	0	0	1
Medical devices	10	17	17	6
Total	41	62	57	43

** Excluding in vitro diagnostics.*

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

• The actual performance of on-site inspections that were initiated in FY 2005 is shown below:

On-site Inspections of Overseas 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

Note: FY 2006: France, Netherlands, Ireland, Denmark, Finland, Austria, USA, South Korea, Indonesia, and South Africa
FY 2007: France, UK, Denmark, Spain, Ireland, Belgium, Italy, Netherlands, USA (including Puerto Rico), China, Singapore, and India
FY 2008: France, Denmark, Sweden, Spain, Ireland, UK, Netherlands, Belgium, Italy, Austria, Germany, Romania, Slovenia, USA (including Puerto Rico), Canada, Mexico, Argentina, China, South Korea, Taiwan, Singapore and India
FY 2009: France, Denmark, Spain, Ireland, UK, Netherlands, Belgium, Italy, Austria, Finland, Germany, Slovenia, USA (including Puerto Rico), Canada, China, South Korea, Taiwan, Thailand, India, and New Zealand
FY 2010: France, Ireland, Belgium, Italy, Portugal, Turkey, Canada, USA (including Puerto Rico), China, South Korea, Taiwan, India, and Vietnam

On-site Inspections of Overseas 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

Note: FY 2006: Ireland, Switzerland, and USA (including Puerto Rico)
FY 2007: France and USA (including Puerto Rico)
FY 2008: Ireland, Italy, UK, Netherlands, Switzerland, Spain, France, USA and Mexico
FY 2009: Switzerland, France, Denmark, USA, Brazil, China, and Singapore
FY 2010: Ireland, Italy, Netherlands, South Korea, France, and USA (including Puerto Rico)

- The processing status of inspections of manufacturing facilities conducted in FY 2010 at overseas 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 Overseas Manufacturing Sites

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs*	614	387	294	390	230
In vitro diagnostics	85	69	69	40	27
Quasi-drugs	73	57	39	41	26
Medical devices	971	1,682	1,191	910	677
Total	1,743	2,195	1,593	1,381	960

** 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 overseas manufacturers, etc., under instructions from MHLW. The number of for-cause inspections conducted in FY 2010 is shown below:

Number of For-cause Inspections (Overseas Manufacturing Sites)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs*	3	5	2	1	1
In vitro diagnostics	0	0	0	0	0
Medical devices	2	0	1	0	4
Total	5	5	3	1	5

** Excluding in vitro diagnostics.*

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

Region	Country	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
Europe	France	1	4	6	5	6	1	23
	Denmark	0	2	3	2	2	0	9
	Ireland	1	2	2	5	3	2	15
	UK	0	0	4	1	3	0	8
	Netherlands	0	3	1	1	5	0	10
	Spain	0	0	3	1	1	0	5
	Italy	0	0	2	5	3	2	12
	Belgium	0	0	1	2	4	3	10
	Austria	0	1	0	2	2	0	5
	Finland	0	1	0	0	2	0	3
	Germany	0	0	0	3	7	0	10
	Sweden	0	0	0	1	0	0	1
	Romania	0	0	0	1	0	0	1
	Slovenia	0	0	0	2	1	0	3
	Portugal	0	0	0	0	0	3	3
	Turkey	0	0	0	0	0	1	1
	Subtotal	2	13	22	31	39	12	119
North, Central and South America	USA	6	20	22	14	18	23	103
	Canada	1	0	0	2	2	1	6
	Mexico	0	0	0	1	0	0	1
	Bahamas	1	0	0	0	0	0	1
	Argentina	0	0	0	2	0	0	2
	Subtotal	8	20	22	19	20	24	113
Asia	China	0	0	5	11	25	10	51
	India	1	0	1	12	4	7	25
	Singapore	0	0	2	4	0	0	6
	South Korea	1	1	0	3	9	10	24
	Indonesia	0	1	0	0	0	0	1
	Taiwan	0	0	0	2	6	1	9
	Thailand	0	0	0	0	2	0	2
	Vietnam	0	0	0	0	0	1	1
	New Zealand	0	0	0	0	1	0	1
	Subtotal	2	2	8	32	47	29	120
Africa	South Africa	0	1	0	0	0	0	1
	Subtotal	0	1	0	0	0	0	1
Grand Total		12	36	52	82	106	65	353

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.

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

Region	Country	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Total
Europe	Ireland	0	3	0	6	0	4	13
	UK	0	0	0	1	0	0	1
	Italy	0	0	0	2	0	2	4
	Netherlands	0	0	0	1	0	1	2
	Switzerland	1	2	0	1	1	0	5
	Spain	0	0	0	1	0	0	1
	France	0	0	1	1	1	1	4
	Denmark	0	0	0	0	1	0	1
	Subtotal	1	5	1	13	3	8	31
North, Central and South America	USA	1	10	10	16	27	19	83
	Mexico	0	0	0	1	0	0	1
	Brazil	0	0	0	0	1	0	1
	Subtotal	1	10	10	17	28	19	85
Asia	China	0	0	0	0	3	0	3
	South Korea	0	0	0	0	0	1	1
	Singapore	0	0	0	0	2	0	2
	Subtotal	0	0	0	0	5	1	6
Grand Total		2	15	11	30	36	28	122

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, periodic meetings (once a month with the offices of new drugs) are conducted for the participation of reviewers in GMP inspections as well as for sharing the progress status of reviews for the timely implementation of GMP inspections.

- For medical devices, regarding applications for Class IV medical devices such as high-risk cell- and tissue-derived medical devices and pacemakers, QMS inspectors and reviewers collaborate with each other 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, for which PMDA is making efforts to provide thorough progress management 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.

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

- In October 2010, PMDA conducted a training program including practical work for medical devices such as pacemakers, biological heart valves, and catheters for placing transvascular stents. From the end of November 2010 to the beginning of December 2010, PMDA conducted a practical training program using orthopedic medical devices.

  In addition, the Agency provided relevant reviewers with other opportunities for learning by using actual devices, and also conducted a training program including practical work at university laboratories studying medical devices, in order to reinforce the training curriculum.

  The Agency also conducted a training program (adverse drug reactions study meeting; pharmacoepidemiology) for safety measures staff in collaboration with the safety division.

c. Lectures and guidance given by skilled experts

- In order to have the staff acquire education and broad perspectives required for reviews and safety measures, PMDA invited domestic and overseas experts to provide special training lectures (24 times), special training sessions on regulatory science (11 times), and training on regulations such as the Pharmaceutical Affairs Act (once).

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 GMS/QMS joint simulated inspection training program provided by MHLW, a workshop on sterilization validation of medical devices, etc.

e. Improvement of training in clinical practice

- In order to enable planning of safety measures in line with the actual medical practice, PMDA dispatched its employees to three medical institutions to do practical training as pharmacists at hospitals.

f. Visits to manufacturing facilities

- As part of learning about manufacturing plants, etc., PMDA conducted visits to facilities (6 manufacturing plants of drugs; 3 manufacturing plants of medical devices, etc.; 1 university laboratory; 1 other laboratory).

(ii) Promotion of exchanges 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 schools of medicine of universities. In FY 2010, in addition to the existing 2 partner universities, University of Tsukuba (Graduate School of Comprehensive Human Sciences) and Yokohama City University (Graduate School of Medicine), PMDA concluded a joint graduate school agreement with 4 universities: 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). In FY 2011, PMDA will accept one graduate student from Gifu Pharmaceutical University as a pre-doctoral fellow to provide research guidance.

- In order to facilitate personnel exchange with National Research Centers for Advanced and Specialized Medical Care, national hospitals, universities, etc., and to secure human resources for clinical area, PMDA explains its work to universities, national hospitals, etc.

- As a part of efforts to promote the diffusion of regulatory science, PMDA makes arrangement as needed when there is a request from universities, etc. for PMDA staff to give lectures (26 universities, 88 lectures).

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

- In association with acceptance of students from graduate schools of the partner university, PMDA developed internal rules in FY 2009, and decided to accept one student on April 1, 2011.

(iii) Efforts to integrate pharmacogenomics into regulatory activities

a. Support to the development of evaluation guidelines

- To facilitate appropriate evaluation of drugs using Omics technologies, biomarkers and other technologies, PMDA voluntarily prepared the Japanese translation of E16 guideline "Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions," which was agreed at the ICH, and contributed to issuance of the MHLW notification (January 2011).

- PMDA also proposed the need for developing basic principles on clinical trials using pharmacogenomics, and had discussions for preparation of the concept.

b. Contribution to establishment of internationally harmonized methods

- At the ICH, PMDA worked with the EU and US agencies to develop E16 guideline "Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions." The final version of the guideline was agreed in August 2010.

- PMDA has held a symposium on biologics each year for forming an international common basis for evaluation of the quality, efficacy and safety of biologics. In August 2010, the "5th

PMDA International Symposium on Biologics" was held with the theme of regenerative medicine by inviting speakers from the EU and US regulatory agencies, etc., and activities and trends in each country were discussed.

(iv) Promotion of appropriate clinical trials

- PMDA conducted consultations for medical institutions, which were subjected to on-site inspection, on issues related to GCP after completion of the inspection. PMDA also made an effort to improve the explanation of case examples by highlighting points to consider in conducting clinical trials through the PMDA website. In order to promote understanding regarding GCP, PMDA held GCP Workshops in Tokyo and Osaka for drug development and regulatory affairs personnel, auditors of pharmaceutical companies, and site management organizations (SMOs) as well as healthcare professionals. In addition, PMDA staff gave lectures at academic conferences and on other occasions where healthcare professionals gathered.

Number of GCP Workshop Participants

Place	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Tokyo	1,303	1,212	1,338	1,165	1,048
Osaka	454	495	543	461	455
Total	1,757	1,707	1,881	1,626	1,503

- PMDA increased the number of GCP on-site inspections at medical institutions while giving consideration to the allocation of PMDA staff at the office in charge.

- With the introduction of new inspection methods such as document-based inspections at sponsor sites, PMDA further promoted the coordination between GCP document-based and on-site inspections.

- To improve the quality of clinical trials in Japan, PMDA tried to educate healthcare professionals and patients about appropriate clinical trials and share further information, through measures such as posting of examples of frequently pointed-out findings on its website, taking into consideration the results of field research at medical institutions, etc.

- PMDA implemented Training for Clinical Research Coordinators (Beginner training - lectures from August to September 2010 and practical training from September 2010 to February 2011; Advanced training - lectures from November 2010 to January 2011; Local data manager training - lectures and practical training in September 2010) to pharmacists and nurses from medical institutions, for the purpose of contributing to the improvement of clinical trial systems at medical institutions from which trainees are dispatched.

Trainees in FY 2010

Beginner training	61
Advanced training	66
Local data manager training	46

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

a. Improvement of provision of information

- In promoting appropriate 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, etc., on the Medical Product Information page of its website, in collaboration with MHLW.

- PMDA cooperated with MHLW to develop Notifications (draft), etc. in relation to the release of re-examination reports, and also 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 2010, the Agency created and released the English version of 3 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"). From among the information on approved new drugs, "review reports" that describe details and results of reviews, and "summaries of product applications" that summarize submitted data, are subject to disclosure for deliberation products, whereas review reports are subject to disclosure for reported products. The information is released on the PMDA website upon conferring with the relevant companies regarding the contents released for each product, based on the Notification Issued by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW.

- In FY 2010, PMDA released 123 review reports (median period from approval to release, 27 days), 84 summaries of product applications (median period from approval to release, 70 days) and 71 re-examination reports (median period from result notification to release, 23 days).

  The percentage of review reports released within one month after approval was 53.7% (33.0% in FY 2009) and the percentage of summaries of product applications released within 3 months after approval was 60.7% (45.7% in FY 2009).

(Review reports on new medical devices)

- In FY 2010, PMDA released 9 review reports (median period from approval to release, 31 days) and 14 summaries of product applications (median period from approval to release, 203 days).

  The percentage of review reports released within one month after approval was 44.4% (38.5% in FY 2009) and the percentage of summaries of product applications released within 3 months after approval was 14.3% (16.7% in FY 2009).

(Review reports on OTC drugs and quasi-drugs)

- It was decided that PMDA should publish review reports on OTC drugs and quasi-drugs, following the issuance of the Notification by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated March 31, 2006, which specifies publication procedures, etc. Furthermore, this Notification was amended on October 31, 2008 to publish summaries of product applications as well. In FY 2010, PMDA disclosed 7 review reports and 7 summaries of product applications on OTC drugs, and 1 review report and 1 summary of product applications on quasi-drugs.

c. Securing of fairness in the utilization of external experts

- It is necessary to secure fairness and transparency of judgment in commissioning external experts. Therefore, based on the "Notice on the Implementation of Expert Discussions at the Pharmaceuticals and Medical Devices Agency (December 25, 2008)," a rule that aims 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, 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, to whom PMDA has asked to participate in Expert Discussions on reviews and safety measures.

(vi) Promotion of internationalization

- 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. 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 United States, the European Union, 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 discussions with the Food and Drug Administration (FDA) and the EU/European Medicines Agency (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 October 2010, where views were exchanged actively.

- PMDA dispatched its executive officers as liaison officers to the USP (US Pharmacopoeia) and the EMA, in order to gather information and exchange views. PMDA also sent a team to the FDA and EMA to study and share ideas on the details of regulatory systems in the US and the EU, including reviews and safety measures.

- PMDA participated in the 5th Summit of Heads of Medicines Regulatory Agencies (the US, Europe, Asian and other countries) held in London in October 2010, and exchanged opinions with regulators in various countries including the FDA and EMA.

- PMDA concluded a confidentiality arrangement with Singapore in April 2010, with UK in October 2010 and with Switzerland in November 2010, and developed a framework to share information.

- A bilateral meeting with China was held in July 2010 to develop a collaborative relationship, and in the meeting, a specific future process of activities of a working group were agreed. In addition, the Japan-China Symposia were held in China in May 2010 and March 2011 to exchange views on pharmaceutical regulatory affairs in both countries and ethnic factors.

- In September 2010, the Japan-China-South Korea Director-General Level Meeting on Pharmaceutical Affairs and the 3rd meeting of the Japan-China-South Korea Working Group were held, where the Terms of Reference of the Working Group was agreed upon. Also, it was decided that Japan and Korea will prepare a concrete plan for the research project on ethnic factors and for the information exchange project on clinical trials, respectively, as the coordinator, while discussing with experts in their own countries.

b. Strengthening of activities for international harmonization

- In FY 2010, PMDA continued to actively participate in international harmonization initiatives 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.

- In order to build a mechanism for exchanging information relating to consultations, reviews, and post-marketing safety measures in cooperation with the US and the EU, PMDA held discussions with the FDA in collaboration with the MHLW.

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

- In FY 2010, PMDA continued to actively participate in Steering Committee Meetings and Expert Working Group Meetings of GHTF[*1], Steering Committee Meetings and Working Group Meetings for HBD[*2] activities, ISO[*3], etc. Particularly for GHTF, PMDA promoted further international harmonization by improving the consistency of Japanese standards with international standards, such as those for preparing data for regulatory submission, which were agreed upon among related countries.

**1 GHTF: Global Harmonization Task Force for Medical Devices*
**2 HBD: Harmonization by Doing*
**3 ISO: International Organization for Standardization*

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

*ICH Expert Working Groups

ICH Meeting in Tallinn

ICH Meeting in Fukuoka

ICH Japan Symposium 2010

Topics discussed in FY 2010

- 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 Residual Solvents – PDE for Cumene (Q3C [R5])
- 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])
- Development Safety Update Report (E2F)
- Genomic Biomarkers Related to Drug Response (E16)
- Q&A on Studies in Support of Special Populations: Geriatrics (E7 IWG)
- 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)
- Virus and Gene Therapy Vector Shedding and Transmission (M6)
- Gene Therapy Discussion Group (GTDG)

* 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/TC/194 (Biological evaluation of medical devices)

ISO/TC/106 (Dentistry)

GHTF SG1 IVD-subgroup (IVD regulation)

GHTF SG1 (Premarket evaluation)

GHTF SG2 (Post-market surveillance/vigilance)

GHTF SG3 (Quality systems)
GFTF SG4 (Auditing)
GHTF SG5 (Clinical safety/performance)
Regulatory Affairs Professionals Society (RAPS)
Harmonization by Doing (HBD)
APEC LSIF RHSC (Life Science Innovation Forum, Regulatory Harmonization Steering Committee)

- PMDA held 4 Expert Discussion meetings on drug names and reported 38 Japanese accepted names (JAN) to MHLW. Five consultations on applications for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in May and November.

c. Promotion of personnel exchanges

- Based on the "Administrative Rules on Overseas Training on a Long-term Basis", PMDA dispatched one employee each to the FDA and the OECD. PMDA selected the employees after soliciting personnel who were interested in being dispatched.

- PMDA received foreign trainees, including one from the China's State Food and Drug Administration (SFDA) and three from Korea Food and Drug Administration (KFDA). PMDA also accepted government research teams from South Korea, Russia, Turkey and Thailand, 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 process and principles of new drug review, etc.

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

- In order to improve communication skills in English, PMDA conducted English conversation training between August 2010 and February 2011. The training was improved by setting more stringent selection criteria for applicants and by introducing a reimbursement system after the trainees paid out of pocket, 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 posted news releases every month on its English website, and also made efforts to improve the provision of English information.

- 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 2010, the Agency prepared and published English translations of 3 review reports. PMDA also released English translations of the Ministerial Ordinance on GCP.

- At the DIA Annual Meetings, etc. held in Japan and the U.S., 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” (Notification from the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated September 28, 2007) which clarifies basic concepts to conduct global clinical trials.

  Of 632 clinical trial notifications submitted in FY 2010, 134 were related to global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

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

Note: The number of global clinical trials has been counted since FY 2007.

- PMDA intends to take an active approach to global clinical trials, etc. In FY 2010, it carried out 66 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 2006	FY 2007	FY 2008	FY 2009	FY 2010
Number of consultations on global clinical trials	22	56	51	56	66

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 such a way that they are inseparable.

- There were approximately 208,000 reports on adverse drug reactions and approximately 16,000 reports on malfunctions of medical devices submitted to PMDA from within and outside of Japan in FY 2010. PMDA inputs the collected information into a database and shares such information with MHLW. In addition, PMDA monitors information on new measures taken for medical products by foreign regulatory agencies including FDA and EMA to consider and evaluate its responses for domestic products on a daily basis, and also reviews 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 within the Agency, 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.

  Additional 2 reports of medication errors that required medical safety measures were submitted to MHLW.

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs	131	204	151	260	339
Medical devices	4	10	37	62	19
Medical safety*	2	1	4	4	5

** "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).

  There were 2 additional safety measures taken by MHLW based on reports from PMDA associated with medication errors:

		FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs	Instructions for revision to precautions in package insert	131	202	141	254	339
	Posting articles and cases on the Pharmaceuticals and Medical Devices Safety Information	24	86	20	29	32
Medical devices	Instructions for revision to precautions in package insert or notifications to instruct self-check	0	8	4	4	3
	Posting articles on the Pharmaceuticals and Medical Devices Safety Information	0	3	2	5	3

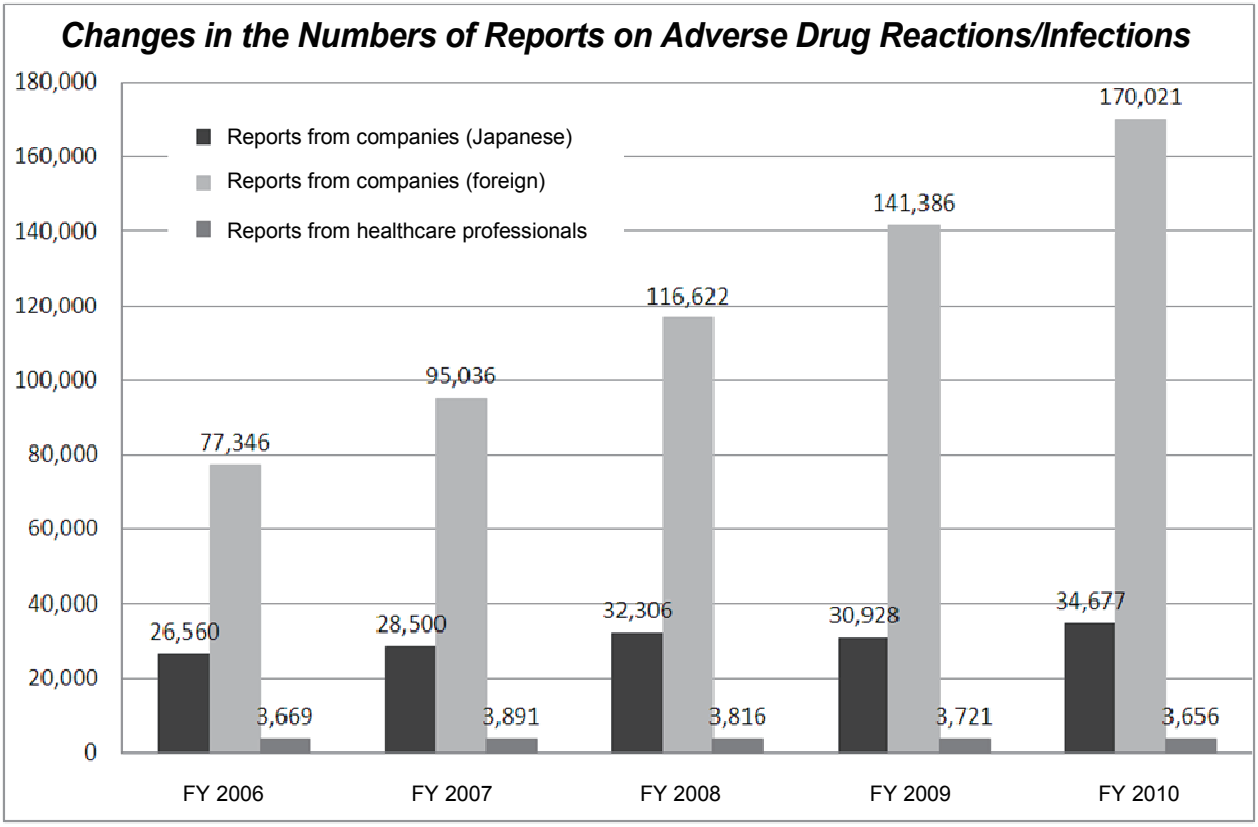
- As collaborative activities with the review offices, the safety offices evaluate adverse drug reaction cases for early post-marketing phase vigilance (EPPV) in cooperation with reviewers of product applications, and staff from the Offices of Safety I and II also participate in the review process (clinical 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/rejection of benefits has been provided to the safety offices and is reflected in the safety measures.

