THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2009

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I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1 History and Objective of PMDA

- As lessons learned from diseases caused by drugs such as thalidomide-induced fetal malformations and subacute myelo-optical neuropathy (SMON), the Fund for Adverse Drug Reactions Suffering Relief was established in October 1979 based on stipulations in the Adverse Drug Reaction Suffering Relief Fund Act (Act No. 55 of 1979), for the purpose of providing prompt relief to patients suffering from adverse drug reactions (ADRs). In 1987, the Fund started R&D-promoting operations under the name of the Fund for Adverse Drug Reaction Relief and R&D Promotion and was then reorganized into the Organization for Pharmaceutical Safety and Research (OPSR/Kiko) 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 and developing the structure as governmental organizations.

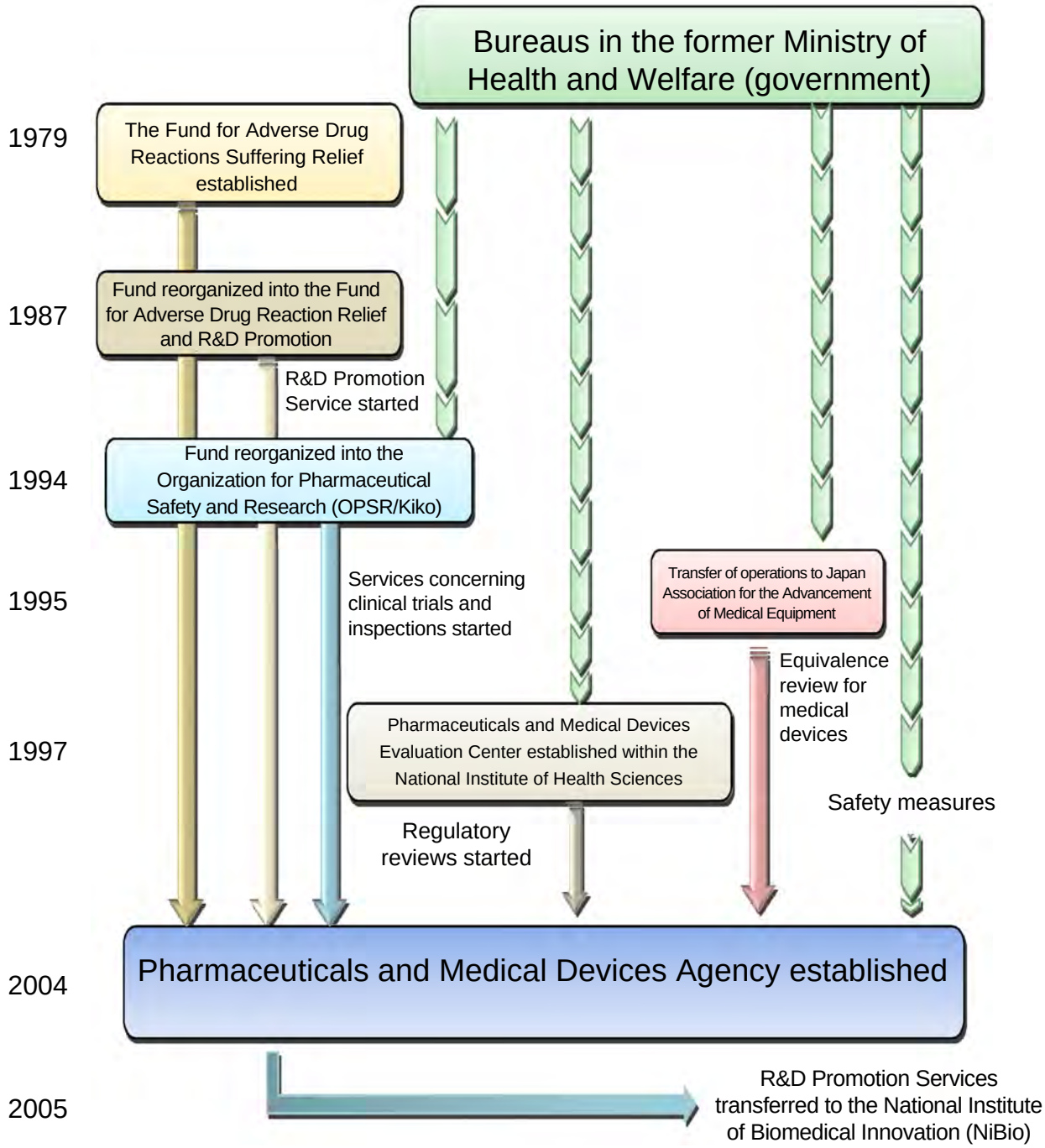
  In the midst of these situations, the Cabinet adopted the Special Service Agency Restructuring Plan in December 2001, in which it was decided that the OPSR/Kiko should be dissolved and that the Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to PMDEC, OPSR/Kiko, 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/Kiko, 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 by 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 reviews the efficacy, safety, and quality of drugs and medical devices for which regulatory approval applications have been submitted, based on the current scientific and technological standards. In addition, PMDA conducts re-examinations/re-evaluations of drugs and medical devices and reviews of applications for confirmation of the quality and safety of cell- and tissue-based products prior to the first-in-man study as well as reviews of applications for confirmation of clinical use of genetically modified biological entities in accordance with 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 implemented 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).

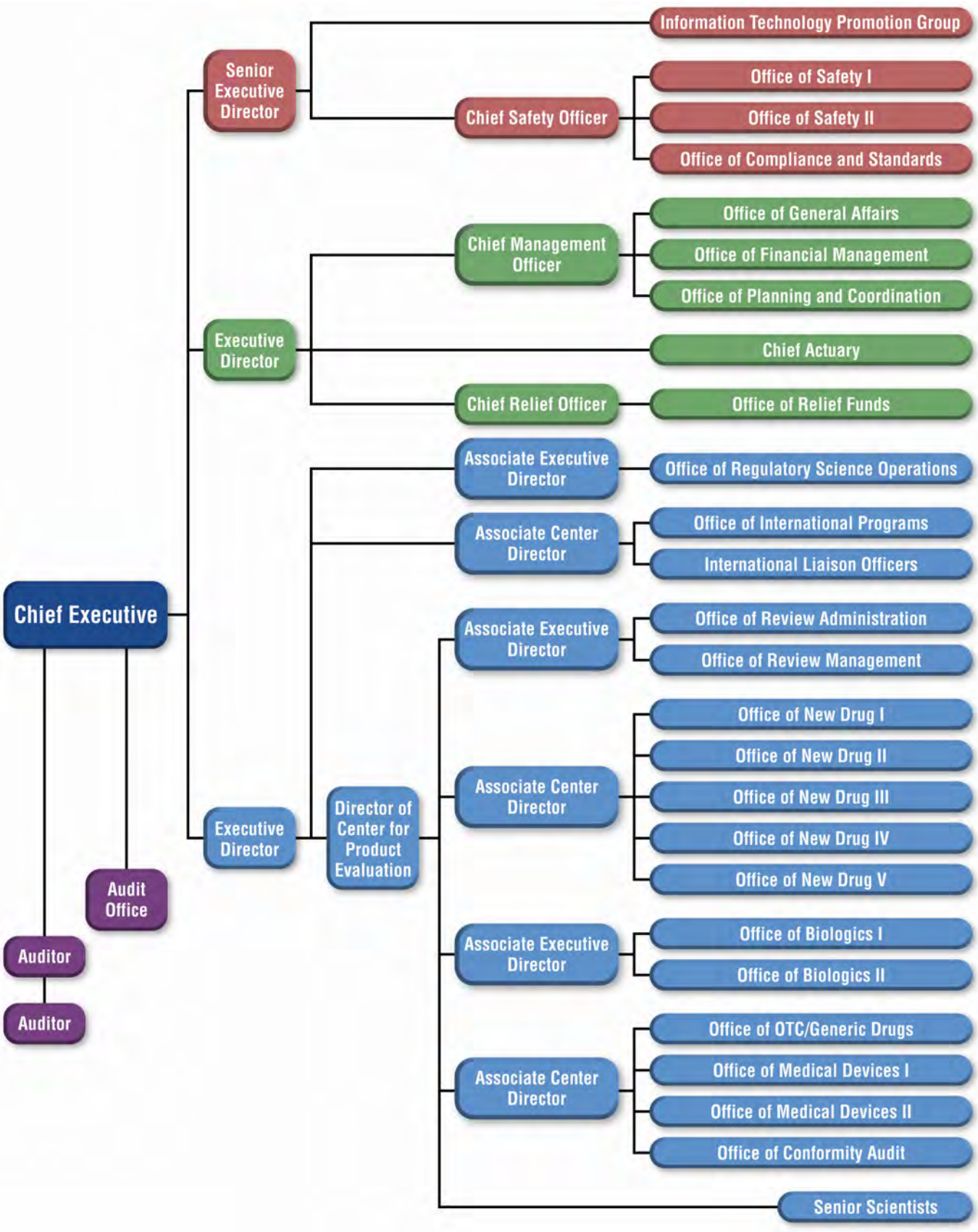
- In addition, on-site and document-based inspections are conducted to determine whether manufacturing facilities and manufacturing control methods for new drugs and medical devices, etc., comply with the requirements of the Ministerial Ordinance on Good Manufacturing Practices (GMP), and whether there is a system for manufacturing products of adequate quality (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 presentations at academic conferences, relating to adverse drug reactions, 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 2009)



II. OPERATING PERFORMANCE FOR FY 2009

PART 1 Development of Fiscal Year 2009 Plan

1.1 Development and Implementation of Fiscal Year 2009 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 2009, submitted it to the Minister of Health, Labour and Welfare at the end of 2008, and is implementing operations in accordance with this plan.

  On November 5, 2009, PMDA notified the Minister of Health, Labour and Welfare of the increase in the budget of specified relief benefits for relief payments, and of the increase in the budget for expediting reviews of unapproved drugs (supplemental budget for FY 2009), pursuant to the "Act on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus."

  The FY 2009 plan was developed based on the newly-created Second Mid-term Targets and Mid-term Plan as well as operating performance for FY 2008 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 2008 and Results of the Final Evaluation on Operating Performance during the Effective Period of the Mid-term Targets

- 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 28, 2009, PMDA received the results of evaluation on its performance for FY 2008 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 19 As and 1 B out of 20 evaluation items (the B was for "expeditious operation and improvement of the system [drugs]").

  Since FY 2008 was the final fiscal year of the effective period of the First Mid-term Targets, the Evaluation Committee of MHLW presented the "Results of the Final Evaluation on Operating Performance during the Effective Period of the Mid-term Targets" on August 28, 2009. The overall evaluation results were determined based on the average evaluation results for the past five years, from FY 2004 to FY 2008, and consisted of 18 As and 2 Bs out of 20 evaluation items (the Bs were for "expeditious operation and improvement of the system [medical devices and clinical trial consultations]").

  "Results of the Evaluation on Operating Performance for FY 2008" and "Results of the Final Evaluation on Operating Performance during the Effective Period of the Mid-term Targets" were released on the website, and were also reported at the Advisory Council Meeting held on October 28, 2009.

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 evaluations conducted by the Evaluation Committee for Incorporated Administrative Agencies of MHLW was reviewed by the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of MIC, which submitted its conclusions as of December 9, 2009, highlighting the following issues concerning the evaluation results for PMDA:

(Opinion from the Commission of MIC on the results of the evaluation for FY 2008)

- Regarding PMDA's reviews of drug applications, the following numerical targets were set up for FY 2008, which was the final fiscal year of the First Mid-term Plan: (1) For new drugs, PMDA aimed to review 80% of all filed applications within a review time of 12 months; and (2) For products designated for priority review by the Minister of Health, Labour and Welfare, PMDA aimed to review 50% of all filed applications within a review time of 6 months. However, the levels of actual performance against these targets were 70% and 33%, respectively, resulting in failure to achieve those targets for new drugs.

  In the Second Mid-term Plan of PMDA starting in FY 2009, the numerical target, for which the total review time including the applicant's time is to be sequentially shortened (by one year by 2011), was set up as a more effective target, toward the goal of resolving the drug lag (circumstances where drugs approved in Europe and the U.S. are not yet approved and provided in Japan) by 2.5 years by FY 2011; and it was decided that reviewers who engage in new drug reviews should be increased three-fold to expedite reviews of drugs (increasing the 112 reviewers in FY 2006 up to 236 by FY 2009). Taking into account these situations, the status of achievement of numerical targets related to shortening of review times for drugs need to be evaluated based on adequate analyses, but the Committee of MHLW has not sufficiently conducted evaluations based on such analyses.

  In future evaluations, PMDA's efforts should be strictly evaluated after clarifying not only the level of achievement of targets for each fiscal year but also factor analysis and improvement measures in the case of non-achievement.

- Regarding PMDA's reviews of medical device applications, the following numerical targets were set up for FY 2008, which was the final fiscal year of the First Mid-term Plan: (1) For new medical devices, PMDA aimed to review 90% of all filed applications within a review time of 12 months; and (2) For products designated for priority review by the Minister of Health, Labour and Welfare, PMDA aimed to review 70% of all filed applications within a review time of 9 months. However, the levels of actual performance against these targets were 75% and 75%, respectively, resulting in failure to achieve those targets for new medical devices.

  In the Second Mid-term Plan of PMDA starting in FY 2009, the numerical target, in which the total review time including the applicant's time is to be sequentially shortened (by 7 months by FY 2013), was set up as a more effective target, toward the goal of solving the device lag (a similar problem to the drug lag but for medical devices) in FY 2013 (shortening the period from filing until approval by 19 months); and it was decided that reviewers should be increased three-fold to expedite reviews of medical devices (increasing the 35 reviewers in FY 2008 up to 69 by FY 2013). Taking into account these situations, the status of achievement of numerical targets related to shortening of review times of medical devices needs to be evaluated under sufficient analyses, but the Committee of MHLW has

not sufficiently conducted evaluations based on such analyses.

In future evaluations, PMDA’s efforts should be strictly evaluated after clarifying not only the level of achievement of targets for each fiscal year but also factor analysis and improvement measures in the case of non-achievement.

(Opinion from the Commission of MIC on the evaluation results during the effective period for the First Mid-term Targets)

When the Commission of MIC developed "Regarding the direction of recommendations in relation to the revision/abolition of main clerical works and projects of incorporated administrative agencies (Notification No. 27 dated December 11, 2007 and Notification No. 29 dated December 21, 2007 from Director of the Commission on Evaluation and Evaluation of Incorporated Administrative Agency; hereinafter the "direction of recommendations"), the Commission of MIC evaluated the performance of PMDA from the standpoint of determining the levels of achievement of individual Mid-term Targets while reviewing the organization and operations of PMDA. The opinions as required under Article 34, Paragraph 3 of the Act on General Rules of Incorporated Administrative Agency (Act No. 103 of 1999) were presented through the direction of recommendations.

It is requested that the Committee of MHLW makes efforts to achieve strict and accurate evaluations each year so that the operations will be improved in quality and streamlined along with the progress of accurate operations in line with the new Mid-term Targets etc. which were developed based on the direction of recommendations.

List of Results of Evaluation of PMDA concerning the Operating Performance during the Effective Period of the First Mid-term Targets

Classification in the mid-term and fiscal year plan			Evaluation items	FY 2008 Performance Evaluation by committee	Final evaluation
Part 1	Improvement in overall operations and quality in services of the PMDA eg. services to the publilc				
	(1) Efficient and flexible operations	1	Operation through target management/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	Improvements in operations of each department, and quality of other services eg. services to the public				
	1 Adverse health effect relief services				
	(1) Expansion and review of dissemination of information regarding the System (2) Proactive public relations activity toward familiarity with the System (3) Expansion of the scale of the consultation office	6	Provision of information on the System and strengthening of the consulatation system	A	A
	(4) Unified management of information through the database (5) Expeditious processing of relief applications through fact-finding study and other measures	7	Expeditious processing of applications and improvement of the system	A	A
	(6) Promotion of appropriate communication of information through cross-functional collaboration (7) Consideration of conducting surveys on adverse health effects, etc.	8	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	A	A
	2 Reviews and related operations/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	B
		12	Expeditious operation and improvement of the system (clinical trial consultations)	A	B
	(2) Improvement in reliability of reviews and related services/post-marketing safety measures	13	Improvement in quality of review and related services/post-marketing safety measures	A	A
		14	Promotion of appropriate clinical trials	A	A
		15	Promotion of transparency of review and related services/ post-marketing safety measures	A	A
	(3) Reinforcement of information management and risk management	16	Collection of ADR information	A	A
		17	Provision of safety information to companies and healthcare professionals	A	A
		18	Provision of safety information to patients and consumers	A	A
Part 3	Budget, income and expenditure plan, and financial plan	19	Budget, income and expenditure plan, and financial plan	A	A
Part 4	Limit of short-term borrowing				
Part 5	Plan for transferring or mortgaging				
Part 6	Use of surplus funds				
Part 7	Other operational issues specified by a ministerial ordinance of the competent ministry				
	(1) Personnel matters (2) Ensuring security	20	Personnel issues 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	2
	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

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, in addition to striving 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 2009, 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 in each office, from October to November 2009, PMDA conducted an interview with its directors about the actual operating performance up to the end of September 2009 in light of the operating plans, and the issues that were pointed out by the directors during this interview were reported in the Board of Directors Meeting that was held in December 2009.

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

- PMDA considers it necessary 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. In addition, PMDA plans to build an organizational system where management decisions by the Chief Executive are promptly reflected in operations.

- To this end, consecutively from FY 2008, 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 liaison and coordination of its general operations.

  Specifically, PMDA has regularly (once a week in principle) held Board of Directors meetings, attended by the Chief Executive and division heads or higher management personnel.

- 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 PMDA's structure of 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 according to the Chief Executive's business judgment (three meetings were held during FY 2009).

- 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 2009), during which reports on the monthly application status for user fees for each review division, reports on the monthly cash flow analysis, and reports on the declared amount of contributions were made.

- PMDA convened an opinion exchange session with organizations of adverse drug reaction sufferers (November).

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

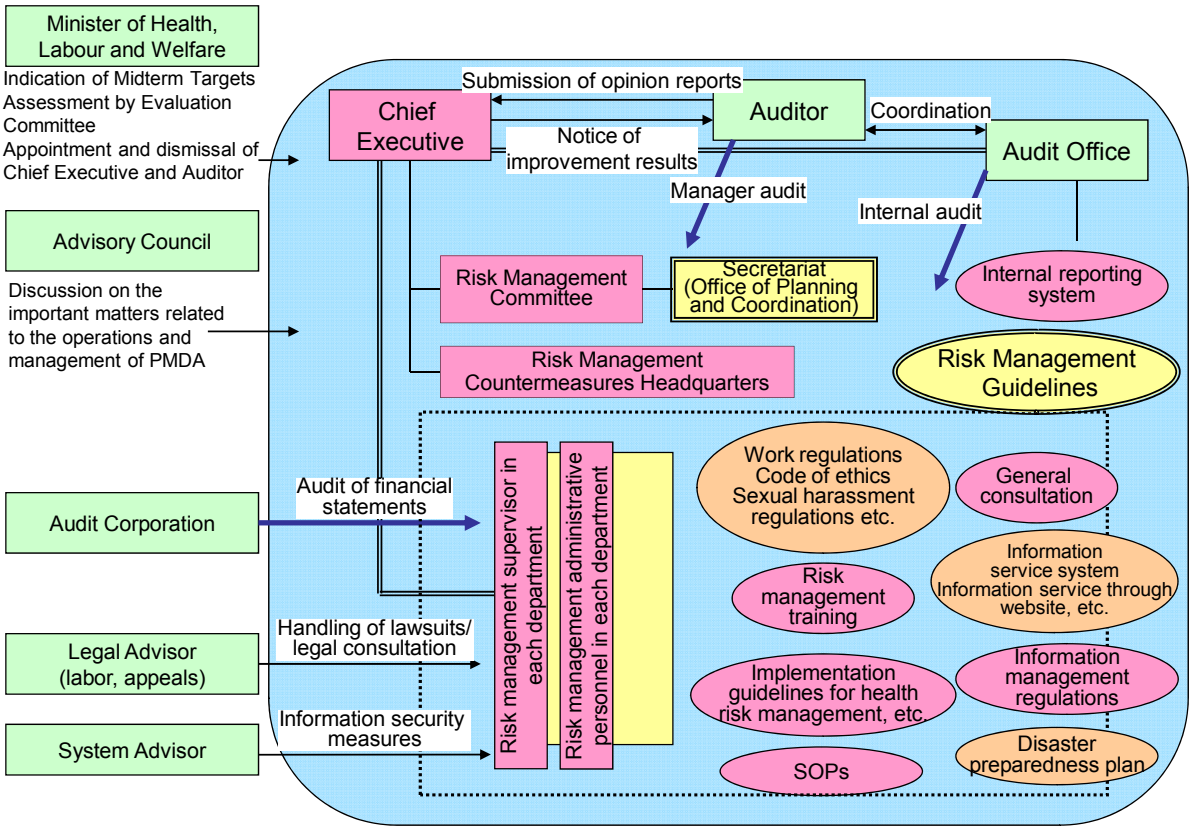
  Further, regarding medical devices and *in vitro* diagnostics, PMDA established a working-level joint task force related to medical devices and *in vitro* diagnostics in February 2007 and convened 4 meetings.

- The Risk Management Committee held 12 meetings in FY 2009 to monitor the risk management of PMDA, and examined the appropriateness of document and information management by reviewing the operational flow.

  PMDA executives and employees have also continued to keep up with their efforts to be familiarized 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. (drugs, medical devices, quasi-drugs, and cosmetics, as well as agents and equipment 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 during the period and decided to improve services to the public by 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 during the period 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.

2.1.(3) Advisory Council meetings

- To create opportunities for exchanges of opinions between academic experts of diverse fields, PMDA established the Advisory Council (chaired by Masaaki Hirobe, Professor Emeritus, University of Tokyo) 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 works to secure fairness and transparency of PMDA's operations, in addition to contributing to streamlining the efficiency of its operations. Under the Advisory Council, the Committee on Relief Services (chaired by Hideaki Mizoguchi, Professor Emeritus, Tokyo Women's Medical University) and the Committee on Review and Safety Operations (chaired by Masaaki Hirobe, Professor Emeritus, University of Tokyo) were also formed to discuss specialized issues relating to operations. The dates of the meetings and specific agendas for FY 2009 are as follows.

Advisory Council—FY 2009

Agenda for the 1st Meeting (June 12, 2009; jointly held with the 1st Meeting of the Committee on Review and Safety Operations)

(1) Annual Report for FY 2008
(2) Financial Report for FY 2008
(3) Organizational restructuring
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions received by commissioned external experts in relation to Expert Discussions
(6) Others

Agenda for the 2nd Meeting (October 28, 2009)

(1) Results of the final evaluation of operating performance during the effective period for the First Mid-term Targets and the results of the evaluations of operating performance for FY 2008
(2) Amendments to the budget for FY 2009
    1) PMDA's actions for unapproved drugs, etc.
    2) Increase in the budget for the specified relief account
(3) Organizational restructuring of PMDA
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions received by commissioned external experts in relation to Expert Discussions
(6) Others

Agenda for the 3rd Meeting (March 16, 2010)

(1) Fiscal year 2010 plan (draft)
(2) Budget for FY 2010 (draft)
(3) Revision of the regulations on employment restrictions for personnel from the private sector (draft)
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions received by commissioned external experts in relation to Expert Discussions
(6) Others

Committee on Relief Services—FY 2009

Agenda for the 1st Meeting (June 11, 2009)

(1) Annual Report for FY 2008
(2) Fiscal year 2009 plan
(3) Organizational restructuring
(4) Standards for the burden of expenses on pharmaceutical companies pursuant to Article 16 of the "Act on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus"
(5) Others

Agenda for the 2nd Meeting (December 14, 2009)

(1) Results of the final evaluation of operating performance during the effective period for the First Mid-term Targets and the results of the evaluations of operating performance for FY 2008
(2) Achievements for the first half of FY 2009, etc.
(3) Amendments to the budget for FY 2009
(4) Results of the survey on awareness of the relief system for adverse health effects in FY 2009 and future public relations
(5) Implementation of health and welfare services (consultation services to address mental issues, etc.)
(6) Others

Committee on Review and Safety Operations—FY 2009

Agenda for the 1st Meeting (June 12, 2009; jointly held with the 1st Meeting of Advisory Council)

*Refer to the 1st Meeting of Advisory Council.

Agenda for the 2nd Meeting (December 8, 2009)

(1) Results of the final evaluation of operating performance during the effective period of the First Mid-term Targets and the results of the evaluations of operating performance for FY 2008
(2) Achievements for the first half of FY 2009 and issues to be addressed hereafter
(3) Amendments to the budget for FY 2009
(4) Organizational restructuring of PMDA
(5) Report on the employment status of personnel from the private sector
(6) Cash contributions received by commissioned external experts in relation to Expert Discussions
(7) 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 disclosed on the PMDA website.

Note: Information on the Advisory Council is available at:
http://www.pmda.go.jp/guide/hyogikaikankei.html

2.1.(4) Approaches for an efficient operation system

- PMDA aims to establish an efficient operation system through flexible personnel allocation tailored to situations, as well as through effective use of external experts.

In review divisions that particularly require flexible approaches, PMDA continued to adopt the group

system where review teams are led by Review Directors who report to the Office Director.

PMDA has continuously invited commissioned external experts to seek their professional opinions relating to scientifically significant matters at Expert Discussions on reviews and safety measures.
(1,099 commissioned external experts are present as of March 31, 2010)

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.
(78 commissioned external experts are present as of March 31, 2010)

- 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 in discussions by commissioned external experts, PMDA developed the Notice of the Implementation of Expert Discussions at the Pharmaceuticals and Medical Devices Agency (December 25, 2008), as a regulation for the conflict of interests that included the establishment of a system that would fully secure transparency and that could be verified by outside parties by releasing review reports and the conflict of interests of commissioned external experts. Reports are made to the Advisory Council and the Committee on Review and Safety Operations on the receipt of cash contributions and contract money 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 increasing the number of its regular staff. Assistance services for the development of the Optimization Plan for Operations and Systems were also commissioned to private companies.

- PMDA has continued to appoint people who have advanced professional expertise regarding information systems in general as well as knowledge of pharmaceutical affairs as information system advisors, 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 2009 as well, meetings of the Committee on Investment in Information Systems, etc. were held. In addition, discussions regarding the operational status of each information system, upgrades for the shared LAN system that serves as the common infrastructure system of PMDA, and improvements in the security of the e-mail system were carried out.

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 recorded in CD-R. 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 the Optimization Plan for Operations and Systems and publicized it on March 28, 2008. Also, PMDA publicized the revised version of the plan in June 2009.

  In FY 2009, PMDA created requirements definition documents to improve existing systems from FY 2010, and also started a two-year plan for preparing for the next systems. The plan includes the following tasks: definition of operational/functional requirements, definition of non-functional requirements for systems such as servers and network infrastructure, calculation of approximate development costs, formulation of various plans which will be needed during the development period, including a plan for data migration to the next systems, and estimation of man-hours.

2.2 Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general administrative expenses

- PMDA was expected to balance the FY 2009 budget for general administrative expenses (excluding expenses for office relocation and retirement allowance) reduced by about 3% compared to the FY 2008 budget, through its continuous efforts to improve operations and increase management efficiency, plus the following additional general administrative expenses:

  1) General administrative expenses to be 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 to be incurred starting in FY 2009 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 to be 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 annual budget relating to general administrative expenses 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 planned budget.