- In FY 2010, PMDA took 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. Improved the efficiency in receiving adverse drug reaction reports from medical institutions by upgrading data input tools
  b. Updated the master files in terms of names of drug products, adverse drug reactions and companies
  c. Upgraded database with malfunctions, introduced the master, etc.
  d. Encouraged staff members to attend academic conferences (a total of 108 participants) and gathered information through the academic conferences that they participated in
  e. Regularly held liaison meetings on both drugs and medical devices every week with MHLW

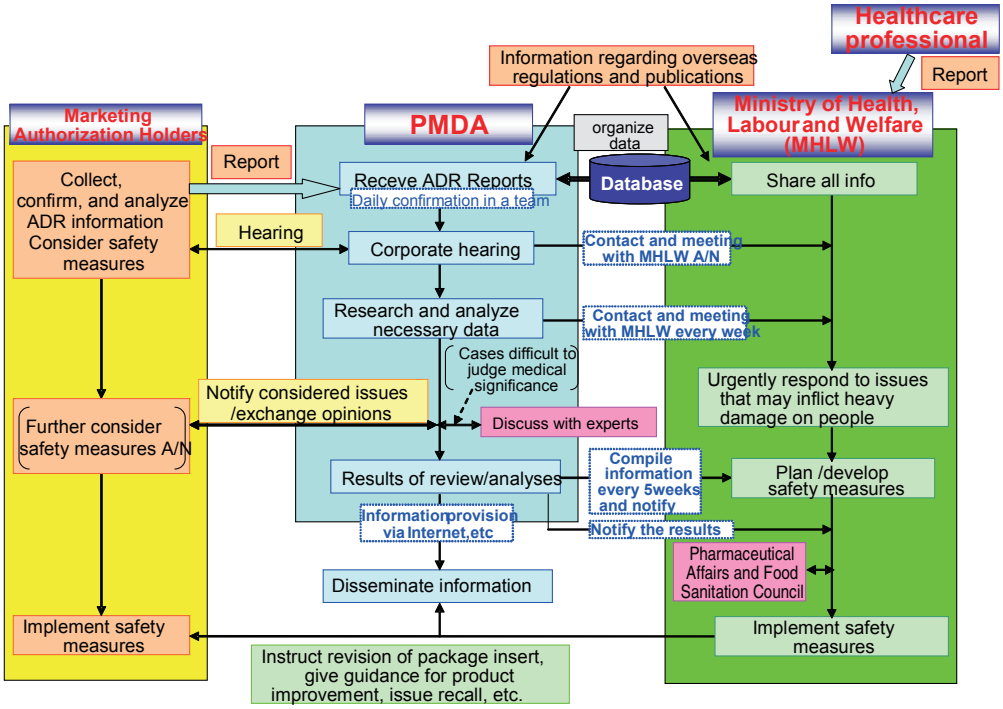
Collection of adverse reaction reports, etc.

1-1) Number of reports relating to drugs

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Reports from companies	106,285	126,181	151,726	175,285	207,772
(cases of adverse drug reactions, Japanese)	(26,309)	(28,231)	(31,455)	(30,814)	(34,578)
(cases of infections caused by drugs, Japanese)	(251)	(269)	(851)	(114)	(99)
(cases of adverse drug reactions, foreign)	(77,314)	(95,015)	(116,592)	(141,364)	(169,994)
(cases of infections caused by drugs, foreign)	(32)	(21)	(30)	(22)	(27)
(research reports)	(818)	(858)	(855)	(933)	(940)
(foreign safety measure reports)	(485)	(695)	(869)	(930)	(1,033)
(periodic infection reports)	(1,076)	(1,092)	(1,074)	(1,108)	(1,101)
Reports from healthcare professionals	3,669	3,891	3,816	3,721	3,656
Total	109,954	130,072	155,542	179,006	211,428



Flowchart for Processing Adverse Reaction Reports

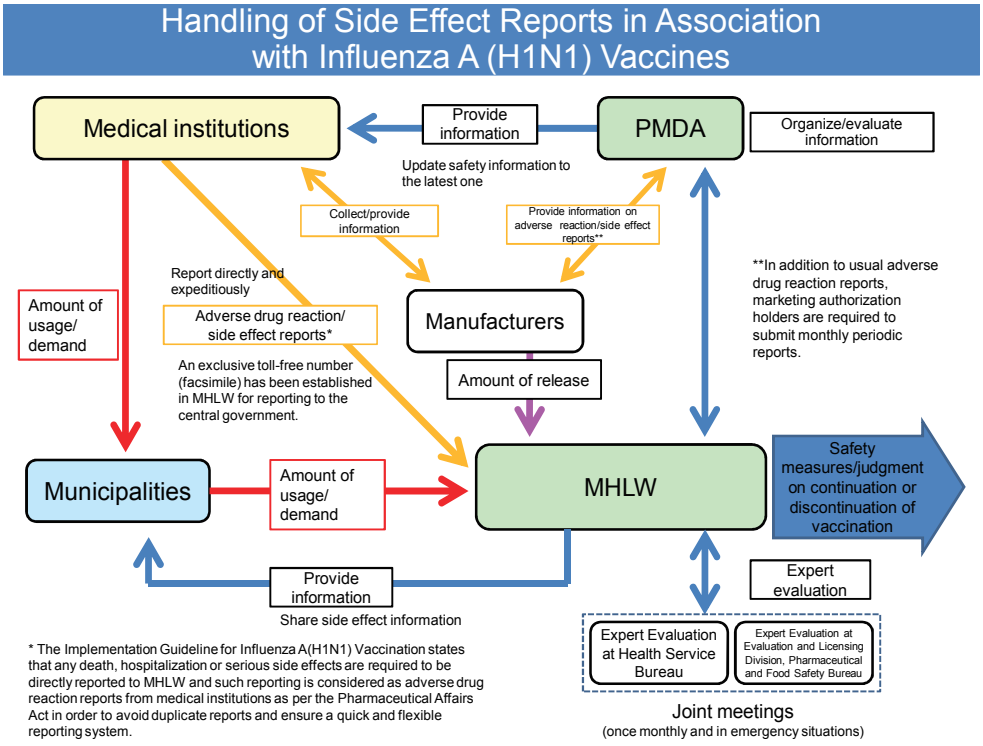


1-2) Report on side effects associated with influenza A (H1N1) vaccines

With regard to the Influenza A (H1N1) Vaccination Program started in October 2010, a scheme 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 in October 1, 2009 and revised in December 15, 2009, Japanese Government Task Force on Influenza A [H1N1]) (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 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 the Program was therefore completed.

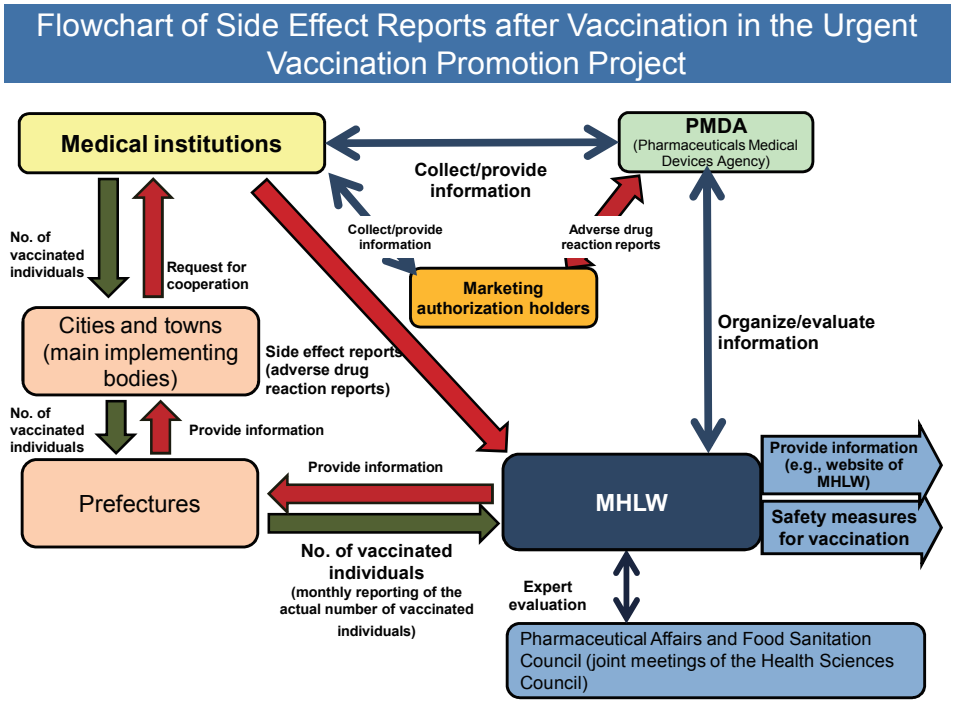
	FY 2009	FY 2010
Number of side effect reports	2,460	684



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

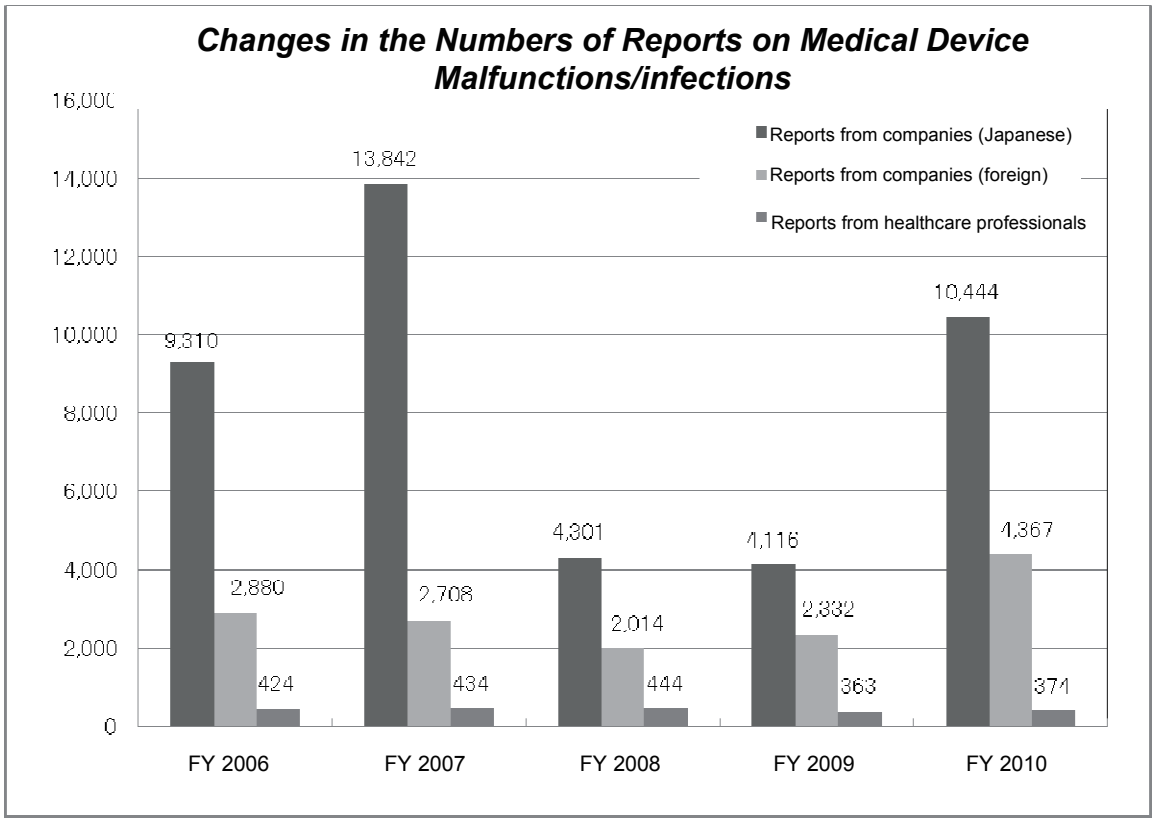
A scheme for the central government to be immediately informed of serious side effects after vaccination with cervical cancer preventive vaccine, Hib vaccine and pediatric pneumococcal conjugate vaccine has been established in accordance with the "Procedure for Urgent Vaccination Promotion" (Appendix to HSB Notification No. 1126-10 from the Health Service Bureau of MHLW and PFSB Notification No. 1126-3 from the Pharmaceutical and Food Safety Bureau of MHLW, dated November 26, 2010, "Implementation of Urgent Vaccination Promotion Program for Cervical Cancer Preventive Vaccine, etc.," 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 effect cases, and contributed to the safety evaluation of vaccines in MHLW.

	Cervical cancer preventive vaccine	Hib vaccine	pediatric pneumococcal conjugate vaccine
Number of side effect reports in FY 2010	176	135	158



2) Number of reports relating to medical devices

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Reports from companies	12,770	17,142	7,137	7,344	15,874
(cases of malfunctions of medical devices, Japanese)	(9,310)	(13,842)	(4,301)	(4,114)	(10,444)
(cases of malfunctions of medical devices, foreign)	(2,880)	(2,708)	(2,014)	(2,332)	(4,367)
(cases of infections caused by medical devices, Japanese)	(0)	(0)	(0)	(2)	(0)
(research reports)	(36)	(15)	(10)	(6)	(27)
(foreign safety measure reports)	(482)	(525)	(748)	(831)	(978)
(periodic infection reports)	(62)	(52)	(64)	(59)	(58)
Reports from healthcare professionals	424	434	444	363	374
Total	13,194	17,576	7,581	7,707	16,248



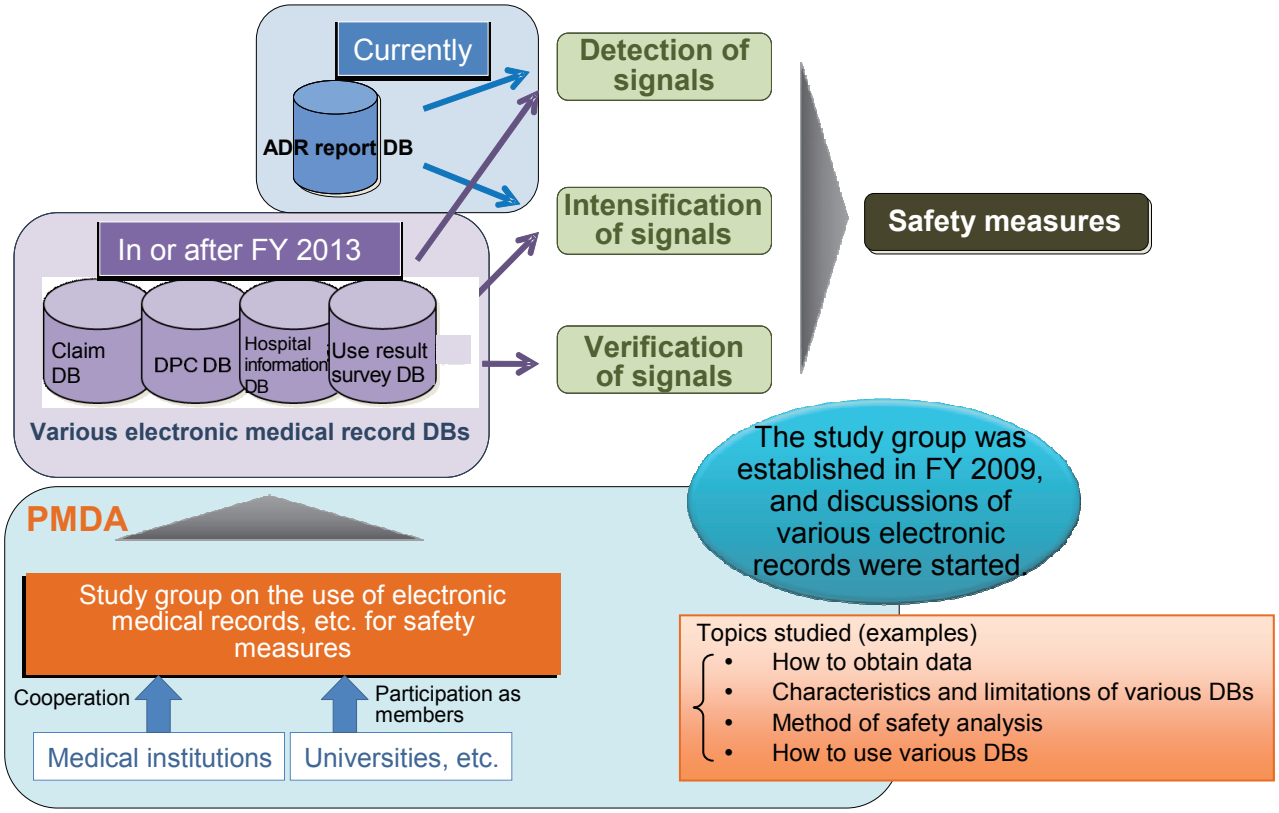
(ii) Sophistication of safety measures

a. Use of electronic medical records, etc.

- In accordance with the 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. Specifically, 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.

- In 2009, PMDA established the “Study group on the use of electronic medical records, etc. for safety measures” (hereinafter, the “Study group on electronic medical records”). The group, composed of external experts, conducted a series of deliberations on each type of data such as claim data and hospital information system data in terms of their advantages/disadvantages, potentials for utilization and limitations, etc.

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



- In FY 2010, PMDA named this project "MIHARI Project" and conducted a pilot study on adverse drug reactions using claim data and hospital information system data, while continuing to seek opinions from the Study group (see the following table).

Investigated data sources	Investigated items	Discussed issues [pilot study]
Claim data	Actual condition of prescription	Analytical methods to clarify the actual condition of prescription of the following drugs: • Amantadine • Thiamazole • Paroxetine • Anti-influenza agents
	Changes before and after safety measures	Analytical methods for changes in the number of patients who received prescriptions of the 4 drugs stated above before and after safety measures
	Risks for adverse reactions	Analysis of the following diseases using a pharmacoepidemiological design • Osteoporosis associated with steroids • Parkinsonism associated with antipsychotic agents
	Pharmacoepidemiological signal detection	Signal detection by PSSA* for the following disease • Parkinsonism associated with antipsychotic agents
	Mechanical signal detection	Discussion in collaboration with a contracted partner (NEC) of signal detection method through supervised learning
Diagnosis Procedure Combination (DPC)	Analysis of data profile (comparison with claim data)	Profile comparison between DPC data and claim data by basic tabulation of cases of anaphylaxis
Hospital information system	Data collection under the Standardized Structured Medical Information Exchange (SS-MIX) standards	• Search criteria for adverse reaction cases, data collection, analysis of data profile (5 hospitals) • Plan for evaluation of the appropriateness of searched cases (2 hospitals)
Adverse drug reaction reports	Provision of adverse reaction report data	Consideration and determination of data items, format, method and criteria for release
Use-results surveys	Development of use-results survey database	Challenges (e.g., data items) associated with development of database

* *PSSA: Prescription Sequence Symmetry Analysis*

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

- In accordance with the Mid-term Plan, PMDA intends to computerize adverse reaction information, such as adverse drug reaction reports and information from use-results surveys, and build databases in order to make use of digitized information in the development of safety measures.

- In FY 2010, PMDA upgraded its system to allow the public to access to adverse reaction reports as compiled in the database. In addition, in a meeting of the sub-committee on use-results surveys database formed under the Study Group on Electronic Medical Records, the Agency proposed the intended use for the use-results surveys database and its data elements based on the format of re-examination submission data. These proposals were examined by the committee members from pharmaceutical companies who were the providers of data from use-results surveys.

c. Sophistication of the data mining method

- In accordance with the 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 2009, by referring to the method for duplicate detection being used at the World Health Organization (WHO), PMDA evaluated the basic performance of the more practical detection model to examine the detection level of duplicate reports, aiming at enhancing the reliability of index values calculated through the signal detection method using data mining (signals: combinations of drugs and adverse drug reactions that are likely to have a causal relationship). In FY 2010, the Agency continued the examination while collecting opinions from experts, and reviewed the appropriateness of the detection formula.

  In FY 2009, PMDA adopted change-point analysis that captures the occurrence tendency (time-series changes in the number of reports on adverse drug reactions), and reviewed safety measures, etc. applied in the past from the statistical aspect. In FY 2010, the Agency continued the review while taking into account opinions from experts, and compared the analytical approach that was newly developed through case studies with other approaches for characterization.

- In addition, PMDA plans to enhance post-marketing safety by actively working on safety measures that are capable of “prediction and prevention” through scientific evaluation and analysis, analyzing adverse drug reactions efficiently with the use of the data mining method to detect signals, introducing risk management to consistently monitor safety information from the development to post-marketing stages, and using electronic medical records.

> 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 Mid-term Plan, PMDA intends to build a system for collecting and evaluating time-series data on the operation status of medical devices such as the incidence rate of malfunctions as a pilot study regarding implantable ventricular-assist devices among high-risk implantable medical devices subject to tracking, so that the system will be appropriately used for safety measures, etc.

> Reference: Medical Devices Subject to Tracking
>
> Medical devices for which it is obligatory for a marketing authorization holder, etc., to create and store records on 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 2010, PMDA facilitated the "Japanese registry for Mechanically Assisted Circulatory Support (J-MACS)" project based on the implementation structures/protocols that were considered 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 the end of March 2011, 19 cases have been registered, mainly consisting of those with an extracorporeal ventricular assist system, which is a comparator.