- In FY 2009, in order to more efficiently execute operations with regard to personnel expenses within the annual budget plan, PMDA promoted general competitive bidding based on the Plan for the Review of Optional Contracts, which was developed in December 2007, and its activities continued from last year aiming to reduce procurement costs arising from rental contracts of personal computers, as well as purchase contracts of expendables, such as additional office furniture and copy papers necessitated by increases in employees.

  Through a negotiation with the owner of the building where PMDA's office is currently located, it became possible to expand and integrate the Agency's office space in response to increases in employees, thereby enabling reinforcement of security and reduction in the rent to a level comparable to that of the new office site as once planned.

  Consequently, PMDA successfully reduced general administrative expenses by 20.9% of its budget size which is subject to efficiency improvements, even excluding factors of the personnel increase that did not achieve the target number and unnecessary office rent, etc.

2.2.(2) Cost control of operating expenses

- PMDA was expected to balance the FY 2009 budget for operating expenses (excluding expenses for office relocation, expenses related to payment of benefits, and single-year expenses due to new project launches, etc.) reduced by about 1% compared to the FY 2008 budget, by increasing operational efficiency through promotion of digitization, plus the following additional operating expenses:

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

  3) Operating expenses to be 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 FY 2009 budget for operating expenses 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 planned budget.

- In FY 2009, PMDA promoted general competitive bidding as well as control of general administrative expenses, based on the Plan for the Review of Optional Contracts. 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 6.8% compared with the budget amount that was the subject of efficiency improvement, even excluding factors of the personnel increase that did not achieve the target number and unnecessary office rent and unused expenses for 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. As a result of that, the ratio of competitive

contract schemes including planning competition and invitation to bids increased by 11.9% compared to the previous fiscal year.

	FY 2008	FY 2009	Change
General competitive bidding (including planning competition and invitation to bids)	101 bids (47.0%) 1,175 million yen (29.6%)	132 bids (58.9%) 1,796 million yen (40.6%)	31 bids (11.9%) 621 million yen (11.0%)
Noncompetitive optional contracts	114 bids (53.0%) 2,797 million yen (70.4%)	92 bids (41.1%) 2,630 million yen (59.4%)	-22 bids (-11.9%) -167 million yen (-11.0%)
Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	91 bids (42.3%) 1,120 million yen (28.2%)	67 bids (29.9%) 725 million yen (16.4%)	-24 bids (-12.4%) -395 million yen (-11.8%)
Total	215 bids 3,972 million yen	224 bids 4,426 million yen	9 bids 454 million yen

2.2.(4) Collection and management of contributions

- Contributions from marketing authorization holders of the industry enable PMDA to secure financial resources for relief 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 management, such as the calculation of transaction value which constitutes the basis of the contribution amount and the management of the data concerning unpaid contributions. PMDA was also able to ensure 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 measures contributions, PMDA set the collection rates to be no less than 99% in the Mid-term Plan. In FY 2009, the collection rates for ADR contributions, infection contributions, and safety measure contributions were 99.6%, 100%, and 99.0%, respectively.

FY 2009 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	743	742	99.9%	3,783
	Pharmacies	7,628	7,598	99.6%	8
	Total	8,371	8,340	99.6%	3,790
Infection contributions	MAHs	97	97	100%	631
Post-marketing safety measures contributions	MAHs of drugs	653	652	99.8%	968
	MAHs of medical devices	2,243	2,168	96.7%	201
	MAHs of drugs & medical devices	199	199	100%	1,185
	Pharmacies	7,628	7,594	99.6%	8
	Total	10,723	10,613	99.0%	2,362

- 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

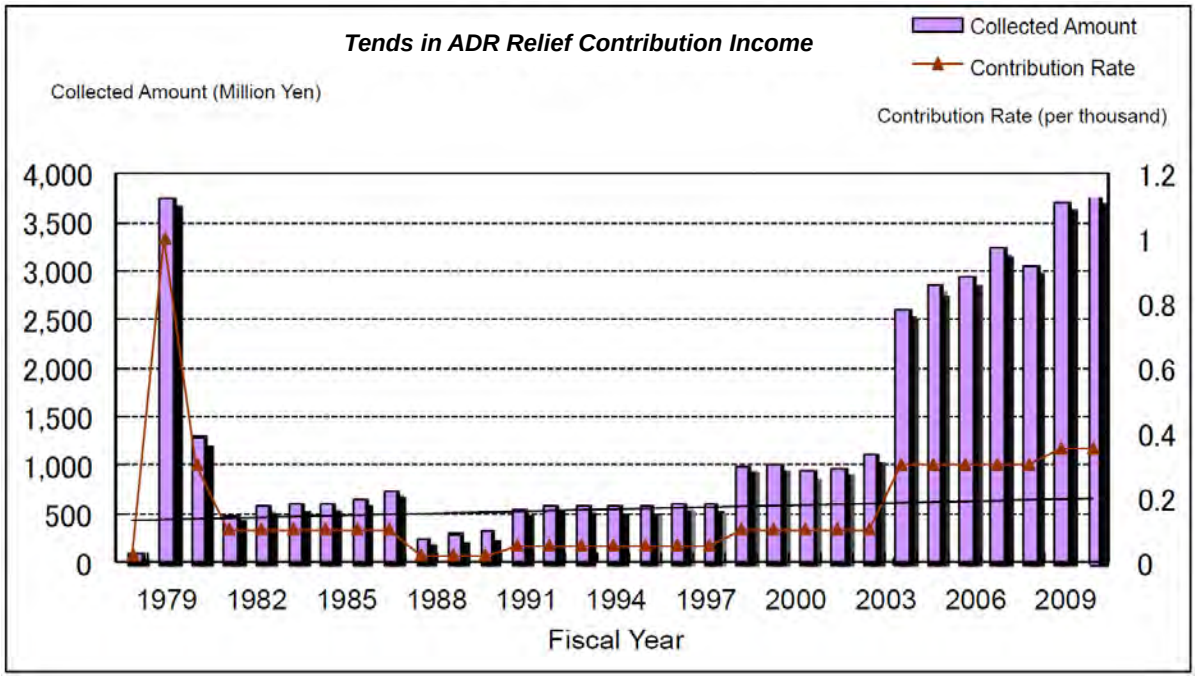
a. Adverse drug reaction fund

To fund the relief service for adverse drug reactions, PMDA has collected contributions to adverse drug reaction funds from marketing authorization holders of approved drugs. In FY 2009, the contribution rate applied to such marketing authorization holders was set at 0.35/1000 and the collected amount was 3,790 million yen.

(Million yen)

Fiscal year	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
MAHs of approved drugs [Number of MAHs]	2,923 [787]	3,240 [778]	3,049 [762]	3,722 [752]	3,783 [742]
MAHs of pharmacy-compounded drugs [Number of MAHs]	10 [9,993]	9 [8,968]	8 [8,309]	8 [8,015]	8 [7,598]
Total amount	2,933	3,249	3,057	3,730	3,790
Contribution rate	0.3/1000	0.3/1000	0.3/1000	0.35/1000	0.35/1000

The amount of adverse drug reaction funds and the contribution rate since the establishment of this service are shown below.



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

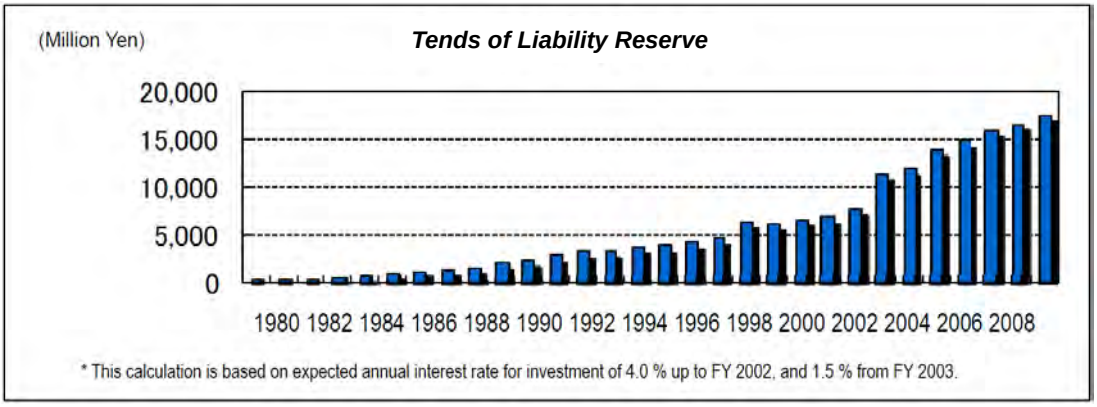
To fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from marketing authorization holders of approved biological products. In FY 2009, the contribution rate applied to such marketing authorization holders was set at 1/1000 and the collected amount was 631 million yen.

(Million yen)

Fiscal year	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
MAHs of approved biological products [Number of MAHs]	553 [105]	556 [101]	574 [98]	620 [96]	631 [97]
Contribution rate	1/1000	1/1000	1/1000	1/1000	1/1000

c. Liability reserve

- To cover the estimated relief benefit service costs 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 2009 was 17,665 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 2009, 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 2,362 million yen.

(Million yen)

Fiscal year	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
MAHs of drugs/ medical devices [Number of MAHs]	1,143 [2,982]	1,211 [3,180]	1,219 [3,094]	1,284 [3,053]	2,354 [3,019]
MAHs of pharmacy-compounded drugs [Number of MAHs]	10 [9,987]	9 [8,960]	8 [8,297]	8 [8,013]	8 [7,594]
Total amount	1,153	1,220	1,227	1,292	2,362
Contribution rate	0.11/1000	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)

2.2.(5) Reduction in personnel expenses and overhaul of the remuneration system

- The personnel expenditure for FY 2009 was reduced by approximately 7.0% (in comparison with personnel expenditure per person for FY 2005) by taking into account the results of the personnel evaluation for the period from April 2008 to March 2009 and appropriately reflecting the results in pay raises, etc.

- PMDA compared the remuneration system for its staff for FY 2008 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
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
Rate of personnel expense reduction (unit personnel expense per person)		-2.7%	-2.8%	-6.0%	-8.5%
Corrected rate of personnel expense reduction (unit personnel expense per person)		-2.7%	-3.3%	-6.6%	-7.0%

Note: Corrected rates have been calculated by excluding amounts equivalent to the recommendations of the National Personnel Authority.

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

- In response to the current public requests addressed to the government, Incorporated Administrative Agencies, etc., to reduce unnecessary expenditures, PMDA developed an internal guidance which stipulates principles for reducing unnecessary expenditures, "Reinforcement of the efforts to reduce unnecessary expenditures (December 22, 2009)," and released the guidance on its website. In addition, PMDA steadily promotes measures such as to ensure that all staff members are thoroughly informed of the efforts.

- To steadily implement the efforts for the cost reductions shown in the guidance in FY 2010, PMDA developed a document titled "Cost-cutting targets toward reduction of unnecessary expenditures in PMDA (March 31, 2010)" which specifies reduction targets such as overtime allowance, expenses related to the use of taxies, electricity cost, off-hours air conditioning usage fee, expenses for the procurement of copy paper, business travel expenses, etc. This document has been released on the website.

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. Since June 2007, PMDA has been receiving comments and opinions via its website as well as telephone/FAX so that citizens can transmit their opinions and requests easily. In FY 2009, PMDA provided the same service.

- Among the 2,167 inquiries that PMDA received in FY 2009, 803 or approximately 40% of the total inquiries received, were those relating to applications and consultations for drugs and medical devices.

	Inquiry/consultation	Complaint	Opinion/request	Other	Total
FY 2009	2,076 (784)	5 (5)	86 (14)	0 (0)	2,167 (803)

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 2009 as well.

- 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 2008, which concerns the operating performance for FY 2008.

- 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.

- Additionally, 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 the improvement of the site map and the improvement of banners related to the relief systems and review services

2.3.(4) Proactive PR activities

- 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 during the period and decided to improve services to the public by proactively providing information in line with the strategic plan. In FY 2009, PMDA held a press study meeting (April 21, 2009) and created newsletters (e-mail magazines for prospective employees), etc. In addition, the Chief Executive himself performed lectures, etc. in Japan and overseas (13 times in Japan and twice overseas).

2.3.(5) Disclosure request for corporate documents

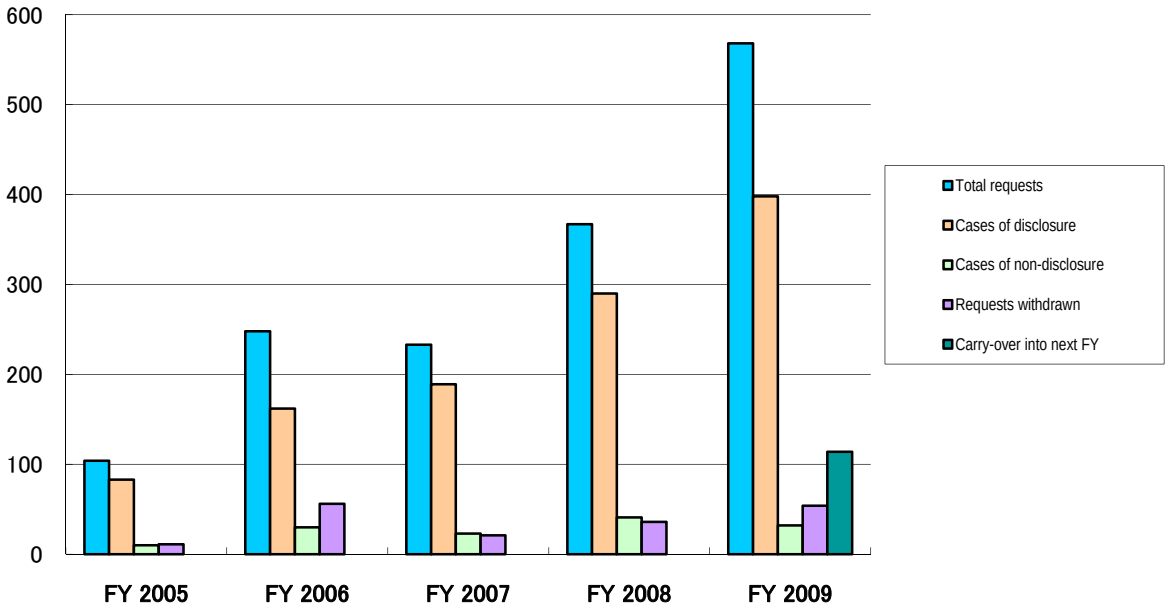
- The status of requests for the disclosure of corporate documents based on the Act on Access to Information Held by Incorporated Administrative Agencies is shown below (for the past five years).

Number of Requests for Disclosure of Corporate Documents

(Unit: Case)

	Total requests	Requests withdrawn	Decisions					Objections	Carry-over into next fiscal year
			Full disclosure	Partial disclosure	Non-disclosure	Documents not existing	Refusal to answer on existence/ non-existence of the document		
FY 2005	104	11	13	70	4	6	0	4	0
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	114

Note: Unhandled requests that carried-over into the next year or later included cases to which the prolongation of due dates for decision of disclosure, etc. pursuant to Article 10, Paragraph 2 of 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, in addition to cases for which requests for disclosure were made at the end of the year.



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.

Number of Requests for Disclosure of Corporate Documents by Requester

(Unit: Case)

Requester/FY	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Individuals	74	113	86	99	103
Corporate (e.g., drug manufacturers)	25	132	143	250	426
Press	5	3	4	18	39
Total	104	248	233	367	568

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 2005	FY 2006	FY 2007	FY 2008	FY 2009	Examples
Product application review	22	90	115	263	377	Marketing notification for products not subject to approval
GLP/GCP/GMP/QMS etc. inspections	69	117	74	52	102	Notice of GCP inspections results
Post-marketing safety	13	40	44	52	89	ADR reports
Others	0	1	0	0	0	Business trip order forms
Total	104	248	233	367	568	

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 the 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 next fiscal year
			Full disclosure	Partial disclosure	Non-disclosure	Documents not existing	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

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

Number of Requests for Disclosure of Personal Information by Requester

(Unit: Case)

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

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	Examples
Office of Relief Funds	3	5	0	Application for decision, etc.
Approval review	0	0	1	Clinical trial notification, etc.
Total	3	5	1	

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

2.3.(7) Auditing and related matters

- In addition to implementing audits through an external accounting firm in accordance with the system 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 2009, PMDA conducted internal audits on the management status of information, the status of contracts, the storage status of cash and cash equivalents, the status of authorization/procedure for payment of travel expenses, and the status of compliance with the rule restricting the employment 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 2008, including the use of review fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2009 on its website.

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

- PMDA publicly announced the follow-up of the Plan for the Review of Optional Contracts on its website in July 2009. Also in May 2009, PMDA developed corrective measures against bids where only one bidder participates, and publicly announced the measures on the website.

2.4 Personnel Issues

2.4.(1) Review of 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 the personnel evaluation during the period from April 2008 to March 2009 in pay raise, etc. in July 2009. In order to ensure the proper implementation of the 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 keep them informed about 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 appropriately implement capacity development 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. PMDA continued to provide these training courses in FY 2009.

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.

(i) New recruit training between April and June 2009
(ii) Training programs one each for mid-level and management-level employees as part of training programs by level
(iii) Human skill training including business etiquette and communications during the new recruit training program, as well as follow-up training for OJT-trainer development
(iv) As general training, English conversation training between July 2009 and February 2010. PMDA also conducted a TOEIC examination once for the purpose of assessing the effect of English conversation training as well as improving the language skills of employees.
(v) As specialized training programs, trainings on case studies and medical writing
(vi) Dispatch of an aggregate of 55 employees to universities in Japan and overseas as well as

foreign drug regulatory authorities for the purpose of training

(vii) Special training programs to mainly learn technical issues (14 sessions), special training programs on regulatory science to nurture employees from a broad perspective through interactions with various knowledgeable persons (8 sessions), and training programs on laws and regulations including the Pharmaceutical Affairs Act to learn the regulatory system, etc. (3 sessions), for which experts and knowledgeable persons belonging to domestic or foreign regulatory authorities, corporations, and universities were invited as lecturers

(viii) One training program by inviting lecturers from organizations of adverse drug reaction sufferers and organizations of patients

(ix) Facility visits (e.g., 4 drug manufacturing plants and 5 medical device manufacturing plants) as an opportunity for learning manufacturing plants, etc.

(x) Dispatch of the employees to two medical institutions for practical training of pharmacists conducted at hospitals

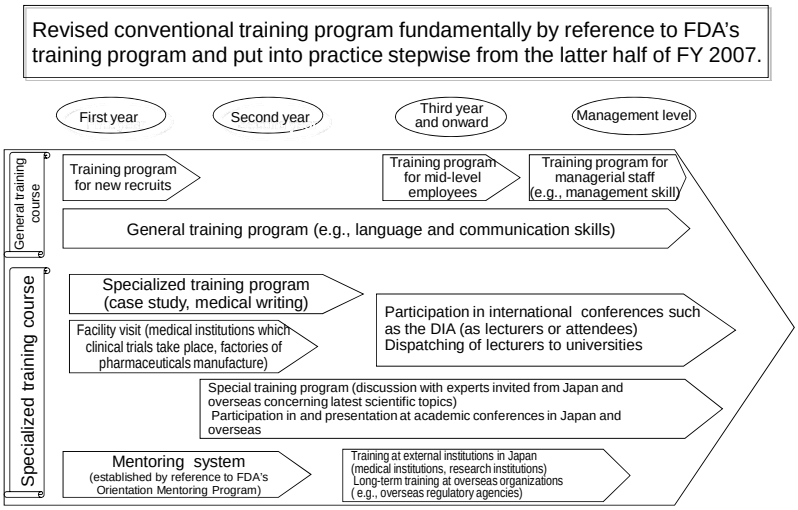
(xi) Dispatch of the employees to technical training programs conducted by external institutions (e.g., training course for experts of pharmaceutical affairs, a visit to Showa University IRB)

(xii) Training actually using medical devices such as pacemakers, biological heart valves, and catheters to place intravascular stents, with cooperation of AMDD member companies. Also, PMDA conducted training on orthopedic medical devices once.

(xiii) Training on in-house documents, and "accounting seminar" to learn the basics of management accounting, as part of the new recruit training. Further, PMDA dispatched one employee each to a grade 3 bookkeeping course and an accounting training course sponsored by the Accounting Center, Ministry of Finance, as external training.

(xiv) Compliance training and personal information protection training once each

Human resource training and development



2.4.(3) Appropriate personnel allocation

- To maintain the expertise of the staff members and operational continuity, PMDA aims to conduct appropriate personnel allocation.

- To achieve this target, PMDA conducted personnel allocation taking the knowledge and work experience of staff members into consideration. PMDA fundamentally avoids short-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

- At PMDA, 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) was set to be 751, and consequently PMDA was 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 technical regular employees 4 times in FY 2009 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 2009 (as of April 1, 2010)

1) Technical employees (4 public recruitments)	
Number of applicants	1,298
Number of employments	58
Number of prospective employees	40
2) Administrative employees (1 public recruitment)	
Number of applicants	80
Number of employments	3

Recruitment Activities (FY 2009)

- Schedule of PMDA information sessions
  - May: Two sessions in Tokyo and one session each in Osaka, Nagoya and Fukuoka (total participants, 240 persons)
  - September to October: Two sessions in Tokyo and one session each in Osaka, Nagoya, Fukuoka, Sendai and Kanazawa (total participants, 399 persons)
  - December: Two sessions in Tokyo and one session each in Osaka and Hiroshima (total participants, 172 persons)
  - February: Two sessions in Tokyo and one session in Osaka (total participants, 127 persons)
- Activities performed in collaboration with directors/employees:
  - Lectures on and explanation of the services at universities, etc. by directors/employees
  - OB/OG visits by young employees
  - Advertising via booth displays at academic conferences, etc. (e.g. distribution of brochures and display of posters at the 26th Live Demonstration in Kokura and the 48th Annual Conference of Japanese Society for Medical and Biological Engineering
- Tools for recruitment activities
  - Brochures for recruitment, posters for recruitment
  - The brochures and posters were sent out to approximately 500 institutions including medical faculties 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, or distributed at information sessions, etc.
- Information to be posted on job information websites
  - Website presenting job offers for new graduates in 2011 (My NAVI 2011, NIKKEI NAVI 2010)
  - Website presenting job information for those seeking a career change (My NAVI Career Change. For 1 month from September 25 and for 1 month from November 24)
  - Number of distributed/subscribed direct mails: 400 (actual 874)
- 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”, 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 beginning of the effective period for the Second Mid-term Plan (beginning of FY 2009)	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	695	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 (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 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 reemployment after retirement 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 reemployment after retirement, 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. PMDA also distributed a handbook on rules to all executives and employees, etc.; and in addition 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 the re-edited handbook 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) Entrance/exit access control

- To ensure security and protect confidential information, PMDA has installed entrance/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 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 order to ensure further strict access control, PMDA has also prescribed restrictions on the entrance/exit control relating to operational management of the security access control system, and has made maximum efforts to thoroughly inform its staff members of these restrictions through the intranet and during new recruit training.

2.5.(2) Security measures for information systems

- Based on the FY 2009 plan, PMDA has 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 increase the use of secure e-mails in the communication to finalize the audio transcription 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	55	421
Within PMDA		489

Note: The numbers of registered companies and issued certificates as of the end of March 2010

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 Adverse Drug Reaction 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 cases of approval/rejection on its website with due consideration to protecting personal information. PMDA has posted cases of approval/rejection of the preceding month on its website starting in February 2010 in order to provide more extensive information on the Relief Systems.
Information on Cases of Approval/Rejection is available at:
http://pmda.go.jp/kenkouhigai/help/information2.htm

From the viewpoint of making the administration of the system more transparent, PMDA disclosed the operating performance for the first half of FY 2009 on its website in December 2009.

(ii) Improvement of brochures, etc.

To reduce the amount of time required for administrative processing of incomplete claim forms and supporting documents, and to make operations more efficient, 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, and distributed the revised brochure. PMDA also posted the brochure (in PDF format) on its website together with animations that summarize details of the brochure, in order to improve the convenience for users.

b) Regarding drug-induced liver injury, PMDA reviewed the instructions on the form of a medical certificate in order to make it easier for doctors to fill in. Also, PMDA posted this revised form on its website.

c) PMDA tried to improve the convenience for requestors by publicizing the fact that claim forms and the brochure can be downloaded from its website.
Claim forms are available at: http://search.pmda.go.jp/fukusayo_dl/

3.1.(2) Proactive PR activities

Activities newly conducted in FY 2009

(i) PMDA conducted an awareness survey on the Relief System for Adverse Health Effects from July to August, targeting the general public and healthcare professionals. The survey was carried out for providing more effective public relations activities by understanding the awareness level of the Relief System for Adverse Health Effects. In September 30, PMDA released the results of the

survey on its website. On the same day, PMDA sent out the report on the survey results to prefectural governments and concerned bodies, etc. PMDA analyzed the report by using external consultants, and created a public relations plan in November based on the results of the analysis. Also, PMDA requested sending/receiving and posting publicity posters at transportation facilities (trains), hospitals, and drug stores, and also conducted publicity activities through newspapers, video displays at hospitals, as well as free magazines.

(ii) PMDA made it possible to download from the website a poster to inform the public of the Relief System for Adverse Health Effects, as pharmacies are required to display such information under the revised Pharmaceutical Affairs Act. The Agency also requested the Japan Pharmaceutical Association to make use of the information.

(iii) PMDA made it possible to download from the website the publicity information to be put in medicine envelopes, and requested the Japan Pharmaceutical Association to make use of the information.

(iv) PMDA requested the Japanese Society of Hospital Pharmacists to make use of the poster and publicity information available from the website.

(v) PMDA requested the Japan Association of Chain Drug Stores to include the information for the public on the Relief System for Adverse Drug Reactions in the “Brochure on the Revised Pharmaceutical Affairs Act” prepared by the Association in June.

(vi) PMDA requested the MR Education & Accreditation Center of Japan to distribute the leaflets on the Relief System for Adverse Health Effects at the MR educational training conducted by the Center in October.

(vii) PMDA published explanatory articles on the Relief System for Adverse Health Effects in two specialized magazines for medical professionals (the Journal of the Japan Medical Association and the Journal of the Japan Pharmaceutical Association).

(viii) PMDA enclosed the leaflet in the “Pharmaceuticals and Medical Devices Safety Information Reporting System” issued by MHLW, and distributed it to prefectural governments and other municipalities.

Activities conducted by direct visits

(i) PMDA participated in medical conferences (the Annual Meeting of the Japanese Dermatological Association, Annual Meeting of the Japan Society of Transfusion Medicine and Cell Therapy, Annual Meeting of the Japanese Society of Allergology, etc.), and distributed brochures and gave presentations about the Relief Systems at 20 different academic conferences.

(ii) At the 23rd Annual Meeting of the Japanese Society for AIDS Research, PMDA displayed posters, published information in the abstract journal, and distributed materials about the Relief Systems.

(iii) PMDA conducted explanations and lectures about the Relief Systems by directly visiting pharmaceutical associations and various training workshops.

- Prefectural pharmaceutical associations (in 17 prefectures)
- Pharmacists exchange meeting of Okayama prefectural chapter
- Workshops for vaccination specialists (at 8 locations in Japan)
- Practical training courses of the Medical Safety Support Center (at 2 locations in Japan)
- The 57th training course for experts of pharmaceutical affairs
- Training program for pharmaceutical affairs expert government officers
- Training program at the headquarters of the National Hospital Organization
- Lecture meeting at the National Cardiovascular Center
- Lecture meeting at Toyama Hospital, International Medical Center of Japan
- Training course of the Osaka Hospital Pharmacists Association
- Training course of the Tokyo Hospital Pharmacists Association
- Training workshop for persons in charge of PMS at the Pharmaceutical Manufacturers'

Association of Tokyo
- Training course for staff in the special wards of Tokyo, etc.