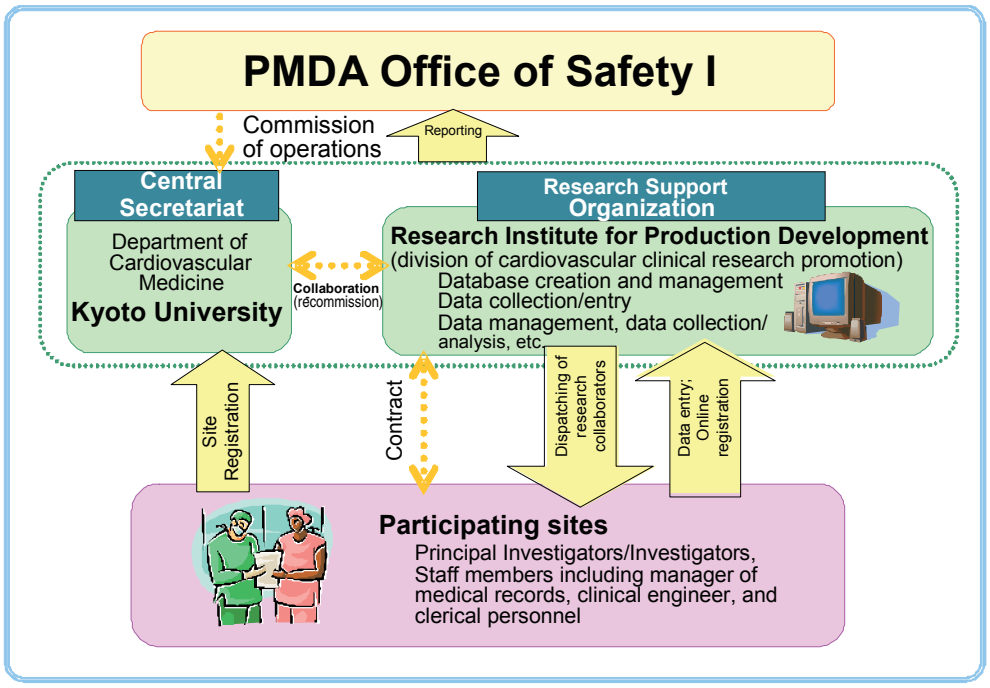
e. Evaluation of malfunctions of medical devices

- In accordance with the Mid-term Plan, PMDA intends to develop scientific evaluation methods by ascertaining the incidence of medical device malfunctions that may unavoidably occur at a constant rate due to the nature of the medical 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 registered patients; 3- to 5-year follow-up period) in patients who underwent their first percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) operation have been collected through an external contract organization.

- In FY 2010, PMDA completed data collection 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), and summarized and analyzed the data. PMDA will continue data collection in FY 2011 and FY 2012 for a five-year period of follow-up.

Implementation System of the Stent Study (FY 2009 - FY 2010)



Medical Product Information site of the PMDA website (http://www.info.pmda.go.jp/kyoten_kiki/port.html) [Japanese only]

(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

- The Agency partially developed a system which allows pharmaceutical companies to access information on adverse reactions to their own product from among the information on adverse drug reactions reported by medical institutions and other companies and analyzed and evaluated by PMDA, so that the company can analyze and deal with the information even before PMDA discloses it as a "line list".

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 consultations by category for FY 2010 is shown below:

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Drugs	567	486	559	619	752
Medical devices	292	260	283	247	171
Medical safety	44	166	172	142	83

- One reason for the reduction in the number of consultations on medical devices is considered to be the improvements in knowledge and understanding on the part of companies as a result of the consultation services provided from FY 2004. In contrast, the increase in the number of consultations on medical safety from FY 2007 to FY 2008 seems to be attributed to the transient rise in the number of consultations on the names of drugs related to new application for replacement of license submitted to change brand names of drugs, as a preventive measure against medical accidents for drugs whose names are similar to those of other products, or whose brand names do not contain the strength of the active ingredient. Consultations conducted in FY 2010 are mainly on the names of new drugs, packaging/labeling, and near-incident cases for drugs/medical devices. PMDA handled all consultations in an appropriate and prompt manner.

c. Support for releasing relevant information for companies

- PMDA has developed a new digitalization tool for medical device package inserts with advanced utility and made it available to companies for free. Meanwhile, the Agency newly developed a tool that works with Microsoft Office 2007.

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 information on 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 2011, PMDA posted 175,360 reports which had been submitted up to November 2010.

- PMDA also upgraded the system for adverse reaction reports from medical institutions to make them available to the public.

- In FY 2010, representatives from the industry, government, and academia discussed measures for releasing adverse reaction reports as database, data elements to be released, etc. in meetings of the sub-committee on adverse reaction report database established under the Study Group on Electronic Medical Records.

- The time from receiving adverse reaction reports to release was decreased to 4 months and the target period for FY 2010 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 information on 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 2011, PMDA posted 51,169 reports submitted up to September 2010.

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

- By the end of FY 2010, PMDA posted 12,256 package inserts of prescription drugs on the Medical Product Information web page. When instructions on revision of a package insert were

issued, PMDA has posted the instructions on the website within 2 days of receiving such information, and made a link to such 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 13,979 instructions for use by the end of FY 2010. Also, PMDA has posted instructions/notifications on revision of instructions for use within 2 days of the issuance of such information, and routinely provided links to the 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 9,884 package inserts were posted on the website as of the end of FY 2010.

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 3,964 package inserts were posted on the website as of the end of FY 2010.

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 2010, manuals for a total of 63 diseases were posted on the website.

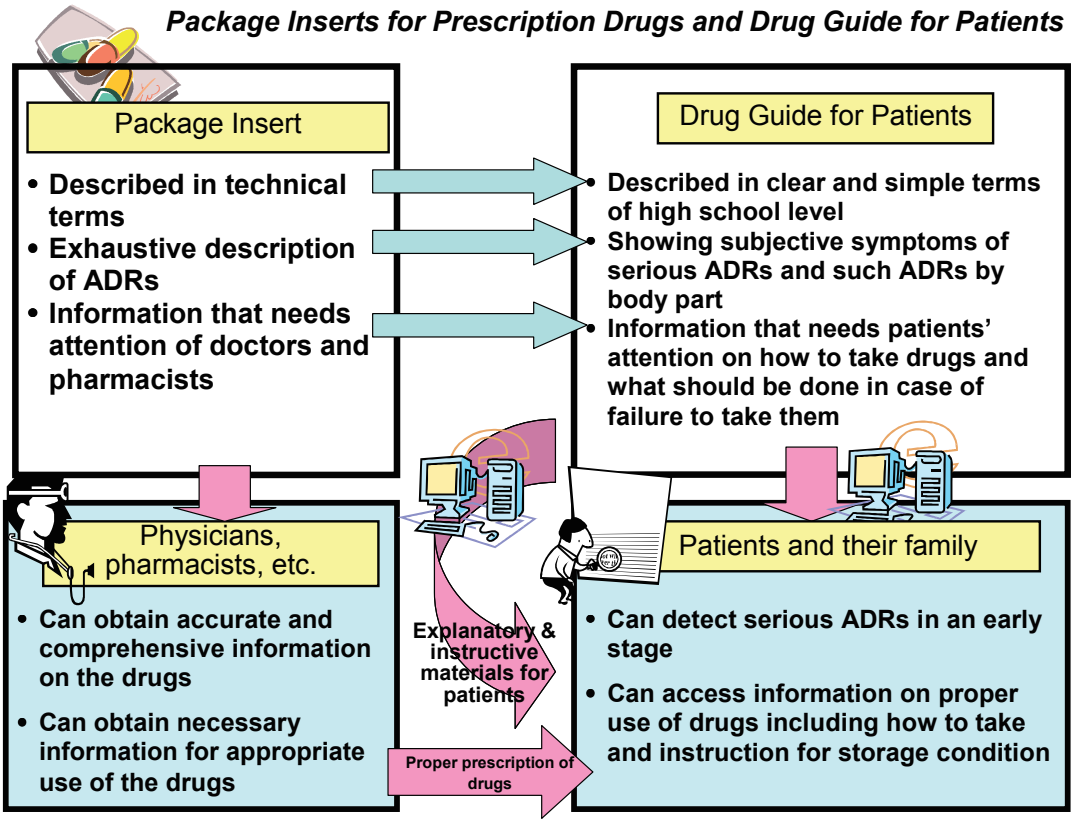
  These manuals contain information for patients and their family members, that allows early detection of serious adverse drug reactions based on subjective symptoms, and also contain methods of their diagnosis and management for healthcare professionals.

k. Publication of the drug guide for patients

- The Drug Guide for Patients, the purpose of which is to make it possible for patients to properly understand prescription drugs and enable detection of serious adverse reactions at an earlier stage, has been available on the PMDA website since January 2006. In FY 2010, 20 active ingredients (which were newly designated or newly marketed) were added to the Drug Guide database, and a total of 330 active ingredients in 2,311 products (1,338 package inserts) were posted by the end of March 2011.

- In accordance with the “Guidelines for Developing the Drug Guide for Patients” (Notification of the Director-General of the Pharmaceutical and Food Safety Bureau, MHLW 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 Labour Sciences Research Grant titled “Research on how to provide patients and people with drug safety information”).

Package Inserts for Prescription Drugs and Drug Guide for Patients



l. Upgrading Medical Product Information web page

- PMDA is also making efforts to enhance and reinforce the provision of information by distributing important post-marketing safety information, such as on revision of precautions in package inserts, to healthcare professionals and relevant people in companies by e-mail whenever such information is issued and by posting various safety information including package inserts, on the Medical Product Information web page: http://www.info.pmda.go.jp/.

- In FY 2010, taking into account opinions given by the website users, PMDA established a search system that allows searching of only contraindications and adverse drug reactions among package insert information on prescription drugs and provided icons linking to applicable contents from the top page. PMDA also developed and released a search system for prescription drugs that allows healthcare professionals, etc. to search for the name and contact information of a company to which inquiries on drugs should be sent.

- PMDA also built a new system that allows searching of review reports of prescription drugs, OTC drugs, medical devices and quasi-drugs with their brand name, time of approval, etc.

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

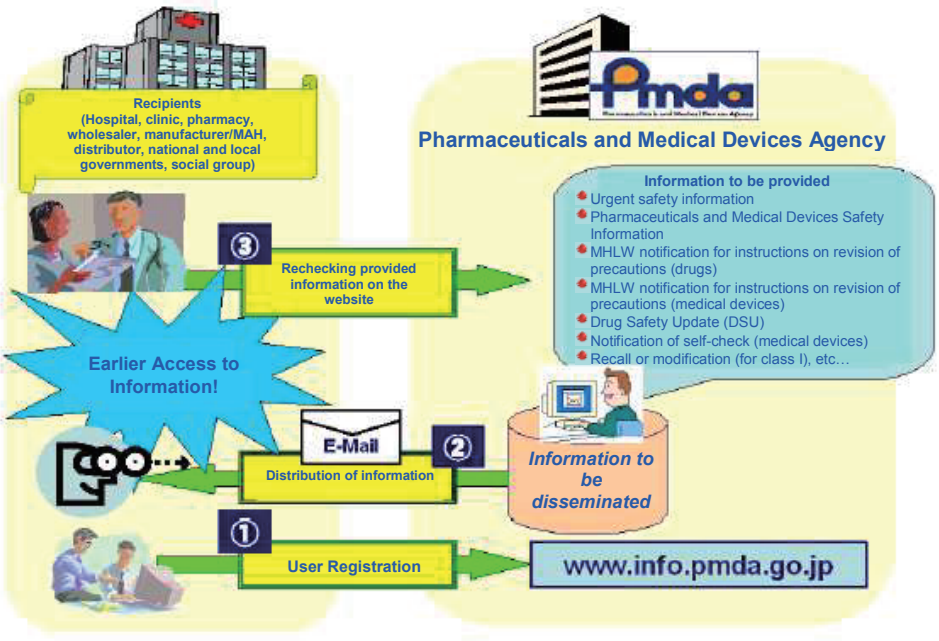
m. Implementation of pharmaceuticals and medical devices information e-mail service

- The "Pharmaceuticals and medical devices information e-mail service" which provides safety information such as revisions to package inserts and Class I recalls, is provided via e-mail to

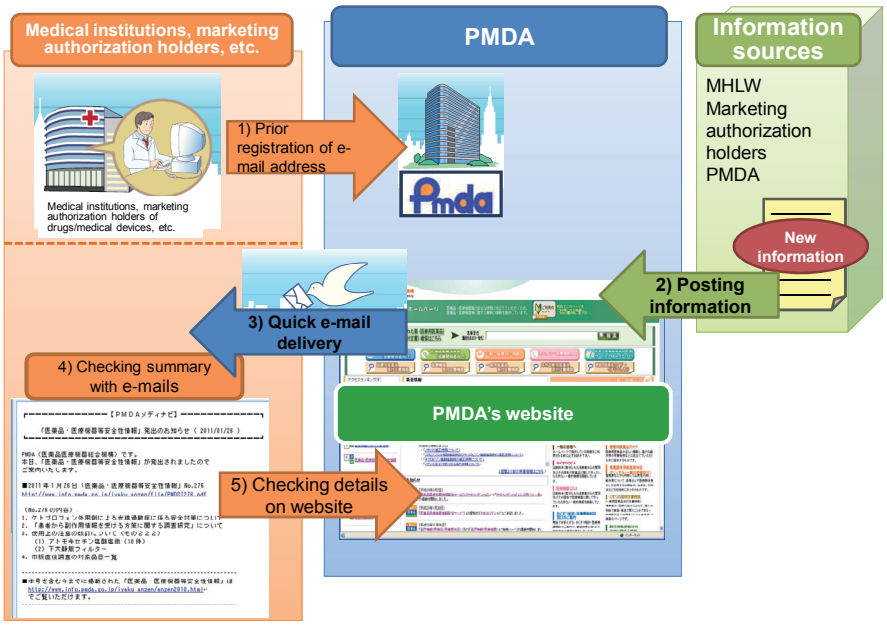
healthcare professionals who subscribe to the service. PMDA accepted candidate nicknames for the service from the public and finally chose "PMDA medi-navi." In addition, taking into account opinions, etc. given at the "Meeting to exchange opinions to promote the Pharmaceutical and Medical Device Information E-mail Service" held by MHLW and opinions, etc. given by the users, PMDA improved the service by reviewing emails to be provided, simplifying the procedure for registration of subscribers and strengthening PR activities in order to make the service more accessible.

- A total of 35,719 e-mail addresses were registered as of the end of March 2011. Approximately 40% of these subscribers were at hospitals and clinics, approx. 20% were pharmacies, approx. 10% were dentist clinics or other medical facilities, and approx. 20% were marketing authorization holders and distributors.

Pharmaceuticals and Medical Devices Information E-mail Service



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



PMDA medi-navi by Content in FY 2010

Contents of e-mails	Number of releases
Recalls (Class I)	32
Pharmaceuticals and Medical Devices Safety Information	11
Drug Safety Update (DSU)	10
Revision of PRECAUTIONS of drugs	14
Revision of PRECAUTIONS of medical devices	1
Notification on self-check (medical devices)	1
PMDA Medical Safety Information	7
Approval information (medical devices)	9
Approval information (prescription drugs)	74
Others	44
Total	203

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 2010, 742 cases associated with drugs and 174 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 916 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: 916 cases	742	174
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.	3	0
2) Cases in which measures have already been taken, or are currently under investigation, by the marketing authorization holder etc.	7	29
3) Cases in which a lack of information is considered to hinder the marketing authorization holder's investigations for measures, or cases that were considered to be a result of human errors or human factors.	732	145

- In addition, in November 2007, PMDA started to issue PMDA Medical Safety Information, which provides precautions for safe use of medical products using charts and other tools 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 reported repeatedly as near-incident cases and adverse drug reaction and malfunction reports as well as events which led to issuance of revisions to package inserts. In FY 2010, 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. 16	April 2010	Precautions in handling electric scalpels (Part 3)
No. 17	May 2010	Precautions in handling of prefilled syringes
No. 18	June 2010	Precautions in handling of lancing devices for capillary blood sampling
No. 19	September 2010	Administration error of concentrated potassium (K) solutions for injection
No. 20	November 2010	Precautions in artificial respiration (No. 3)
No. 21	January 2011	Precautions in flow rate programming of infusion pumps
No. 22	February 2011	Precautions in handling blood tubing sets used for blood purification

o. Information provision in English

- To promote provision of information on safety measures to overseas users, PMDA translated 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, and posted the translations on its English website.

p. Implementation 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. Implementation 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 2010, the number of persons receiving consultations was 8,846 (12,336 calls) for drugs, and 574 (622 calls) for medical devices.
- Regarding generic drugs, requests for consultation have been accepted from not only general consumers but also healthcare professionals such as doctors and pharmacists since May 2007 as consultations on generic drugs. In FY 2010, the number of persons receiving consultations was 617. General consumers accounted for 90.3% of them, whereas doctors/pharmacists accounted for 3.3%.

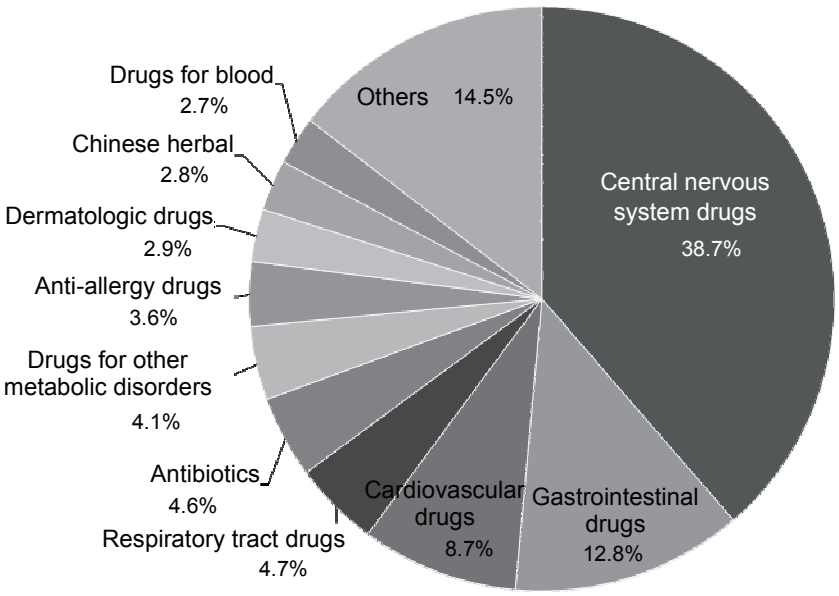
Number of Consultations on Drugs/Medical Devices

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Consultations on drugs	8,459 [34.5 cases/day]	8,696 [35.5 cases/day]	8,479 [34.9 cases/day]	9,316 [38.5 cases/day]	8,846 [36.4 cases/day]
(of which, consultations on generic drugs)	-	(122)	(143)	(687)	(617)
Consultations on medical devices	376 [1.5 cases/day]	564 [2.3 cases/day]	639 [2.6 cases/day]	558 [2.3 cases/day]	574 [2.4 cases/day]

Contents of Consultations on Drugs

Contents of consultation	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
(1) Safety	5,697 (48.7%)	5,731 (45.9%)	6,347 (50.6%)	5,727 (42.4%)	5,553 (45.0%)
(2) Indications	1,175 (10.0%)	1,175 (9.4%)	954 (7.6%)	1,079 (8.0%)	890 (7.2%)
(3) Administration and Dosage	828 (7.1%)	1,072 (8.6%)	836 (6.7%)	746 (5.5%)	784 (6.4%)
(4) Interactions	691 (5.9%)	715 (5.7%)	732 (5.8%)	753 (5.6%)	784 (6.4%)
(5) Active Ingredient	219 (1.9%)	236 (1.9%)	214 (1.7%)	251 (1.9%)	181 (1.5%)
Others	3,086 (26.4%)	3,548 (28.4%)	3,450 (27.5%)	4,960 (36.7%)	4,144 (33.6%)
Total	11,696 (100.0%)	12,477 (100.0%)	12,533 (100.0%)	13,516 (100.0%)	12,336 (100.0%)

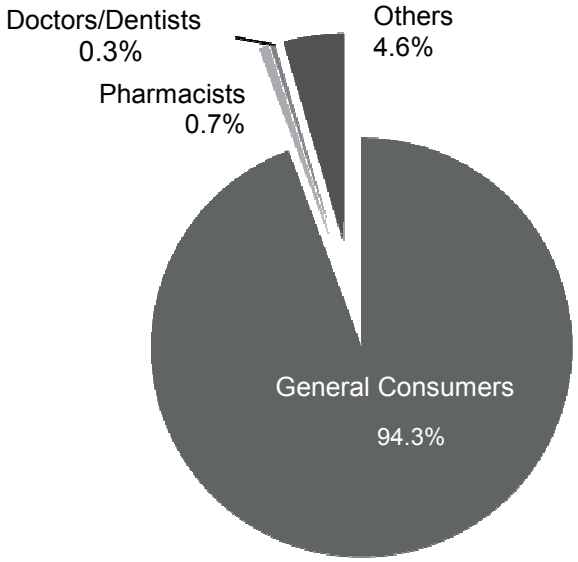
Number of Consultations on Drugs by Therapeutic Category (FY 2010)



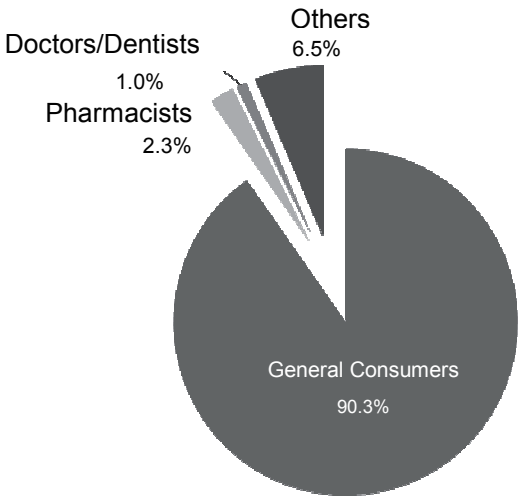
n=17,222

Breakdown of Persons Receiving Consultations on Drugs in FY 2010 (by Profession, etc.)

Consultations on drugs (n = 8,846)

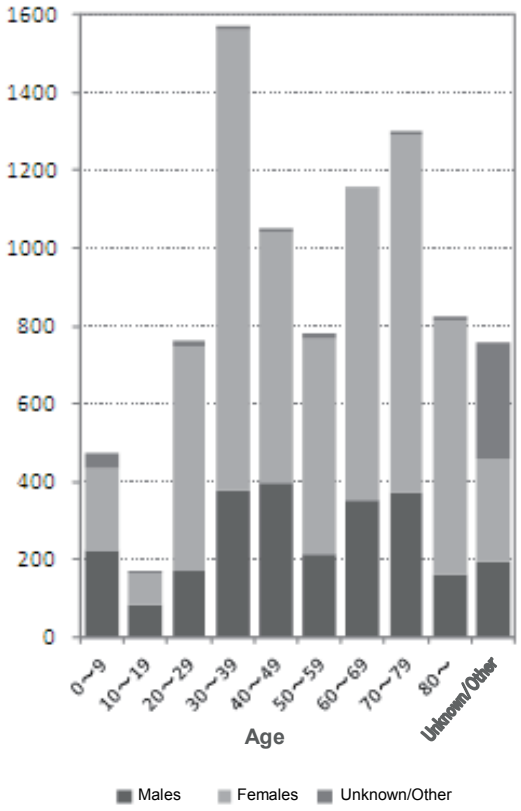


Consultations on generic drugs (n = 617)

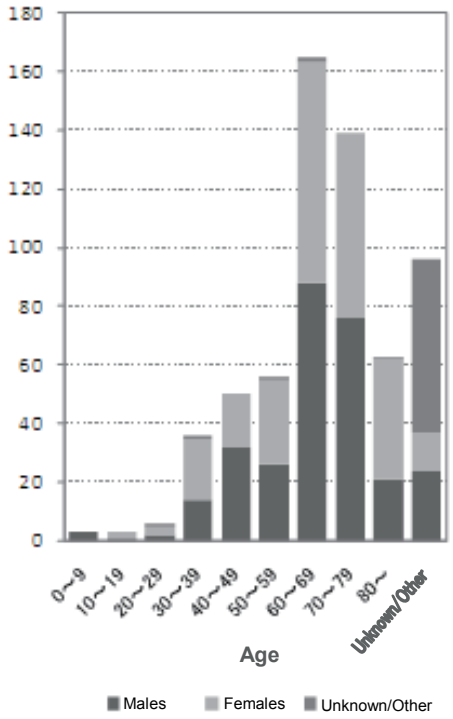


Breakdown of Persons Receiving Consultations on Drugs in FY 2010 (by Age and Gender)

Consultations on drugs (n = 8,846)



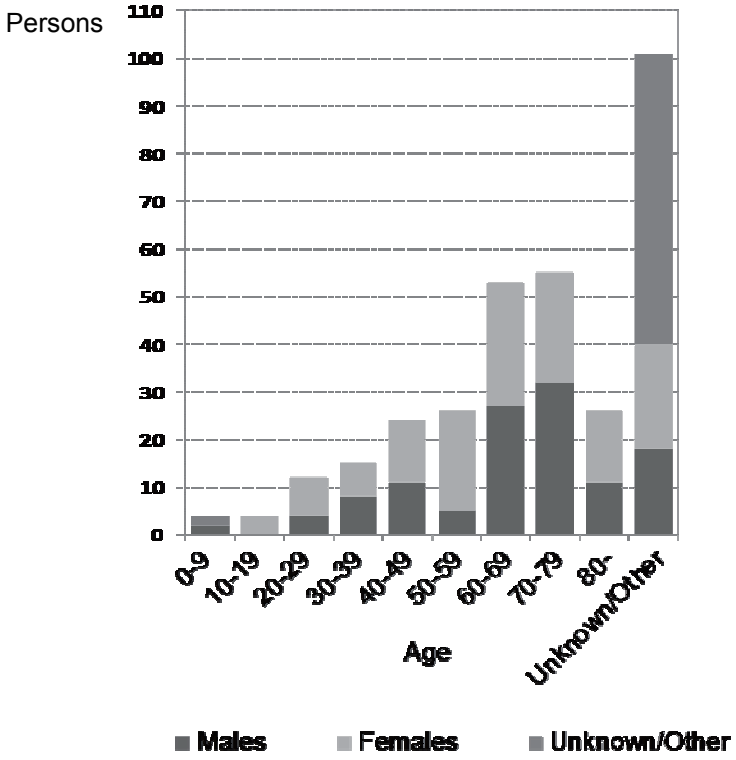
Consultations on generic drugs (n = 617)



Contents of consultations on medical devices

Contents of consultation	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
(1) Safety	62 (10.7%)	91 (11.0%)	96 (10.6%)	74 (12.0%)	78 (12.5%)
(2) Indications	101 (17.4%)	85 (10.3%)	90 (10.0%)	59 (9.6%)	61 (9.8%)
(3) Performance	45 (7.7%)	37 (4.5%)	46 (5.1%)	27 (4.4%)	17 (2.7%)
(4) Directions for use	16 (2.8%)	12 (1.5%)	17 (1.9%)	15 (2.4%)	12 (1.9%)
Others	357 (61.4%)	599 (72.7%)	653 (72.4%)	441 (71.6%)	454 (73.0%)
Total	581 (100.0%)	824 (100.0%)	902 (100.0%)	616 (100.0%)	622 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2010 (by Age and Gender)*



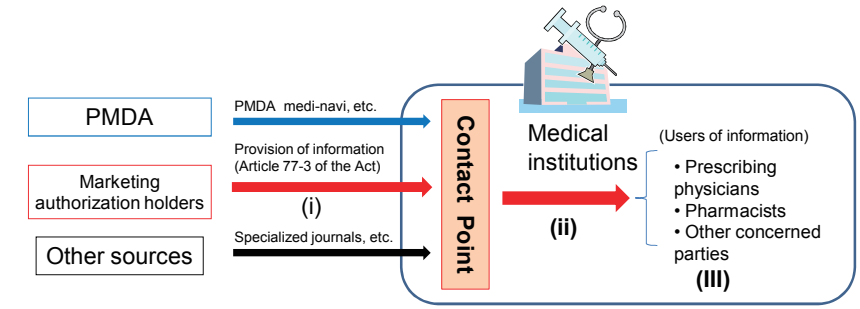
** Summary results from a total of 320 persons consisting of general consumers and consultants of consumer affairs centers.*

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 clarify the status of communication and use of safety information on drugs, etc. in medical institutions, and conducted a mail-in questionnaire survey among hospitals (8679 institutions) nationwide.

  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 Clarify the Status of Communication/Use of Information within Medical Institutions



[Method of survey]

•Written questionnaire survey
•On-site survey

Major points to be clarified are:

(i) Is information communicated appropriately within medical institutions?

(ii) <u>Is information communicated to right persons at the right time?</u>

(iii) <u>Do medical institutions take appropriate actions (use information) at the right time upon receipt of information?</u>

Number of Posted Products on the Medical Product Information Web Page as of the End of March 2011

Posted information	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Package inserts*1					
Prescription drugs	12,341	13,090	13,287	13,050	12,256
Medical devices	3,995	5,462	8,164	11,213	13,979
OTC drugs	3,306	7,437	8,356	9,513	9,884
In vitro diagnostics			2,237	3,301	3,984
Drug Guide for Patients*1	237 active ingredients (1,240 products)	270 active ingredients (1,567 products)	294 active ingredients (1,958 products)	312 active ingredients (1,920 products)	330 active ingredients (2,311 products)
Safety information issued by MHLW • Instruction of revisions of package inserts • Pharmaceuticals and Medical Devices Safety Information • Press release	294	323	350	376	409
Urgent safety information (by pharmaceutical companies)	24	24	24	24	24
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])	31	41	51	61	71
Notification of safety measures for medical devices					
Notification of self-check	45	45	47	49	50
Notification of revisions of labeling	21	28	30	32	33
Other related notification	35	54	57	66	74
Information about case reports on suspected ADR	48,584	84,094	110,879	142,084	175,360
Information about case reports on suspected malfunction	17,345	34,226	42,405	46,551	51,169
Notification related to preventive measures for medical accidents	21	26	44	56	68
PMDA Medical Safety Information	-	3	9	15	22
Manuals for management of individual serious adverse drug reactions	9	25	38	63	63
Information about approved new drugs • Review reports, summaries of product applications	261 active ingredients (559 products)	308 active ingredients (642 products)	373 active ingredients (763 products)	445 active ingredients (895 products)	513 active ingredients (1,034 products)
A list of prescription drugs on which Quality Information Package (Orange Book) was published	481 active ingredients/ formulations (3,737 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 about recalls of drugs or medical devices*2	2,128	2,777	3,448	1,979	1,977
Pharmaceuticals and medical devices information e-mail service (PMDA medi-navi)					
E-mails issued*3	93	87	107	188	203
Subscribers	6,762	11,965	20,707	27,410	35,719
Number of site visitors*4	391 million	497 million	642 million	754 million	873 million

**1 When necessary, an addition or deletion was conducted.*

**2 Addition was conducted when necessary, and the information is deleted after two years in principle.*

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

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

s. Launch of 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. Accordingly, PMDA started to provide information to healthcare professionals and related associations to promote proper use of drugs. In FY 2010, the Agency provided information on one active ingredient, salazosulfapyridine.

III. SUPPLEMENTARY INFORMATION

Table 1. Products Approved in FY 2010: New Drugs

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Apr. 16, 2010	1	Nesp Injection 10 μg/1 mL Plastic Syringe Nesp Injection 15 μg/1 mL Plastic Syringe Nesp Injection 20 μg/1 mL Plastic Syringe Nesp Injection 30 μg/1 mL Plastic Syringe Nesp Injection 40 μg/1 mL Plastic Syringe Nesp Injection 60 μg/0.6 mL Plastic Syringe Nesp Injection 120 μg/0.6 mL Plastic Syringe Nesp Injection 180 μg/0.9 mL Plastic Syringe (Kyowa Hakko Kirin Co., Ltd.)	Approval Approval Approval Approval Approval Approval Approval Approval	Darbepoetin alfa (genetical recombination)	Drugs with a new route of administration and a new indication for the treatment of renal anemia.
1	Apr. 16, 2010	2	Soliris for Intravenous Infusion 300 mg (Alexion Pharma K.K.)	Approval	Eculizumab (genetical recombination)	A drug with a new active ingredient indicated to reduce hemolysis in patients with paroxysmal nocturnal hemoglobinuria. [Orphan drug]
1	Jun. 18, 2010	3	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of moderate to severe ulcerative colitis (for use only in patients who have not sufficiently responded to conventional treatments).
1	Jun. 18, 2010	4	Pariet Tablets 10 mg (Eisai Co., Ltd.)	Change	Sodium rabeprazole	A drug with a new additional indication and a new dosage for the treatment of non-erosive reflux disease.
1	Jul. 23, 2010	5	Takepron Capsules 15 Takepron OD Tablets 15 (Takeda Pharmaceutical Company Limited)	Change Change	Lansoprazole	Drugs with a new additional indication and a new dosage for prevention of recurrence of gastric ulcer or duodenal ulcer in patients treated with low-dose aspirin.
1	Aug. 20, 2010	6	Takepron Capsules 15 Takepron OD Tablets 15 (Takeda Pharmaceutical Company Limited)	Change Change	Lansoprazole	Drugs with a new additional indication and a new dosage for prevention of recurrence of gastric ulcer or duodenal ulcer in patients treated with nonsteroidal anti-inflammatory drugs.
1	Oct. 27, 2010	7	Humira 40mg for S.C. Injection Syringe 0.8 mL (Abbott Japan Co., Ltd.)	Change	Adalimumab (genetical recombination)	A drug with new additional indications and a new dosage for the remission induction and maintenance therapy for moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatment).
1	Oct. 27, 2010	8	Minclea Catapasm for Internal Use 0.8% (Nihon Pharmaceutical Co., Ltd.)	Approval	*l*-Menthol	A drug with a new additional indication and a new dosage and in an additional dosage form for the inhibition of gastric peristalsis in endoscopy of the upper gastrointestinal tract.
1	Oct. 27, 2010	9	Radiogardase Capsule 500 mg (Nihon Medi-Physics Co., Ltd.)	Approval	Iron(III)hexacyanoferrate(II)	A drug with a new active ingredient indicated for the reduction of internal contamination with radioactive cesium. [Expedited review]
1	Dec. 21, 2010	10	Pariet Tablets 10 mg Pariet Tablets 20 mg (Eisai Co., Ltd.)	Change Change	Sodium rabeprazole	Drugs with new dosages for the treatment of reflux esophagitis.
1	Jan. 21, 2011	11	Altat Capsules 37.5 Altat Capsules 75 (Aska Pharmaceutical Co., Ltd.)	Change Change	Roxatidine acetate hydrochloride	Drugs with new additional pediatric dosages. These drugs are indicated for gastric ulcer, duodenal ulcer, stomal ulcer, Zollinger-Ellison syndrome, reflux esophagitis, preanesthetic medication and improvement of gastric mucosal lesions (erosion, bleeding, redness, edema) during acute gastritis or acute exacerbation phase of chronic gastritis.
1	Mar. 10, 2011	12	Exal for Inj. 10 mg (Nippon Kayaku Co., Ltd.)	Change	Vinblastine sulfate	A drug with a new additional indication and a new dosage for the treatment of Langerhans cell histiocytosis. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
2	Apr. 16, 2010	13	Unisia Combination Tablets LD Unisia Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Candesartan cilexetil/amlodipine besilate	New combination drugs indicated for the treatment of hypertension.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	May 13, 2010	14	Tambocor Tablets 50 mg Tambocor Tablets 100 mg (Eisai Co., Ltd.)	Change Change	Flecainide acetate	Drugs with a new additional indication and a new dosage for the treatment of tachyarrhythmia (paroxysmal atrial fibrillation/flutter, paroxysmal supraventricular tachycardia, ventricular tachycardia) in children. [Expedited review]
2	Jul. 23, 2010	15	Micamlo Combination Tablets AP (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Telmisartan/amlodipine besilate	A new combination drug indicated for the treatment of hypertension.
2	Jul. 23, 2010	16	Volibris Tablets 2.5 mg (GlaxoSmithKline K.K.)	Approval	Ambrisentan	A drug with a new active ingredient indicated for the treatment of pulmonary arterial hypertension. [Orphan drug]
2	Sep. 10, 2010	17	Ancaron Tablets 100 (Sanofi-Aventis K.K.)	Change	Amiodarone hydrochloride	A drug with a new additional indication for the treatment of arterial fibrillation with cardiac failure (impaired cardiac function).
2	Oct. 27, 2010	18	Samsca Tablets 15 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval	Tolvaptan	A drug with a new active ingredient indicated for the treatment of fluid retention in heart failure patients who have not responded sufficiently to other diuretics to such as loop diuretics.
2	Oct. 27, 2010	19	Revolade Tablets 12.5 mg Revolade Tablets 25 mg (GlaxoSmithKline K.K.)	Approval Approval	Eltrombopag olamine	Drugs with a new active ingredient indicated for the treatment of chronic idiopathic thrombocytopenic purpura. [Orphan drug]
2	Jan. 21, 2011	20	Memary Tablets 5 mg Memary Tablets 10 mg Memary Tablets 20 mg (Daiichi Sankyo Company, Limited)	Approval Approval Approval	Memantine hydrochloride	Drugs with a new active ingredient indicated for inhibition of progression of symptoms of dementia in moderate and severe Alzheimer's dementia.
2	Jan. 21, 2011	21	Reminyl Tablets 4 mg Reminyl Tablets 8 mg Reminyl Tablets 12 mg Reminyl OD Tablets 4 mg Reminyl OD Tablets 8 mg Reminyl OD Tablets 12 mg Reminyl Oral Solution 4 mg/mL (Janssen Pharmaceutical K.K.)	Approval Approval Approval Approval Approval Approval Approval	Galantamine hydrobromide	Drugs with a new active ingredient indicated for inhibition of progression of symptoms of dementia in mild and moderate Alzheimer's dementia.
2	Jan. 21, 2011	22	Prazaxa Capsules 75 mg Prazaxa Capsules 110 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval	Dabigatran etexilate methanesulfonate	Drugs with a new active ingredient indicated for prevention of ischemic stroke and systemic embolism in patients with nonvalvular atrial fibrillation.
2	Jan. 21, 2011	23	Romiplate for S.C. Injection 250 μg (Kyowa Hakko Kirin Co., Ltd.)	Approval	Romiplostim (genetical recombination)	A drug with a new active ingredient indicated for the treatment of chronic idiopathic thrombocytopenic purpura. [Orphan drug]
2	Jan. 21, 2011	24	Arixtra Injection 5 mg Arixtra Injection 7.5 mg (GlaxoSmithKline K.K.)	Approval Approval	Fondaparinux sodium	Drugs with new additional indications and new dosages for the treatment of acute pulmonary thromboembolism and acute deep vein thrombosis.
2	Feb. 23, 2011	25	Warfarin Tablets 0.5 mg Warfarin Tablets 1 mg Warfarin Tablets 5 mg (Eisai Co., Ltd.)	Change Change Change	Warfarin potassium	Drugs with new additional pediatric dosages. These drugs are indicated for the treatment and prophylaxis of thromboembolism (e.g., phlebothrombosis, myocardial infarction, pulmonary embolism, brain embolism, slowly-progressive cerebral thrombosis). [Public knowledge-based application after PAFSC's preliminary assessment]
2	Mar. 30, 2011	26	Lipidil Tablets 53.3 mg Lipidil Tablets 80 mg (Aska Pharmaceutical Co., Ltd.) Tricor Tablets 53.3 mg Tricor Tablets 80 mg (Abbott Japan Co., Ltd.)	Approval Approval Approval Approval	Fenofibrate	Drugs in new dosage forms and with new dosages indicated for the treatment of hyperlipemia (including familial hyperlipemia).
3-1	Apr. 16, 2010	27	Rozerem Tablets 8 mg (Takeda Pharmaceutical Company Limited)	Approval	Ramelteon	A drug with a new active ingredient indicated for the improvement of difficulty with sleep onset in insomnia.
3-1	Apr. 16, 2010	28	Lyrica Capsules 25 mg Lyrica Capsules 75 mg Lyrica Capsules 150 mg (Pfizer Japan Inc.)	Approval Approval Approval	Pregabalin	Drugs with a new active ingredient indicated for the treatment of postherpetic neuralgia.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Jul. 23, 2010	29	E Keppra Tablets 250 mg E Keppra Tablets 500 mg (UCB Japan Co., Ltd.)	Approval Approval	Levetiracetam	Drugs with a new active ingredient 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	Oct. 27, 2010	30	Botox for Injection 50 Units Botox for Injection 100 Units (GlaxoSmithKline K.K.)	Change Change	Botulinum toxin type A	Drugs with new additional indications and new dosages for the treatment of upper and lower limb spasticity.
3-1	Oct. 27, 2010	31	Zyprexa Tablets 2.5 mg Zyprexa Tablets 5 mg Zyprexa Tablets 10 mg Zyprexa Fine Granules 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 manic symptoms in patients with bipolar disorder.
3-1	Oct. 27, 2010	32	Kenketsu Venoglobulin IH 5% I.V. 2.5 g/50 mL (Benesis Corporation)	Change	Polyethylene glycol treated human normal immunoglobulin	A drug with a new additional indication and a new dosage for the improvement of muscular weakness in polymyositis/dermatomyositis (for use only when steroids are not sufficiently effective). [Orphan drug]
3-1	Oct. 27, 2010	33	Invega Tablets 3 mg Invega Tablets 6 mg Invega Tablets 9 mg (Janssen Pharmaceutical K.K.)	Approval Approval Approval	Paliperidone	Drugs with a new active ingredient indicated for the treatment of schizophrenia.
3-1	Oct. 27, 2010	34	Lyrica Capsules 25 mg Lyrica Capsules 75 mg Lyrica Capsules 150 mg (Pfizer Japan Inc.)	Change Change Change	Pregabalin	Drugs with a new additional indication for the treatment of peripheral neuropathic pain.
3-1	Jan. 21, 2011	35	Nerbloc Intramuscular Injection 2500 Unit (Eisai Co., Ltd.)	Approval	Botulinum toxin type B	A drug with a new active ingredient indicated for the treatment of spasmodic torticollis (cervical dystonia).
3-2	Apr. 16, 2010	36	DuoTrav Combination Ophthalmic Solution (Alcon Japan Ltd.)	Approval	Travoprost/timolol maleate	A new combination drug indicated for the treatment of glaucoma and ocular hypertension.
3-2	Apr. 16, 2010	37	Fentos Tape 1 mg Fentos Tape 2 mg Fentos Tape 4 mg Fentos Tape 6 mg Fentos Tape 8 mg (Hisamitsu Pharmaceutical Co., Inc.)	Approval Approval Approval Approval Approval	Fentanyl citrate	Drugs with a new route of administration indicated for analgesia in various types of cancer associated with moderate to severe pain which cannot be managed by treatments with non-opioid analgesics or weak opioid analgesics (for use only in patients who switch from an opioid analgesic).
3-2	Apr. 16, 2010	38	Cosopt Ophthalmic Solution (Banyu Pharmaceutical Co., Ltd.)	Approval	Dorzolamide hydrochloride/timolol maleate	A new combination drug indicated for the treatment of glaucoma and ocular hypertension in patients who have not responded sufficiently to other glaucoma drugs.
3-2	Jul. 23, 2010	39	Tramal Capsules 25 mg Tramal Capsules 50 mg (Nippon Shinyaku Co., Ltd.)	Approval Approval	Tramadol hydrochloride	Drugs with a new route of administration indicated for analgesia in various types of cancer with mild to moderate pain.
3-2	Aug. 20, 2010	40	Precedex Intravenous Solution 200 μg "Hospira" (Hospira Japan Co., Ltd.) Precedex Intravenous Solution 200 μg "Maruishi" (Maruishi Pharmaceutical Co., Ltd.)	Change Change	Dexmedetomidine hydrochloride	Drugs with a new additional dosage indicated for sedation during artificial respiration and after weaning in patients in intensive care.
3-2	Oct. 27, 2010	41	Acref Oral Transmucosal Fentanyl Citrate 200μg Acref Oral Transmucosal Fentanyl Citrate 400μg Acref Oral Transmucosal Fentanyl Citrate 600μg Acref Oral Transmucosal Fentanyl Citrate 800μg (Mitsubishi Tanabe Pharma Corporation)	Approval Approval Approval Approval	Fentanyl citrate	Drugs with a new route of administration indicated for the analgesia of breakthrough pain in patients with cancer receiving a potent opioid analgesic at fixed time.
3-2	Oct. 27, 2010	42	OneDuro Patch 0.84 mg OneDuro Patch 1.7 mg OneDuro Patch 3.4 mg OneDuro Patch 5 mg OneDuro Patch 6.7 mg (Janssen Pharmaceutical K.K.)	Approval Approval Approval Approval Approval	Fentanyl	Drugs in new dosage forms indicated for the analgesia in various types of cancer with moderate to severe pain which cannot be managed by treatments with non-opioid analgesics and weak opioid analgesics (for use only in patients who switch from an opioid analgesic).
3-2	Oct. 27, 2010	43	MaQaid Intravitreal Injection 40 mg (Wakamoto Co., Ltd.)	Approval	Triamcinolone acetonide	A drug with a new route of administration indicated for the visualization of the vitreous body during vitreous surgery.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-2	Feb. 23, 2011	44	Norspan Tape 5 mg Norspan Tape 10 mg Norspan Tape 20 mg (Mundipharma K.K.)	Approval Approval Approval	Buprenorphine	Drugs with a new active ingredient indicated for analgesia of chronic pain associated with osteoarthritis and lumbago which cannot be managed by treatments with non-opioid analgesics.
4	Jun. 18, 2010	45	(1) Takepron Capsules 15 Takepron Capsules 30 (2) Takepron OD Tablets 15 Takepron OD Tablets 30 (Takeda Pharmaceutical Company Limited) (3) Omepral Tablets 10 Omepral Tablets 20 (AstraZeneca K.K.) (4) Omeprazon Tablets 10 mg Omeprazon Tablets 20 mg (Mitsubishi Tanabe Pharma Corporation) (5) Pariet Tablets 10 mg (Eisai Co., Ltd.) (6) Pasetocin Capsule 125 Pasetocin Capsule 250 (7) Pasetocin Tablets 250 (Kyowa Hakko Kirin Co., Ltd.) (8) Sawacillin Capsules 250 (9) Sawacillin Tablets 250 (Astellas Pharma Inc.) (10) Amolin Capsules 125 Amolin Capsules 250 (11) 10% Amolin Fine Granules (Takeda Pharmaceutical Company Limited) (12) Clarith Tab. 200 (Taisho Pharmaceutical Co., Ltd.) (13) Klaricid Tablets 200 mg (Abbott Japan Co., Ltd.) (14) Flagyl Oral Tablet 250 mg (Shionogi & Co., Ltd.) (15) Lansap 400 Lansap 800 (Takeda Pharmaceutical Company Limited)	Change Change	(1)(2) Lansoprazole (3)(4) Omeprazole (5) Sodium rabeprazole (6)(7)(8)(9)(10)(11) Amoxicillin hydrate (12)(13) Clarithromycin (14) Metronidazole (15) Lansoprazole/amoxicillin hydrate/clarithromycin	Drugs with a new additional indication for *helicobacter pylori (H. pylori)* eradication therapy for gastric MALT lymphoma, for the stomach after endoscopic treatment of early gastric cancer, and for idiopathic thrombocytopenic purpura, in *H. pylori* infection.
4	Jun. 18, 2010	46	Zovirax for I.V. Infusion 250 Zovirax Tablets 200 Zovirax Tablets 400 Zovirax Granules 40% (GlaxoSmithKline K.K.) Zobiclobill Tab. 200 Zobiclobill Tab. 400 (Nihon Pharmaceutical Industry Co.,Ltd.) Natazil for I.V. Infusion 250 mg (Fujiyakuhin Co., Ltd.) Tomill Kit for I.V. Infusion 250 mg (Mitsubishi Tanabe Pharma Corporation) Viruhexal Tablets 200 mg Viruhexal Tablets 400 mg Viruhexal for I.V. Infusion 250 mg Viruhexal Granule 40% (Sandoz K.K.) Astric Dry Syrup 80% (Nippon Kayaku Co., Ltd.) Grosparl Syrup 8% Grosparl Granules 40% (Takata Seiyaku Co., Ltd.) Vercusron Tablets 200 Vercusron Tablets 400 Vercusron Granules 40% Vercusron for Intravenous Infusion 250 mg Vercusron Injection 250 (Towa Pharmaceutical Co., Ltd.) Acirovec Tablets 200 Acirovec Tablets 400 Acirovec Granules 40% Acirovec DS 80% Acirovec for Intravenous Infusion 250 mg (Sawai Pharmaceutical Co., Ltd.) Vizocross Tablets 200 Vizocross Tablets 400 Vizocross Granules 40% (Taisho Pharm. Ind., Ltd.)	Change Change	Aciclovir	Drugs with new additional indications and a new additional dosage for herpes simplex, prevention of herpes simplex virus infection in hematopoietic stem cell transplantation, herpes zoster, and prevention of recurrence of genital herpes (oral dosage form), and neonatal herpes simplex virus infection (injectable dosage form) based on the discussion of the Investigational Committee on Pediatric Drug Therapies.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
			Actidas for Intravenous Infusion 250 mg	Change		
			Actidas Tablets 400	Change		
			Actidas Tablets 200	Change		
			Actidas Kit	Change		
			(Shiono Chemical Co., Ltd.)			
			Aciclovir Tablets 200 mg "Mylan"	Change		
			Aciclovir Tablets 400 mg "Mylan"	Change		
			(Mylan Seiyaku Ltd.)			
			Pharrax Tablets 200	Change		
			Pharrax Tablets 400	Change		
			(Kyorin Rimedio Co., Ltd.)			
			Aciclovin Tablets 200	Change		
			Aciclovin Intravenous Infusion 250 mg	Change		
			Aciclovin Granules 40%	Change		
			Aciclovin Tablets 400	Change		
			(Nichi-Iko Pharmaceutical Co., Ltd.)			
			Acilomin Tablets 200	Change		
			Acilomin Tablets 400	Change		
			(Medisa Shinyaku Inc.)			
			Aciclovir Tablets 200 mg "Tanabe"	Change		
			Aciclovir Tablets 400 mg "Tanabe"	Change		
			Aciclovir Granules 40% "Tanabe"	Change		
			Zobistat Granules 40%	Change		
			(Choseido Pharmaceutical Co., Ltd.)			
			Aciclovir Injection 250 mg "Kayaku"	Change		
			Clovate Tab. 200	Change		
			Clovate Tab. 400	Change		
			(Pola Pharma Inc.)			
			Acycril Bag for I.V. Infusion 250 mg/100 mL	Change		
			Acycril for I.V. infusion 250 mg	Change		
			(I'rom Pharmaceutical Co.,Ltd.)			
			Vicclox I.V. Infusion 125 mg	Change		
			Vicclox I.V. Infusion 250 mg	Change		
			Vicclox Tablets 200	Change		
			Vicclox Tablets 400	Change		
			Vicclox Granules 40%	Change		
			Vicclox Syrup 8%	Change		
			(Kobayashi Kako Co., Ltd.)			
			Acivir Oral Jelly 200 mg	Change		
			Acivir Oral Jelly 800 mg	Change		
			(Nichi-Iko Pharmaceutical Co., Ltd.)			
			Ailax Tablets 200 mg	Change		
			Ailax Tablets 400 mg	Change		
			(Tatsumi Kagaku Co., Ltd.)			
			Actios Tablets 200	Change		
			Actios Tablets 400	Change		
			Actios for Intravenous Infusion 250 mg	Change		
			Actios for Intravenous Infusion 250 mg Kit	Change		
			Actios Granules 40%	Change		
			(Taiyo Pharmaceutical Industry Co., Ltd.)			
4	Jul. 23, 2010	47	Pasil Intravenous Drip Infusion 300 mg	Change	Pazufloxacin mesilate	Drugs with new additional indications for the treatment of *Streptococcus pneumoniae* and sepsis and a new dosage in an additional dosage form.
			Pasil Intravenous Drip Infusion 500 mg	Change		
			Pasil Intravenous Drip Infusion 1000 mg	Approval		
			(Toyama Chemical Co., Ltd.)			
			Pazucross Injection 300	Change		
			Pazucross Injection 500	Change		
			Pazucross Injection 1000 mg	Approval		
			(Mitsubishi Tanabe Pharma Corporation)			
4	Sep. 10, 2010	48	Inavir Dry Powder Inhaler 20 mg	Approval	Laninamivir octanoate hydrate	A drug with a new active ingredient indicated for the treatment of influenza A or B virus infections.
			(Daiichi Sankyo Company, Limited)			
4	Oct. 27, 2010	49	Cravit Intravenous Drip Infusion 500 mg/100 mL	Approval	Levofloxacin hydrate	Drugs with a new route of administration indicated for the treatment of pneumonia, secondary infection of chronic respiratory disease, typhoid, paratyphoid, anthrax, brucellosis, plague, tularemia and Q fever.
			Cravit Intravenous Drip Infusion 500 mg/20 mL	Approval		
			(Daiichi Sankyo Company, Limited)			
4	Oct. 27, 2010	50	Rapiacta 300 mg Bag for Intravenous Drip Infusion	Change	Peramivir hydrate	Drugs with new additional pediatric dosages for influenza A or B virus infection.
			Rapiacta 150 mg Vial for Intravenous Drip Infusion			
			(Shionogi & Co., Ltd.)	Change		