Activities conducted conventionally

(i) PMDA conducted publicity activities through a brochure titled "Do You Know about Relief Systems?" which explains the Relief Systems in simple words.
- Enclosed the brochure in the Journal of Japan Medical Association (about 170,000 copies) and the Journal of Japan Pharmaceutical Association (about 102,000 copies).
- Posted the brochure in electronic medium (PDF format) and animation version (14 minutes) that summarizes the details of the brochure, on the PMDA website.
- Distributed the brochure to universities/colleges (colleges of pharmacy, faculties of pharmaceutical sciences), clinical training hospitals, university hospitals, nurse training facilities, etc.

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

(iii) PMDA placed the summary of the Relief Systems in programs and abstract journals of two academic conferences including the Japanese Society of National Medical Services.

(iv) PMDA placed the publicity of the Relief System for Adverse Drug Reactions in a magazine on drug safety updates (DSU) published by the Federation of Pharmaceutical Manufacturers' Associations of JAPAN, and then distributed the magazine to all medical institutions.

(v) PMDA distributed the brochures introducing the Relief Systems to medical institutions through the Japanese Red Cross Society Blood Center (24,600 copies).

(vi) PMDA placed the summary of the Relief Systems in "medication record book" published by the Japan Pharmaceutical Association and prefectural pharmaceutical associations.

(vii) PMDA placed the summary of the Relief Systems in a brochure "Useful Information on Medicines" published by MHLW and the Japan Pharmaceutical Association.

Publicity through the Brochure

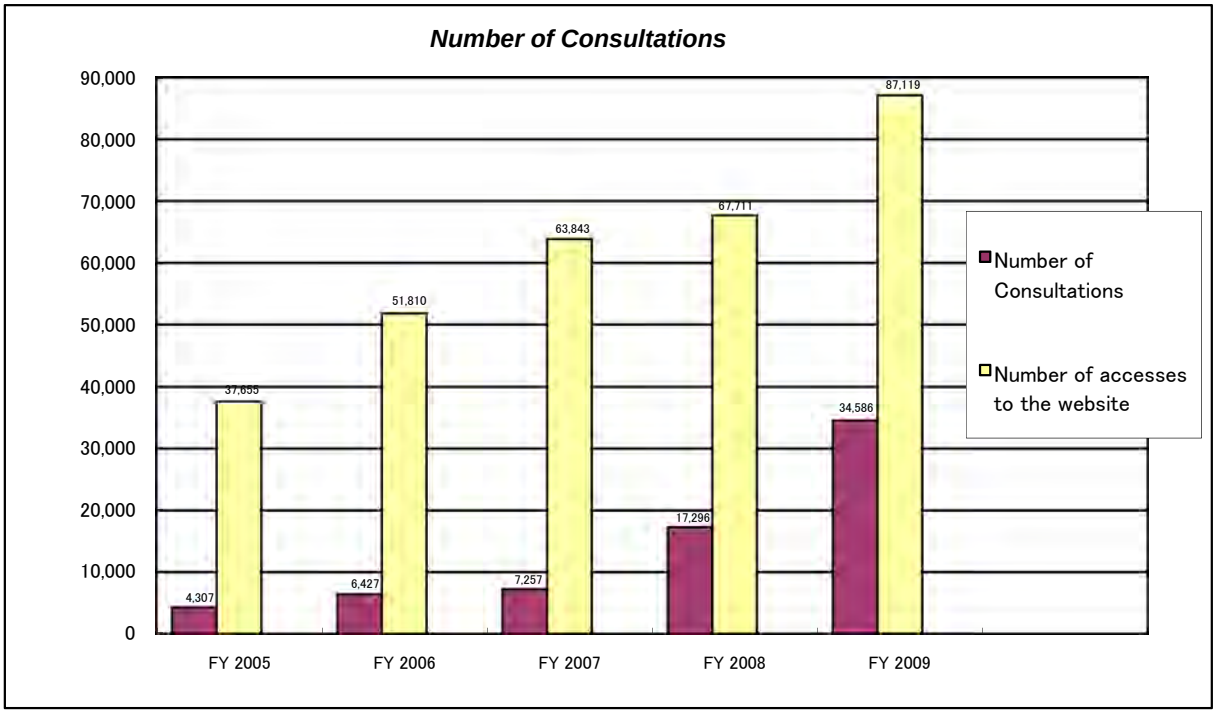
3.1.(3) Management of the consultation service

- In FY 2009, the numbers of consultations and accesses to the website were 34,586 and 87,119, respectively, with ratios of 200% and 129% compared with the previous fiscal year.

- Regarding telephone consultations, PMDA has conducted operations with setting up a toll free number since FY 2005, and placing exclusive staff. The Agency made it possible to use the toll-free number from mobile phones and public phones in 2008. With these measures, the Agency has improved the convenience for users. The increases in the number in FY 2009 are attributable to descriptions of the Relief System for Adverse Drug Reaction and "PMDA's toll-free number" on the outer boxes of OTC drugs based on a voluntary agreement in the pharmaceutical industry. Because telephone calls for inquiries and complaints about particular products have markedly increased, PMDA set up a preliminary guidance (tape recording) which explains the main points of the telephone consultation service since September 25, 2009 to reduce the number of such calls (3,208 in September → 932 in October), while securing the accessibility of people for whom consultations are needed.

- On the website, PMDA started to distribute animations explaining the summary of the Relief Systems, and also tried to keep the people who seek consultation informed of the fact that the request form, etc. can be downloaded.

Fiscal Year	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	Compared with FY 2008
Number of consultations	4,307	6,427	7,257	17,296	34,586	200%
Number of accesses to the website	37,655	51,810	63,843	67,711	87,109	129%



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

3.1.(4) Central management of information through databases

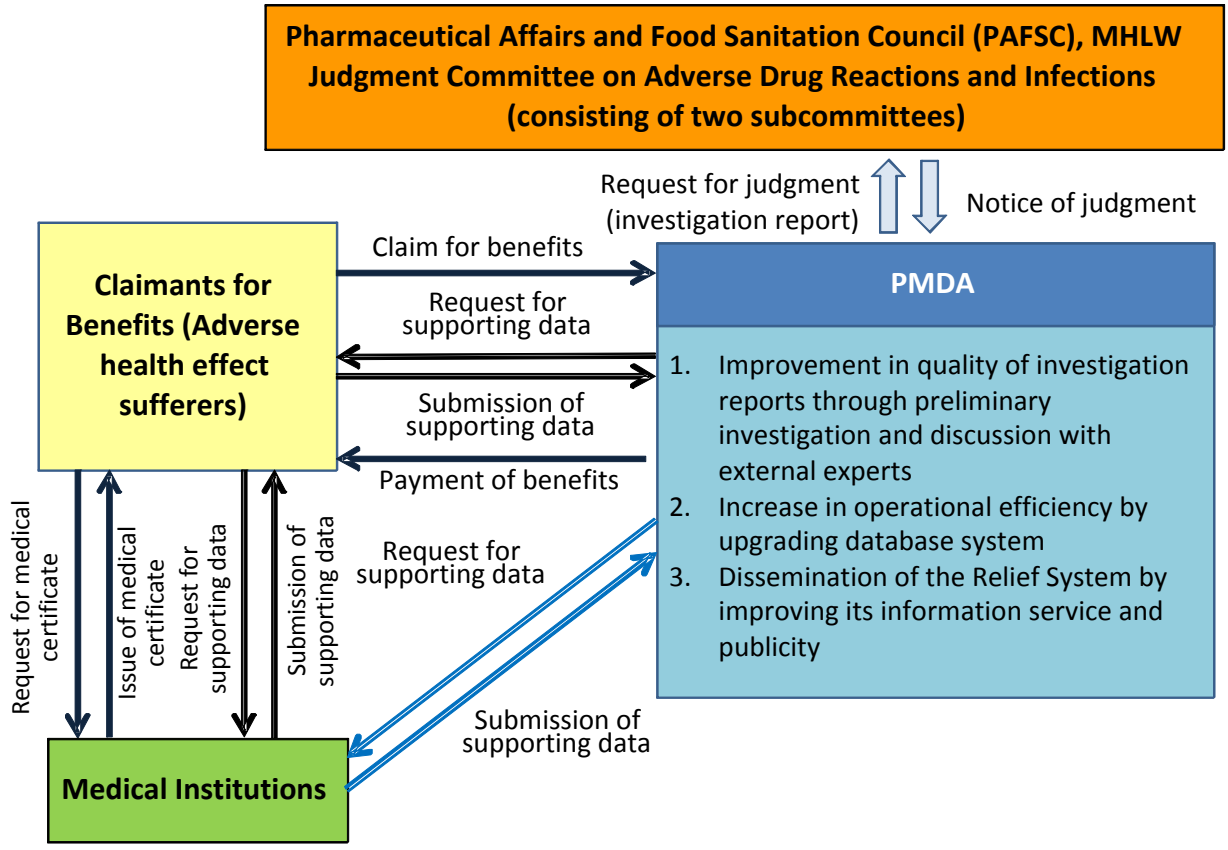
- To make operations more efficient and swift, PMDA upgraded the System of Relief Fund Services and the System of Contributions Collection.

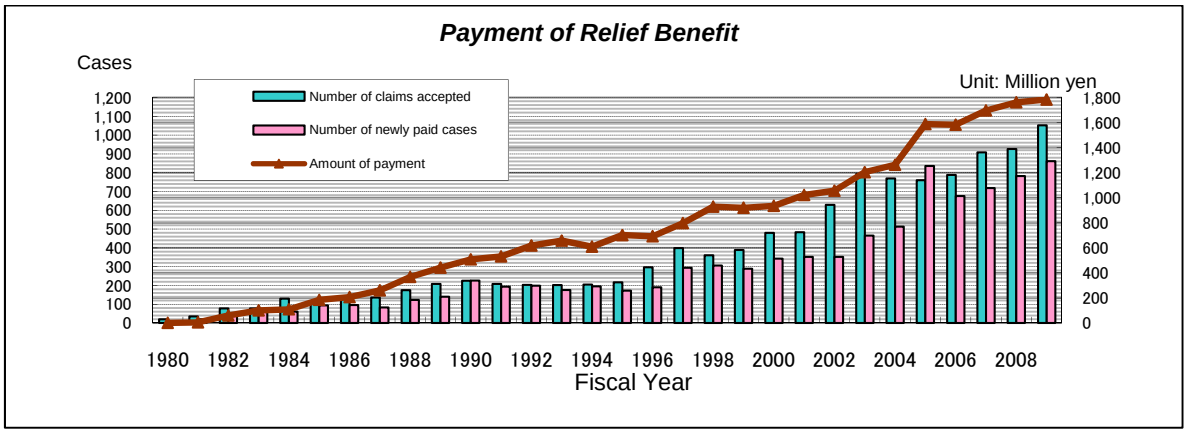
  In addition, PMDA plans to launch the third phase development of the Integration and Analysis System for Databases on Relief Benefits Services in FY 2010 for improvements such as (1) expanding both progress management and the function to control the workload of the staff in charge and (2) expanding the search function to make more effective use of information accumulated in the system to date. For this reason, the Agency defined the requirements for the development in FY 2009.

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: (1) Fact-finding investigations of the incident included in the claim, (2) Preparation of a summary chart tracing the case over time, and (3) Preparation of investigation reports, etc.

Flow of Adverse Health Effect Relief Services





FY 2009

- Relief services for adverse drug reactions
  Number of claims: 1,052
  Number of cases of approval/rejection: 990 (of which 861 were judged approved)
- Relief services for infections
  Number of claims: 6
  Number of cases of approval/rejection: 10 (of which 8 were judged approved)

In the Second Mid-term Plan, PMDA planned to exercise judgment within 6 months for more than 60% of the total number of judged cases (regardless of approval/rejection). In FY 2009, the initial year of the Second Mid-term Plan, PMDA planned to increase the number of claims judged within 6 months amid a tendency toward increase in the number of claims, while ensuring that more than 70% of claims are processed within 8 months of the standard administrative processing time. As the

performance in FY 2009, the rate of claims processed within the standard administrative processing time was 74.0%, showing that the level of more than 70% was maintained; and the number of claims processed within 6 months was 360, showing a higher number than that of the previous fiscal year (355).

(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 and 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 2009 is shown below:

Fiscal Year		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Number of claims		760	788	908	926	1,052
Number of judged cases		1,035	845	855	919	990
	Approved	836	676	718	782	861
	Rejected	195	169	135	136	127
	Withdrawn	4	0	2	1	2
Cases in progress*		681	624	677	684	746
Achievement rate†		12.7%	65.3%	74.2%	74.3%	74.0%
Median processing time		11.2 months	6.6 months	6.4 months	6.5 months	6.8 months

* *The numbers obtained at the end of each fiscal year.*
† *The percentages of the cases judged within 8 months of the standard administrative processing time out of the total number of the cases judged during the fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2009 by type of benefit are shown below.

(Cases)

Fiscal Year		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Number of claims		760	788	908	926	1,052
Types of benefits	Medical expenses	602	643	730	769	902
	Medical allowances	659	694	786	824	943
	Disability pensions	78	60	70	79	71
	Pension for raising handicapped children	5	14	10	7	11
	Bereaved family pensions	41	31	33	26	36
	Lump-sum benefits for bereaved families	48	51	72	49	50
	Funeral expenses	84	88	105	78	83

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

c. Judgment status by type of benefit

The status of judgments made in FY 2009 by type of benefit is shown below:

(Thousand yen)

Types	FY 2005		FY 2006		FY 2007	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	717	78,527	572	67,502	603	67,603
Medical allowances	757	70,073	624	60,034	651	62,668
Disability pensions	33	653,143	35	692,446	42	730,007
Pension for raising handicapped children	17	40,639	6	30,131	7	35,760
Bereaved family pensions	44	502,468	22	493,010	20	501,454
Lump-sum benefits for bereaved families	32	228,708	34	229,446	39	286,373
Funeral expenses	74	14,010	53	10,386	63	12,661
Total	1,674	1,587,567	1,346	1,582,956	1,425	1,696,525

Types	FY 2008		FY 2009	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	659	75,339	763	86,666
Medical allowances	711	62,055	813	70,963
Disability pensions	27	747,362	26	804,251
Pension for raising handicapped children	7	40,127	7	50,804
Bereaved family pensions	22	523,455	18	545,843
Lump-sum benefits for bereaved families	47	335,977	30	215,342
Funeral expenses	72	14,391	46	9,914
Total	1,545	1,798,706	1,703	1,783,783

Note 1: "Number of cases" means judged cases. "Amount paid" means benefits paid for both new and existing cases.

Note 2: Since the payment figures are rounded off to the nearest thousand yen, the figures' sum does not always match the sum of the payment amounts.

(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 and 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 human beings or other living matter (excluding plants), which are designated as special products requiring extreme 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 2009 is shown below.

Fiscal Year		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Number of claims		5	6	9	13	6
Number of judgments		6	7	5	11	10
	Approved	3	7	3	6	8
	Rejected	3	0	2	5	2
	Withdrawn	0	0	0	0	0
Cases in progress*		2	1	5	7	3
Achievement rate†		50.0%	100.0%	100.0%	100.0%	100.0%
Median processing time		5.6 months	3.8 months	3.8 months	5.2 months	5.4 months

* *The numbers obtained at the end of each fiscal year.*

† *The percentages of the cases judged within 8 months of the standard administrative processing time out of the total number of the cases judged during the fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2009 by type of benefit are shown below.

(Cases)

Fiscal Year		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Number of claims		5	6	9	13	6
Types of benefits	Medical expenses	5	5	7	11	5
	Medical allowances	5	5	8	13	6
	Disability pensions	0	0	1	0	0
	Pension for raising handicapped children	0	0	0	0	0
	Bereaved family pensions	0	1	0	0	0
	Lump-sum benefits for bereaved families	0	0	0	1	0
	Funeral expenses	0	1	0	1	0

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

c. Judgment status by type of benefit

The status of judgments made in FY 2009 by type of benefit is shown below.

(Thousand yen)

Types of benefits	FY 2005		FY 2006		FY 2007		FY 2008		FY 2009	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	3	475	6	473	3	102	5	204	6	375
Medical allowances	3	249	6	497	3	352	6	386	8	567
Disability pensions	—	—	—	—	—	—	—	—	—	—
Pension for raising handicapped children	—	—	—	—	—	—	—	—	—	—
Bereaved family pensions	—	—	1	1,387	—	2,378	—	2,378	—	2,378
Lump-sum benefits for bereaved families	—	—	—	—	—	—	1	7,135	—	—
Funeral expenses	—	—	1	199	—	—	1	199	—	—
Total	6	724	14	2,556	6	2,833	13	10,302	14	3,320

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

3.1.(6) Promotion of appropriate communication of information through collaboration between operational divisions

- To enhance collaboration with the other divisions within PMDA, information on cases judged to be accepted/rejected were provided for relief benefits for adverse drug reactions in FY 2009, and information on claims and information on cases judged to be accepted/rejected were provided for relief benefits for infections in FY 2009, to the Offices of Safety, etc. with due consideration to protecting personal information.

3.1.(7) Surveys on actual state of health damage caused by adverse drug reactions (investigative research as part 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 (Article 15, Paragraph 1, Item 1-b of the Act on the Pharmaceuticals and Medical Devices Agency).

Investigative Research for Improvements in QOL of Sufferers of Severe and Rare Adverse Health Effects Caused by Pharmaceuticals:

As part of health and welfare services, PMDA established an Investigative Research Team for Improvements in the Quality of Life 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, for which general measures for disabled people do not necessarily provide sufficient support. 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 2009, the data on the operating performance for FY 2008 were organized at a meeting of the above-mentioned Research Team held on July 30, and also its results were publicly announced on the website after reporting to the Committee on Relief Services.

Contents of the Research

PMDA collects, analyzes, and evaluates reports, such as survey forms, etc., from sufferers from adverse health effects regarding the condition of various efforts in their daily life (68 volunteers in FY 2009).

Investigative Research Team

Leader:	Kazuaki Miyata	President of Nihon Fukushi 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	Section Director, Research Section, Planning and Research Division, the National Center for Persons with Severe Intellectual Disabilities, Nozominosono

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 mentally deep

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 2009, 22 consultations were performed.

Distribution of the Benefit Recipient Card:

For beneficiaries of the Relief System for Adverse Health Effects, a service to issue a portable size card 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 2009, the card was issued to 161 persons.

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

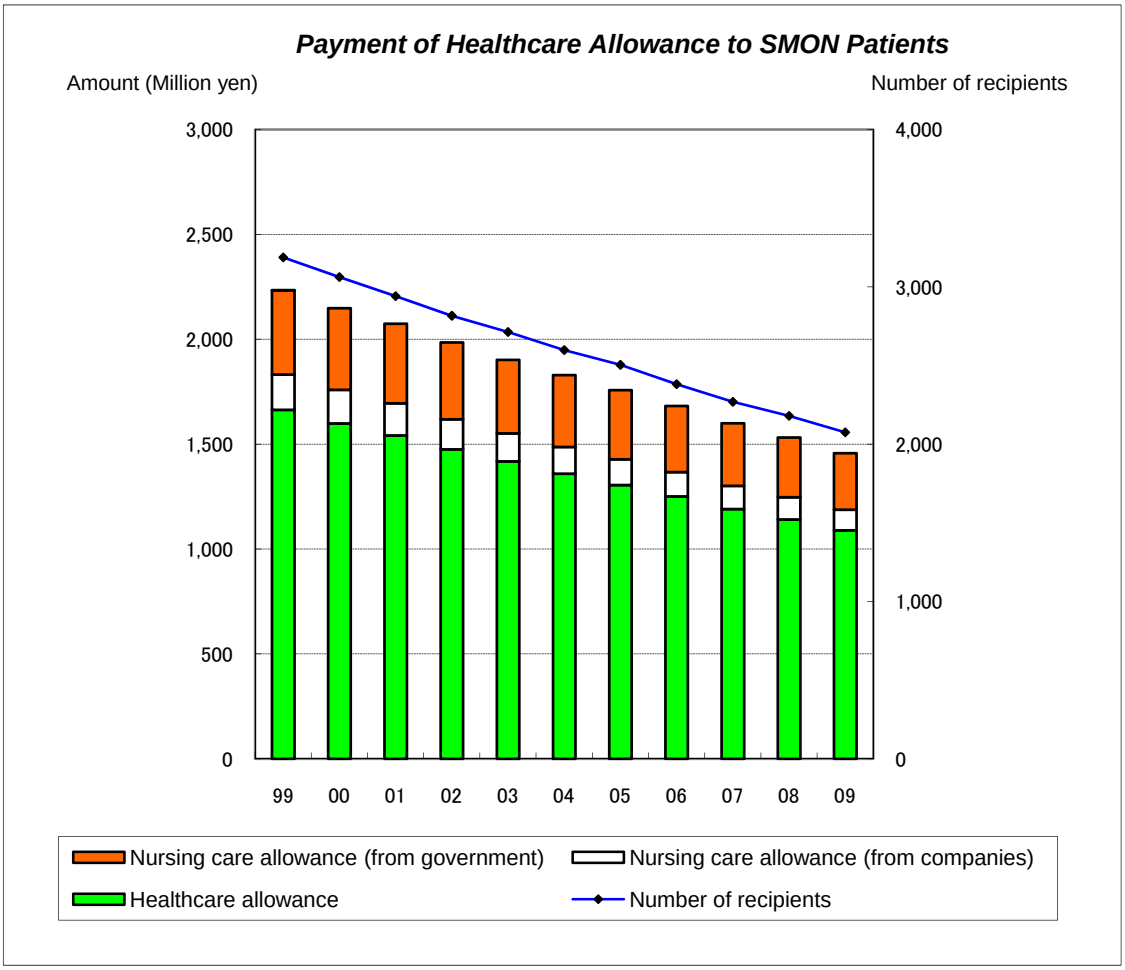
PMDA appropriately provided healthcare allowances, etc. to SMON patients and HIV-positive patients affected through blood products under commission of relevant organizations, giving due consideration to the confidentiality of personal information.

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

- PMDA provides healthcare allowances and nursing care allowances to SMON patients for whom a settlement has been reached in court. In FY 2009, the number of patients receiving such allowances was 2,075, and the total amount paid was 1,458 million yen.

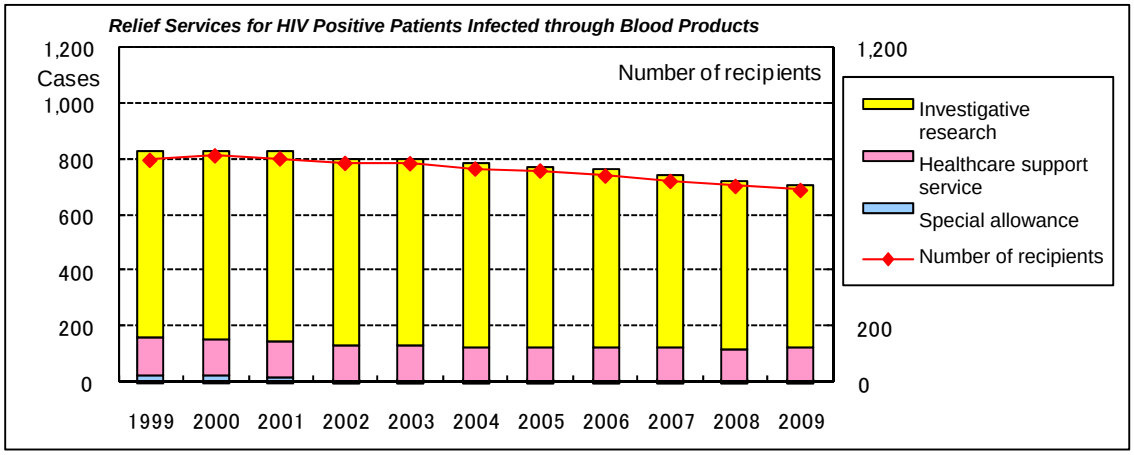
Fiscal year		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Number of recipients		2,504	2,381	2,269	2,180	2,075
Amount paid (thousand yen)		1,757,774	1,683,500	1,601,134	1,531,745	1,457,724
Break down	Healthcare allowance	1,305,168	1,251,622	1,191,245	1,140,517	1,089,491
	Nursing care allowance (from companies)	330,086	315,027	299,108	284,981	268,749
	Nursing care allowance (from the government)	122,520	116,850	110,781	106,247	99,485

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 2009, 566 HIV-positive patients received allowances relating to the investigative research, 120 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 688, and the total amount paid was 531 million yen.
  a. Payment of healthcare allowances for HIV-positive patients, 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 2005		FY 2006		FY 2007	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	638	341,017	618	334,653	604	327,857
Healthcare support service	121	210,300	120	210,000	117	224,796
Special allowance	3	8,706	3	8,678	3	8,084
Total	762	560,023	741	553,331	724	560,737

Fiscal year	FY 2008		FY 2009	
	Number of Recipients	Amount paid (Thousand yen)	Number of Recipients	Amount paid (Thousand yen)
Investigative research	587	320,122	566	313,676
Healthcare support service	121	211,800	120	210,600
Special allowance	2	6,300	2	6,300
Total	710	538,222	688	530,576

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 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 on January 16, 2008. The number of benefit recipients was 661, with 13,748 million yen as the total amount paid in FY 2009.

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

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; ensure that drugs and medical devices are used properly, prevent health hazards, and respond 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 consultation/review and post-marketing safety measures, and to organically link the operations to achieve the Mid-term Targets and FY 2009 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 shortening the time between approval of new drugs in the United States and approval in Japan by 2.5 years by FY 2011.