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Dec. 21, 2010	51	Cravit Ophthalmic Solution 1.5% (Santen Pharmaceutical Co., Ltd.)	Approval	Levofloxacin hydrate	A drug with a new dosage of the 1.5% formulation for the treatment of blepharitis, dacryocystitis, hordeolum, conjunctivitis, meibomianitis, and keratitis (including corneal ulcer) and sterilization during the ophthalmic perioperative period.
4	Mar. 10, 2011	52	Meropen for Intravenous Drip Infusion Vial 0.25 g Meropen for Intravenous Drip Infusion Vial 0.5 g Meropen for Intravenous Drip Infusion Kit 0.5 g (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change	Meropenem hydrate	Drugs with a new dosage (the maximum daily dose has been changed) in patients with general infections that are severe and refractory.
5	Dec. 21, 2010	53	Sodium Phosphate Corrective Injection 0.5 mmol/mL (Otsuka Pharmaceutical Factory, Inc.)	Approval	N/A for this combination drug	A combination prescription drug with similar formulations to be used for the correction of electrolyte levels of electrolyte fluids. [Expedited review]
5	Dec. 21, 2010	54	Lunabell Tablets (Nobelpharma Co., Ltd.)	Change	Norethisterone/ ethinylestradiol	Drugs with a new additional indication for the treatment of functional dysmenorrhoea.
5	Dec. 21, 2010	55	Kindaly 4E Kindaly 4D Kindaly AF-4P (Fuso Pharmaceutical Industries, Ltd.)	Approval Approval Approval	N/A for this combination drug	Combination prescription drugs with similar formulations to be used as the perfusate of dialysis-based artificial kidneys in chronic renal failure (use in patients whose blood sugar level is not controlled well with sugarless dialysate and when other bicarbonate dialysate is not sufficiently effective to improve hyperkalemia and hypermagnesemia, or when hypercalcemia may occur).
5	Jul. 23, 2010	56	Yaz Combination Tablets (Bayer Yakuhin, Ltd.)	Approval	Drospirenone/ethinylestradiol betadex	A new combination drug with a new active ingredient indicated for the treatment of dysmenorrhea.
5	Feb. 23, 2011	57	Prostandin 20 for Injection (Ono Pharmaceutical Co., Ltd.)	Change	Alprostadil alfadex	A drug with a new route of administration and a new dosage for a new additional indication for the diagnosis of erectile disturbance.
5	Feb. 23, 2011	58	Norlevo Tablets 0.75 mg (Sosei Co., Ltd.)	Approval	Levonorgestrel	A drug with a new additional indication and a new dosage for emergency contraception.
6-1	Apr. 16, 2010	59	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of ankylosing spondylitis in patients who have not responded sufficiently to conventional treatments. [Orphan drug]
6-1	Apr. 16, 2010	60	Diquas Ophthalmic Solution 3% (Santen Pharmaceutical Co., Ltd.)	Approval	Diquafosol sodium	A drug with a new active ingredient indicated for the treatment of dry eye.
6-1	Jul. 23, 2010	61	Orencia for I.V. Infusion 250 mg (Bristol-Myers K.K.)	Approval	Abatacept (genetical recombination)	A drug with a new active ingredient indicated for the treatment of rheumatoid arthritis (for use only in patients who have not sufficiently responded to conventional treatments).
6-1	Jul. 23, 2010	62	Synvisc Intraarticular Injection 2 mL (Genzyme Japan K.K.)	Approval	Sodium hyaluronate crosslinked polymer and sodium hyaluronate crosslinked polymer crosslinked with vinylsulfone	A drug with a new active ingredient indicated for pain relief in patients with knee osteoarthritis who have not responded sufficiently to conservative non-drug treatment and oral drug treatment.
6-1	Jul. 23, 2010	63	Pulmicort 100 μg Turbuhaler 112 doses Pulmicort 200 μg Turbuhaler 56 doses Pulmicort 200 μg Turbuhaler 112 doses (AstraZeneca K.K.)	Change Change Change	Budesonide	Drugs with a new additional pediatric dosage indicated for the treatment of bronchial asthma.
6-1	Jul. 23, 2010	64	Allelock Tablets 2.5 Allelock Tablets 5 Allelock OD Tablets 2.5 Allelock OD Tablets 5 (Kyowa Hakko Kirin Co., Ltd.)	Change Change Change Change	Olopatadine hydrochloride	Drugs 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	Oct. 27, 2010	65	Nevanac Ophthalmic Suspension 0.1% (Alcon Japan Ltd.)	Approval	Nepafenac	A drug with a new active ingredient indicated for the treatment of postoperative inflammation in intraocular surgery.
6-1	Oct. 27, 2010	66	Xyzal Tablets 5 mg (GlaxoSmithKline K.K.)	Approval	Levocetirizine hydrochloride	A drug with a new active ingredient indicated for the treatment of allergic rhinitis, urticaria, eczema/dermatitis, pruigo and cutaneous pruritus.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Oct. 27, 2010	67	Humira 40 mg for S.C. Injection Syringe 0.8 mL (Abbott Japan Co., Ltd.)	Change	Adalimumab (genetical recombination)	A drug with a new additional indication of ankylosing spondylitis (for use only in patients who have not sufficiently responded to conventional treatment). [Priority review]
6-1	Nov. 16, 2010	68	Pulmicort Respules 0.25 mg Pulmicort Respules 0.5 mg (AstraZeneca K.K.)	Change Change	Budesonide	Drugs with new additional adult and pediatric (5 years of age and older) dosages for the treatment of bronchial asthma.
6-1	Jan. 21, 2011	69	Stelara Subcutaneous Injection 45 mg (Janssen Pharmaceutical K.K.)	Approval	Ustekinumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of plaque psoriasis and psoriatic arthritis in patients who have not responded sufficiently to conventional treatments.
6-1	Jan. 21, 2011	70	Alvesco 50 μg Inhaler 112 puffs Alvesco 100 μg Inhaler 112 puffs Alvesco 100 μg Inhaler 56 puffs Alvesco 200 μg Inhaler 56 puffs (Teijin Pharma Limited)	Change Change Approval Change	Ciclesonide	Drugs with a new additional pediatric dosage indicated for the treatment of bronchial asthma.
6-1	Jan. 21, 2011	71	Calonal Fine Gran. 20% Calonal Fine Gran. 50% Calonal Tab. 200 Calonal Tab. 300 Calonal Powder (Showa Yakuhin Kako Co., Ltd.) Cocarl Dry Syr. 40% Cocarl Tab. 200 mg (Sanwa Kagaku Kenkyusho Co., Ltd.) Calsil Fine Granules 20% Calsil Tablets 200 (Taiyo Pharmaceutical Industry Co., Ltd.) Anyrume Fine Granules 20% Anyrume Tablets 200 mg Anyrume Tablets 300 mg Pyrinazin Powder (Choseido Pharmaceutical Co., Ltd.) Napa (Mylan Seiyaku Ltd.)	Change Change Change Change Change Change Change Change Change Change Change Change Change Change	Acetaminophen	Drugs with a new additional indication for the treatment of osteoarthritis and with an expanded dosage of acetaminophen.
6-1	Feb. 23, 2011	72	Rheumatrex Capsules 2 mg (Pfizer Japan Inc.) Methotrexate Tablets 2 mg "Tanabe" (Mitsubishi Tanabe Pharma Corporation) Methotrexate Cap. 2 mg "Mylan" (Mylan Seiyaku Ltd.) Trexamette Capsules 2 mg (Shiono Chemical Co., Ltd.) Methotrexate Capsules 2 mg "Towa" (Towa Pharmaceutical Co., Ltd.) Metolate Tablets 2 mg (Santen Pharmaceutical Co., Ltd.) Methotrexate Cap. 2 mg "Sawai" (Sawai Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change	Methotrexate	Drugs with a revised indication and an expanded dosage for the treatment of rheumatoid arthritis (limitation of patients to be treated was abolished).
6-1	Feb. 23, 2011	73	Mohrus Tape 20 mg Mohrus Tape L 40 mg (Hisamitsu Pharmaceutical Co., Inc.)	Change Change	Ketoprofen	Drugs with new additional indications for the treatment of myalgia and post-traumatic swelling/pain.
6-1	Feb. 23, 2011	74	Endoxan for Injection 100 mg Endoxan for Injection 500 mg Endoxan Tablets 50 mg (Shionogi & Co., Ltd.)	Change Change Change	Cyclophosphamide	Drugs with a new additional indication and new dosages for treatment-resistant rheumatic disease in adults and children. [Public knowledge-based application after PAFSC's preliminary assessment]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Apr. 16, 2010	75	Nesina Tablets 6.25 mg Nesina Tablets 12.5 mg Nesina Tablets 25 mg (Takeda Pharmaceutical Company Limited)	Approval Approval Approval	Alogliptin benzoate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes (for use only in patients with inadequate glycemic control by following treatments: 1. Treatment by diet and exercise only 2. In addition to treatment by diet and exercise, treatment by alpha-glucosidase inhibitor).
6-2	Apr. 16, 2010	76	Metact Combination Tablets LD Metact Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Pioglitazone hydrochloride/metformin hydrochloride	New combination drugs indicated for the treatment of type 2 diabetes (only when a concomitant use of pioglitazone hydrochloride with metformin hydrochloride is deemed appropriate).
6-2	Jun. 18, 2010	77	Amaryl 0.5 mg Tablets Amaryl 1 mg Tablets Amaryl 3 mg Tablets (Sanofi-Aventis K.K.)	Change Change Change	Glimepiride	Drugs with a new dosage 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. 23, 2010	78	Forteo S.C. Injection Kit 600 μg Forteo S.C. Injection Cart 600 μg (Eli Lilly Japan K.K.)	Approval Approval	Teriparatide (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of osteoporosis with a high risk of fracture.
6-2	Jul. 23, 2010	79	Viviant Tablets 20 mg (Pfizer Japan Inc.)	Approval	Bazedoxifene acetate	A drug with a new active ingredient indicated for the treatment of postmenopausal osteoporosis.
6-2	Aug. 20, 2010	80	Nesina Tablets 6.25 mg Nesina Tablets 12.5 mg Nesina Tablets 25 mg (Takeda Pharmaceutical Company Limited)	Change Change Change	Alogliptin benzoate	Drugs with a new additional indication for the treatment of type 2 diabetes mellitus in patients who have not responded sufficiently to thiazolidinediones along with diet and exercise therapies.
6-2	Oct. 27, 2010	81	Byetta Subcutaneous Injection 5 μg Pen 300 Byetta Subcutaneous Injection 10 μg Pen 600 Byetta Subcutaneous Injection 10 μg Pen 300 (Eli Lilly Japan K.K.)	Approval Approval Approval	Exenatide	Drugs 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 treatment with sulfinylurea [including concomitant treatment with biguanides or thiazolidines] along with diet and exercise therapies).
6-2	Jan. 21, 2011	82	Surepost Tablets 0.25 mg Surepost Tablets 0.5 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval Approval	Repaglinide	Drugs with a new active ingredient indicated for the improvement of postprandial changes of blood glucose in type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to either [1] diet and exercise therapies alone or [2] alpha-glucosidase inhibitors along with diet and exercise therapies).
6-2	Jan. 21, 2011	83	Feburic Tablet 10 mg Feburic Tablet 20 mg Feburic Tablet 40 mg (Teijin Pharma Limited)	Approval Approval Approval	Febuxostat	Drugs with a new active ingredient indicated for the treatment of gout and hyperuricemia.
6-2	Jan. 21, 2011	84	Sonias Combination Tablets LD Sonias Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Pioglitazone hydrochloride/glimepiride	New combination drugs indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of pioglitazone hydrochloride with glimepiride is deemed appropriate).
6-2	Jan. 21, 2011	85	Edirol Capsule 0.5 μg Edirol Capsule 0.75 μg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval	Eldecalcitol	Drugs with a new active ingredient indicated for the treatment of osteoporosis.
6-2	Feb. 23, 2011	86	Nesina Tablets 6.25 mg Nesina Tablets 12.5 mg Nesina Tablets 25 mg (Takeda Pharmaceutical Company Limited)	Change Change Change	Alogliptin benzoate	Drugs with new additional indications for the treatment of type 2 diabetes mellitus in patients who have not responded sufficiently to sulfonylureas or biguanides along with diet and exercise therapies.
6-2	Mar. 10, 2011	87	L-Cartin Tablets 100 mg L-Cartin Tablets 300 mg (Otsuka Pharmaceutical Co., Ltd.)	Change Change	Levocarnitine chloride	Drugs with a new additional indication and new dosages for the treatment of carnitine deficiency. [Public knowledge-based application after PAFSC's preliminary assessment]
6-2	Mar. 23, 2011	88	Novolin R FlexPen Novolin R 100 IU/mL Novolin 30R FlexPen Novolin N FlexPen InnoLet 30R (Novo Nordisk Pharma Ltd.)	Approval Approval Approval Approval Approval	Insulin human (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated. However, 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.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Apr. 16, 2010	89	Vectibix for Intravenous Infusion 100 mg (Takeda Pharmaceutical Company Limited) Vectibix for Intravenous Infusion 100 mg "Takeda Bio" (Takeda Bio Development Center Limited)	Approval Approval	Panitumumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable, advanced or recurrent colorectal cancer with wild-type KRAS.
Oncology drugs	Jun. 25, 2010	90	Revlimid Capsules 5 mg (Celgene K.K.)	Approval	Lenalidomide hydrate	A drug with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Jun. 18, 2010	91	LenaDex Tablets 4 mg (Celgene K.K.)	Approval	Dexamethasone	A drug with a new additional indication and a new dosage for the treatment of multiple myeloma. [Expedited review]
Oncology drugs	Jul. 23, 2010	92	Torisel Injection 25 mg (Pfizer Japan Inc.)	Approval	Temsirolimus	A drug with a new active ingredient indicated for the treatment of unresectable or metastatic renal cell carcinoma.
Oncology drugs	Jul. 23, 2010	93	Abraxane I.V. Infusion 100 mg (Taiho Pharmaceutical Co., Ltd.)	Approval	Paclitaxel	A drug in a new dosage form and with a new dosage indicated for the treatment of breast cancer.
Oncology drugs	Aug. 20, 2010	94	Immucyst Intravesical 81 mg (Nippon Kayaku Co., Ltd.)	Change	Freeze-dried bacillus of Calmette and Guerin for intravesical use (Connaught strain)	A drug with a new additional dosage indicated for the treatment of superficial bladder cancer and carcinoma in situ of bladder.
Oncology drugs	Aug. 20, 2010	95	Revlimid Capsules 5 mg (Celgene K.K.)	Change	Lenalidomide hydrate	A drug with a new additional indication and a new dosage for the treatment of myelodysplastic syndrome associated with a deletion 5q cytogenetic abnormality. [Orphan drug]
Oncology drugs	Oct. 27, 2010	96	Treakisym Injection 100 mg (SymBio Pharmaceuticals Limited)	Approval	Bendamustine hydrochloride	A drug with a new active ingredient indicated for the treatment of relapsed or refractory indolent B-cell non-Hodgkin's lymphoma and mantle cell lymphoma. [Orphan drug]
Oncology drugs	Nov. 16, 2010	97	Taxotere 20 mg for I.V. Infusion Taxotere 80 mg for I.V. Infusion (Aanofi-Aventis K.K.)	Change Change	Docetaxel hydrate	Drugs with new dosages for the treatment of breast cancer, non-small cell lung cancer, gastric cancer, head and neck cancer and ovarian cancer.
Oncology drugs	Dec. 21, 2010	98	Tasigna Capsules 150 mg Tasigna Capsules 200 mg (Novartis Pharma K.K.)	Approval Change	Nilotinib hydrochloride hydrate	Drugs with new additional indications and a new dosage for the treatment of chronic- or accelerated-phase chronic myelocytic leukaemia.
Oncology drugs	Jan. 21, 2011	99	Vidaza for Injection 100 mg (Nippon Shinyaku Co., Ltd.)	Approval	Azacitidine	A drug with a new active ingredient indicated for the treatment of myelodysplastic syndrome. [Orphan drug]
Oncology drugs	Feb. 23, 2011	100	Hycamtin for Injection 1.1 mg (Nippon Kayaku Co., Ltd.)	Change	Nogitecan hydrochloride	A drug with a new additional indication and a new dosage for the treatment of ovarian cancer which has progressed after cancer chemotherapy. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 23, 2011	101	Xeloda Tablet 300 (Chugai Pharmaceutical Co., Ltd.)	Change	Capecitabine	A drug with a new additional indication and a new dosage for the treatment of unresectable advanced or recurrent gastric cancer. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Feb. 23, 2011	102	Gemzar Injection 200 mg Gemzar Injection 1 g (Eli Lilly Japan K.K.)	Change Change	Gemcitabine hydrochloride	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	Mar. 10, 2011	103	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 unresectable advanced or recurrent gastric cancer with HER2 overexpression. [Priority review]
AIDS drugs	Dec. 8, 2010	104	Kaletra Combination Tablets (Abbott Japan Co., Ltd.)	Change	Lopinavir/ritonavir	A drug with new dosages for the treatment of HIV infection. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Biologicals	Oct. 27, 2010	105	Adsorbed Pandemic Influenza Vaccine (H5N1) "Kaketsuken" (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Inactivated influenza virus, H5N1 (whole virion)	A drug with a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
Biologicals	Jan. 14, 2011	106	Freeze-dried Live Attenuated Measles, Rubella Combined Vaccine "Hokken" (The Kitasato Institute)	Approval	Freeze-dried live attenuated measles, rubella combined vaccine	A drug with a new active ingredient indicated for the prevention of measles and rubella.
Biologicals	Jan. 17, 2011	107	Encevac for Subcutaneous Injection (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Approval	Freeze-dried, cell culture-derived Japanese encephalitis vaccine (inactivated)	A drug with a new active ingredient indicated for the prevention of Japanese encephalitis. [Expedited review]
Blood products	May 13, 2010	108	Venoglobulin IH 5% I.V. 2.5 g/50 mL (Benesis Corporation)	Change	Polyethylene glycol treated human normal immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	May 13, 2010	109	Kenketsu Venilon-I for Intravenous Injection 2500 mg (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change	Freeze-dried sulfonated human normal immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	May 13, 2010	110	Kenketu Glovenin-I for I.V. Injection 2500 mg (Nihon Pharmaceutical Co., Ltd.)	Change	Freeze-dried polyethylene glycol treated human normal immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	May 13, 2010	111	Nisseki Polyglobin-N 5% I.V. 2.5 g/50 mL (Japanese Red Cross Society)	Change	pH4-treated acidic human normal immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	May 13, 2010	112	Sanglopor I.V. Infusion 2.5 g (CSL Behring AG; designated marketing authorization holder, CSL Behring K.K.)	Change	Freeze-dried pH4 treated human immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	May 13, 2010	113	Gammagard for Intravenous Injection 2.5 g (Baxter Limited)	Change	Freeze-dried ion-exchange-resin treated human normal immunoglobulin	A drug with a new dosage indicated for the treatment of hypogammaglobulinemia or agammaglobulinemia.
Blood products	Jun. 18, 2010	114	Epogin Subcutaneous Injection Syringe 24000 (Chugai Pharmaceutical Co., Ltd.)	Approval	Epoetin beta (genetical recombination)	A drug with a new dosage in a new additional dosage form indicated for autologous blood storage.

Table 2. Products Approved in FY 2010: New Medical Devices

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Aug. 23, 2010 Total review time: 1055 days Regulatory review time: 385 days	Aug. 2, 2004 Domestic clinical study results	1	Bausch&Lomb Ortho-k (B.L.J. Company, Ltd.)	Approval	Instrument & apparatus 72 Orthokeratology contact lens	An orthokeratology contact lens for patients with myopia and myopic astigmatism to reshape the corneal anterior surface by wearing it during sleep and correct the unaided vision after removal of the lens. A clinical study was conducted to confirm the efficacy and safety of this product. (The original product is in a reexamination period)
1	Sep. 1, 2010 Total review time: 908 days Regulatory review time: 517 days	Jun. 7, 2004 Domestic clinical study results	2	My Emerald (Technopia Co., Ltd.)	Approval	Instrument & apparatus 72 Orthokeratology contact lens	An orthokeratology contact lens for patients with myopia and myopic astigmatism to reshape the corneal anterior surface by wearing it during sleep and correct the unaided vision after removal of the lens. A clinical study was conducted to confirm the efficacy and safety of this product. (The original product is in a reexamination period)
1	Sep. 1, 2010 Total review time: 908 days Regulatory review time: 170 days	Jun. 7, 2004 No clinical study results	3	Visual Emerald (Technopia Co., Ltd.)	Approval	Instrument & apparatus 72 Orthokeratology contact lens	An orthokeratology contact lens for patients with myopia and myopic astigmatism to reshape the corneal anterior surface by wearing it during sleep and correct the unaided vision after removal of the lens. Application for multiple brand name of "My Emerald". (The original product is in a reexamination period)
1	Mar. 9, 2011 Total review time: 538 days Regulatory review time: 182 days	Aug. 9, 1996 Domestic clinical study results	4	Cochlear Baha System (Cochlear Ltd.)	Approval	Instrument & apparatus 73 Bone-anchored hearing aid	A bone-anchored hearing aid that transmits sound vibrations to the bone to improve the ability to hear environmental sounds and speech sounds. A clinical study was conducted to evaluate the efficacy and safety of this product in patients who are not expected to achieve improvement with existing treatments.
3-1	Apr. 2, 2010 Total review time: 119 days Regulatory review time: 104 days	Sep. 22, 2006 No clinical study results	5	Angioguard (Johnson & Johnson K.K.)	Change	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	A device to prevent distal emboli by capturing and removing embolic substances including thrombi while a stent is placed in the carotid artery. Application for a partial change to add Rapid Exchange (RX) type to the delivery system. (A partial change in the reexamination period)
3-1	Apr. 30, 2010 Total review time: 458 days Regulatory review time: 223 days	Aug. 11, 2004 Foreign clinical study results	6	Merci Retriever (Century Medical,Inc.)	Approval	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. A clinical study was conducted to evaluate its efficacy and safety in thrombectomy for cerebral infarction. [Priority review]
3-1	Jul. 6, 2010 Total review time: 617 days Regulatory review time: 162 days	Oct. 31, 2007 Foreign clinical study results	7	GuardWire Protection System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	A balloon-type device to prevent distal emboli by capturing and removing embolic substances including thrombi released while a stent is placed in the carotid artery. The efficacy (the effect of preventing distal emboli) and safety of this product were evaluated based on a clinical study for a carotid artery stent used in combination with this product. (The original product is in a reexamination period)
3-1	Mar. 9, 2011 Total review time: 439 days Regulatory review time: 202 days	- Domestic and foreign clinical study results	8	Nobori (Terumo Corporation)	Approval	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a stent to be inserted and placed at the site of a lesion to maintain the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. The stent is coated with biolimus A9 with cytostatic effect to topically inhibit neointimal proliferation that is thought to be a cause of in-stent restenosis. Clinical studies were conducted to evaluate the efficacy and safety of this product with high-novelty coating.
3-2	Jun. 14, 2010 Total review time: 620 days Regulatory review time: 238 days	Nov. 6, 2007 Foreign clinical study results	9	Bard Agento I.C. (Medicon,Inc.)	Approval	Instrument & apparatus 51 Antimicrobial endotracheal tube	An endotracheal tube inserted into the trachea for airway management. The device has a hydrophilic silver coating with antimicrobial activity to reduce the incidence and delay the onset of ventilator-associated pneumonia (VAP). A clinical study was conducted to verify its effects on reducing the incidence and delaying the onset of VAP.
3-2	Aug. 23, 2010 Total review time: 320 days Regulatory review time: 213 days	Jun. 27, 2008 No clinical study results	10	TALENT Thoracic Stent Graft System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft for thoracic aortic aneurysm used to prevent blood flow into the thoracic aortic aneurysm and its rupture. Application for a partial change to alter the delivery system and the method of sterilization. (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)	Approval/ Partial Change	Classification Generic Name	Notes
4	Apr. 30, 2010 Total review time: 497 days Regulatory review time: 251 days	Dec. 7, 2007 Foreign clinical study results	11	The Crosser System (USCI Japan, Ltd.)	Approval	Instrument & apparatus 51 Oscillating peripheral artery recanalization catheter system	A medical device used to facilitate guidewire recanalization with mechanical vibration for a stenotic lesion in the peripheral vessel that a conventional guidewire for angioplasty cannot cross in percutaneous transluminal angioplasty. A clinical study was conducted to confirm its efficacy and safety in the treatment of a stenotic lesion that a conventional guidewire for angioplasty cannot cross.
4	Jun. 14, 2010 Total review time: 766 days Regulatory review time: 476 days	Aug. 13, 2002 Domestic clinical study results	12	ELVeS Laser (Integral Corporation)	Approval	Instrument & apparatus 31 Diode laser	A system intended for endovenous laser treatment of varicose veins of lower extremities. Endovenous laser irradiation obstructs a target vessel and blocks blood flow in the saphenous vein that causes varicose veins of lower extremities. A clinical study was conducted to confirm its efficacy and safety using stripping, a standard treatment, as a control.
4	Dec. 8, 2010 Total review time: 447 days Regulatory review time: 127 days	- Domestic and foreign clinical study results	13	DuraHeart Left Ventricular Assist System (Terumo Corporation)	Approval	Instrument &apparatus 7 Implantable ventricular assist device	An implantable left ventricular assist device intended for use to improve the blood circulation in patients with end-stage heart failure who require cardiac transplantation. In addition to clinical studies conducted in Europe, where it was used earlier than in Japan, clinical studies were also conducted to investigate the efficacy and safety of this product to the target patients and to confirm the conformity to the medical environment in Japan. [Orphan device]
4	Dec. 8, 2010 Total review time: 688 days Regulatory review time: 160 days	- Domestic clinical study results	14	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Approval	Instrument &apparatus 7 Implantable ventricular assist device	An implantable left ventricular assist device intended for use to improve the blood circulation in patients with end-stage heart failure who require cardiac transplantation. Clinical studies were conducted to investigate the efficacy and safety of this product to the target patients and to confirm the conformity to the medical environment in Japan. [Orphan device]
6	Jun. 11, 2010 Total review time: 49 days Regulatory review time: 18 days	Jul. 2, 1998 No clinical study results	15	KYPHON BKP System (Medtronic Sofamor Danek Co., Ltd.)	Change	Instrument & apparatus 58 Single-use vertebral body restoration device	A treatment system used in percutaneous kyphosis correction in acute painful spinal compression fracture performed for restoration of the height of fractured vertebral body, fixation of the vertebral body, and pain relief. Addition of a manufacturing site. (A partial change in the reexamination period)
6	Jun. 14, 2010 Total review time: 500 days Regulatory review time: 373 days	Aug. 8, 2006 Foreign clinical study results	16	X-STOP PEEK Implant (Medtronic Sofamor Danek Co., Ltd.)	Approval	Medical products 4 Single-use interspinous implant device	An implant to be implanted 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. A clinical study was conducted to verify its efficacy and safety with regard to the mechanism to physically broaden the gap between the upper and lower spinous processes.
Specified Partial Change	Jan. 27, 2011 Total review time: 90 days Regulatory review time: 75 days	2003/5/14 No clinical study results	17	PDA Occlusion Set (Japan Lifeline Co., Ltd.)	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 that transdermally places an occluder at the site of patent ductus arteriosus using a delivery system for occlusion of the arterial canal. Addition of an outside manufacturer of the raw material for an occluder end screw and a delivery cable screw. (A partial change in the reexamination period)
Biologics	Mar. 18, 2011 Total review time: 310 days Regulatory review time: 240 days	- No clinical study results	18	Jace (Japan Tissue Engineering Co., Ltd.)	Change	Instrument & apparatus 7 Human autogenous transplant	An autologous-cultured epidermis in the shape of a sheet, which is manufactured by culturing keratinocytes isolated from patients' skin tissue, using Green's technique. It is applied to the wound surface of severe burn patients for wound closure through epithelialization. Application for a partial change to alter the method of mycoplasma testing and the subculture process for keratinocytes, etc in the manufacturing process. (A partial change in the reexamination period)

Table 3. Products Approved in FY 2010: Improved Medical Devices (with Clinical Data)