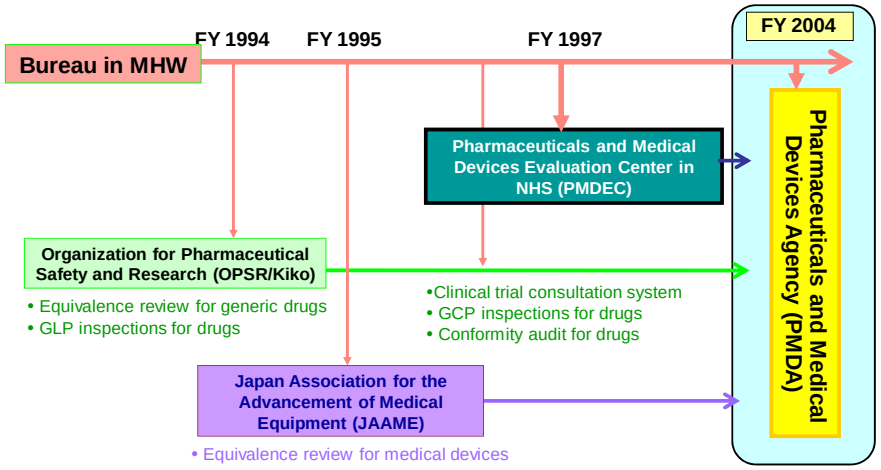
(i) Implementation of appropriate and prompt reviews

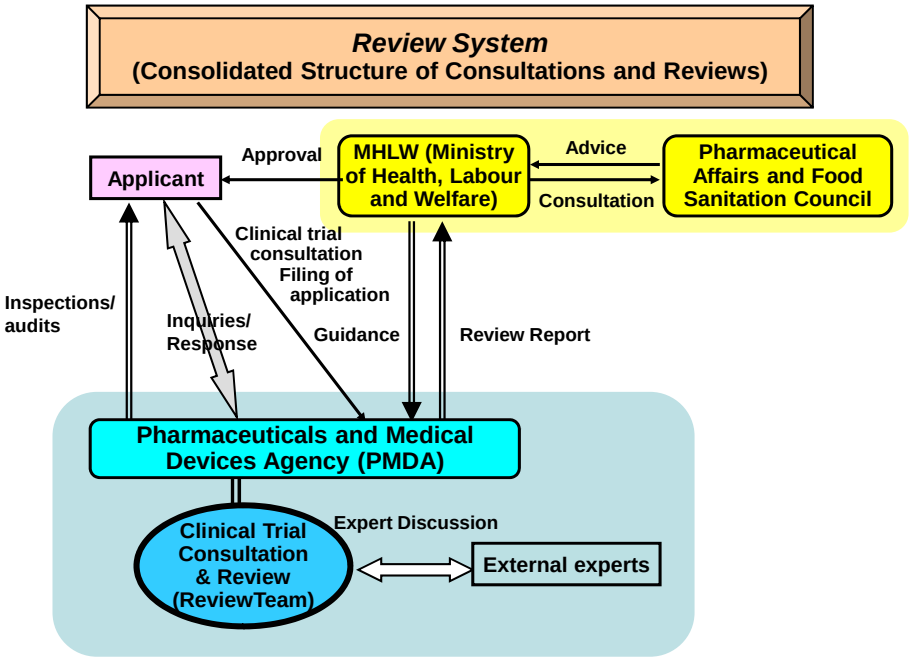
a. Implementation structure for clinical trial consultations and reviews

- 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.

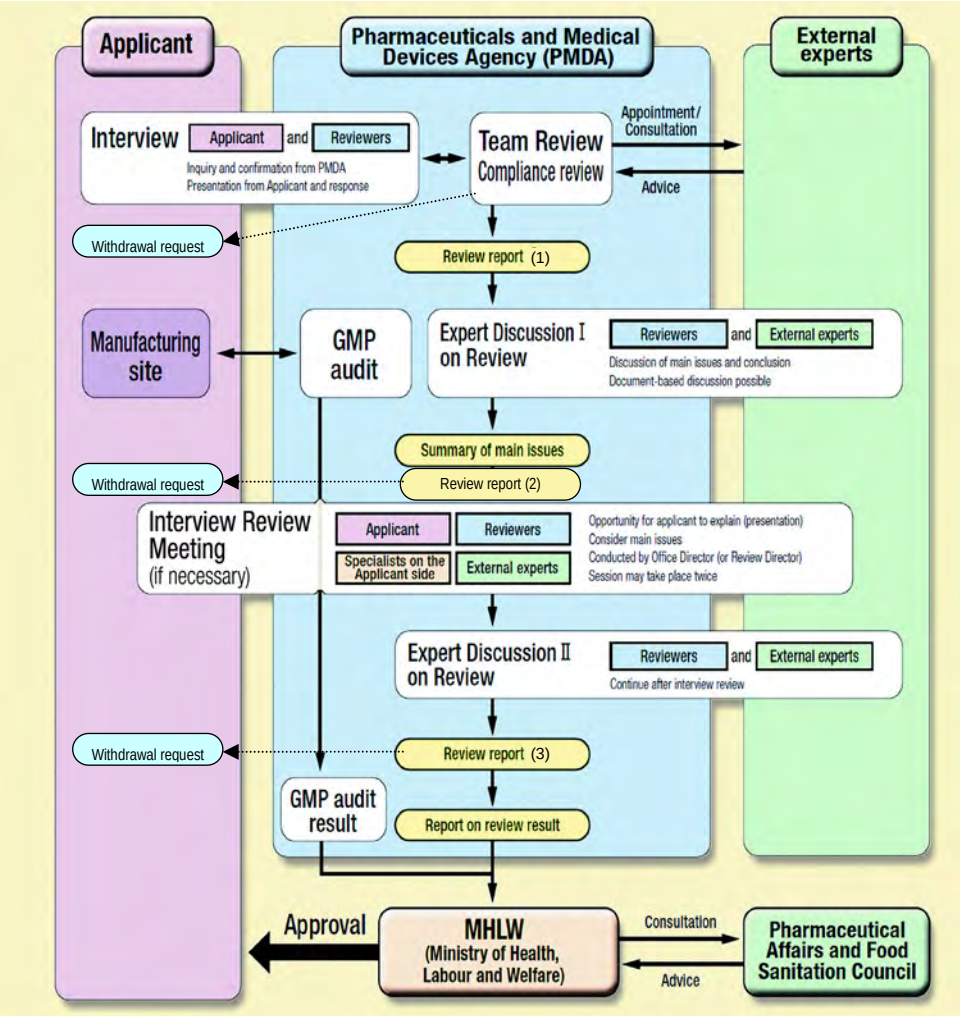
  1) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the “Pharmaceuticals and Medical Devices Agency (PMDA)” was established through the integration of three separate organizations that were responsible for reviews and related 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 Review Services in FY 2009

Reviews:

Drugs

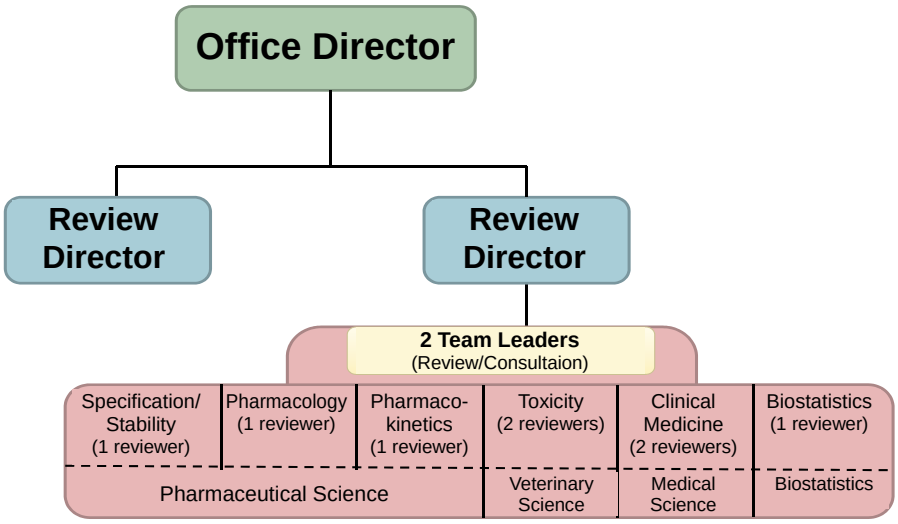
(1) Number of Expert Discussions conducted: 224
(168 in written form, 56 through meetings)

(2) Applications deliberated at the Drug Committees (PAFSC): 63
Applications reported to the Drug Committees (PAFSC): 44

- 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



- PMDA increased the number of reviewers in the drug review offices responsible for the therapeutic categories where many new drug applications were filed and likely to remain pending. Also in April 2009, the Agency established the Office of New Drug V dedicated to oncology drugs and re-organized the categories among some review offices, thus enhancing its review system.

- Reviews of new drugs were implemented after establishing a dedicated office and team to each therapeutic category as shown below:

Therapeutic Categories in the Offices of New Drugs

Name of office	Therapeutic 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 for internal use, 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	Blood coagulation factor products, gene therapy, confirmation under Cartagena Act
	Bio-CMC	Quality of antibody 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 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 control and coordination of reviews of new drugs. In FY 2009, based on the experience of implementing the system in the initial year, this scheme was further integrated into the review system.

- 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 the progress. The Committee thus monitored operational progress, and particularly for new drugs, comprehensively considered relevant information and approaches for solving issues.

- 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 2009. 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 (10 meetings were held in FY 2009).

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

- The progress of the PMDA review had been informed to the applicants at meetings, etc. by the directors of review divisions in each review stage. In order to further properly notify the progress of review, the procedures for information sharing entitled, “Way of Information Sharing between an Applicant and Pharmaceuticals and Medical Devices Agency during the Review Process for New Drugs” was developed (March 19, 2009). In accordance with the procedures, information was smoothly shared with applicants at each stage of review. At the same time, meetings were held appropriately upon the applicant’s request by the office directors to explain the progress and outlook of reviews.

c. Standardization of review

- As the basic concept of review, “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, etc.

- 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 851 PMDA staff members participated in 316 domestic and international academic conferences and seminars.

- In order to periodically grasp the needs of academic societies and patients regarding drugs 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, by reorganizing the “Investigational Committee for Usage of Unapproved Drugs” and the “Investigational Committee on Pediatric Drug Therapies,” 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 of such types

of development. To respond to these demands, consultations on pharmacogenomics/biomarkers have been conducted beginning 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. Members of respective review teams participate in all relevant clinical trial consultations.

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 dissolution of solid oral dosage forms is examined to confirm appropriate quality and appropriate dissolution specifications are established based on the data submitted by these marketing authorization holders. The re-evaluations of quality are conducted to ensure that the quality of solid oral dosage forms is maintained at a certain level.

- In FY 2009, 164 products underwent re-examinations, 0 product underwent re-evaluation for drug efficacy, and 12 products underwent re-evaluation for quality.

Implementation Status of Re-examinations/Re-evaluations

		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Products that underwent re-examination		28	152	95	235	164
Re-evaluation	Products that underwent re-evaluation for drug efficacy	0	0	0	0	0
	Products that underwent re-evaluation for quality	206	70	434	89	12

Note: Number of products for which re-examination was completed in respective fiscal year.

g. Promotion of digitization for reviews and related services

- 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 for reference only.

- This new application/review system enables PMDA to manage the progress for 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 2009, 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 developments to promptly and efficiently perform reviews and inspections.

  1) Digitization of documents related to past consultations

     - PMDA digitized documents related to past consultations, which had been archived in paper media, and converted them into PDF format through a general competitive bidding process, and thus reduced the costs for storage of paper documents.

  2) Development of the Web application platform for medical devices

     - The percentage of paper-based submission of medical device applications is still high. The information included in those applications is manually entered into the review system by PMDA staff members, resulting in low efficiency with the risk of incorrect entry. For this reason, the Web application platform for medical devices running in conjunction with the main system was developed through a general competitive bidding process, in order to improve the efficiency of medical device reviews.

  3) Improvement of the medical device review support system

     - The device system used for management of information and progress of medical device reviews was improved, through the general competitive bidding process, to handle the division of Office of Medical Devices into two offices. This improvement made the system more user-friendly and facilitated the acceleration of reviews of new medical devices.

  4) The migration of a review-related authentication system, etc.

     - The migration of a review-related authentication system and the procurement of hardware, etc. were carried out through the general competitive bidding process. As a result, the replacement of obsolete hardware and the employment of the redundant system configuration improved the system reliability, thereby optimizing reviews and related services.

  5) Conversion of final decision documents for regulatory approval for drugs etc. and submitted documents into electronic media

- Final decision documents for regulatory approval for drugs etc. and submitted documents were converted into image data, which can reduce space and be stored for a long time, through the general competitive bidding process. PMDA promoted the efficiency and acceleration of reviews by using the search function to view these image data.

6) Digitization of documents submitted in clinical trial notifications for drugs, documents submitted in applications for drugs, etc.

- As a project to accelerate reviews that is funded by grants according to the “guideline for the management of funds related to the project to accelerate reviews of unapproved drugs” among the “funds for measures to address unapproved drugs, new-type influenza, etc.,” the digitization of documents submitted in clinical trial notifications and product applications for drugs, etc. was implemented through the general competitive bidding process. The digitization of these documents contributed to the enhancement of the efficiency of review operations.

7) Building of a database system on excipients that are used in already-approved drug products

- Similarly to the above, as a review acceleration project, the building of a database system on excipients was implemented through the general competitive bidding process. This enabled the enhancement of the efficiency of surveillance on excipients that are used in already-approved drug products, which relied on paper documents in the past.

8) IT literacy training

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

h. Improvement of environments for eCTD

- Based on the requirements defined in FY 2007 for review-related function for eCTD, the eCTD viewer system was improved through the general competitive bidding process, to newly add the review comment control function. The reviews using the eCTD viewer system were greatly enhanced. As a result of this improvement, submission of paper documents for applications is unnecessary if an eCTD is filed as the original.

i. Development of Japanese Pharmacopoeia

- In FY 2009, the Japanese Pharmacopoeia Draft Committee held a total of 97 meetings, and posted information on the PMDA website to seek public comments regarding 206 official monographs (98 new articles, 93 amendments, 15 deletions), 23 general testing methods (2 new methods, 21 amendments), 11 ultraviolet-visible reference spectra, 13 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 supplement of the 16th edition of the Japanese Pharmacopoeia (JP) (to be published as a Ministerial Notification 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
New monographs	102	90	1	106	-
Amendments	276	171	1	122	2

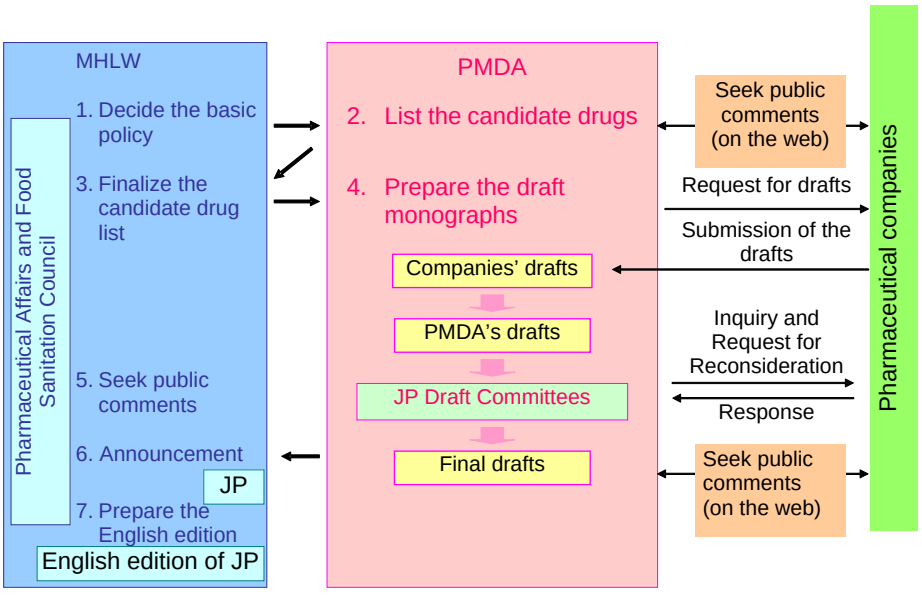
Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for General Notices, General Rules for Preparations, General Rules for Crude Drugs, General Tests, Processes, and Apparatus, and General Information. PMDA provided a report on those drafts to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

Ministerial Notification on the Japanese Pharmacopoeia (JP) by MHLW

Ministerial Notification on the JP (month and year announced)	15th edition of the JP (March 2006)	1st supplement to the 15th edition of the JP (September 2007)	Amendments to the 15th JP(March 2009)
New monographs	102	90	1
Amendments	272	170	1
Deletion	8	6	0
Total number of monographs	1,483	1,567	1,568

- 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 website of JP-related information. In addition, the Agency gives information on international harmonization of pharmacopoeial standards to overseas users on the English website of JP-related information.
  (URL: http://www.std.pmda.go.jp/jpPUB/index_e.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 clinical trial consultation stage, PMDA has offered prior assessment consultations as a pilot scheme since FY 2009. (Category 1, 1 product; Category 2, 1 product; Category 3-1, 1 product; Category 4, 3 products; Biological Products, 1 product)

  Taking into account the results of the pilot scheme, the clinical trial consultation working group prepared the Q&A document while exchanging opinions with the industry (January 05, 2010).

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 were placed in three review teams, and actions 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 were taken on a trial basis.

(iii) Target-setting to solve the drug lag

- The targets for total review time (from application date to approval date; same below) for drug applications submitted on or after April 1, 2004, the regulatory review time (including the review time for the Ministry of Health, Labour and Welfare; same below), 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.) submitted to PMDA were reviewed by review teams consisting of experts in pharmaceutical science, medicine, veterinary medicine, biostatistics, etc.

- With regard to review services for new drugs, in order to ensure consistency among the review teams and carry out review work promptly and appropriately, PMDA developed the "Procedures for Reviews of New Drugs" regarding reviews and related procedures, and the SOPs for various operations.

- The status of reviews for new drugs in FY 2009 is shown below:

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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	4.9	13.7	12.3 (19.4)	15.4 (19.1)	11.9 (24.5)
Regulatory review time [months]	2.8	6.4	4.9 (7.7)	7.3 (8.3)	3.6 (6.7)
Applicant's time [months]	2.2	6.0	6.5 (12.0)	6.8 (11.4)	6.4 (15.9)
Number of approved applications	9	20	20	24	15

Note 1: Products covered were those for which applications were filed in or after FY 2004. Refer to the "Table 1. Products Approved in FY 2009: New Drugs" in the Supplementary Information for the number of products.

Note 2: 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 necessity (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 15 applications were approved in FY 2009. In FY 2009, 12 applications requesting priority reviews of drugs regarded as having particularly high medical necessity were submitted.

  Of the 12 products for which priority reviews were requested, 2 applications were judged to be "applicable" as priority review products, and 4 were "not applicable," and 6 are currently under consideration.

- The median total review time for priority review products was 11.9 months in FY 2009. The median regulatory review time was 3.6 months, showing the achievement of the target, whereas the applicant's time was 6.4 months, which was longer than the target.

  Among approved applications in FY 2009, priority review products accounted for 14% and the percentage was lower than that in FY 2008 (31%).

b. Review times for new drugs (standard 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 Products)

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	18.1	20.3	20.7 (29.5)	22.0 (27.6)	19.2 (24.8)
Regulatory review time [months]	10.3	12.8	12.9 (17.7)	11.3 (18.5)	10.5 (15.3)
Applicant's time [months]	7.2	6.9	7.9 (11.2)	7.4 (14.1)	6.7 (10.7)
Number of approved applications	15	29	53	53	92

Note 1: Products covered were those for which applications were filed in or after FY 2004. Refer to the " Table 1. Products Approved in FY 2009: New Drugs" in the Supplementary Information for the number of products .

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

- In FY 2009, the median total review time for standard products was shortened to 19.2 months, compared with 22.0 months in FY 2008. The median regulatory review time was shortened by 0.8 months compared with that in FY 2008, and the median applicant's time was also shortened by 0.7 months. The number of approved applications was markedly increased from the previous fiscal year.

- As for the applications submitted before the establishment of PMDA (in or before March 2004) and the applications submitted after the establishment of PMDA (in or after April 2004), PMDA reviewed those in the order of their submission, giving full consideration to the target time for reviews. Meanwhile, PMDA has requested the applicants to withdraw applications that were considered to be difficult to approve due to a lack of response by the applicants to inquiries made by PMDA.

- Of the applications submitted in or before March 2004, 134 were processed through approvals or withdrawals by FY 2009.

Median Regulatory TC Metrics for Standard Review

	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 2009	2.1 months (2.4 months) 46 applications	0.5 months (0.9 months) 48 applications	3.9 months (7.6 months) 97 applications	2.4 months (3.3 months) 91 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 there was 1 application which was not subject to Expert Discussion, the number is different from 92 applications which is the number of approvals in standard reviews.

- The number of applications under review at the end of FY 2009 was 142 (including 13 orphan drugs; 7 priority reviews excluding orphan 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 (1)	106 (0)	28 (2)	6 [-2]
FY 2004	87	78 (0)	9 (0)	0
FY 2005	57	49 (0)	7 (1)	1 [-1]
FY 2006	102 (1)	90 (12)	9 (1)	3 [-13]
FY 2007	92 (5)	71(43)	10 (3)	11 [-46]
FY 2008	81 (-1)	46 (39)	3 (2)	32 [-41]
FY 2009	105	13 (13)	3 (3)	89 [89]
Total	664	453 (107)	69 (12)	142 [-14]

Note 1: In the number of applications on or before March 31, 2004, there was 1 additional application (1 application was later changed to be included in "Applications").

Note 2: In the number of applications in FY 2006, there was 1 additional application (1 application was later changed to new drugs from other category during the review).

Note 3: In the number of applications in FY 2007, there were 7 additional applications (7 applications were later changed to be included in "Applications") and 2 deleted applications (2 separate applications for a single active ingredient was integrated into 1 application, 1 application was changed to be not included in "Applications").

Note 4: As the number of applications in FY 2008, there were 2 additional applications (1 application was later changed to be included in "Applications", and 1 application was changed to new drugs from other category during the review), and 3 deleted applications (2 separate applications for a single active ingredient was integrated into 1 application, and there were 3 such dual applications).

Note 5: Values in parentheses in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2009 (included in values on their left).

Note 6: Values in brackets indicate difference from FY 2008.

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 2009	Number of processed applications	55	73	105	107
	Median total review time	76.0 days	394.0 days	27.0 days	59.0 days

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

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

(vi) Promotion of international harmonization and global clinical trials

- From the viewpoint of promoting international activities as a whole during the effective period 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. The Agency aims to proactively promote international activities in line with the said strategic plans and 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 specific system for exchanging information, etc., relating to consultations, reviews, and post-marketing safety measures in cooperation with the US and the EU, PMDA holds discussions with the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in collaboration with the MHLW. However, no individual discussion with the EU was made in FY 2009.

- PMDA collected information on the review system and post-marketing safety measures of the FDA, EMA, etc. Specifically, a bilateral meeting with the FDA was held in June 2009, where opinions 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 exchanged opinions.

- PMDA also participated in the 4th Summit of Heads of Medicines Regulatory Agencies (the US, Europe, Asian and other countries) held in Ottawa in October 2009, and exchanged opinions with regulators in various countries including the FDA and EMA. At around the same time, PMDA concluded a confidentiality arrangement with Canada and developed a system to exchange information.

- In consideration of recent increases in simultaneous clinical trials/development of drugs among three East Asian countries (Japan, China and South Korea), the 1st meeting of the Japan-China-South Korea Working Group was held in August 2009 to promote collaborative relationships among the regulatory authorities of the three countries and to re-confirm the importance of drug development in East Asia, where discussions focusing on ethnic factors

were conducted. In December 2009, the 2nd Japan-China-South Korea Director-General Level Meeting on Pharmaceutical Affairs and the 2nd meeting of the Japan-China-South Korea Working Group were held, where the outline of the Working Group was agreed upon. Also, it was decided that Japan will prepare a concrete plan for the research project on ethnic factors as the coordinator while contacting experts in the other two countries.

b. Strengthening of activities for international harmonization

- In FY 2009, PMDA continued to actively participate in international harmonization meetings such as ICH, and promoted further international harmonization. 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.

- Specifically, PMDA actively cooperated in efforts toward the development of international standards and the international regulatory harmonization through participation in Steering Committee Meetings and Expert Working Group Meetings of ICH, etc., as well as in the Expert Working Group Meeting of PDG.

- In order to build a specific system for exchanging information, etc., relating to consultations, reviews, and post-marketing safety measures in cooperation with the US and the EU, PMDA holds 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

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

*ICH Expert Working Groups

ICH Meeting in Yokohama

ICH Meeting in St. Louis

ICH Japan Symposium 2009

Topics discussed in FY 2009

- Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use (S2 [R1])
- Nonclinical Evaluation for Anticancer Pharmaceuticals (S9)
- Impurities: Guideline for Residual Solvents PDE for Cumene (Q3C [R5])
- Impurities: Guideline for Metal Impurities (Q3D)
- Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions (Q4B)
- Development and Manufacturing of Drug Substances (Q11)
- Q&A on Quality (Q-IWG)
- Q&A on CTD-Quality Documents (CTD-Q)
- Electronic Standards for Transmission of Regulatory Information (M2)
- Non-Clinical Safety Studies for the Conduct of Human Clinical Trials (M3 [R2])
- Data Elements and Standards for Drug Dictionaries (M5)
- Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals (S6 [R1])
- Data Elements for Transmission of Individual Case Safety Reports (E2B [R3])
- Development Safety Update Report (E2F)
- 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)

- Genomic Biomarkers Related Drug Response (E16)
- 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)
*WHO INN (international nonproprietary names) meeting

- PMDA held four Expert Discussion meetings on drug names and reported 30 Japanese accepted names (JAN) to MHLW. Eleven application consultations for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conference on INN in April 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 four from Indonesia and one from the U.S. (Mansfield trainee). The Agency also accepted investigation teams from the China’s State Food and Drug Administration (SFDA) and Korea Food and Drug Administration (KFDA), and provided explanations regarding Japanese pharmaceutical regulatory affairs.

- PMDA expressed to China and South Korea that the Agency intends to accept trainees. Consequently, PMDA decided to accept trainees from FY 2010 onwards, and prepared for this.

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 July 2009 and February 2010. PMDA improved the training by setting more stringent selection criteria for applicants and introducing a reimbursement system after the trainees paid out of pocket, resulting in an increase in the rate of attendance for training and enhancement in the students’ English conversation/presentation skills. For the purpose of improving linguistic skill, PMDA performed a TOEIC examination for employees who requested it. In addition, PMDA developed a “challenge training program” that allows young staff to participate in international academic conferences, aiming to nurture internationally-minded human resources.

e. Improvement and strengthening of international publicity and information provision

- PMDA made efforts to improve the provision of English information by reorganizing its English website to make it easier to view and set up a new page dedicated to international activities.

- In order to provide information on its reviews and related services and post-marketing safety measures to international audiences, PMDA has created and released the English translations of the review reports and safety information on its website. In FY 2009, the Agency prepared and published the English translations of 7 review reports.

- At the DIA Annual Meetings, etc. held in Japan, the U.S., and Europe, PMDA provided lectures on its reviews and safety measures to improve the international recognition of PMDA, and also made booth exhibitions for the publicity of PMDA's operations.

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 560 clinical trial notifications submitted in FY 2009, 113 were related to global clinical trials.

- PMDA decided on an active approach to global clinical trials, etc. In FY 2009, it received 61 applications for consultations on global clinical trials for drugs with new active ingredients, of which 56 were carried out.

(v) Efficient implementation of clinical trial consultations

a. Implementation of priority consultations

- In FY 2009, there were no requests for designation for priority consultations on drugs that are considered to have particularly high medical necessity. Two ingredients for which priority consultations were requested in FY 2008 were accepted and there were no requests rejected as inapplicable. PMDA conducted a total of 6 priority consultations related to the designated ingredients.

- In FY 2009, PMDA tried to expand and reinforce the consultation categories by introducing the "prior assessment consultations for drugs" on a trial basis, and "consultations on pharmacogenomics/biomarkers."

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 a clinical trial consultation to consultation or to the first meeting of a priority consultation by establishment of the procedural guidance and appropriate improvements in operation. The target duration from consultation request to consultation, about 2 months, has been firmly maintained.

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

Number of Clinical Trial Consultations (CTCs)

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Requests for CTC	339 (243)	473 (327)	435 (325)	342 (326)	407
Conducted CTCs	218	288	281	315	370
Withdrawals	14	7	21	23	23
Total (Conducted CTCs and withdrawals)	232	295	302	338	393

Number of Prior Assessment Consultations for Drugs Conducted

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Requests for CTC	-	-	-	-	33
Conducted CTCs	-	-	-	-	33
Withdrawals	-	-	-	-	0
Total (Conducted CTCs and withdrawals)	-	-	-	-	33

Number of Consultations on Pharmacogenomics/Biomarkers Conducted

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Requests for CTCs	-	-	-	-	1
Conducted CTCs	-	-	-	-	1
Withdrawals	-	-	-	-	0
Total (Conducted CTCs and withdrawals)	-	-	-	-	1

Note 1: Values in parentheses do not include consultations re-requested after rejection (in accordance with the scheduling method for requests submitted by July 2008).