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Jun. 2, 2010 Total review time: 789 days Regulatory review time: 426 days	Aug. 16, 2006 Clinical evaluation report	1	Intralase FS Laser (AMO Japan K.K.)	Approval	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	A Nd:Glass laser (wave length 1053 nm) surgical instrument used for creation of a corneal flap in LASIK (laser in-situ keratomileusis) and for cut/resection in keratoplasty. Creation of a corneal flap, lamellar and penetrating cut/incision can be performed with this product, instead of using a keratome or scalpel, in LASIK and keratoplasty. A clinical evaluation report summarizing the results of post-marketing clinical studies conducted by the manufacturer in the USA and literature searches were submitted to evaluate its efficacy and safety.
1	Jul. 21, 2010 Total review time: 411 days Regulatory review time: 186 days	Dec. 6, 2005 Domestic clinical study results	2	Aime Aquafinity (Asahi Kasei Aime Co., Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	A soft contact lens using silicone hydrogel for correcting visual acuity in myopia, hyperopia and astigmatism. The lens is made from a novel material that aims to improve the comfort in wearing while maintaining high oxygen permeability.
1	Nov. 22, 2010 Total review time: 423 days Regulatory review time: 243 days	Jan. 30, 2007 Domestic clinical study results	3	Alcon Acrysof IQ Restor Single-Piece (Alcon Japan Ltd.)	Change	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal posterior chamber lens to be inserted into an aphakic eye after cataract surgery for correcting near and distance visual acuity. A model with an additional power of 3.0D (focal distance: approximately 40 cm) was added in this application, while the additional power of the existing model is 4.0D (focal distance: approximately 30 cm). A clinical study was conducted to evaluate the efficacy and safety of the additional model.
1	Feb. 2, 2011 Total review time: 92 days Regulatory review time: 13 days	- Domestic clinical study results	4	Fall in Eyez (Destiny International Co., Ltd.)	Approval	Instrument & apparatus 72-2 Reusable colored contact lenses not for correcting visual acuity	A reusable colored contact lens that is not for correcting visual acuity that is indicated for daily wear and replaced monthly. Since equivalence to the approved product was not demonstrated with regard to the compounding ratio of the raw material monomer and cross-linker, a clinical study was conducted to evaluate its efficacy and safety.
2	Jun. 2, 2010 Total review time: 1098 days Regulatory review time: 610 days	- Clinical evaluation report	5	Oral Moisture Checking Device Mucus (Life Co., Ltd.)	Approval	Instrument & apparatus 21 Body constituent analysis instrument	A device used as a diagnostic aid that quantifies dryness of oral mucosa by converting an impedance level at the dorsum of the tongue measured by bioelectrical impedance analysis (BIA) technique to an amount of water. Quantification using this product is different from conventional gum test and Saxon test in that the measurement time is as short as approximately 2 seconds and measurement is possible regardless of the presence or absence of patient's consciousness. A clinical evaluation report summarizing the results of literature searches was submitted with regard to the appropriateness of a cut-off level for the degree of dryness and a correlation with the existing methods.
2	Aug. 31, 2010 Total review time: 1516 days Regulatory review time: 768 days	The main body is not subject to regulatory control as a medical device. January 5, 2005 (only resin part for gingival protection) Domestic clinical study results	6	Tion In Office (GC Corporation)	Approval	Dental 2 Dental bleaching material	A dental bleaching agent exclusively designated for office bleaching containing hydrogen peroxide solution and urea hydrogen peroxide as major ingredients. This product was improved to achieve efficient bleaching using a reactor containing visible light-titanium oxide. A clinical study was conducted to evaluate the bleaching performance and safety of this product in discolored human teeth.
3-1	Dec. 2, 2010 Total review time: 308 days Regulatory review time: 258 days	Oct. 10, 2008 Jul. 13, 2009 (38 mm added) Foreign clinical study results	7	Taxus Liberté Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A stent system consisting of a stent and delivery catheter. The stent is coated with antineoplastic agent paclitaxel to topically inhibit neointimal proliferation. Application for a partial change to add a product with a stent length of 38 mm to the existing products for extending the target lesion length from 28 mm to 34 mm. A clinical study was conducted to evaluate the efficacy and safety of a 38-mm-long stent.
3-1	Dec. 14, 2010 Total review time: 595 days Regulatory review time: 345 days	Dec. 11, 2008 Foreign clinical study results	8	Express SD Renal Artery Dilatation Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Stent for blood vessel	A balloon dilating stent system developed for maintaining vascular patency of an atherosclerotic lesion occurring at the opening of the renal artery. A clinical study was conducted to evaluate the efficacy and safety of this product in maintaining vascular dilatation when it was placed at an atherosclerotic lesion occurring at the entrance of the renal artery.
3-1	Feb. 23, 2011 Total review time: 1052 days Regulatory review time: 600 days	Jun. 26, 2006 Foreign clinical study results	9	COOK Vascular Stent (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Stent for iliac artery	This product consists of a stent and delivery system used for treatment of symptomatic vascular diseases such as a stenotic lesion with a reference vessel diameter of 5-9 mm in the iliac artery. A clinical study was conducted to evaluate the efficacy and safety of this product in maintaining vascular patency when it was placed at a stenotic lesion in the iliac artery.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
3-2	Apr. 28, 2010 Total review time: 1083 days Regulatory review time: 829 days	Sep. 21, 2006 Foreign clinical study results	10	ASD Occlusion System (Japan Lifeline Co., Ltd.)	Change	Medical products 4 Prosthetic material for artificial cardiac membrane	A device used for occlusion of ostium secundum atrial septal defect by transdermally placing an occluder (septal occluder) made from a nickel-titanium alloy wire in an atrial septal defect (ASD). This is a partial change approval application to add a septal occluder MF type with a smaller waist diameter to enable placement of the device at multiple atrial septal defects. A clinical study was conducted to evaluate the occlusion performance of this product in multiple defects of the atrial septum.
3-2	Jun. 14, 2010 Total review time: 377 days Regulatory review time: 152 days	Apr. 5, 2007 Foreign clinical study results	11	Tegaderm CHG Dressing (3M Health Care Limited)	Approval	Medical products 4 Antibacterial catheter dressing and protecting material	A catheter dressing and protecting material that covers and protects an insertion site of a vascular catheter. A gel pad included in this device contains an antibacterial agent chlorhexidine gluconate that inhibits regrowth of skin bacterial flora at the insertion site. A clinical study was conducted to evaluate whether use of this product inhibited regrowth of skin bacterial flora on normal skin and the performance of fixation of a catheter with this product in patients inserted with a catheter.
3-2	Sep. 29, 2010 Total review time: 2009 days Regulatory review time: 676 days	Apr. 23, 1998 (IDE Approval) Domestic clinical study results	12	Bioglue Surgical Adhesive (Century Medical, Inc.)	Approval	Medical products 4 Surgical adhesive	A surgical adhesive containing bovine serum albumin and glutaraldehyde as major ingredients. This product is used for adhesion and hemostasis at an artificial blood vessel suture site associated with closure of aortic dissection and aortic dissection lumen (including dissecting aneurysm of the aorta). A clinical study was conducted to evaluate the degree of adhesion (efficacy) and safety of this product in such surgeries.
3-2	Dec. 17, 2010 Total review time: 521 days Regulatory review time: 216 days	Apr. 15, 2008 Jul. 15, 2008 (change to the current product) Foreign clinical study results	13	TALENT Abdominal Stent Graft System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	A stent graft for abdominal aortic aneurysm used to prevent blood flow into abdominal aortic aneurysm and prevent rupture of aortic aneurysm. A clinical study was conducted to evaluate the efficacy and safety of stent graft treatment for abdominal aortic aneurysm.
3-2	Mar. 16, 2011 Total review time: 866 days Regulatory review time: 215 days	May. 21, 2008 Foreign clinical study results	14	COOK Zenith TX2 TAA Endovascular Graft (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	This product consists of a stent graft and delivery system used for endovascular treatment of descending thoracic aortic aneurysm. It consists of a self-expanding stainless-steel stent and polyester graft. A clinical study was conducted to evaluate the efficacy and safety of stent graft treatment for thoracic aortic aneurysm.
4	Jun. 23, 2010 Total review time: 545 days Regulatory review time: 289 days	May. 16, 2008 Foreign clinical study results	15	Acuity Spiral (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A spirally-molded lead to be placed in the coronary vein for CRT. A clinical study was conducted to demonstrate that the safety and efficacy of this product were within an acceptable range compared to the existing products.
4	Jul. 5, 2010 Total review time: 1036 days Regulatory review time: 528 days	May. 21, 2004 Foreign clinical study results	16	ZOLL AED Plus Automated External Defibrillator (Zoll Medical Corporation)	Approval	Instrument & apparatus 12 Automatic defibrillator for non-healthcare professionals	A semi-automatic external defibrillator using biphasic defibrillation waveform dedicated for use by non-healthcare professionals, equipped with a pad with an acceleration sensor to enable the display of the rate and depth of chest compression during cardiopulmonary resuscitation. A clinical study was conducted to confirm the efficacy and safety of defibrillator function using biphasic waveform.
4	Aug. 23, 2010 Total review time: 482 days Regulatory review time: 302 days	Oct. 1, 2004 Foreign clinical study results	17	Precision Plus SCS System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 12 Implantable stimulator for pain relief	An implantable stimulator for pain relief to be applied to patients with chronic refractory pain in the trunk and extremities who are not sufficiently responsive to pain relief therapy with drugs or nerve block. It can be charged non-invasively from outside the body. A clinical study was conducted to evaluate the safety and efficacy of this product for relief of chronic pain.
4	Sep. 3, 2010 Total review time: 1326 days Regulatory review time: 229 days	Jun. 20, 2005 Foreign clinical study results	18	Revolution 2 (Volcano Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Central circulation system intravascular ultrasound catheter	A catheter for intravascular ultrasound diagnostic imaging with a built-in ultrasound transducer for imaging intravascular lumen and vascular wall using ultrasound. The ultrasonic frequency of this product is 45 MHz. A clinical study was conducted to primarily evaluate system-related adverse events.
4	Oct. 8, 2010 Total review time: 259 days Regulatory review time: 157 days	- Foreign clinical study results	19	Attain Ability Straight Leads (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A tined lead to be placed in a coronary vein for CRT. A clinical study was conducted to demonstrate that the safety and efficacy of this product were within an acceptable range compared to the existing products.
4	Dec. 7, 2010 Total review time: 326 days Regulatory review time: 173 days	Jan. 29, 2010 Foreign clinical study results	20	Accent DR ACC (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Dec. 7, 2010 Total review time: 326 days Regulatory review time: 173 days	Jan. 29, 2010 Foreign clinical study results	21	Accent RF DR ACC (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 7, 2010 Total review time: 326 days Regulatory review time: 173 days	Jan. 29, 2010 Foreign clinical study results	22	Anthem ACC (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable pulse generator that delivers CRT. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in the patient's biventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 7, 2010 Total review time: 326 days Regulatory review time: 173 days	Jan. 29, 2010 Foreign clinical study results	23	Anthem RF ACC (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable pulse generator that delivers CRT. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in the patient's biventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 9, 2010 Total review time: 324 days Regulatory review time: 168 days	Jan. 29, 2010 Foreign clinical study results	24	Nuance DR RF (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 9, 2010 Total review time: 324 days Regulatory review time: 168 days	Jan. 29, 2010 Foreign clinical study results	25	Nuance DR (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 14, 2010 Total review time: 897 days Regulatory review time: 377 days	May. 15, 2008 Foreign clinical study results	26	Ovatio CRT-D (Sorin CRM)	Approval	Instrument & Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT, with the function of a defibrillator. A clinical study was conducted to evaluate the efficacy and safety of this product as a CRT-D system.
4	Dec. 14, 2010 Total review time: 482 days Regulatory review time: 226 days	Oct. 27, 2009 Foreign clinical study results	27	Paradym CRT-D (Sorin CRM)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT, with the function of a defibrillator. A clinical study was conducted to evaluate the efficacy and safety of this product as a CRT-D system.
4	Dec. 17, 2010 Total review time: 366 days Regulatory review time: 168 days	- Foreign clinical study results	28	AnalyST Accel RF VR (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	Automatic implantable defibrillator with the function of single-chamber bradycardia pacing. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular threshold were submitted to evaluate the efficacy and safety of this function.
4	Dec. 17, 2010 Total review time: 365 days Regulatory review time: 167 days	- Foreign clinical study results	29	AnalyST Accel RF DR (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Dual-chamber automatic implantable defibrillator	Automatic implantable defibrillator with the function of dual-chamber bradycardia pacing. Results from clinical studies of a different model with a function to automatically adjust pulse amplitude according to a change in patient's ventricular and atrial thresholds were submitted to evaluate the efficacy and safety of this function.
4	Dec. 17, 2010 Total review time: 365 days Regulatory review time: 167 days	Jan. 29, 2010 Foreign clinical study results	30	Promote Accel RF (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT. A clinical study was conducted to evaluate the efficacy and safety of a function to automatically adjust pulse amplitude according to a change in the patient's biventricular and atrial thresholds.
4	Mar. 29, 2011 Total review time: 456 days Regulatory review time: 161 days	- Foreign clinical study results	31	Situs 2 OTW Lead (Sorin CRM)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A bipolar left ventricular pacing lead for coronary veins and its accessory connected to CRT-P and CRT-D and used during cardiac resynchronization treatment. The first left ventricular pacing lead of the company. Results from clinical studies were submitted to evaluate its efficacy and safety.
5	Apr. 30, 2010 Total review time: 231 days Regulatory review time: 151 days	- Domestic clinical study results	32	Cellsorba E (Asahi Kasei Kuraray Medical Co., Ltd.)	Change	Instrument & apparatus 7 Purifie for blood cell removal	Application for a partial change to add a miniaturized column to the approved product "Cellsorba E (approval No.: 21300BZZ00440000)."A clinical study was conducted to evaluate the efficacy and safety of this product in patients with pediatric active ulcerative colitis.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
5	Sep. 14, 2010 Total review time: 487 days Regulatory review time: 255 days	- Domestic clinical study results	33	PTEG Kit (Akita Sumitomo Bakelite Co., Ltd.)	Approval	Instrument & apparatus 51 Enteral feeding kit for long-term use	An enteral feeding tube and its insertion kit used in a procedure for percutaneous trans-esophageal insertion and placement of a catheter in the gastrointestinal tract to provide enteral feeding and decompression to patients for whom it is difficult to perform gastrostomy. A clinical study was conducted to evaluate the efficacy and safety of percutaneous trans-esophageal gastro-tubing (PTEG) in patients receiving enteral feeding or decompression.
5	2010/10/21 Total review time: 325 days Regulatory review time: 200 days	- Domestic clinical study results	34	Toraylight NV (Toray Industries, Inc.)	Approval	Instrument & apparatus 7 Hollow-fiber dialyzer	A hollow fiber dialyzer. Because equivalence to the approved products was not demonstrated with regard to the semipermeable membrane material, a clinical study was conducted to evaluate its efficacy and safety.
5	Dec. 1, 2010 Total review time: 404 days Regulatory review time: 248 days	- Domestic clinical study results	35	Maxiflux (Nipro Corporation)	Approval	Instrument & apparatus 7 Hemodiafilter	A hollow fiber membrane hemodiafilter. Because equivalence to the approved products was not demonstrated with regard to the semipermeable membrane material and performance profile, a clinical study was conducted to evaluate its efficacy and safety.
5	Feb. 2, 2011 Total review time: 687 days Regulatory review time: 344 days	- Domestic clinical study results	36	Fibroscan (InterMedical Co., Ltd.)	Approval	Instrument & apparatus 12 Versatile ultrasound diagnostic imaging device	A device to measure non-invasively liver stiffness using ultrasonic waves, etc. A clinical study was conducted to evaluate whether it could qualitatively measure the stiffness of the liver.
6-1	Sep. 14, 2010 Total review time: 837 days Regulatory review time: 329 days	Sep. 5, 2002 Domestic clinical study results	37	Trabecular Metal Modular Acetabular System (Zimmer K.K.)	Approval	Medical products 4 Artificial hip joint, acetabular component	A locking ring used to fix a titanium alloy acetabular cup and liner that are used at the pelvic side to replace the function of the hip joint during hip replacement arthroplasty (including revision hip replacement arthroplasty). The outer surface is coated with a consecutive 3-D dodecahedron porous structure made from tantalum to ensure direct fixation to the bone. A clinical study was conducted to evaluate the efficacy and safety of this device with this novel surface structure.
6-1	Nov. 9, 2010 Total review time: 855 days Regulatory review time: 237 days	Jul. 19, 2001 Feb. 12, 2002 Domestic clinical study results	38	Trabecular Metal Monoblock (Zimmer K.K.)	Approval	Medical products 4 Artificial knee joint, patellar and tibial component	A tibia component to be implanted at the tibial side to reconstruct the function of the knee joint and a patellar component to be implanted in the patella during knee replacement arthroplasty (including revision knee replacement arthroplasty). While the shape and size of this product are equal to those of the approved product, a metal part and ultrahigh molecular weight polyethylene part are compressed to form an integrated architecture. In addition, improved bone fixation and reduced stress shielding on bone are expected because of a new raw material (consecutive 3-D dodecahedron porous structure made from tantalum) used in this product. A clinical study was conducted to evaluate the efficacy and safety of this device with improved structure, etc.
6-2	Jan. 6, 2011 Total review time: 1011 days Regulatory review time: 496 days	- Domestic clinical study results	39	Biohesive (Alcare Co., Ltd.)	Approval	Medical products 4 Antibacterial wound dressing and protecting material	A wound dressing and protecting material used to protect wound reaching subcutaneous adipose tissue, maintain a moist environment, promote healing and relieve pain. With hydrocolloid material as a base material, this product contains sulfadiazine silver 0.05% to improve hygiene inside the dressing material. Since equivalence to the approved product was not demonstrated with regard to this structure, a clinical study was conducted to evaluate its efficacy and safety.
8	Feb. 23, 2011 Total review time: 208 days Regulatory review time: 67 days	- Domestic clinical study results	40	Visceral Fat Area Measurement Device HDS-2000 (Omron Healthcare Co., Ltd.)	Approval	Instrument & apparatus 21 Body constituent analysis instrument	A body constituent analysis instrument that estimates and shows a cross-sectional area of visceral fat based on bioelectrical impedance level and major axis and minor axis of cross-sectional area of the abdomen. It is indicated for secondary screening (detection of cross-sectional area of visceral fat $\leqq 100\ cm^2$) of patients who are tested positive according to the diagnostic criteria using abdominal circumference, one of the diagnostic criteria for metabolic syndrome. A clinical study was conducted to evaluate the estimation precision of the cross-sectional area of visceral fat in relation to correlation with the cross-sectional area of visceral fat obtained from CT images.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs, etc. Instructed by MHLW in FY 2010

Post-marketing safety measures implemented by MHLW in FY 2010

	Drugs	Medical devices
Revision of PRECAUTIONS instructed	341	3
Information published in the Pharmaceuticals and Medical Devices Safety Information	33	3

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

Revision of PRECAUTIONS in the package inserts of drugs, instructed by MHLW in FY 2010

Date	Drug name
Apr. 27, 2010	1. Infliximab (genetical recombination) 2. Liraglutide (genetical recombination) 3. Clopidogrel sulfate 4. Alogliptin benzoate 5. Sitagliptin phosphate hydrate 6. Vildagliptin 7. Adalimumab (genetical recombination) 8. Etanercept (genetical recombination) 9. Tacrolimus hydrate (oral dosage form, injectable dosage form) 10. Atomoxetine hydrochloride 11. Sertraline hydrochloride 12. Paroxetine hydrochloride hydrate 13. Fluvoxamine maleate 14. Vecuronium bromide Rocuronium bromide 15. Clopidogrel sulfate 16. Ofloxacin (oral dosage form) Levofloxacin hydrate (oral dosage form) (low-dose) 17. Levofloxacin hydrate (oral dosage form) (high-dose) 18. Darunavir ethanolate 19. Ribavirin (tablets) 20. Freeze-dried, cell culture-derived Japanese encephalitis vaccine (inactivated) 21. Recombinant adsorbed hepatitis B vaccine (yeast-derived) 22. Peginterferon alfa-2a (genetical recombination)
Jun. 1, 2010	1. Furosemide 2. Oxytocin 3. Dinoprost 4. Dinoprostone 5. Deferasirox 6. Colchicine 7. Mirtazapine 8. Efonidipine hydrochloride ethanolate 9. Famotidine 10. Purified human menopausal gonadotrophin Human menopausal gonadotrophin 11. Human chorionic gonadotrophin 12. Follitropin beta (genetical recombination) 13. Follitropin alfa (genetical recombination) (75 IU, 450 IU, 900 IU) 14. Follitropin alfa (genetical recombination) (150 IU) 15. Estriol (injectable dosage form) Chlormadinone acetate/Mestranol Norethisterone/Mestranol Norgestrel/Ethinylestradiol Hydroxyprogesterone caproate/Estradiol benzoate Hydroxyprogesterone caproate/Estradiol dipropionate 16. Norethisterone/Ethinylestradiol (preparation with the indication for dysmenorrhoea) 17. Clomifene citrate cyclofenil 18. Gonadorelin acetate (1.2 mg, 2.4 mg)

Date	Drug name
	19. Estriol (vaginal tablet) 20. Alendronate sodium hydrate (oral dosage form) Etidronate disodium Sodium risedronate hydrate 21. Alendronate sodium hydrate (injectable dosage form) Incadronate disodium hydrate Zoledronic acid hydrate Pamidronate disodium hydrate 22. Minodronic acid hydrate 23. Tamoxifen citrate 24. Over-the-counter Drugs (antitussives and expectorants) Preparations containing codeine phosphate hydrate Preparations containing dihydrocodeine phosphate Preparations containing hydrocodeine phosphate sekisanol
Jul. 6, 2010	1. Olmesartan medoxomil Olmesartan medoxomil/Azelnidipine Telmisartan Telmisartan/Hydrochlorothiazide Valsartan Valsartan/Amlodipine besilate Valsartan/Hydrochlorothiazide 2. Yokukansan 3. Phenytoin Phenytoin/Phenobarbital Phenytoin/Phenobarbital/Caffeine and sodium benzoate Phenytoin sodium 4. Desogestrel/Ethinylestradiol Norethisterone/Ethinylestradiol (preparations with the indication of contraception) Levonorgestrel/Ethinylestradiol 5. Protamine sulfate 6. Enoxaparin sodium 7. Tegafur/Gimeracil/Oteracil potassium 8. Over-the-counter Drugs Yokukansan
Aug. 10, 2010	1. Amitriptyline hydrochloride Amoxapine Imipramine hydrochloride Clomipramine hydrochloride Setiptiline maleate Duloxetine hydrochloride Dosulepin hydrochloride Trazodone hydrochloride Trimipramine maleate Nortriptyline hydrochloride Maprotiline hydrochloride Mianserin hydrochloride Mirtazapine Milnacipran hydrochloride Lofepramine hydrochloride 2. Sertraline hydrochloride Paroxetine hydrochloride hydrate 3. Fluvoxamine maleate 4. Dienogest 5. Cladribine 6. Amphotericin B (liposome preparation)

Date	Drug name
	7. Amphotericin B [non-liposome preparation (injectable dosage form)] 8. Salazosulfapyridine (tablet, suppository) 9. Enoxacin hydrate Tosufloxacin tosilate hydrate (oral dosage form) Pazufloxacin mesilate Lomefloxacin hydrochloride (oral dosage form) 10. Garenoxacin mesilate hydrate 11. Sitafloxacin hydrate Prulifloxacin 12. Ciprofloxacin Ciprofloxacin hydrochloride 13. Sparfloxacin 14. Norfloxacin (oral dosage form) 15. Didanosine 16. Raltegravir potassium 17. Tocilizumab (genetical recombination)
Aug. 26, 2010	1. Influenza HA vaccine Influenza A (H1N1) HA vaccine Influenza A (H1N1) Emulsion HA Vaccine Cell-culture Derived Influenza A (H1N1) Emulsion HA Vaccine
Sep. 16, 2010	1. Thalidomide
Sep. 28, 2010	1. Goserelin acetate (1.8 mg) 2. Goserelin acetate (3.6 mg) 3. Goserelin acetate (10.8 mg) 4. Leuprorelin acetate 5. Solifenacin succinate 6. Alglucosidase alfa (genetical recombination) 7. Adalimumab (genetical recombination) 8. Pemetrexed sodium hydrate 9. Erlotinib hydrochloride 10. Gefitinib 11. Bicalutamide Flutamide 12. Alprazolam Diazepam (oral dosage form) Nitrazepam Haloxazolam 13. Estazolam Nimetazepam Brotizolam Lorazepam 14. Oxazolam Quazepam Cloxazolam Clorazepate dipotassium Chlordiazepoxide Tofisopam Triazolam Prazepam Fludiazepam Flutazolam Flutoprazepam Flurazepam hydrochloride Mexazolam

Date	Drug name
	Medazepam Rilmazafone hydrochloride hydrate Lormetazepam Clotiazepam 15. Diazepam (injectable dosage form) 16. Flunitrazepam 17. Bromazepam 18. Midazolam 19. Ethyl loflazepate 20. Clonazepam 21. Clobazam 22. Etizolam 23. Landiolol hydrochloride 24. Infliximab (genetical recombination) 25. Somatropin (genetical recombination) 26. Sitagliptin phosphate hydrate 27. Adalimumab (genetical recombination) 28. Etanercept (genetical recombination) 29. Irinotecan hydrochloride hydrate 30. Miriplatin hydrate 31. Rituximab (genetical recombination) 32. Glucagon Glucagon (genetical recombination) 33. Iodine addition products of the ethylesters of the fatty acids obtained from poppyseed oil (MIRIPLA suspension vehicle)
Oct. 12, 2010	1. Liraglutide (genetical recombination) 2. Ketoprofen (cream) 3. Ketoprofen (gel, lotion) 4. Ketoprofen (tape, poultice) 5. Over-the-counter Drugs Preparations containing ketoprofen (dermatologic preparation)
Oct. 26, 2010	1. Keigairengyoto Nijutsuto 2. Ryutanshakanto 3. Aliskiren fumarate 4. Ramosetron hydrochloride (oral dosage form 2.5 μg, 5 μg) 5. Imidafenacin 6. Yttrium (^{90}Y) ibritumomab tiuxetan (genetical recombination) Indium (^{111}In) ibritumomab tiuxetan (genetical recombination) 7. Sorafenib tosilate 8. Vancomycin hydrochloride (ophthalmic agent) 9. Itraconazole 10. Over-the-counter Drugs Keigairengyoto Nijutsuto 11. Over-the-counter Drugs Ryutanshakanto
Nov. 30, 2010	1. Atomoxetine hydrochloride 2. Carteolol hydrochloride (ophthalmic solution) 3. Lanthanum carbonate hydrate 4. Thiamazole 5. Cilostazol 6. Sugammadex sodium

Date	Drug name
	7. Deferoxamine mesilate 8. Capecitabine 9. Gefitinib 10. Etravirine 11. Yellow fever vaccine
Jan. 11, 2011	1. Pilsicainide hydrochloride hydrate (oral dosage form) 2. Pilsicainide hydrochloride hydrate (injectable dosage form) 3. Ciclosporin (oral dosage form, injectable dosage form) 4. Imatinib mesilate Nilotinib hydrochloride hydrate 5. Sunitinib malate 6. Mianserin hydrochloride 7. Trichlormethiazide Hydrochlorothiazide Benzylhydrochlorothiazide Indapamide Benzylhydrochlorothiazide/Reserpine/Carbazochrome Meticrane 8. Mefruside Tripamide 9. Losartan potassium/Hydrochlorothiazide 10. Agalsidase alfa (genetical recombination) 11. Sitagliptin phosphate hydrate 12. Temozolomide 13. Miriplatin hydrate 14. Entecavir hydrate 15. Freeze-dried, cell culture-derived Japanese encephalitis vaccine (inactivated) 16. Perflubutane 17. Iodine addition products of the ethylesters of the fatty acids obtained from poppyseed oil (MIRIPLA suspension vehicle) 18. Remifentanil hydrochloride
Feb. 15, 2011	1. Isosorbide 2. Unseiin Gorinsan 3. San'oshashinto 4. Mesalazine (tablet 250 mg, 500 mg, granule, enema) 5. Mesalazine (tablet 400 mg) 6. Dried thyroid Liothyronine sodium 7. Levothyroxine sodium hydrate 8. Goserelin acetate 9. Oxybutynin hydrochloride 10. Pirfenidone 11. Actinomycin D 12. Cisplatin (excluding intra-arterial injection) 13. Tamoxifen citrate 14. Minocycline hydrochloride (oral dosage form, injectable dosage form) 15. Prulifloxacin 16. Ribavirin (capsules) 17. Interferon beta (for administration in combination with ribavirin) 18. Over-the-counter Drugs Unseiin Gorinsan

Date	Drug name
	19. Over-the-counter Drugs San'oshashinto
Mar. 22, 2011	1. Aripiprazole 2. Tolvaptan 3. Pioglitazone hydrochloride Pioglitazone hydrochloride/Glimepiride Pioglitazone hydrochloride/Metformin hydrochloride 4. Tacrolimus hydrate (oral dosage form, injectable dosage form) 5. Lenalidomide hydrate 6. Sanilvudin 7. Freeze-dried live attenuated mumps vaccine 8. Anti-human thymocyte immunoglobulin, rabbit 9. Acetaminophen (preparations that are not indicated for osteoarthritis) 10. Isopropylantipyrine/Acetaminophen/Allylisopropylacetylurea/Anhydrous caffeine 11. Oxypertine Olanzapine Carpipramine hydrochloride hydrate Carpipramine maleate Quetiapine fumarate Clocapramine hydrochloride hydrate Clozapine Chlorpromazine hydrochloride Chlorpromazine hydrochloride/Promethazine hydrochloride/Phenobarbital Chlorpromazine hibenzate Chlorpromazine phenolphthalinate Spiperone Sultopride hydrochloride Sulpiride Zotepine Timiperone Trifluoperazine maleate Nemonapride Paliperidone Pipamperone hydrochloride Pimozide Fluphenazine decanoate Fluphenazine maleate Prochlorperazine maleate Prochlorperazine mesilate Blonanserin Propericiazine Bromperidol Perphenazine Perphenazine hydrochloride Perphenazine fendizoate Perphenazine maleate Perospirone hydrochloride hydrate Mosapramine hydrochloride Moperone hydrochloride Risperidone Levomepromazine hydrochloride Levomepromazine maleate 12. Trazodone hydrochloride 13. Haloperidol 14. Haloperidol decanoate 15. Salicylamide /Acetaminophen/Anhydrous caffeine/ Chlorpheniramine maleate (for adults)

Date	Drug name
	Salicylamide/Acetaminophen/Anhydrous caffeine/ Promethazine methylenedisalicylate (for adults) 16. Salicylamide/Acetaminophen/Anhydrous caffeine/ Chlorpheniramine maleate (for pediatric) Salicylamide/Acetaminophen/Anhydrous caffeine/ Promethazine methylenedisalicylate (for pediatric) 17. Amiodarone hydrochloride (injectable dosage form) 18. Olmesartan medoxomil Olmesartan medoxomil/Azelnidipine 19. Beraprost sodium 20. Diprophylline/Dihydrocodeine phosphate/ dl-Methylephedrine hydrochloride/ Diphenhydramine salicylate/Acetaminophen/ Bromovalerylurea Ephedra herb extract/Caffeine and sodium benzoate/ Magnesium oxide/Acetaminophen/Scopolia extract 21. Tiotropium bromide hydrate 22. Minocycline hydrochloride (dental) 23. Azathioprine 24. Everolimus (0.25 mg·0.5 mg·0.75 mg) 25. Gusperimus hydrochloride 26. Ciclosporin (oral dosage form, injectable dosage form) 27. Mycophenolate mofetil 28. Mizoribine 29. Everolimus (5 mg) 30. Efavirenz 31. Saquinavir mesilate 32. Nevirapine 33. Peramivir hydrate 34. Laninamivir octanoate hydrate 35. Itraconazole 36. Basiliximab (genetical recombination) 37. Muromonab-CD3 38. Monobasic sodium phosphate monohydrate and anhydrous dibasic sodium phosphate 39. Over-the-counter Drugs Nanpao
Mar. 29, 2011	1. Pneumococcal polysaccharide conjugate vaccine (adsorbed) Haemophilus Type b Conjuegate Vaccine (Tetanus Toxoid Conjugate)

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

Medical safety measures for drugs instructed by MHLW in FY 2010

Date	Drug name
Oct. 28, 2010	Methylergometrine maleate preparations Ritodrine hydrochloride preparations

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

Table 5. Revision of PRECAUTIONS and Notifications on Instruction of Self-check for Medical Devices in FY 2010

Revision of PRECAUTIONS for medical devices instructed in FY 2010

Date	Title
Dec. 3, 2010	Revision of Package Insert of Inferior Vena Cava Filter

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

Notifications on instruction of self-check for medical devices issued in FY 2010

Date	Title
Jun. 9, 2010	Self-checks, etc. for handling of bipolar electrode used along with electrosurgical device Reference: Handling of bipolar electrode used along with electrosurgical device (request for provision of information to users)
Mar. 31, 2011	Post-marketing safety measures for plasma gas sterilizers

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

Table 6. FY 2010 Pharmaceuticals and Medical Devices Safety Information (No. 268-278)

Date	No.	Contents
Apr. 28, 2010	268	1. Manuals for Management of Individual Serious Adverse Drug Reactions 2. Project of Japan Drug Information Institute in Pregnancy 3. Important Safety Information [1] Atorvastatin Calcium Hydrate, Simvastatin, Pitavastatin Calcium, Pravastatin Sodium, Fluvastatin Sodium, Rosuvastatin Calcium, Amlodipine Besilate/Atorvastatin Calcium Hydrate [2] Cetuximab (Genetical Recombination) 4. Revision of PRECAUTIONS (No.215) Aripiprazole (and 6 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
May 26, 2010	269	1. Project to Collect and Analyze Medical “Near-Miss” Incidents from Pharmacies 2. Important Safety Information [1] Clopidogrel Sulfate [2] Sitagliptin Phosphate Hydrate, Vildagliptin, Liraglutide (Genetical Recombination), Alogliptin Benzoate [3] Tacrolimus Hydrate (oral dosage form, injectable dosage form) 3. Revision of PRECAUTIONS (No.216) Infliximab (Genetic Recombination) (and 15 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jun. 30, 2010	270	1. Association between the use of TNF Blockers and Malignancies 2. Important Safety Information [1] Deferasirox [2] Furosemide 3. Revision of PRECAUTIONS (No. 217) Oxytocin (and 21 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Project to survey provision and availability of information on appropriate use of drugs
Jul. 28, 2010	271	1. Precautions in Handling of Bipolar Electrode Used along with Electrosurgical Device 2. Important Safety Information [1] Olmesartan Medoxomil, Olmesartan Medoxomil/Azelnidipine, Telmisartan, Telmisartan/Hydrochlorothiazide, Valsartan, Valsartan/Amlodipine Besilate, Valsartan/Hydrochlorothiazide [2] Yokukansan 3. Revision of Precautions (No. 218) Phenytoin (and 5 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Sep. 29, 2010	272	1. Safety Measures Against Bisphosphonate-related Osteonecrosis and Osteomyelitis of Jaw: Review Process and Implementation 2. Revision of Precautions (No. 219) Amitriptyline Hydrochloride (and 16 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 26, 2010	273	1. The Relief System for Sufferers from Adverse Drug Reactions and Diseases Infected from Biological Products 2. Summary of the Report on Adverse Reactions Associated with the Influenza A (H1N1) Vaccines in the 2009 Season 3. Important Safety Information [1] Influenza HA Vaccine, Influenza A (H1N1) HA Vaccine, Influenza A (H1N1) HA Emulsion Vaccine, Cell-culture Derived Influenza A (H1N1) HA Emulsion

Date	No.	Contents
		Vaccine [2] Thalidomide 4. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Reports on adverse reactions associated with seasonal influenza vaccines in FY 2009 (Conclusion of the Vaccine Adverse Reaction Review Committee)
Nov. 24, 2010	274	1. Important Safety Information [1] Adalimumab (Genetical Recombination) [2] Erlotinib Hydrochloride [3] Gefitinib [4] Goserelin Acetate [5] Solifenacin Succinate [6] Bicalutamide, Flutamide [7] Pemetrexed Sodium Hydrate [8] Leuprorelin Acetate 2. Revision of Precautions (No. 220) Alglucosidase alfa (Genetical Recombination) (and 22 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 24, 2010	275	1. Safety Measures for Use of the Antidiabetic Drugs with New Action Mechanisms (DPP-4 inhibitors and GLP-1 receptor agonists) 2. Important Safety Information [1] Keigairengyoto, Nijutsuto [2] Ryutanshakanto 3. Revision of Precautions (No. 221) Aliskiren Fumarate (and 8 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jan. 26, 2011	276	1. Safety Measures Against Photosensitivity Due to Topical Ketoprofen 2. Research on System for Receiving Adverse Reaction Information from Patients 3. Revision of Precautions (No. 222) (1) Atomoxetine Hydrochloride (and 10 others) (2) Inferior Vena Cava Filter 4. List of Products Subject to Early Post-marketing Phase Vigilance
Mar. 1, 2011	277	1. Safety Measures for Gemtuzumab Ozogamicin (genetical recombination) 2. Important Safety Information [1] Imatinib Mesilate, Nilotinib Hydrochloride Hydrate [2] Sunitinib Malate [3] Pilsicainide Hydrochloride Hydrate 3. Revision of Precautions (No. 223) Ciclosporin (oral and injectable dosage form) (and 13 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Mar. 23, 2011	278	1. Revision of Package Insert of Inferior Vena Cava Filter 2. Promotion of Safety Measures Using the PMDA medi-navi 3. Important Safety Information [1] Isosorbide [2] Unseiin 4. Revision of Precautions (No. 224) Gorinsan (and 17 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance

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

Table 7. FY 2010 PMDA Medical Safety Information

No.	Date published	Title
16	April 2010	Precautions in Handling Electric Scalpels (Part 3)
17	May 2010	Precautions in Handling of Prefilled Syringes
18	June 2010	Precautions in Handling of Lancing Devices for Capillary Blood Sampling
19	September 2010	Administration Error of Concentrated Potassium (K) Solutions for Injection
20	November 2010	Precautions in Artificial Respiration (No. 3)
21	January 2011	Precautions in Flow Rate Programming of Infusion Pumps
22	February 2011	Precautions in Handling Blood Tubing Sets Used for Blood Purification

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, 2010)

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		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		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		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		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		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	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		Domestic		739,800	739,800
						Article 17 (4) 1-b (1)	
				Overseas		933,500 + travel expenses	933,500 + travel expenses
						Article 17 (4) 1-b (2)	
		Biological drugs/Radiopharmaceuticals		Domestic		666,100	666,100
						Article 17 (4) 1-a (1)	
				Overseas		844,400 + travel expenses	844,400 + travel expenses
						Article 17 (4) 1-a (2)	
		Sterilized drugs/Sterilized quasi-drugs		Domestic		201,300	201,300
						Article 17 (4) 1-c (1)	
				Overseas		229,800 + travel expenses	229,800 + travel expenses
						Article 17 (4) 1-c (2)	
		Other drugs/quasi-drugs		Domestic		141,200	141,200
						Article 17 (4) 1-d (1)	
				Overseas		155,400 + travel expenses	155,400 + travel expenses
						Article 17 (4) 1-d (2)	
		Package, labeling, storage, external testing, etc.		Domestic		63,800	63,800
						Article 17 (4) 2-a, Article 17 (5) 1-a	
				Overseas		84,800 + travel expenses	84,800 + travel expenses
						Article 17 (4) 2-b, Article 17 (5) 1-b	
	Renewal of the above	Biological drugs/ Radiopharmaceuticals	Basic	Domestic		436,000	436,000
						Article 17 (4) 3-a (1)	
				Overseas		554,200 + travel expenses	554,200 + travel expenses
						Article 17 (4) 3-a (2)	
			Addition of products	Domestic		30,500	30,500
						Article 17 (4) 3-a (1)	
				Overseas		30,500	30,500
						Article 17 (4) 3-a (2)	
		Sterilized drugs/ Sterilized quasi-drugs	Basic	Domestic		380,000	380,000
						Article 17 (4) 3-b (1)	
				Overseas		480,000 + travel expenses	480,000 + travel expenses
						Article 17 (4) 3-b (2)	
			Addition of products	Domestic		12,400	12,400
						Article 17 (4) 3-b (1)	
				Overseas		12,400	12,400
						Article 17 (4) 3-b (2)	
		Other drugs/ quasi-drugs	Basic	Domestic		336,500	336,500
						Article 17 (4) 3-c (1)	
				Overseas		409,400 + travel expenses	409,400 + travel expenses
						Article 17 (4) 3-c (2)	
			Addition of products	Domestic		9,600	9,600
						Article 17 (4) 3-c (1)	
				Overseas		9,600	9,600
						Article 17 (4) 3-c (2)	
		Package, labeling, storage, external testing, etc.	Basic	Domestic		258,500	258,500
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		338,100 + travel expenses	338,100 + travel expenses
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
			Addition of products	Domestic		6,700	6,700
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		6,700	6,700
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	

Classification				User fees		
				Review	Inspection	Total
GLP inspection of drugs						
GLP		Domestic			2,062,400	2,062,400
					Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
		Overseas			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		Domestic		2,723,200	2,723,200
					Article 17 (3) 2-a	
			Overseas		3,011,900 + travel expenses	3,011,900 + travel expenses
					Article 17 (3) 2-b	
	Line extension products		Domestic		720,800	720,800
					Article 17 (3) 2-c	
			Overseas		751,800 + travel expenses	751,800 + travel expenses
					Article 17 (3) 2-d	
GCP inspection of generic drugs			Domestic		645,200	645,200
					Article 17 (3) 2-e	
			Overseas		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		Domestic		2,193,300	2,193,300
					Article 17 (9) 2-b (1)	
			Overseas		2,409,600 + travel expenses	2,409,600 + travel expenses
					Article 17 (9) 2-b (2)	
	Line extension products		Domestic		752,600	752,600
					Article 17 (9) 2-b (3)	
			Overseas		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		Domestic		739,800 Article 17 (4) 1-b (1)	739,800
				Overseas		933,500 + travel expenses Article 17 (4) 1-b (2)	933,500 + travel expenses
		Biological medical devices, specially controlled medical devices (class Ⅳ), etc.		Domestic		666,100 Article 17 (4) 1-a (1)	666,100
				Overseas		844,400 + travel expenses Article 17 (4) 1-a (2)	844,400 + travel expenses
		Sterilized medical devices		Domestic		201,300 Article 17 (4) 1-c (1)	201,300
				Overseas		229,800 + travel expenses Article 17 (4) 1-c (2)	229,800 + travel expenses
		Other medical devices		Domestic		141,200 Article 17 (4) 1-d (1)	141,200
				Overseas		155,400 + travel expenses Article 17 (4) 1-d (2)	155,400 + travel expenses
		Package, labeling, storage, external testing, etc.		Domestic		63,800 Article 17 (4) 2-a, Article 17 (5) 1-a	63,800
				Overseas		84,800 + travel expenses Article 17 (4) 2-b, Article 17 (5) 1-b	84,800 + travel expenses
	Renewal of the above	Biological medical devices, specially controlled medical devices (class Ⅳ), etc.	Basic	Domestic		436,000 Article 17 (4) 3-a (1)	436,000
				Overseas		554,200 + travel expenses Article 17 (4) 3-a (2)	554,200 + travel expenses
			Addition of products	Domestic		30,500 Article 17 (4) 3-a (1)	30,500
				Overseas		30,500 Article 17 (4) 3-a (2)	30,500
		Sterilized medical devices	Basic	Domestic		380,000 Article 17 (4) 3-b (1)	380,000
				Overseas		480,000 + travel expenses Article 17 (4) 3-b (2)	480,000 + travel expenses
			Addition of products	Domestic		12,400 Article 17 (4) 3-b (1)	12,400
				Overseas		12,400 Article 17 (4) 3-b (2)	12,400
		Other medical devices	Basic	Domestic		336,500 Article 17 (4) 3-c (1)	336,500
				Overseas		409,400 + travel expenses Article 17 (4) 3-c (2)	409,400 + travel expenses
			Addition of products	Domestic		9,600 Article 17 (4) 3-c (1)	9,600
				Overseas		9,600 Article 17 (4) 3-c (2)	9,600
		Package, labeling, storage, external testing, etc.	Basic	Domestic		258,500 Article 17 (4) 3-d (1), Article 17 (5) 2-a	258,500
				Overseas		338,100 + travel expenses Article 17 (4) 3-d (2), Article 17 (5) 2-b	338,100 + travel expenses
			Addition of products	Domestic		6,700 Article 17 (4) 3-d (1), Article 17 (5) 2-a	6,700
				Overseas		6,700 Article 17 (4) 3-d (2), Article 17 (5) 2-b	6,700
GLP inspection of medical devices							
	GLP			Domestic		2,062,400 Article 17 (3) 1-a, Article 17 (9) 2-a (1)	2,062,400
				Overseas		2,282,600 + travel expenses Article 17 (3) 1-b, Article 17 (9) 2-a (2)	2,282,600 + travel expenses
GCP inspection of medical devices							
	GCP			Domestic		635,300 Article 17 (3) 3-a	635,300
				Overseas		918,400 + travel expenses Article 17 (3) 3-b	918,400 + travel expenses
Re-examination of medical devices							
	New medical devices				502,600 Article 17 (8) 2-a	624,600 Article 17 (9) 1-c	1,127,200
	Medical devices other than new ones				51,600 Article 17 (8) 2-b		51,600
	GPSP			Domestic		610,700 Article 17 (9) 2-b (5)	610,700
				Overseas		949,000 + travel expenses Article 17 (9) 2-b (6)	949,000 + travel expenses

8-3. List of user fees under the 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 (face-to-face)			
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	4,239,400 yen per consultation	
	Consultation before start of early phase II study for drugs	1,623,000 yen per consultation	
	Consultation before start of late phase II study for drugs	3,028,400 yen per consultation	
	Consultation after completion of phase II study for drugs	6,011,500 yen per consultation	
	Pre-application consultation for drugs	6,011,400 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	2,675,600 yen per consultation	
	Consultation on GLP/GCP compliance for drugs	2,875,500 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	
	Consultation on pharmacogenomics/biomarkers	3,028,400 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/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	
	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/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 cell- and tissue-based 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 advance 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 advance payment
All test items (for drugs or medical devices)	Domestic	2,062,400 yen per facility	
	Overseas	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 advance 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		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

Reform Plan for the Pharmaceuticals and Medical Devices Agency

1. Human resources (downsizing of the organization)

Effects of the reform

Number of staff reduced

- Associate Center Director: 1
- Non-regular experts: 10

<FY 2009>

- Associate Center Directors: 3
- Non-regular experts: 95

<FY 2010>

- Associate Center Directors: 3
- Non-regular experts : 85 (-10)

<FY 2011>

- Associate Center Directors: 2 (-1)
- Non-regular experts : 75 (-10)

Based on budget screening

The number of active employees dispatched from the central government (120 employees) will be reduced, and the percentage of PMDA-hired regular employees among all employees above the level of division director (95 employees) will be increased to 50% or higher within four years.

Former national government employees

	FY 2009	FY 2010	No. of change
Board members	1/6 members	0/6 members	-1
Staff members	7/515 staff members	11/599 staff members	4

Future actions

Employment of 11 staff members was continued because they were employed through open recruitment as employees with expertise.

Note: The 11 staff members, including 4 added in FY 2009, are qualified pharmacists or dentists, who passed the selection examination for technical employees through public recruitment.

2. Property (sale of surplus assets)

Estimated treasury payment

—

[*PMDA owns no fixed assets such as land and buildings.]

3. Funds (reduction of grants from the central government)

Amount reduced

90 million yen

<FY 2009>

Operating cost grants 570 million yen

<FY 2010>

Operating cost grants 440 million yen

<FY 2011>

Operating cost grants 350 million yen

[Approximately 20.3% reduction in the overall operating cost grants]

4. Reform of administrative work and projects

1. Human resources reform

(i) Expansion of review services and safety measures — Based on budget screening

- Promote the expansion of reviews and related services by increasing reviewers in accordance with the Mid-term plan toward complete resolution of the drug lag and device lag (drug lag to be resolved by FY 2011 and device lag by FY 2013)
- Improve the consultation system based on the needs of relevant companies, etc.
  → Request for including the "Project for promoting regulatory affairs consultations on R&D strategy for drugs and medical devices" in the special category "Recovery of Lively Japan" in the government budget

(ii) Expansion and strengthening of training

- Dispatch staff to medical institutions and international academic conferences, improve training programs for mid-level and management-level employees

(iii) Promotion of the diffusion of regulatory science

- Promote the Joint Graduate School Program, contribute to development of international standards

(iv) Awareness raising of employees

- Execute operations from the viewpoint of users and promote measures for reduction of unnecessary expenditures
- Active on the international stage
- Clarify the career path (provide rough career models for promotion to the management-level after experiencing training, personnel exchange, etc.) — Based on budget screening

(v) Reinforcement of governance — Based on budget screening

- Establish an external expert panel to discuss career paths and dispatch of active government employees
- The number of active employees dispatched from the central government (120 employees) will be reduced, and the percentage of PMDA-hired regular employees among all employees above the level of division director (95 employees) will be increased to 50% or higher within four years.
- Improve the direct opinion exchange between the Chief Executive and employees

(vi) Personnel exchange with the private sector (academia, medical institutions, industry)

2. Cost reform

(i) Reexamination of optional contracts and radical reduction in unnecessary expenses
(ii) Increase in operating efficiency through information ties among the services of reviews, safety measures and relief
(iii) Reflection of opinions of the public and relevant parties to operations

3. Information reform

(i) Information provision from the viewpoint of ordinary citizens
(ii) Information provision responding to the internationalization