Note 2: Prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers have been conducted since FY 2009.

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: Prior assessment consultations for drugs are conducted for the categories of quality, non-clinical: toxicity, non-clinical: pharmacology, non-clinical: pharmacokinetics, and 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 upon request, 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 2009, PMDA provided a total of 393 consultations (including 23 withdrawals), basically responding to all of the consultations requested.

- PMDA aimed to complete the process from a consultation to finalization of meeting records in 30 business days for 60% of all consultations conducted. In FY 2009, the meeting records were finalized for 305 out of 328 consultations (93.0%) within 30 business days after 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 outlook for the consultation is presented to the applicant beforehand (preliminary outlook disclosure system).

Number of Clinical Trial Consultations for Drugs by Category in FY 2009

Category	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Total
Category 1 (Gastrointestinal drugs etc.)	4	1	8	2	3	2	4	2	2	3	3	1	35
Category 6-2 (Hormone drugs)	3	3	5	3	2	2	3	4	2	3	1	4	35
Category 2 (Cardiovascular drugs)	2	3	6	5	4	6	4	5	5	3	5	4	52
Category 5 (Drugs for the urogenital system etc.)	1	1	0	1	2	2	2	1	1	1	2	5	19
In vivo diagnostics	0	0	0	0	0	1	0	0	0	0	0	0	1
Radiopharmaceuticals	1	0	0	1	1	0	0	0	1	0	1	0	5
Category 3-1 (Central nervous system drugs etc.)	5	3	5	6	2	2	2	2	4	4	4	3	42
Category 3-2 (Anesthetic drugs, etc.)	0	3	1	2	1	2	4	3	2	2	1	1	22
Category 4 (Antibacterial agents etc.)	1	2	0	2	7	10	2	1	2	3	3	2	35
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 6-1 (Respiratory tract drugs etc.)	3	2	2	4	1	1	9	2	2	3	1	2	32
Oncology drugs	2	1	5	6	5	9	3	5	5	4	6	3	54
Blood products	1	1	1	0	1	2	1	0	0	0	1	0	8
Bio-CMC	1	2	0	0	0	0	0	1	2	2	2	1	11
Biological products	1	1	1	1	1	1	1	2	2	0	0	5	16
Cell- and tissue-based products	0	0	0	0	0	0	0	0	0	0	0	1	1
[Re-listed] Prior assessment (pre-NDA review) for drugs	0	0	7	6	8	5	1	0	0	0	3	3	33
Pharmacogenomics/biomarkers	0	0	0	0	1	0	0	0	0	0	0	0	1
GLP/GCP compliance (for priority review)	0	0	0	0	0	0	1	0	0	0	0	0	1
Total	25	23	34	33	31	40	36	28	30	28	30	32	370
Withdrawals	2	3	3	1	2	1	2	3	1	3	1	1	23
Grand Total	27	26	37	34	33	41	38	31	31	31	31	33	393

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, and 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.

(vi) 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, 2010, the number of commissioned experts is 1,099 including external experts commissioned for issues relating to safety measures)

- The number of Expert Discussions conducted in FY 2009 was 224 (168 in written form; 56 through meetings)

b. Support to the development of national guidelines

- PMDA cooperated with the government to develop national guidelines for evaluating products to which new technologies have been applied (Notification for products derived from human [auto] and human [allogenic] cell- and tissue and the related Administrative Notice on Q&A; Evaluation guidelines regarding biosimilars/follow-on biologics and the related Administrative Notice on Q&A).

  PMDA also 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, and to administer drugs to each patient in more appropriate conditions, there are expectations for the application of pharmacogenomics to drug development. Aspects such as how pharmacogenomics should be used in clinical trials and reviews had been considered by the Pharmacogenomics Discussion Group (PDG) within PMDA; but to deal with the progress in this field, the PDG was reorganized expansively into the PMDA Omics Project (POP). The team 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 2009, PMDA periodically held internal meetings and 3 unofficial meetings with companies, etc. to exchange opinions on pharmacogenomics, biomarkers, etc.

  In FY 2009, PMDA started to provide consultations on pharmacogenomics/biomarkers and built a system which enables determination of appropriateness of biomarkers for each drug. The Agency actually gave advice for one case.

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 2005		FY 2006		FY 2007		FY 2008		FY 2009	
	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	0	1	1	0	2	2	1	0	1	1
Gene therapy products	0	0	1	0	0	2	0	0	0	0

- 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 2005	FY 2006	FY 2007	FY 2008	FY 2009
No. of preliminary reviews for first-class use Median review time	0 -	0 -	1 -	0 -	0 -
No. of preliminary reviews for second-class use Median review time	22 -	12 -	8 -	24 -	11 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 from FY 2009, no previous data were available.

d. Improvement of the consultation system for drugs using the latest technologies

- 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 of such types of development. In order to respond to these needs, PMDA has been conducting consultations on pharmacogenomics/biomarkers starting from FY 2009.

- To support venture companies that possess development technologies but are not able to develop new drugs very efficiently just because of being not familiar with the pharmaceutical regulatory system, in FY 2009 PMDA continued to conduct venture company support consultations in which PMDA explains the pharmaceutical regulatory system and the procedures and data required for applications. (FY 2009: 7 consultations for drugs)

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 2nd meeting held on July 30, 2009 and the 3rd meeting held on March 12, 2010. In addition,

PMDA will promptly deal 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 851 PMDA staff members participated in 316 domestic and international academic conferences and seminars.

b. Promotion of digitization in reviews

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

c. Development of Japanese Pharmacopoeia

- See 3.2.(1).(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) Target-setting 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 2009).

- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2009 are as follows:

Targets

Products	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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Generic drugs	1,919	2,152	3,278	1,980	3,271
Of which: Number of approved applications filed in or after April 2004	1,782	2,029	3,228	1,960	3,245
Median review time (for the applications filed in or after April 2004)	7.3 months	4.0 months	4.5 months	5.3 months	7.5 months
OTC drugs	1,570	1,030	1,329	1,821	2,171
Of which: Number of approved applications filed in or after April 2004	1,163	923	1,309	1,807	2,166
Median review time (for the applications filed in or after April 2004)	7.8 months	6.3 months	4.0 months	3.5 months	4.6 months
Quasi-drugs	2,611	2,287	2,236	2,340	2,221
Of which: Number of approved applications filed in or after April 2004	2,575	2,275	2,230	2,339	2,220
Median review time (for the applications filed in or after April 2004)	5.3 months	5.5 months	5.2 months	5.0 months	4.8 months
Total	6,100	5,469	6,843	6,141	7,663
Of which: Number of approved applications filed in or after April 2004	5,520	5,227	6,767	6,106	7,631

Note 1: The medians for OTC drugs and quasi-drugs in FY 2007, FY 2008, and FY 2009 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 2005	1,829	1,919	221	2,159
	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
OTC drugs	FY 2005	1,131	1,570	144	2,207
	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
Quasi-drugs	FY 2005	2,286	2,611	118	1,495
	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

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 2009	0	0	4	1	0	33	10	7	0	2	6	58	1	1,627	1,749
Approved in FY 2009	0	0	0	0	0	20	4	0	0	0	0	3	0	1,486	1,513

Category of application	Insecticides	Total
Filed in FY 2009	10	10
Approved in FY 2009	3	3

Former category of application	1	2	3	4-1	4-2	OTC test agents	Total
Approved in FY 2009	0	14	29	82	530	0	655

(Quasi-drugs)

Category of application	1, 3	2	Total
Filed in FY 2009	121	2,450	2,571
Approved in FY 2009	54	2,167	2,221

Note 1: The categories of application for OTC drugs were amended on January 1, 2009. Categories 1, 2, 3, 4-1 and 4-2 in the column of "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 a new active ingredient (Direct OTC drugs)
2: Drugs with a new active ingredient 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 category
1: Drugs with a new active ingredient (Direct OTC drugs)
2: Drugs with a new route of administration
3-1: Drugs with a new indication
3-2: Drugs in a new dosage form
3-3: Drugs with a new dosage
4: Drugs with a new active ingredient for OTC (Switch OTC drugs)
5-1: OTC drugs with a new route of administration
5-2: OTC drugs with a new indication
5-3: OTC drugs in a new dosage form
5-4: OTC drugs with a new dosage
6: New OTC combination drugs
7-1: OTC combination drugs with similar prescription
7-2: OTC drugs in a similar dosage form
8: Other drugs (relatively less innovative drugs and drugs that are not innovative)

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

Note 3: Each application belongs to the category 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 that of insecticides and rodenticides for which applications for approval as quasi-drugs were filed

- The median regulatory review times in FY 2009 were 7.5 months for generic drugs (target: 10 months), 4.6 months for OTC drugs (8 months), and 4.8 months for quasi-drugs (5.5 months), showing target achievement for all categories.

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

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Generic drugs	941	628	1,135	601	1,004

- For generic drugs, PMDA conducted 1,004 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

- In FY 2009, PMDA sought opinions and requests from the industry through the Federation of Pharmaceutical Manufacturers' Associations of JAPAN, regarding pre-application consultations for generic drugs. PMDA intends to continue discussions centering on these opinions and requests.

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

- In FY 2009, PMDA organized the framework for the new consultation system through a series of discussions with the Japan Self-Medication Industry. The Agency has been seeking public comments since the end of March 2010, toward the start of the new consultation system on a trial basis in June 2010.

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

- In FY 2009, PMDA started exchanging opinions with the persons in charge at the secretariat of the Japan Cosmetic Industry Association regarding issues such as how to conduct pre-application consultations for quasi-drugs in future. PMDA intends to continuously exchange opinions with the Association.

Medical devices

- Based on the “Action Program to Accelerate Reviews of Medical Devices” in December 2008, the Agency intends to take various measures with the aim of shortening the time to the approval of new medical devices by 19 months (consisting of 12 months before and 7 months after the filing of application).

(i) Implementation of appropriate and prompt reviews

a. Implementation structure for clinical trial consultations and reviews

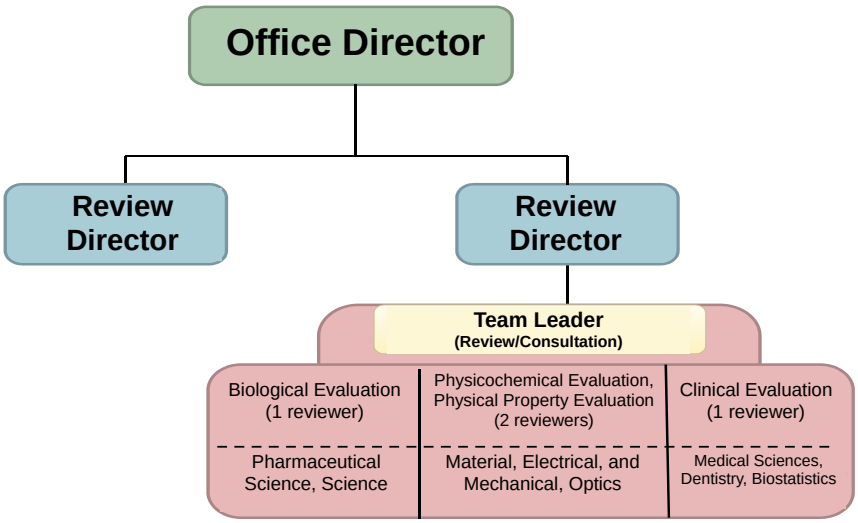
Actual Results of Reviews in FY 2009

Reviews:
Medical devices and *in vitro* diagnostics
(i) Number of Expert Discussions conducted: 81
(62 in written form, 19 through meetings)
(ii) Applications deliberated at the Committee on Medical Devices and *in vitro* Diagnostics (PAFSC): 19
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (PAFSC): 43 (38 for medical devices, 5 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 reinforced the review system by reorganizing the office of medical devices into Office of Medical Devices I and Office of Medical Devices II in August 2009.

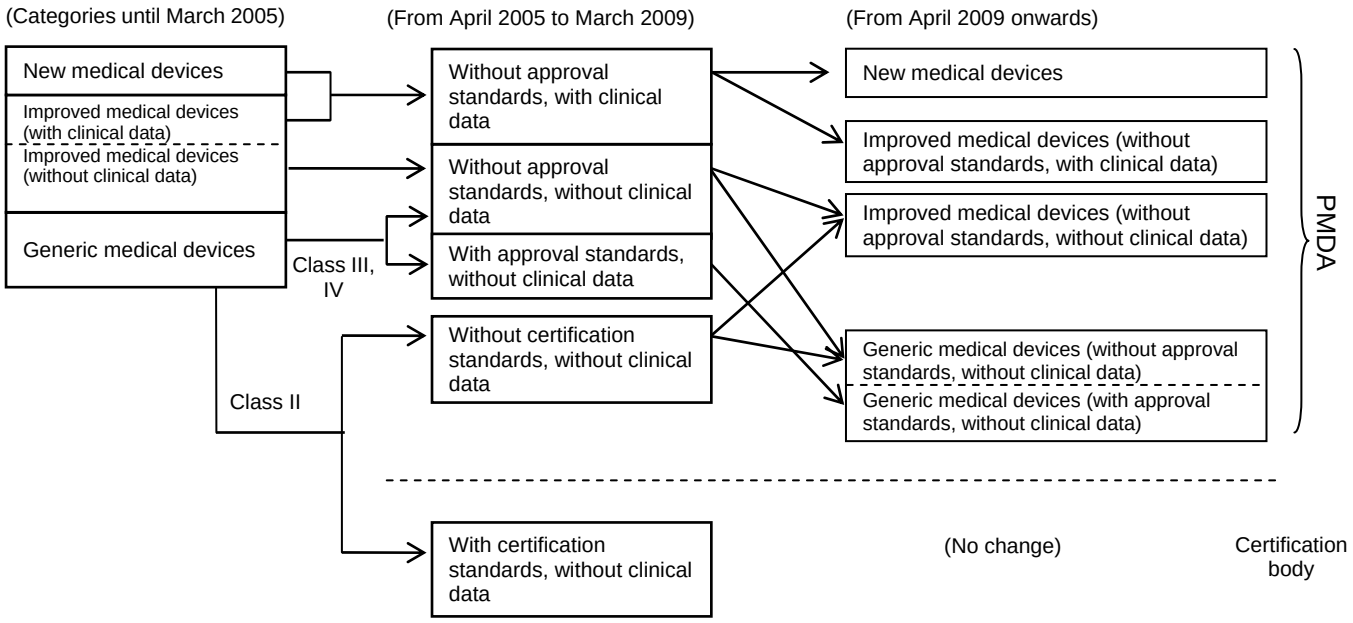
- Reviews of new medical devices were implemented upon establishing a team to each therapeutic category as shown below:

Therapeutic Categories in the Office of Medical Devices

Name of office	Therapeutic 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	Mainly for orthopedic surgery, plastic surgery, 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 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 numbers II, III, and IV are categories of medical devices by risk level. Class II refers to those with relatively low risk for the human body, Class III refers to those with relatively high risk for 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, etc.

• See 3.2.(1).(i).d *[New drugs]*

• Efforts were made based on the examination results 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.

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 more than one category in FY 2009.

d. Promotion of digitization in reviews

• See 3.2.(1).(i).g *[New drugs]*

e. Standardization of review

• As the basic concepts of reviews, from the viewpoint of clarification of review standards, a guideline "Points to Consider in Preparing Applications for New Medical Devices, etc."

prepared in FY 2008 was explained to the reviewers in charge. The information was also posted on the website and has been used for reviews, etc.

- In FY 2009, PMDA prepared the “Guideline for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices and improved medical device)” 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 directors of the review division assessed the operational progress on a routine basis. Based on the reports from these directors, the Director and Associate Center Directors of the Center for Product Evaluation provided necessary guidance at the Reveiw Segment Meeting for Progress Management.

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

- PMDA released a guideline “Points to Consider in Preparing Applications for Generic Medical Devices” in March 2009, and explained to the reviewers in charge. The information was posted on the PMDA website and has been utilized for reviews, etc. In addition, PMDA is continuously considering about the preparation of a guidance aiming for the rationalization of application documents of improved medical devices.

(ii) Introduction of new review systems

a. Introduction of prior assessment consultations

- Based on the results of a questionnaire survey on clinical trial consultations which was conducted with the cooperation of the industry, PMDA discussed appropriate consultation categories and considered reviewing the operational method.

- PMDA started designing the prior assessment consultation system under agreement with the industry regarding its concept, aiming toward the introduction of the system in FY 2010.

b. Implementation of the short-term review system for approvals for partial changes in specific information

- Among 3 products applied for in FY 2008 and 38 products applied for in 2009, 30 products that completed review were approved within 2 months of waiting time on the applicant side (excluding the conformity audit period).

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 four meetings, and the Expert Committee on Medical Device Review Guidelines held three meetings in FY 2009.

  The numbers of established standards for approval and certification reported to MHLW in FY 2009 were as follows:

Reported in:	FY 2006	FY 2007	FY 2008	FY 2009	Total
Approval standards	6	7	5	2	20
Certification standards	0	14	86	64	164
Review guidelines	0	1	2	6	9

- The number of standards established by MHLW in FY 2009 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	Total
Approval standards	0	17	8	10	-2*	5	38
Certification standards	363	9	24	0	17	68	481
Review guidelines	0	0	0	0	3	1	4

* *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 2009)

Medical device certification standards (68 established, 0 revised standards), medical device approval standards (5 established, 1 revised standards), review guidelines (1 established, 0 revised standard)	
Date of issue	Name of standard
MHLW Ministerial Notification No. 36 dated January 28, 2010	67 certification standards including the standard for motorized liquid crystal thermography devices
PFSB Notification No. 0525004 dated May 25, 2009	Approval standards for dental implant
PFSB Notification No. 1120-2 dated November 20, 2009	Approval standards for artificial kidney machine
PFSB Notification No. 1120-7 dated November 20, 2009	Approval standards for artificial lung
PFSB Notification No. 1120-10 dated November 20, 2009	Approval standards for neuroendoscopes
PFSB Notification No. 1120-13 dated November 20, 2009	Approval standards for vascular endoscopes
PFSB Notification No. 1203-1 dated December 3, 2009	Review guidelines for intramedullary nails 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 FY 2009, PMDA started providing information on the status of establishments/revisions of JIS standards for medical devices (related to revisions of certification standards, etc.), and also started providing information to overseas users by setting up 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, but 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 cooperated in the activities of the MHLW and industry in relation to the preparation of Q&A concerning the interpretation of MHLW Notifications on the clarification of the necessity, or not, of clinical data.

- PMDA considered issues such as the 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.

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

- PMDA introduced the equivalence review method for generic medical devices applied for in FY 2009 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. Sixty-eight certification standards were established in FY 2009.

(iii) Target-setting 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 reviews.

- 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 prepared the "Procedures for Review of New Medical Devices," which describes review and related procedures, and developed SOPs relating to various operations. 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 2009 is shown below:

a. Review times for new medical devices (priority 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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	-	14.2	15.7	28.8	13.9
Regulatory review time [months]	-	5.7	8.6	5.8	6.0
Applicant's time [months]	-	-	-	-	7.7
Number of approved applications	0	1	4	4	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, previous values are not available.

• Reviews of applications for orphan medical devices and other devices that are regarded as having particularly high medical necessity (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 products. In FY 2009, 4 products (all were new medical devices) were approved (however, application for one of the products was made before FY 2003). There was one application requesting priority review of a medical device regarded as having particularly high medical necessity. For this application, the request for priority review was withdrawn. Meanwhile, one application under consideration at the end of FY 2008 was designated for priority review.

b. Review times for new medical devices (standard 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 Products)

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	10.3	15.7	15.1	14.4	11.0
Regulatory review time [months]	1.8	3.2	7.7	9.8	6.8
Applicant's time [months]	-	-	-	-	7.1
Number of approved applications	5	14	19	12	33

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.

- The median total review time for priority review products was 13.9 months in FY 2009, showing achievement of the target.

  On the other hand, the median total review time for standard review products was 11.0 months in FY 2009, showing achievement of the target. In addition, the number of approvals exceeded those of past years more new medical devices were approved than in any past year.

- For applications submitted before the establishment of PMDA (in or before March 2004) and applications submitted after the establishment of PMDA (in or after April 2004), PMDA processed reviews taking the target review time sufficiently into consideration. However, 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.

- As to the applications submitted in or before March 2004, PMDA processed 129 of these applications through approvals or withdrawals by FY 2009. In order to achieve the target for the review time earlier, PMDA plans to progress with reviews of such application vigorously.

- The number of product under review at the end of FY 2009 was 42 (including 3 orphan medical devices and 1 priority review product 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 (1)	75 (0)	3 [-1]
FY 2004	56	35 (4)	18 (1)	3 [-5]
FY 2005	7	7 (0)	0	0
FY 2006	23 (-1)	18 (2)	3 (0)	2 [-2]
FY 2007	37	28 (8)	4 (3)	5 [-11]
FY 2008	32	21 (20)	0 (0)	11 [-20]
FY 2009	24	5 (5)	1 (1)	18 [18]
Total	311	168 (40)	101 (5)	42 [-21]

Note 1: Values in the "Applications" column are the numbers of those submitted for new medical devices.
Note 2: The number of approved products includes those approved as improved medical devices.
Note 3: The number of the "Applications" in FY 2006 decreased by one because one application switched to other category during the review.
Note 4: Values in parentheses in the columns of "Approved" and "Withdrawn" indicate those processed in FY 2009 (included in values on their left).
Note 5: Values in brackets indicate difference from FY 2008.

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 2009	Number of processed applications	20	21	22	36
	Median total review time*	24.5 days	217.0 days	152.0 days	30.0 days

Note 1: The days shown in each review process are the median of the total review time (the sum of reviewers' and applicants' time clocks).
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 refer to devices that do not fall under "new medical devices" or "generic medical devices" and is not novel enough to be subject to re-examination, but are not substantially equivalent to existing medical devices in terms of structure, usage, indications, or performance (medical devices requiring clinical evaluation).

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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	-	-	-	-	17.2
Regulatory review time [months]	-	-	-	-	10.4
Applicant's time [months]	-	-	-	-	6.6
Number of approved applications	-	-	-	-	30

Note 1: Products covered were those for which applications were filed in or after FY 2004.
Note 2: The "Number of approved applications" was counted after the applications filed in or before FY 2008 were re-categorized according to the new system implemented from FY 2009.
Note 3: Because the target for this category was set up beginning in FY 2009, no previous values were available.

- There were 30 improved medical devices (with clinical data) approved in FY 2009, and the median total review time was 17.2 months. The target review time for FY 2009 could not be achieved. The possible reason for this is that in this fiscal year, which was the initial year of the Action Program, old applications were handled intensively so that the future targets could be achieved.

  The median regulatory review time was 10.4 months, and the median applicant's time was 6.6 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 2009

Improved medical devices (with clinical data)	Applications	Approved	Withdrawn	Under review
FY 2009	34	1 (1)	0 (0)	33
Total	34	1 (1)	0 (0)	33

Note 1: Values in parentheses indicate those processed in FY 2009 (included in values on their left).
Note 2: The number of applications was counted based on the categorization of the day the application was filed or the request was received.

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

- Improved medical devices refer to devices that do not fall under "new medical devices" or "generic medical devices" and is not novel enough to be subject to re-examination but are not substantially equivalent to existing medical devices in terms of structure, usage, indications, or performance (medical devices not requiring clinical evaluation).

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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	-	-	-	-	13.2
Regulatory review time [months]	-	-	-	-	8.5
Applicant's time [months]	-	-	-	-	3.9
Number of approved applications	-	-	-	-	158

Note 1: Products covered were those for which applications were filed in or after FY 2004.
Note 2: The "Number of approved applications" was counted after the applications filed in or before FY 2008 were re-categorized according to the new system implemented from FY 2009.
Note 3: Because the target for this category was set up beginning in FY 2009, no previous values were available.

- The number of improved medical devices (without clinical data) approved in FY 2009 was 158, and the median total review time for these applications was 13.2 months, showing non-achievement of the target value for FY 2009.

  The median regulatory review time was 8.5 months, and the median applicant's time was 3.9 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 2009

Improved medical devices (without clinical data) Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	137	22 (22)	0 (0)	115
Total	137	22 (22)	0 (0)	115

Note 1: Values in parentheses indicate those processed in FY 2009 (included in values on their left)
Note 2: The number of applications was counted based on the categorization of the day the application was filed or the request was received.

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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Total review time [months]	-	-	-	-	12.9
Regulatory review time [months]	-	-	-	-	5.9
Applicant's time [months]	-	-	-	-	3.6
Number of approved applications	-	-	-	-	1,797

Note 1: Products covered were those for which applications were filed in or after FY 2004.
Note 2: The "Number of approved applications" was counted after the applications filed in or before FY 2008 were re-categorized according to the new system 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 2009 was 1,797, and the median total review time was 12.9 months, showing non-achievement of the target value for FY 2009. The median regulatory review time was 5.9 months, and the median applicant's time was 3.6 months.

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

Review Status of Generic Medical Devices Applications Filed in FY 2009

Generic medical devices Filed in:	Applications	Approved	Withdrawn	Under review
FY 2009	1,127	451 (451)	8 (8)	668
Total	1,127	451 (451)	8 (8)	668

Note 1: Values in parentheses indicate those processed in FY 2009 (included in values on their left)
Note 2: The number of applications was counted based on the categorization of the day the application was filed or the request was received.

- For improved medical devices (without clinical data) and generic medical devices, the target values for FY 2009 could not be achieved.

  Target values for the FY 2009 could not be achieved probably because older applications filed in past years were processed intensively in this fiscal year when the Action Program was introduced, aiming to achieve the targets for the future. Meanwhile, the total number of approvals was 1,275, showing an increase compared with 962 corresponding approvals in FY 2008 (excluding applications for transition of licensed products to a new category due to the change in regulations as an exceptional measure).

(iv) Promotion of international harmonization and global clinical trials

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

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

- PMDA collected information of the review system and post-marketing safety measures from FDA, while exchanging information with the FDA on operational methods and other issues. PMDA also participated in the 4th Summit of Heads of Medicines Regulatory Agencies (the US, Europe, Asian and other countries) held in Ottawa in October 2009, and exchanged opinions with regulators from various countries including the FDA.

b. Strengthening of activities for international harmonization

- In FY 2009, PMDA continued to actively participate in Steering Committee Meetings and Expert Working Group Meetings of GHTF[*1,] Steering Committee Meetings and Working Group Meeting for HBD[*2] activities, ISO[*3], etc. Particularly in GHTF meetings, PMDA promoted further international harmonization by improving the consistency of Japanese standards with international standards such as those for developing data for review, 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 medical devices that PMDA participated in (relating to reviews and post-marketing safety measures)]
  ISO/TC/198 (Sterilization of health care products)
  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)

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

c. Promotion of personnel exchanges

- See 3.2.(1).(iv).c *[New drugs]*

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

- See 3.2.(1).(iv) d *[New drugs]*

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

- See 3.2.(1).(iv).e *[New drugs]*

(v) 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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Requests for CTC	33	46	76	87	130
(Medical devices)	32	43	75	84	122
(*In vitro* diagnostics)	1	3	1	3	8
Conducted CTCs	30	42	72	76	110
(Medical devices)	29	39	71	74	104
(*In vitro* diagnostics)	1	3	1	2	6
Withdrawals	0	0	0	2	1
(Medical devices)	0	0	0	2	1
(*In vitro* diagnostics)	0	0	0	0	0
Total (Conducted consultations and withdrawals)	30	42	72	78	111
(Medical devices)	29	39	71	76	105
(*In vitro* diagnostics)	1	3	1	2	6

Note: Requests for CTC: The number of submitted written requests for arrangement of schedule for each fiscal year

- A total of 111 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 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 2009, the meeting records were finalized for 78 out of 113 consultations (69.0%) within 30 business days from the consultation.

Number of Clinical Trial Consultations for Medical Devices by Category in FY 2009

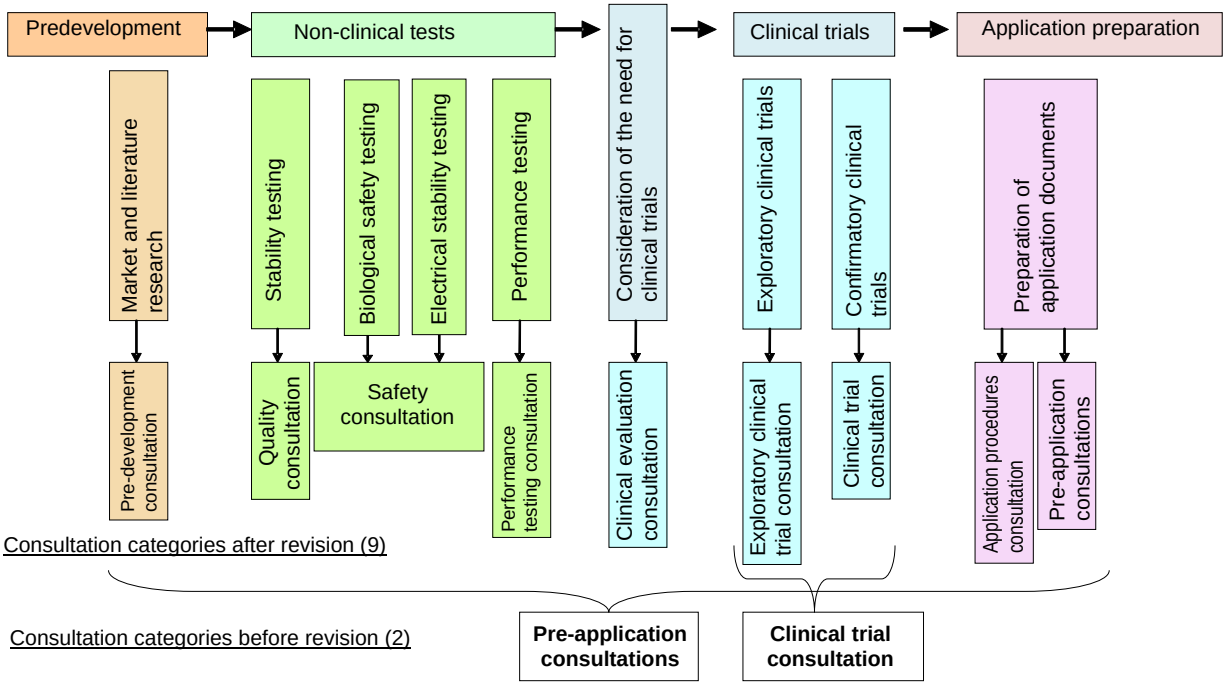
Consultation category	Number of clinical trial consultation requests	Number of clinical trial consultations conducted	Withdrawals	Total (Conducted consultations and withdrawals)
Pre-development consultation for medical devices	25	19	0	19
Safety consultation for medical devices (excluding biological devices)	2	1	0	1
Quality consultation for medical devices (excluding biological devices)	3	1	0	1
Safety consultation for biological medical devices	0	0	0	0
Quality consultation for biological medical devices	0	0	0	0
Performance testing consultation for medical devices	4	4	0	4
Clinical evaluation consultation for medical devices	14	12	0	12
Exploratory clinical trial consultation for medical devices	4	3	1	4
Clinical trial/pre-application consultation for medical devices	39	40	0	40
Clinical trial/pre-application consultation for *in vitro* diagnostics	8	6	0	6
Application procedure consultation for medical devices	28	21	0	21
Application procedure consultation for *in vitro* diagnostics	0	0	0	0
Additional consultation for medical devices	3	3	0	3
Additional consultation for *in vitro* diagnostics	0	0	0	0
Consultation for preparation of documents for cell- and tissue-derived products	0	0	0	0
Total	130	110	1	111

d. Review of consultation categories

- Since FY 2007, in order to promote 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.

Expansion of the Consultation Menu by Development Stage

- Facilitating development and speed up reviews by providing detailed advice that meets various needs at each stage of development -



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

- In FY 2009, the working-level joint task force on medical devices and *in vitro* diagnostics, comprised of MHLW, PMDA, and the industry, started up a working group for utilizing the consultation system and has considered reviewing the categorization of consultation.

(vi) Promotion of evaluation of new technologies

a. Use of external experts

- See 3.2.(1).(vi).a *[New drugs]*

b. Support to the development of national guidelines

- See 3.2.(1).(vi).b *[New drugs]*

- PMDA cooperated with the MHLW to develop “Points to Consider for the Assessment of Next-generation Medical Devices (fracture reduction support systems, joint surgery support systems, cell sheets for cell therapy for severe heart failure, and corneal epithelial cell sheets) (PFSB/ELD/OMDE Notification No. 0118-1 dated January 18, 2010),” and also tried to thoroughly disseminate the Notification.

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

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

d. Improvement of the consultation system for medical devices 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 has been conducting consultations on pharmacogenomics/biomarkers starting from FY 2009.

- To support venture companies that possess development technologies but are not able to develop new medical devices very efficiently just because of not being familiar with the pharmaceutical regulatory system, PMDA accepted and implemented applications for venture company support consultations in which PMDA explains the pharmaceutical regulatory system and the procedures and materials required for applications (FY 2009: 1 consultation for a medical device).

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

- See 3.2.(1).(vi).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 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 reliability assessment for new drugs

- PMDA conducted efficient document-based and on-site inspections and reliability 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), the Ministerial Ordinance on Good Post-Marketing Surveillance Practice (GPMSP) and the reliability standards for the submitted documents/data.

- 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, resulting in no delays caused by GLP/GCP inspections in the reviews in FY 2009.

Numbers of Conducted GLP/GCP/GPSP Inspections and Reliability Assessment

		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Document-based inspections/ reliability assessment		136	426	774	942	1,136
	Drugs	135	251	234	293	246
	Medical devices	1	175	540	649	890
GLP inspections		39	31	27	43	26
	Drugs	37	23	23	32	18
	Medical devices	2	8	4	11	8
GCP inspections		131	149	132	198	175
	New drugs	120	137	122	182	164
	Generic drugs	11	12	9	15	10
	Medical devices	0	0	1	1	1
GPSP inspections		82	103	107	79	65

Note 1: Values for GLP, GCP, and GPSP inspections in or after FY 2005 are the number of notifications after evaluation was conducted.

Note 2: In the columns for GPSP inspections, inspections completed in FY 2005 to FY 2008 were conducted as GPMSP inspections. Inspections completed in FY 2009 were conducted as GPMSP inspections or GPSP inspections.

Note 3: GLP: Good Laboratory Practices

Note 4: GCP: Good Clinical Practices

Note 5: GPMSP: Good Post-Marketing Surveillance Practices

Note 6: GPSP: Good Post-Marketing Study Practices

a. Promotion of document-based inspection on sites

- As part of GLP/GCP/GPSP inspections for new drugs, PMDA introduced a method whereby its staff members visit companies and conduct document-based inspection in FY 2009, and conducted 52 inspections (61%) based on this method.

  [Note: Document-based GLP/GCP/GPSP inspections have been originally conducted at PMDA.]

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.

(ii) Efficient implementation of data reliability assessment for re-examination

- PMDA has conducted reliability assessment as to whether or not data submitted for re-examination of approved new drugs were collected and prepared in compliance with the data reliability standards for product applications, etc.

- In FY 2009, the number of completed assessments was 66.

Number of Data Reliability Assessment for Re-examination

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Reliability assessment for re-examination	96	123	119	83	66

- PMDA has conducted reliability assessment as to whether or not data submitted for re-evaluation of approved drugs were collected and prepared in compliance with the data reliability standards for product applications, etc.

  In FY 2009, no assessment relating to re-evaluation of oral prescription drugs (quality re-evaluations) was conducted.

Number of Data Reliability Assessment for Re-evaluation

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Reliability assessment for re-evaluation	206	145	31	0	0

- PMDA set up a review meeting with experts in the section of post-marketing surveillances of companies that are marketing approval holders of new drugs, and exchanged opinions regarding issues related to reliability assessment of data for re-examination, as well as regarding improvement of the efficiency of assessment.

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

  * *Ministerial Ordinance on Good Manufacturing Practice (GMP) for Drugs and Quasi-drugs (MHLW Ministerial Ordinance No.179 of 2004)*

  † *Ministerial Ordinance on Quality Management System (QMS) for Medical Devices and In vitro Diagnostics (MHLW Ministerial Ordinance No.169 of 2004)*

  Note 1: GMP: Good Manufacturing Practice

  Note 2: QMS: Quality Management System

b. Building of the inspection system

- PMDA continued to recruit GMP/QMS specialists and the number of inspectors is 40 as of April 1, 2009. At the same time, PMDA is promoting 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 2009 are shown below:

GMP/QMS Inspections Conducted under the Revised Pharmaceutical Affairs Act

	FY 2005				FY 2006				
	Requested	Completed		Withdrawn	In progress	Requested	Completed		Withdrawn	In progress
Drugs*	203	53	(35)	1	149	1,039	783	(180)	24	381
In vitro diagnostics	22	9	(0)	0	13	63	32	(4)	1	43
Quasi-drugs	5	0	(0)	0	5	0	5	(0)	0	0
Medical devices	101	32	(4)	0	69	638	300	(20)	29	378
Total	331	94	(39)	1	236	1,740	1,120	(204)	54	802

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

	FY 2009				
	Requested	Completed		Withdrawn	In progress
Drugs*	2,228	2,000	(297)	71	969
In vitro diagnostics	115	107	(3)	5	36
Quasi-drugs	3	3	(0)	0	2
Medical devices	1,201	1,285	(66)	39	237
Total	3,547	3,395	(366)	115	1,244

** 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 2009 are shown below:

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

	FY 2005		FY 2006		FY 2007	
	Total processing time	PMDA processing time	Total processing time	PMDA processing time	Total processing time	PMDA processing time
Drugs*	78 days	59.5 days	161 days	117 days	170 days	111 days
In vitro diagnostics	101 days	101 days	149 days	100 days	158 days	88 days
Quasi-drugs	-	-	142 days	72 days	-	-
Medical devices	131 days	104 days	161 days	110 days	157 days	88 days

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

** Excluding in vitro diagnostics.*

• The processing status of inspections of manufacturing facilities conducted in FY 2009 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 2005		FY 2006		FY 2007		FY 2008		FY 2009	
Drugs*	12	(8)	30	(23)	16	(14)	8	(6)	40	(25)
In vitro diagnostics	1	(1)	6	(6)	2	(2)	2	(2)	4	(2)
Medical devices	2	(1)	1	(0)	0	(0)	1	(1)	2	(1)
Total	15	(10)	37	(29)	18	(16)	11	(9)	46	(28)

** 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 2009 is shown below:

Number of For-cause Inspections (Domestic Manufacturers)

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs*	15	11	27	13	12
In vitro diagnostics	0	0	1	1	3
Medical devices	0	0	2	0	0

** Excluding in vitro diagnostics.*

• PMDA conducts simple consultations on GMP/QMS inspections. The number of simple consultations on GMP/QMS inspections conducted in FY 2009 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

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

** 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

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

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

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

- The processing status of inspections of manufacturing facilities conducted in FY 2009 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 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs*	69	614	387	294	390
In vitro diagnostics	9	85	69	69	40
Quasi-drugs	29	73	57	39	41
Medical devices	127	971	1,682	1,191	910
Total	234	1,743	2,195	1,593	1,381

** 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 2009 is shown below:

Number of For-cause Inspections (Overseas Manufacturing Sites)

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs*	2	3	5	2	1
In vitro diagnostics	0	0	0	0	0
Medical devices	0	2	0	1	0
Total	2	5	5	3	1

** 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	Total
Europe	France	1	4	6	5	6	22
	Denmark	0	2	3	2	2	9
	Ireland	1	2	2	5	3	13
	UK	0	0	4	1	3	8
	Netherlands	0	3	1	1	5	10
	Spain	0	0	3	1	1	5
	Italy	0	0	2	5	3	10
	Belgium	0	0	1	2	4	7
	Austria	0	1	0	2	2	5
	Finland	0	1	0	0	2	3
	Germany	0	0	0	3	7	10
	Sweden	0	0	0	1	0	1
	Romania	0	0	0	1	0	1
	Slovenia	0	0	0	2	1	3
	Subtotal	2	13	22	31	39	107
North, Central and South America	USA	6	20	22	14	18	80
	Canada	1	0	0	2	2	5
	Mexico	0	0	0	1	0	1
	Bahamas	1	0	0	0	0	1
	Argentina	0	0	0	2	0	2
	Subtotal	8	20	22	19	20	89
Asia	China	0	0	5	11	25	41
	India	1	0	1	12	4	18
	Singapore	0	0	2	4	0	6
	South Korea	1	1	0	3	9	14
	Indonesia	0	1	0	0	0	1
	Taiwan	0	0	0	2	6	8
	Thailand	0	0	0	0	2	2
	New Zealand	0	0	0	0	1	1
	Subtotal	2	2	8	32	47	91
Africa	South Africa	0	1	0	0	0	1
	Subtotal	0	1	0	0	0	1
Grand Total		12	36	52	82	106	288

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	Total
Europe	Ireland	0	3	0	6	0	9
	UK	0	0	0	1	0	1
	Italy	0	0	0	2	0	2
	Netherlands	0	0	0	1	0	1
	Switzerland	1	2	0	1	1	5
	Spain	0	0	0	1	0	1
	France	0	0	1	1	1	3
	Denmark	0	0	0	0	1	1
	Subtotal	1	5	1	13	3	23
North, Central and South America	USA	1	10	10	16	27	64
	Mexico	0	0	0	1	0	1
	Brazil	0	0	0	0	1	1
	Subtotal	1	10	10	17	28	66
Asia	China	0	0	0	0	3	3
	Singapore	0	0	0	0	2	2
	Subtotal	0	0	0	0	5	5
Grand Total		2	15	11	30	36	94

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 to implement GMP inspections timely.

- 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 of products that are actually manufactured 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 created a method of assessment (draft) by referring to the five-level evaluation models (Kirkpatrick; Jack Phillips) that are used world-wide.

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

- In September 2009, PMDA conducted a training program including practical work for medical devices such as pacemakers, biological heart valves, and catheters for placing transvascular stents. In December 2009, PMDA conducted practical training program using orthopedic medical devices.

  In addition, the Agency provided relevant reviewers with other opportunities for learning by using actual devices, in order to reinforce the training curriculum.

  The Agency also conducted basic training (WHO adverse drug reactions monitoring; pharmacoepidemiology) for persons in charge of safety measures 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 programs (14 times in FY 2009), special training on regulatory science (8 times in FY 2009), and training on regulations such as the Pharmaceutical Affairs Act (3 times in FY 2009).

d. Education and training of GMP/QMS inspectors

- GMP/QMS inspectors of PMDA participated in a training program at the National Institute of Public Health, a GMS/QMS joint simulated inspection training program provided by MHLW, a workshop on QMS for medical devices and *in vitro* diagnostics, etc. The Agency also conducted a special training lecture on PIC/S.

e. Improvement of training in clinical practice

- In order to enable planning of safety measures in line with the actual clinical practice, PMDA dispatched its employees to two 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 (4 manufacturing plants of drugs; 5 manufacturing plants of medical devices, etc.).

(ii) Promotion of cooperation with foreign regulatory agencies

- Based on the PMDA International Strategic Plan, the Agency carried forward liaison/coordination and personnel exchanges with regulatory agencies in the US, the EU and Asian countries, to promote collaborations with regulatory agencies in those countries.

- 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 interested in being dispatched.

- PMDA dispatched its executive officers as liaison officers to the USP and the EMA, where the Agency gathered information and exchanged opinions. PMDA sent a team to the FDA and EMA to study the details of regulatory systems in the EU and the US, including reviews and safety measures, and exchange opinions.

(iii) 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 and colleges. In FY 2009, the Agency concluded a joint graduate school agreement with two universities: University of Tsukuba and Yokohama City University. The program is scheduled to be implemented from FY 2010.

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

- PMDA developed working regulations regarding the employment status of graduate students to be accepted under the joint graduate school agreement (Effective on April 01, 2010).

(iv) Efforts to integrate pharmacogenomics into regulatory activities

a. Support to the development of evaluation guidelines

- With regard to pharmacogenomics and biomarkers, PMDA held periodic meetings in collaboration with responsible bureaus and divisions of MHLW to develop national evaluation guidelines.

b. Contribution to establishment of internationally harmonized methods

- See 3.2.(1).(vi).b *[New drugs]*

- With regard to pharmacogenomics, PMDA has conducted teleconference, etc. with persons in charge at regulatory agencies in the EU and the US, to promote provision of information and to reinforce collaboration.

- 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 October 2009, the "4th PMDA International Symposium on Biologics" was held with the theme of regenerative

medicine by inviting speakers from a European regulatory agency, etc., and activities and trends in each country were discussed.

(v) 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 GLP/GCP/GPSP Inspection page of the PMDA website. In order to promote understanding regarding GCP, PMDA held GCP Workshops in Tokyo and Osaka for people in charge of drug development and regulatory affairs and 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
Tokyo	1,303	1,212	1,338	1,165
Osaka	454	495	543	461
Total	1,757	1,707	1,881	1,626

- 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 matters 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 in August 2009 and practical training from September 2009 to March 2010; Advanced training - lectures from November 2009 to January 2010; Local data manager training - lectures and practical training in September 2009) to pharmacists and nurses from medical institutions, for the purpose of contributing to the development of clinical trial systems at medical institutions from which trainees are dispatched.

Trainees in FY 2009

Beginner training	59
Advanced training	89
Local data manager training	39

(vi) 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, and also with the cooperation of MHLW, provided information on the application review of new drugs, etc., on the Medical Product Information page of its website.

- PMDA cooperated with MHLW to develop Notifications (draft), etc. in relation to the release of re-examination reports of new drugs, and also started posting re-examination reports in FY 2009 on its website.

- In order to provide information on PMDA's review services and post-marketing safety measures to foreign countries, PMDA has created and released the English version of review reports on its English website. In FY 2009, the Agency created and released the English version of 7 review reports.

b. Release of information related to review reports

(Review reports on new drugs)

- Based on the submitted information, new drugs are classified into two 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 the details and results of reviews, and "Summaries of Product Application" 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 for disclosure 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 2009, PMDA released 109 review reports (median period from approval to posting, 43 days) and 70 summaries of product applications (median period from approval to posting, 96 days).

(Review reports on new medical devices)

- In FY 2009, PMDA released 13 review reports (median period from approval to posting, 62 days) and 6 summaries of application dossiers (median period from approval to posting, 131 days).

(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 2009, PMDA disclosed 4

review reports and 7 summaries of product applications on OTC drugs, and 1 review report and 6 summaries of product applications on quasi-drugs.

(vii) Securing of fairness in the utilization of external experts

- Based on the need to secure fairness and transparency of judgment in commissioning external experts, PMDA developed the “Notice on the Implementation of Expert Discussions at 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 verify the judgment process. Reports are made to the Advisory Council and the Committee on Review and Safety Operations regarding the receipt of cash contributions and contract money by the external experts to whom PMDA has asked to participate in Expert Discussions on reviews and safety measures.

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

(i) Basic direction of post-marketing safety measures

- In order to improve the safety of marketed drugs and medical devices, and to enable patients and healthcare professionals to use them properly, PMDA has been working hard to ensure that reviews and safety measures function in such a way that they are inseparable, by collecting and examining post-marketing safety information efficiently, processing the information speedily, planning appropriate safety measures and providing easily understandable safety information promptly.

- There are approximately 175,000 reports on adverse drug reactions submitted to PMDA from within and outside of Japan each year, and approximately 7,000 reports on malfunctions of medical devices from within and outside of Japan are submitted to PMDA yearly. PMDA inputs the collected information into a database and shares such information with MHLW. In addition, PMDA is making efforts to take effective safety measures for drugs and medical devices in the post-marketing stage by enhancing cooperation between the review offices and safety offices, as well as between the relief office and safety offices.

- In addition to reviewing such adverse drug reaction reports and malfunction reports with representatives from MHLW every week based on daily reviews conducted by the supervising team in PMDA, the Agency gathers opinions from experts once every 5 weeks and proposes necessary safety measures, such as for revision of precautions in package inserts. Issues that require a particular urgent measure are responded to immediately.

- PMDA distributes 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 is also making efforts to enhance and reinforce the provision of information by posting various safety information regarding package inserts, labeling, etc., on the Medical Product Information web page: http://www.info.pmda.go.jp/.

- PMDA completed the system development and introduction of the system into the operational process, so that new safety information can be detected and analyzed by finding any relevance

with different kinds of information on adverse drug reactions (data mining method), in order to establish measures to prevent adverse drug reactions from occurring.

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.

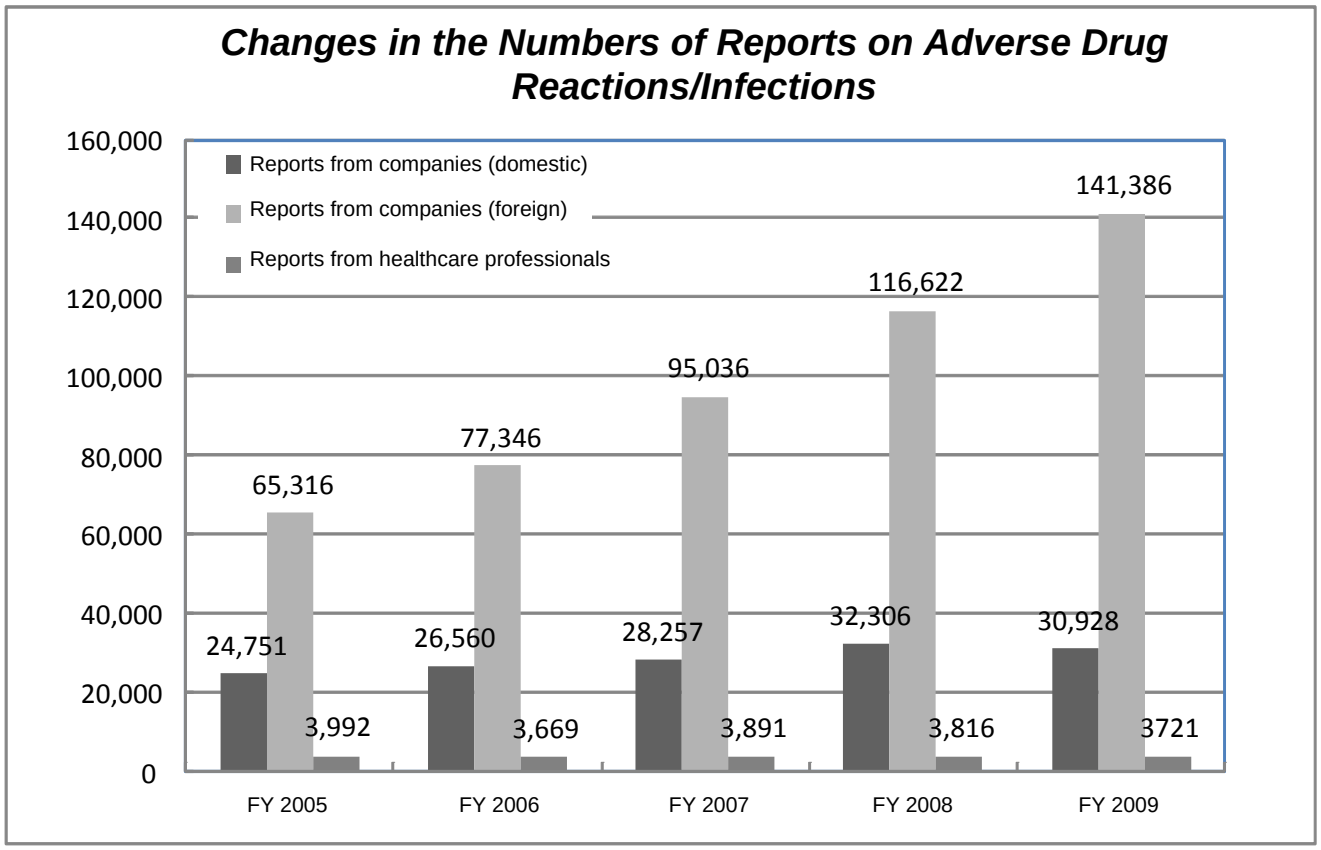
Specifically, the data mining method is used for detecting combinations (signals) of drugs and adverse drug reactions that are likely to have a causal relationship from the database of individual cases of adverse drug reactions.

- 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 applying electronic medical records.

Collection of adverse reaction reports, etc.

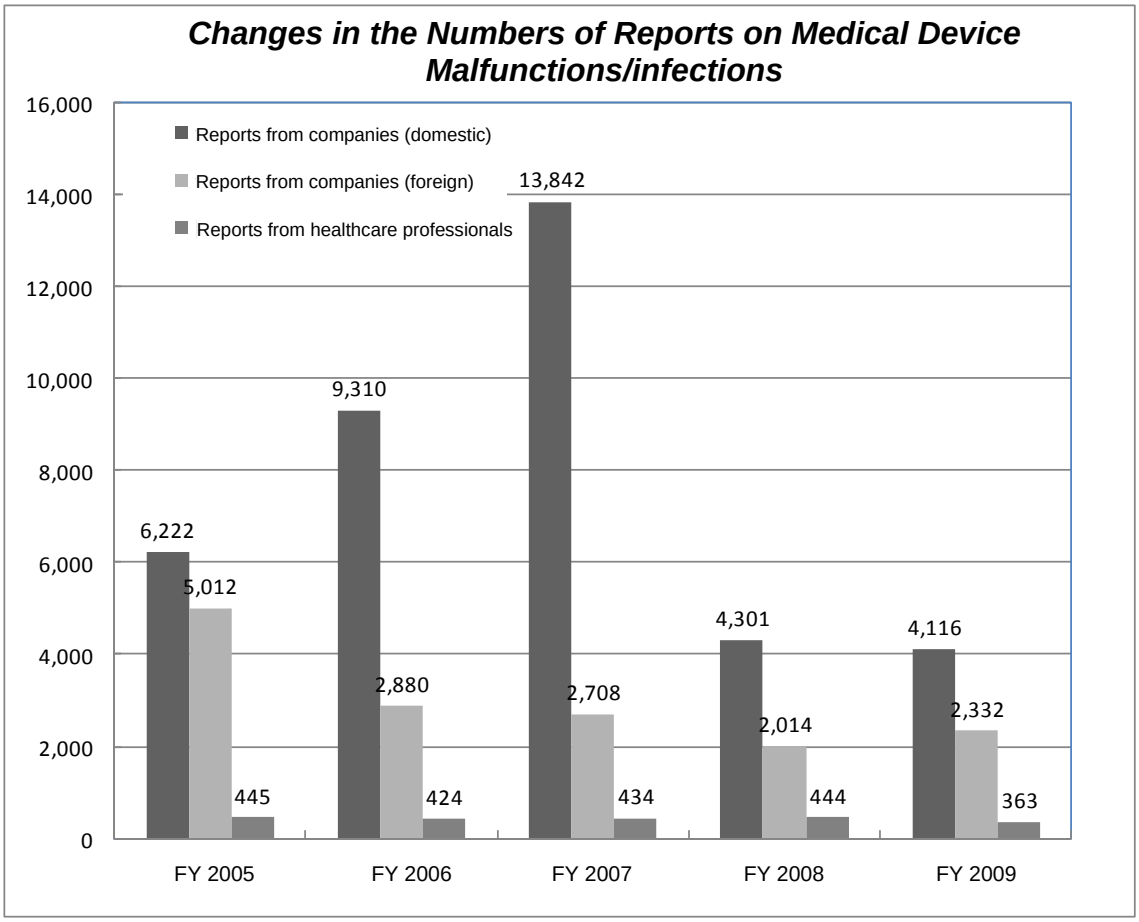
1) Number of reports relating to drugs

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Reports from companies	92,678	106,285	125,938	151,726	175,285
(cases of adverse drug reactions, Japanese)	(24,523)	(26,309)	(27,988)	(31,455)	(30,814)
(cases of infections caused by drugs, Japanese)	(228)	(251)	(269)	(851)	(114)
(cases of adverse drug reactions, foreign)	(64,650)	(77,314)	(95,015)	(116,592)	(141,364)
(cases of infections caused by drugs, foreign)	(666)	(32)	(21)	(30)	(22)
(research reports)	(971)	(818)	(858)	(855)	(933)
(foreign corrective action reports)	(563)	(485)	(695)	(869)	(930)
(periodic infection reports)	(1,077)	(1,076)	(1,092)	(1,074)	(1,108)
Reports from healthcare professionals	3,992	3,669	3,891	3,816	3,721
Total	96,670	109,954	129,829	155,542	179,006

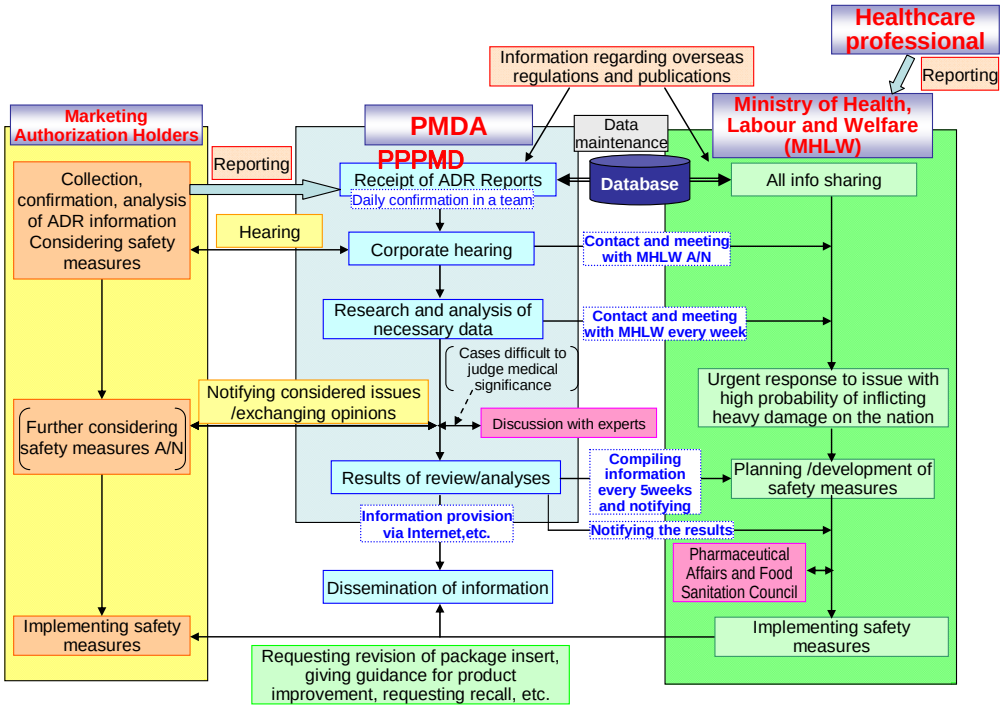


2) Number of reports relating to medical devices

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Reports from companies	11,802	12,770	17,142	7,137	7,344
(cases of malfunctions of medical devices, Japanese)	(6,222)	(9,310)	(13,842)	(4,301)	(4,114)
(cases of malfunctions of medical devices, foreign)	(5,012)	(2,880)	(2,708)	(2,014)	(2,332)
(cases of infections caused by medical devices, Japanese)	(0)	(0)	(0)	(0)	(2)
(research reports)	(37)	(36)	(15)	(10)	(6)
(foreign corrective action reports)	(436)	(482)	(525)	(748)	(831)
(periodic infection reports)	(95)	(62)	(52)	(64)	(59)
Reports from healthcare professionals	445	424	434	444	363
Total	12,247	13,194	17,576	7,581	7,707



Flowchart for Processing Adverse Reaction Reports



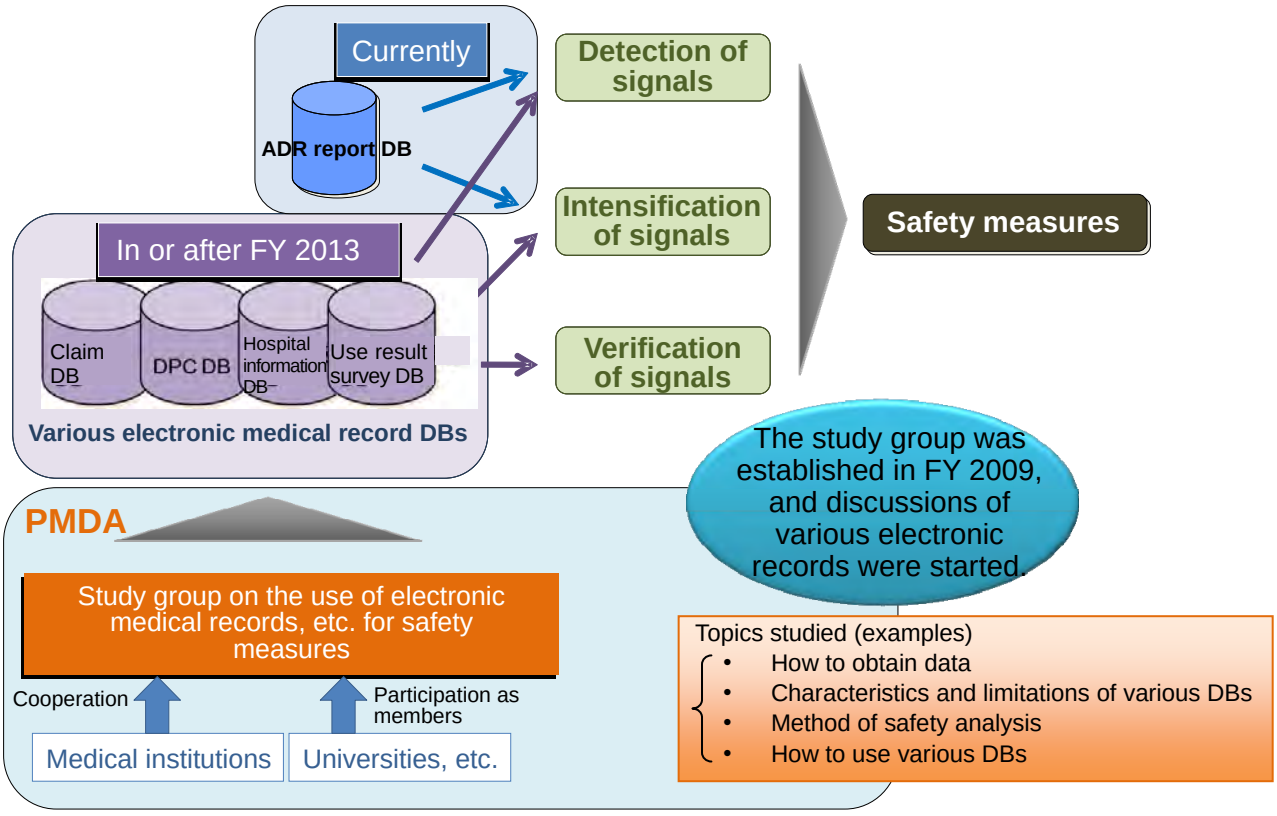
(ii) Sophistication of safety measures

a. Use of electronic medical records, etc.

- According to the Mid-term Plan, PMDA plans to organize the access infrastructure for the databases of medical records including health insurance claim data (hereinafter referred to as “claim data”), by FY 2013, perform pharmacoepidemiological analyses, and evaluate pharmaceutical risks quantitatively. Specifically, the Agency intends to start making use of such infrastructures on a trial basis in FY 2011, and by FY 2013 establish a system for conducting investigations on the incidence of adverse drug reactions and pharmacoepidemiological analyses.

- In July 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, held a total of five meetings by the end of the fiscal year and conducted a series of deliberations on each type of data such as claim data and hospital information system data regarding their advantages/disadvantages, potentials for utilization and limitations, etc.

Study on the Introduction of New Databases (DBs) for the Drug Safety Evaluation Process



- Taking into account that secondary use of the national database of claim data may become possible in the near future, in FY 2009 PMDA purchased commercially-available database of claim data. PMDA started to research what analysis is possible particularly for safety evaluation, and conducted a pilot study on anaphylaxis as the first study. Specifically, PMDA performed data compilation, etc. by drug therapeutic class, by means of extracting adverse

drug reaction cases of anaphylaxis/anaphylactic shock as entered in the “names of injuries/diseases”, from a commercially-available database of claims (data on about 400,000 patients for whom health insurance claims were issued in a particular period of 4 years in a certain health insurance union). In FY 2010, PMDA intends to obtain data on not only adverse drug reaction cases but all patients to whom drugs were administered in order to calculate the incidence rates, etc., and then post the organized results (report) on the website. PMDA also intends to undertake pilot studies on different themes and to research analysis methods. In addition, the Agency will study the potential for comprehensive analysis of claim data to detect signals.

- With regard to hospital information systems, PMDA conducted a pilot study to extract information on adverse drug reactions from 5 medical institutions in Shizuoka prefecture that are equipped with the standardized storage using the specification of SS-MIX (Standardized Structured Medical Information Exchange project by the MHLW). The study focused on more than one well-known association between a drug and an adverse reaction such as “rhabdomyolysis caused by statin drugs.” In this study, PMDA identified technical challenges for the secondary use of data from more than one hospital information system as a basic investigation to carry forward this theme expansively in the future. The technical challenges are related to differences in data among facilities, potential for integration of retrieved and detected data, and preparation of data sets for analysis.

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

- According to the Mid-term Plan, PMDA intends to computerize information on adverse drug reactions, such as those from use-results surveys, and build databases in order to make use of digitized information in the development of safety measures.

- In FY 2009, PMDA established a sub-committee on use-results surveys, etc. under the Study Group on Electronic Medical Records. Pharmaceutical companies as the providers of data from use-results surveys were also asked to participate in the sub-committee as members. In two meetings held, one each in August and December 2009, representatives from industry, the government, and academia discussed various issues related to building of databases and providing of data, such as clarification of the purposes of database, and standardization, utilization, and users of data.

c. Sophistication of the data mining method

- According to 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 plans to improve the approach on an as-needed basis by referring to overseas examples.

- In FY 2009, PMDA examined the detection level of duplicate reports in order to enhance 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). By referring to the method for duplicate detection being used at the World Health Organization (WHO), the Agency evaluated the basic performance of the new detection model, which is more practical and allows shorter calculation time, by using sample duplicate reports.

- PMDA also studied the methods of capturing time-series changes in the number of reports on adverse drug reactions. In this study, in addition to the occurrence tendency index which is already incorporated in the operational system for safety measures, the Agency adopted the change-point analysis and reviewed some safety measures applied in the past from the statistical aspect, in terms of changes in the number of reports before and after the safety measures taken. In addition, among cases reported during the 4-week pilot study period, PMDA examined the adverse reactions that were judged to have a change (increase) in the occurrence tendency index beyond the pre-determined threshold level and classified the factors that are possible causes. PMDA thus considered the characteristics and usability of the detection methods.

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.

Specifically, this is a method to find out, for example, a time point where the number of reports per month may rapidly increase for a certain combination of drug and adverse drug reaction.

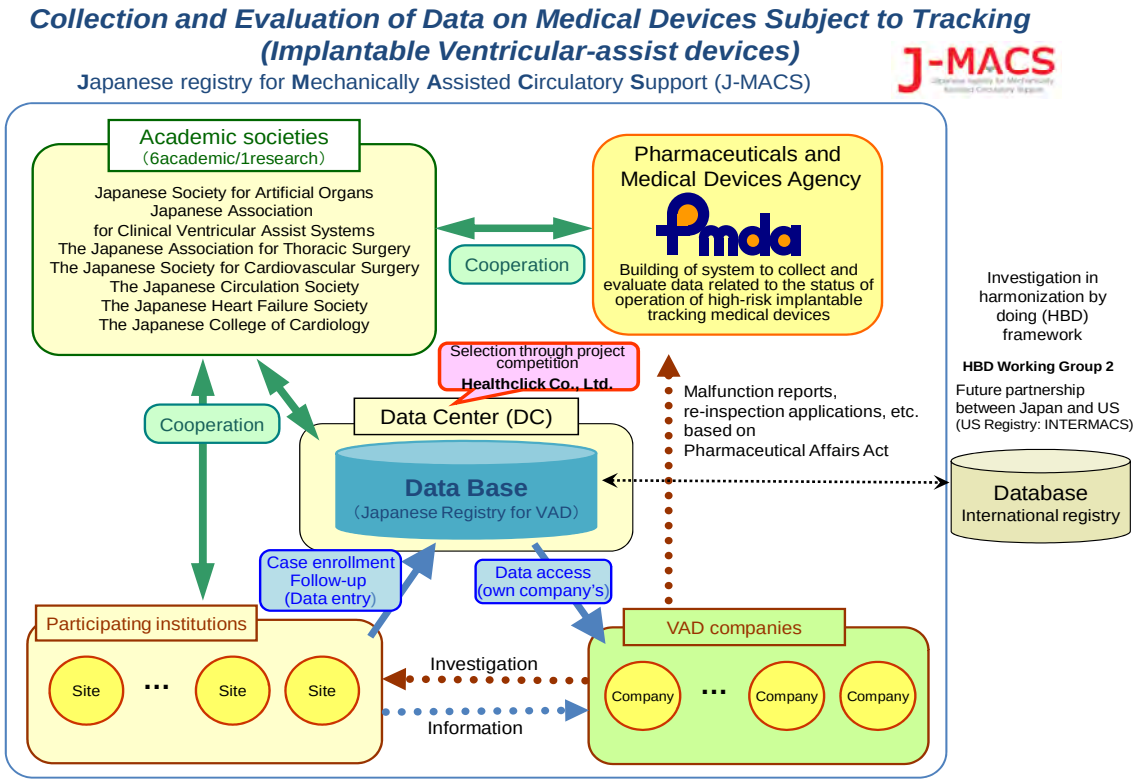
d. Collection and evaluation of data on medical devices subject to tracking (implantable ventricular-assist devices)

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

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, etc. Under the Pharmaceutical Affairs Act, such devices are categorized as designated medical devices.

- At the end of March 2010, the first release of a web-based entry system called J-MACS for the registry of implantable artificial heart assist systems (patient registration) was finished, based on the implementation structures/protocols that were considered in detail under the industry-government-academia collaboration in the First Mid-term Plan. The preparations for registration of post-marketing patient data at 6 participating medical institutions were completed. In FY 2010, PMDA intends to start collecting data from medical institutions and to examine operational challenges toward the full-scale operation in or after FY 2011.



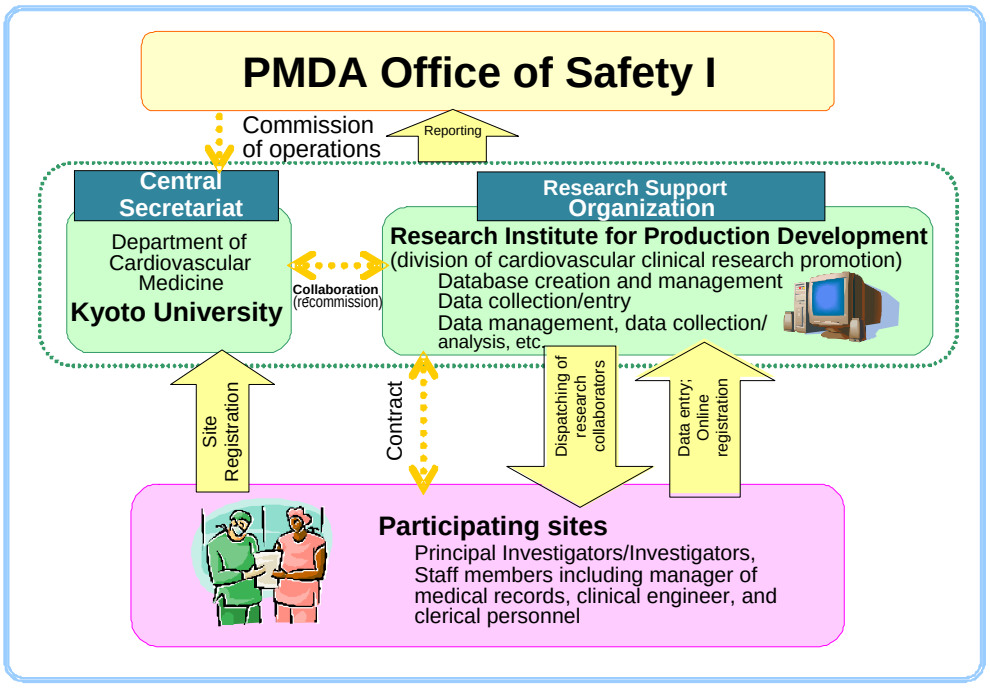
e. Evaluation of malfunctions of medical devices

- According to 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 the first percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) operation have been collected through an external contract organization.

- In FY 2009, since all enrolled patients who can continue the study have undergone follow-up for 2 full years, the second interim analysis was performed by using data on 9,206 patients with PCI (13,144 lesions) at 23 facilities from among data collected until December 25, 2009. At the end of March 2010, PMDA posted an “interim report” summarizing patients' baseline background information on the website, since the study is still under way.

Implementation System of 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) Proper assessment of reports of adverse drug reactions and medical device malfunctions

- Adverse drug reaction reports, medical device malfunction reports, infection reports, research reports, etc., from marketing authorization holders of drugs and medical devices under the Pharmaceutical Affairs Act have been required to be submitted directly to PMDA since April 2004. These reports are entered into the PMDA database and maintained so that information can be shared with MHLW.

- In addition, adverse drug reaction reports, infections reports, etc., that are submitted by healthcare professionals (doctors, pharmacists, etc.) to the Minster of Health, Labour and Welfare are entered into the PMDA database and maintained so that information can be shared with MHLW.

- In assessing reports of adverse drug reaction and medical device malfunctions, PMDA has been closely working with the Safety Division of the Pharmaceutical and Food Safety Bureau at MHLW to hold weekly reviews on both drugs and medical devices, seek opinions from experts approximately once every 5 weeks, and report on proposals for necessary safety measures, such as for revision of precautions in package inserts, to MHLW. Issues that require a particular urgent measure are responded to immediately.

- The number of reports (the number of active ingredients for drugs, and the number of generic names for medical devices) submitted to MHLW on products for which measures were necessary (such as for revision of package inserts) in FY 2009 is as follows:

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs	240	131	204	151	261
Medical devices	18	4	10	37	62
Medical safety*	2	2	1	4	4

** "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 in FY 2009 based on reports from PMDA are as follows (includes duplicated measures):

		FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs	Instructions for revision to precautions in package insert	212	131	202	141	261
	Posting articles and cases on the Pharmaceuticals and Medical Devices Safety Information	26	24	86	20	29
Medical devices	Instructions for revision to precautions in package insert or notifications to instruct self-check	7	0	8	4	4
	Posting articles on the Pharmaceuticals and Medical Devices Safety Information	7	0	3	2	5

- With regard to cooperation with the review offices within PMDA, approaches such as participation of personnel from the Offices of Safety I and II in the review process (clinical trial consultations, consideration of post-marketing survey plans, consideration of draft package inserts, Expert Discussions, etc.) of new drugs and new medical devices, as well as cooperation in adverse drug reaction case evaluations for early post-marketing phase vigilance (EPPV) are being implemented. As for 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 and is reflected in the safety measures.

- In FY 2009, PMDA took the following approaches 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 by using data input tools
  b. Updated the master files consisting of drug product and company names
  c. Encouraged staff members to attend academic conferences (a total of 54 participants) and gathered information through the academic conferences that they participated in
  d. Regularly held liaison meetings on both drugs and medical devices every week with MHLW

(iv) 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 is developing a system which allows pharmaceutical companies to access information on adverse reactions caused by 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 consultations from companies

- In order to contribute to the improvement of post-marketing safety measures in companies, PMDA responded to 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 2009 is shown below:

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Drugs	557	567	486	559	619
Medical devices	553	292	260	283	247
Medical safety	46	44	166	172	142

- 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 is attributed to the sudden rise in the number of pre-application consultations on new application for change or replacement of brand name 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 quantity of the active ingredient. Consultations conducted in FY 2009 are mainly on the names of new drugs and packaging/labeling, and on near-incident cases for drugs/medical devices. PMDA handled all consultations in an appropriate and prompt manner.

c. Support for disclosing relevant information for companies

- PMDA developed a new digital tool for medical device package inserts with advanced utility and made it available to companies for free.

- PMDA translated into English the PMDA Medical Safety Information and the Pharmaceuticals and Medical Devices Safety Information prepared by MHLW, and posted the translations on its English website.

d. Disclosure of adverse drug reaction cases

- From among the contents of all adverse reaction reports that have been submitted by companies since April 2004, PMDA has disclosed 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 2010, PMDA posted 142,084 reports which had been submitted up to November 2009.

- The time from receiving reports to disclosure was decreased to 5 months and the target period for FY 2009 was achieved.

e. Disclosure of medical device malfunction cases

- From among the contents of all reports on medical device malfunctions that have been submitted by companies since April 2004, PMDA has disclosed 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 2010, PMDA posted 46,551 reports submitted up to November 2009.

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 2009, PMDA posted 13,050 package inserts of prescription drugs on the Medical Product Information web page. When instructions on revision of a package insert were issued, PMDA 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 package inserts of medical devices

- For medical devices as well, PMDA has disclosed package inserts since FY 2005. The Agency disclosed 11,213 package inserts by the end of FY 2009. Also, PMDA has posted instructions/notifications on revision of package inserts within 2 days of the issuance of such information, and routinely provided links to the package inserts.

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

- Regarding OTC drugs, the revised Pharmaceutical Affairs Act was enforced in June 2009. Prior to the enforcement, PMDA made efforts such as securing of information supply and consultation systems according to the level of risk associated with the drugs, securing of qualifications of professionals engaged in selling drugs, and development of an environment that can respond appropriately to consultations as well as provide appropriate information. As a part of the efforts, PMDA started posting package inserts of OTC drugs on the website in March 2007. A total of 9,513 package inserts were put on the website as of the end of FY 2009.

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 3,301 package inserts were posted on the website as of the end of FY 2009.

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

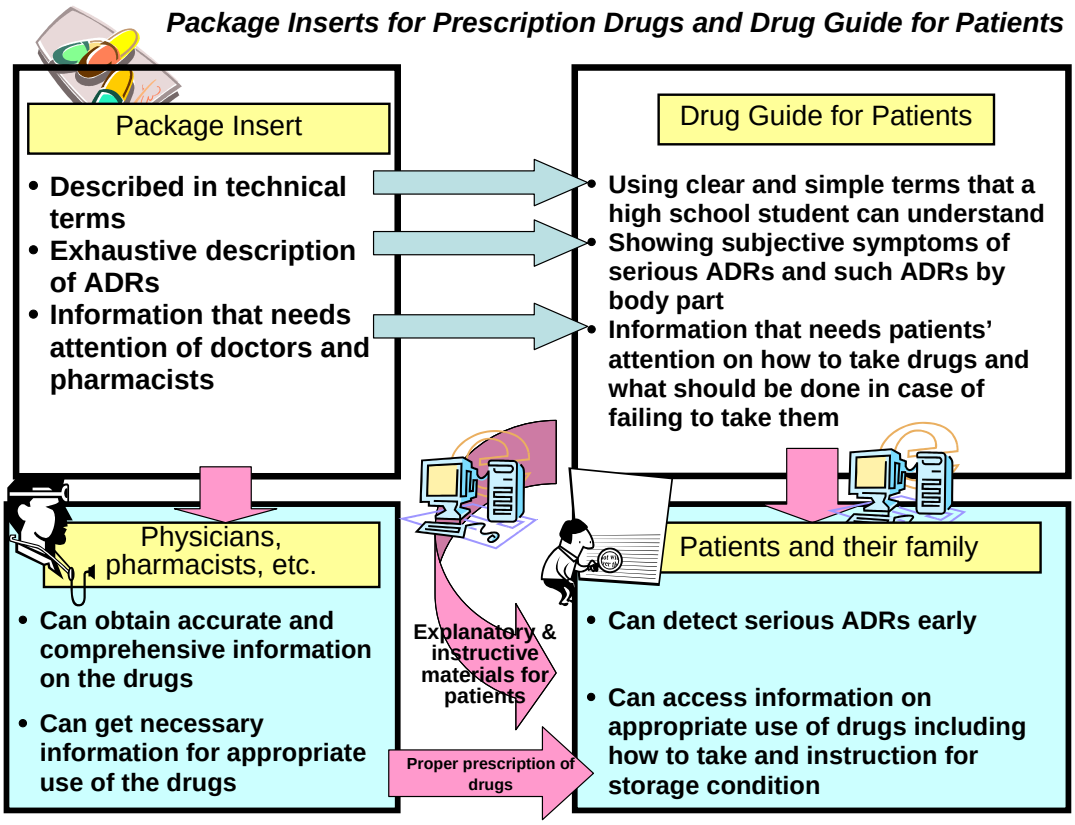
- The manuals for management of individual serious adverse drug reactions prepared by MHLW have been made available on the PMDA website since November 2006. In FY 2009, manuals for 25 diseases were added to the website (total number of diseases, 63).

  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 posted on the PMDA website since January 2006. In FY 2009, 18 active ingredients (which were newly designated or newly marketed) were added to the Drug Guide database, and a total of 312 active ingredients in 1,920 products (1,356 package inserts) were posted by the end of March 2010. Meanwhile, the number of products was reduced through sorting out and integrating generic drugs and other arrangements.

- 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”).



l. Upgrading Medical Product Information web page

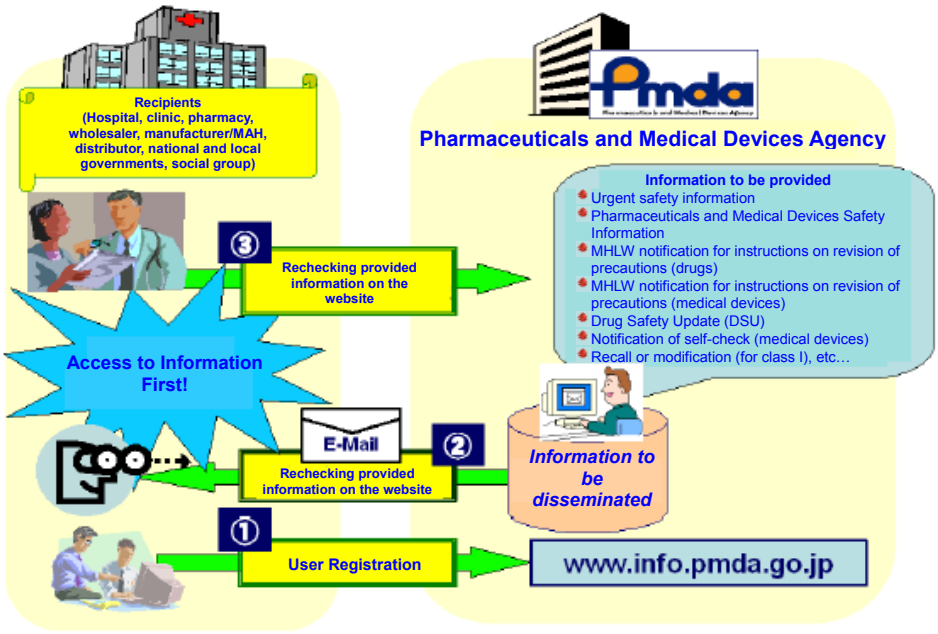
- In FY 2009, taking into account opinions given by the website users, PMDA improved the user interface of its website by setting up a search window for package insert information on prescription drugs at the upper part of the top page and providing distinct icons linking to existing and new content, so that users can more easily find target information.

m. 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 enhanced this service by adding approval information to the contents.

- A total of 27,410 e-mail addresses were registered as of the end of March 2010. Approximately 40% of these subscribers were hospitals and clinics, approx. 20% were pharmacies, approx. 10% were dentist clinics or other medical facilities, approx. 10% were marketing authorization holders, and approx. 10% were distributors.

Pharmaceuticals and Medical Devices Information E-mail Service



Push E-mail Service by Content in FY 2009

Contents of e-mails	Number of releases
Recalls (Class I)	76
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)	2
PMDA Medical Safety Information	6
Approval information (medical devices)	10
Approval information (prescription drugs)	43
Others	15
Total	188

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" published by the Japan Council for Quality Health Care. In FY 2009, 562 cases associated with drugs and 153 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 715 cases for which deliberations were completed by MHLW, the details of the cases were posted on the Medical Product Information web page.

Cases	Drugs	Medical devices
Total applicable cases: 715 cases	562	153
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.	6	2
2) Cases in which measures have already been taken, or are currently being investigated, by the marketing authorization holder etc.	13	19
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.	543	132

- In addition, in November 2007, PMDA started to issue 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 the issuance of revisions to package inserts.

In FY 2009, the following six 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.10	May 2009	Good management and maintenance of automated external defibrillators (AEDs)
No.11	August 2009	Precautions in artificial respiration (No.2)
No.12	September 2009	Misconnection of tourniquet cuff
No.13	October 2009	Medical gas mix-ups
No.14	February 2010	Precautions in handling electric scalpels (Part 1)
No.15	March 2010	Precautions in handling electric scalpels (Part 2)

o. Implementation of post-marketing safety workshops

- PMDA co-hosted the workshops on the effective use of safety information with the Japan Pharmacists Education Center on the theme of "Information on Pharmaceuticals for Appropriate Use – Toward Early Detection of Adverse Drug Reactions." The workshops were held in 4 regions in Japan (September 2009, Sendai; November 2009, Hiroshima; January 2010, Nagoya; and March 2010, Tokyo). Similarly, at workshops held by outside parties and at academic conferences, PMDA gave presentations on the recent revision of precautions in package inserts, the effective use of the Medical Product Information web page, and PMDA's consultation services.

p. 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 2009, the number of persons receiving consultations was 9,316 (13,516 calls) for drugs, and 558 (616 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 2009, the number of persons receiving consultations was 687. General consumers accounted for 93.2% of them, whereas doctors/pharmacists accounted for 2.0%.

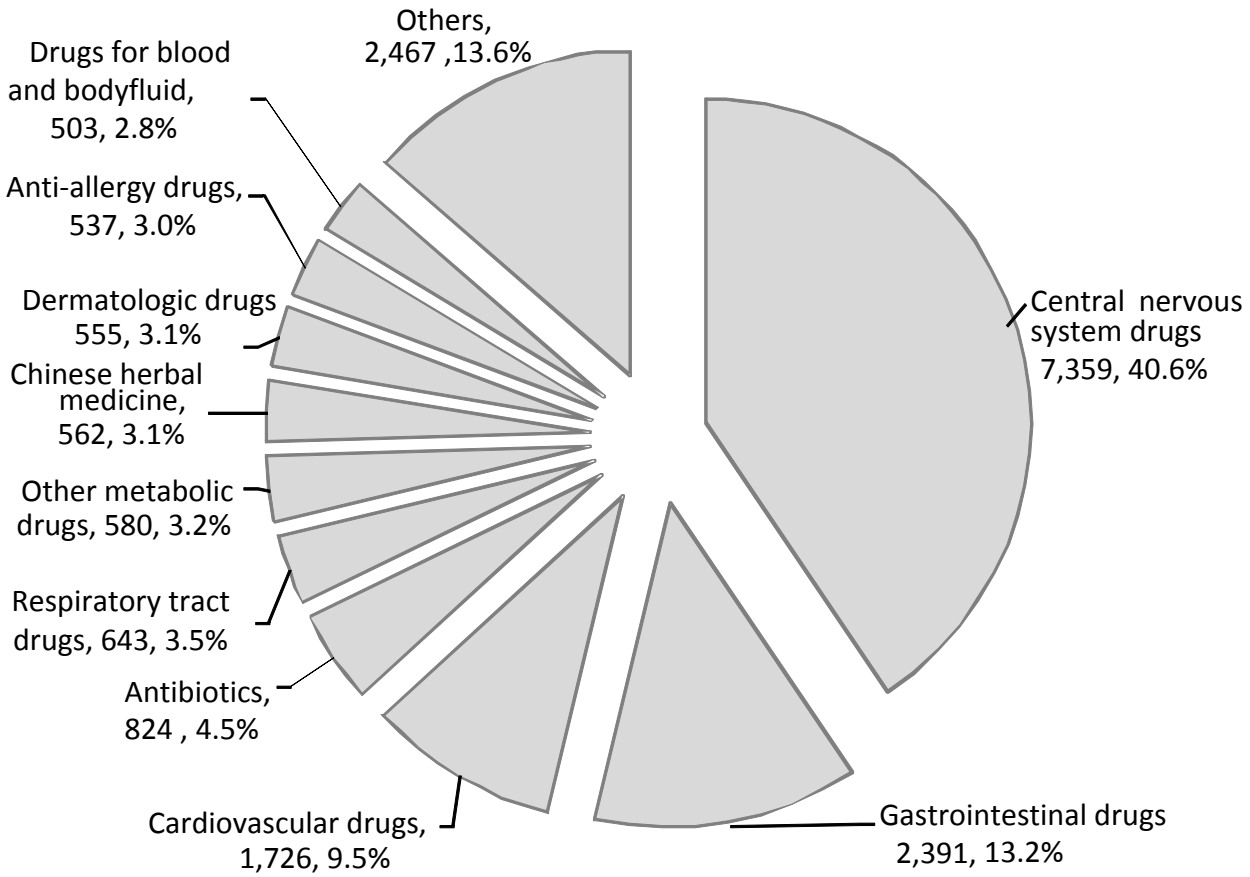
Number of Consultations on Drugs/Medical Devices

	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Consultations on drugs	7,741 30.0 cases/day	8,459 34.5 cases/day	8,696 35.5 cases/day	8,479 34.9 cases/day	9,316 38.5 cases/day
(consultations on generic drugs)	-	-	(122)	(143)	(687)
Consultations on medical devices	166 1.0 cases/days	376 1.5 cases/day	564 2.3 cases/day	639 2.6 cases/day	558 2.3 cases/day

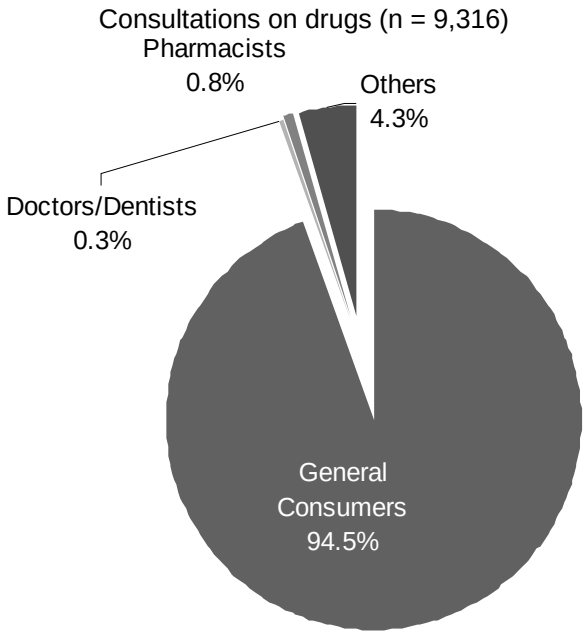
Contents of Consultations on Drugs

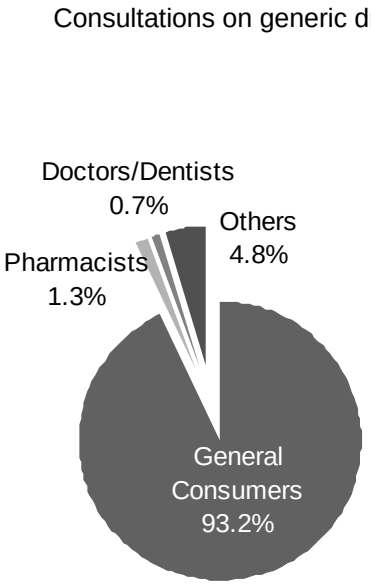
Contents of consultation	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
(1) Safety	5,968 (56.8%)	5,697 (48.7%)	5,731 (45.9%)	6,347 (50.6%)	5,727 (42.4%)
(2) Indications	1,132 (10.8%)	1,175 (10.0%)	1,175 (9.4%)	954 (7.6%)	1,079 (8.0%)
(3) Administration and Dosage	771 (7.3%)	828 (7.1%)	1,072 (8.6%)	836 (6.7%)	746 (5.5%)
(4) Interactions	628 (6.0%)	691 (5.9%)	715 (5.7%)	732 (5.8%)	753 (5.6%)
(5) Active Ingredient	161 (1.5%)	219 (1.9%)	236 (1.9%)	214 (1.7%)	251 (1.9%)
Others	1,845 (17.6%)	3,086 (26.4%)	3,548 (28.4%)	3,450 (27.5%)	4,960 (36.7%)
Total	10,505 (100.0%)	11,696 (100.0%)	12,477 (100.0%)	12,533 (100.0%)	13,516 (100.0%)

Number of Consultations on Drugs by Therapeutic Category (FY 2009)

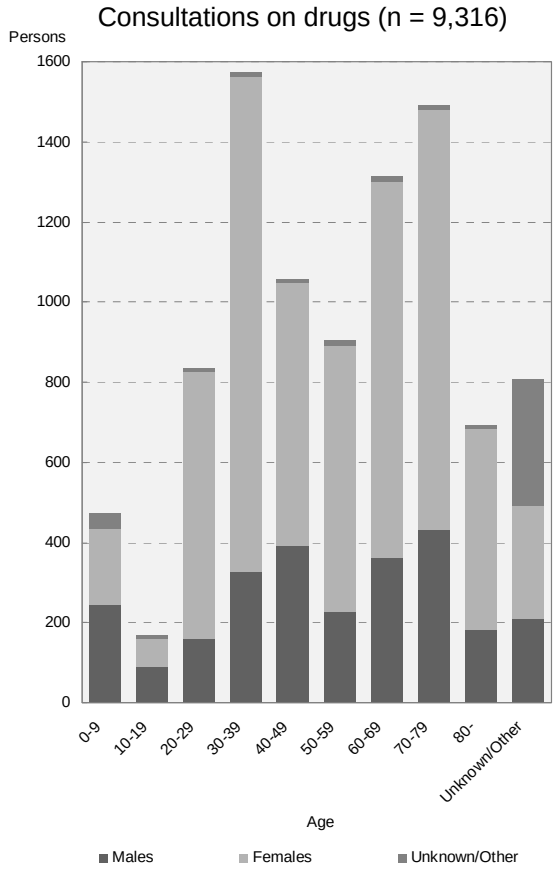


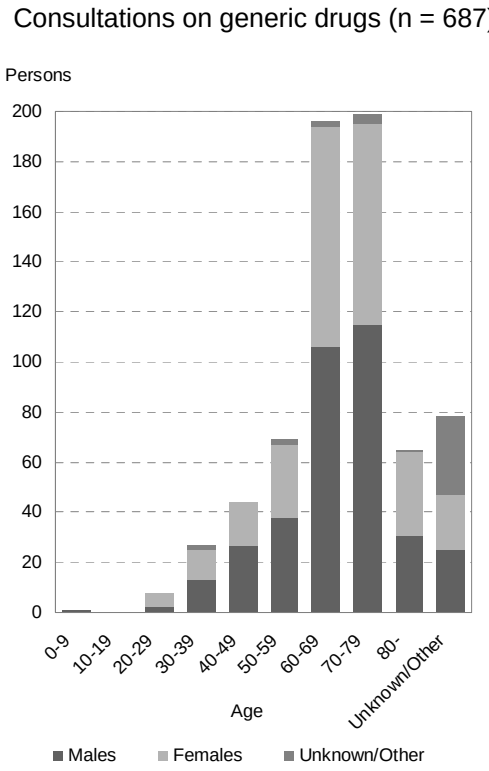
Breakdown of Persons Receiving Consultations on Drugs in FY 2009 (by Profession, etc.)





Breakdown of Persons Receiving Consultations on Drugs in FY 2009 (by Age and Gender)

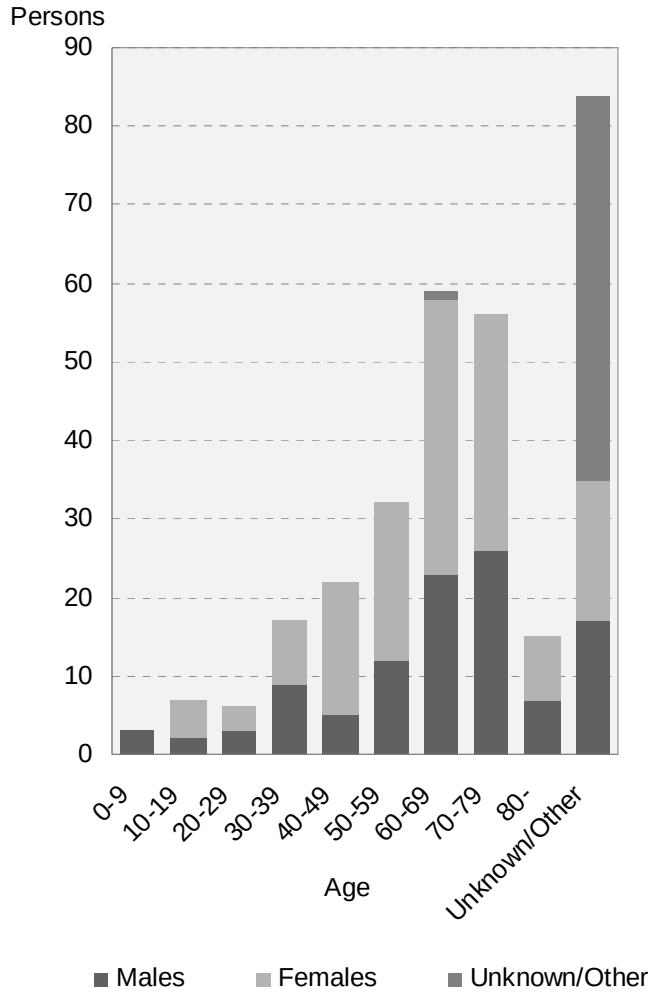




Contents of consultations on medical devices with consumers

Contents of consultation	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
(1) Safety	32 (9.9%)	62 (10.7%)	91 (11.0%)	96 (10.6%)	74 (12.0%)
(2) Indications	64 (19.8%)	101 (17.4%)	85 (10.3%)	90 (10.0%)	59 (9.6%)
(3) Performance	25 (7.7%)	45 (7.7%)	37 (4.5%)	46 (5.1%)	27 (4.4%)
(4) Directions for use	12 (3.7%)	16 (2.8%)	12 (1.5%)	17 (1.9%)	15 (2.4%)
Others	190 (58.8%)	357 (61.4%)	599 (72.7%)	653 (72.4%)	441 (71.6%)
Total	323 (100.0%)	581 (100.0%)	824 (100.0%)	902 (100.0%)	616 (100.0%)

Breakdown of Persons Receiving Consultations on Medical Devices in FY 2009 (by Age and Gender)



Number of Posted Products on the Medical Product Information Web Page as of the End of March 2010

Posted information	Number of posted information				
	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009
Package inserts [*1]					
Prescription drugs	11,819	12,341	13,090	13,287	13,050
Medical devices	1,524	3,995	5,462	8,164	11,213
OTC drugs	-	3,306	7,437	8,356	9,513
In vitro diagnostics				2,237	3,301
Drug Guide for Patients [*1]	23 active ingredients (150 products)	237 active ingredients (1,240 products)	270 active ingredients (1,567 products)	294 active ingredients (1,958 products)	312 active ingredients (1,920 products)
Safety information issued by MHLW - Instruction of revisions of package inserts - Pharmaceuticals and Medical Devices Safety Information - Press release	267	294	323	350	376
Urgent safety information (by pharmaceutical companies)	23	24	24	24	24
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])	21	31s	41	51	61
Notification of safety measures for medical devices					
Notification of self-check	45	45	45	47	49
Notification of revisions of labeling	20	21	28	30	32
Other related notification	33	35	54	57	66
Information about case reports on suspected ADR	3,884	48,584	84,094	110,879	142,084
Information about case reports on suspected malfunction	1,750	17,345	34,226	42,405	46,551
Notification related to preventive measures for medical accidents	18	21	26	44	56
PMDA Medical Safety Information	-	-	3	9	15
Manuals for management of individual serious adverse drug reactions	-	9	25	38	63
Information about approved new drugs	203 active ingredients	261 active ingredients	308 active ingredients	373 active ingredients	445 active ingredients
- Review reports, summaries of product applications	(435 products)	(559 products)	(642 products)	(763 products)	(895 products)
A list of prescription drugs on which Quality Information Package (Orange Book) was published	481 active ingredients/ formulation (3,737 products)	481 active ingredients/ formulation (3,737 products)	811 active ingredients/ formulation (3,900 products)	811 active ingredients/ formulation (3,900 products)	811 active ingredients/ formulation (3,900 products)
Information about withdrawals of drugs or medical devices [*2]	1,453	2,128	2,777	3,448	1,979
Pharmaceuticals and medical devices information e-mail service					
E-mails issued [*3]	92	93	87	107	188
Subscribers	2,892	6,762	11,965	20,707	27,410
Number of site visitors [*4]	289 million	391 million	497 million	642 million	754 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*

III. SUPPLEMENTARY INFORMATION

Table 1. Products Approved in FY 2009: New Drugs

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Apr. 22, 2009	1	Niflec (Ajinomoto Co., Inc.)	Change	N/A for this combination drug	A drug with a new additional indication and a new dosage for cleansing of gastrointestinal tract for pretreatment of barium enema X-ray examination.
			Gasmotin Tablets 2.5 mg Gasmotin Tablets 5 mg Gasmotin Powder (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change	Mosapride citrate hydrate	Drugs with a new additional indication and a new dosage for adjunctive treatment to pretreatment with orally gastrointestinal lavage solution for barium enema X-ray examination.
1	Jul. 7, 2009	2	Prograf Capsules 0.5 mg Prograf Capsules 1 mg Prograf Capsules 5 mg (Astellas Pharma Inc.)	Change Change Change	Tacrolimus hydrate	Drugs with a new additional indication and a new dosage for the treatment of refractory (steroid-resistant/steroid-dependent) active ulcerative colitis (limited to moderate-to-severe cases).
1	Oct. 16, 2009	3	Emend Capsules 80 mg Emend Capsules 125 mg Emend Capsules Set (Ono Pharmaceutical Co., Ltd.)	Approval Approval Approval	Aprepitant	Drugs with a new active ingredient indicated for the treatment of digestive symptoms (nausea and vomiting, including delayed phase) resulting from the administration of antineoplastic agents (cisplatin, etc.).
1	Oct. 16, 2009	4	Feron for Injection 6 MIU Feron for Injection 3 MIU Feron for Injection 1 MIU (Toray Industries, Inc.)	Change	Interferon beta	Drugs with a new additional indication and a new dosage for the improvement of viraemia in chronic hepatitis C on concomitant administration with ribavirin.
			Rebetol Capsule 200 mg (Schering-Plough K.K.)	Change	Ribavirin	A drug with a new additional indication and a new dosage for the improvement of viraemia in chronic hepatitis C on concomitant administration with interferon beta.
1	Oct. 16, 2009	5	Asacol Tablets 400 mg (Zeria Pharmaceutical Co., Ltd.)	Approval	Mesalazine	A drug in a new dosage form and with a new dosage indicated for the treatment of ulcerative colitis (excluding severe case).
1	Jan. 20, 2010	6	Aloxi I.V. Injection 0.75 mg (Taiho Pharmaceutical Co., Ltd.)	Approval	Palonosetron hydrochloride	A drug with a new active ingredient indicated for the treatment of digestive symptoms (nausea and vomiting, including delayed phase) resulting from the administration of antineoplastic agents (cisplatin, etc.).
1	Jan. 20, 2010	7	Epoetin Alfa BS Injection 750 syringe [JCR] Epoetin Alfa BS Injection 1500 syringe [JCR] Epoetin Alfa BS Injection 3000 syringe [JCR] Epoetin Alfa BS Injection 750 [JCR] Epoetin Alfa BS Injection 1500 [JCR] Epoetin Alfa BS Injection 3000 [JCR] (JCR Pharma	Approval Approval Approval Approval Approval Approval	Epoetin kappa (genetical recombination) [epoetin alfa biosimilar 1]	Follow-on biologics indicated for the treatment of renal anemia in patients on dialysis and anemia of prematurity.
1	Mar. 12, 2010	8	Protecadin Tablet 5 Protecadin Tablet 10 (Taiho Pharmaceutical Co., Ltd.)	Change Change	Lafutidine	Drugs with a new additional indication for the treatment of reflux esophagitis.
2	Apr. 22, 2009	9	Micombi Combination Tablets AP (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Telmisartan/ hydrochlorothiazide	New combination drugs indicated for the treatment of hypertension.
		10	Micombi Combination Tablets BP (Nippon Boehringer Ingelheim Co., Ltd.)	Approval		
2	Jul. 7, 2009	11	Caduet Combination Tablets 1ban Caduet Combination Tablets 2ban Caduet Combination Tablets 3ban Caduet Combination Tablets 4ban (Pfizer Japan Inc.)	Approval Approval Approval Approval	Amlodipine besilate/atorvastatin calcium hydrate	New combination drugs indicated for the treatment of comorbidity of hypertension or angina pectoris and hypercholesterolemia or familial hypercholesterolemia.
2	Jul. 7, 2009	12	Rasilez Tablets 150 mg (Novartis Pharma K.K.)	Approval	Aliskiren fumarate	A drug with a new active ingredient indicated for the treatment of hypertension.
2	Oct. 16, 2009	13	Adcirca Tablets 20 mg (Eli Lilly Japan K.K.)	Approval	Tadalafil	A drug with a new indication and a new dosage for the treatment of pulmonary arterial hypertension.
2	Jan. 20, 2010	14	Exforge Combination Tablets (Novartis Pharma K.K.)	Approval	Valsartan/amlodipine besylate	A new combination drug indicated for the treatment of hypertension.
2	Jan. 20, 2010	15	Rezaltas Combination Tablets LD Rezaltas Combination Tablets HD (Daiichi Sankyo Co., Ltd.)	Approval Approval	Olmesartan medoxomil/ azelnidipine	New combination drugs indicated for the treatment of hypertension.

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Apr. 22, 2009	16	Risperdal Consta Intramuscular Injection 25 mg Risperdal Consta Intramuscular Injection 37.5 mg Risperdal Consta Intramuscular Injection 50 mg (Janssen Pharmaceutical K.K.)	Approval Approval Approval	Risperidone	Drugs with a new route of administration indicated for the treatment of schizophrenia.
3-1	Apr. 22, 2009	17	Strattera Capsules 5 mg Strattera Capsules 10 mg Strattera Capsules 25 mg (Eli Lilly Japan K.K.)	Approval Approval Approval	Atomoxetine hydrochloride	Drugs with a new active ingredient indicated for the treatment of attention-deficit/hyperactivity disorder (AD/HD) in children. [Expedited review]
3-1	Apr. 22, 2009	18	Clozaril Tablets 25 mg Clozaril Tablets 100 mg (Novartis Pharma K.K.)	Approval Approval	Clozapine	Drugs with a new active ingredient indicated for the treatment of treatment-resistant schizophrenia.
3-1	Jul. 7, 2009	19	Remeron Tablets 15 mg (Schering-Plough K.K.) Reflex Tablets 15 mg (Meiji Seika Kaisha, Ltd.)	Approval Approval	Mirtazapine	Drugs with a new active ingredient indicated for the treatment of depression.
3-1	Oct. 16, 2009	20	Paxil Tablets 10 mg Paxil Tablets 20 mg (GlaxoSmithKline K.K.)	Change Change	Paroxetine hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of social anxiety disorder.
3-1	Oct. 16, 2009	21	Prograf Capsules 0.5 mg Prograf Capsules 1 mg Prograf Granules 0.2 mg Prograf Granules 1 mg (Astellas Pharma Inc.)	Change Change Change Change	Tacrolimus hydrate	Drugs with a revised indication for the treatment of myasthenia gravis (limitation of patients to be treated was abolished.) [Orphan drug]
3-1	Jan. 20, 2010	22	Bi•Sifrol Tablets 0.125 mg Bi•Sifrol Tablets 0.5 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Change Change	Pramipexole hydrochloride hydrate	Drugs with a new additional indication and a new dosage for the treatment of moderate to severe idiopathic restless legs syndrome.
3-1	Jan. 20, 2010	23	Cymbalta Capsules 20 mg Cymbalta Capsules 30 mg (Shionogi & Co., Ltd.)	Approval Approval	Duloxetine hydrochloride	Drugs with a new active ingredient indicated for the treatment of depression.
3-1	Jan. 20, 2010	24	Kenketsu Venilon-I for Intravenous Injection 500 mg (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change	Freeze-dried sulfonated human normal immunoglobulin	A drug with a new additional indication and a new dosage for the improvement of neurological disorder in patients with Churg-Strauss syndrome or allergic granulomatous angiitis (for use only when steroids are not sufficiently effective). [Orphan drug]
3-2	Jul. 7, 2009	25	Lumigan Ophthalmic Solution 0.03% (Senju Pharmaceutical Co., Ltd.)	Approval	Bimatoprost	A drug with a new active ingredient indicated for the treatment of glaucoma and ocular hypertension.
3-2	Aug. 20, 2009	26	DisCoVisc 1.0 Ophthalmic Viscoelastic Substance (Alcon Japan Ltd.)	Approval	Sodium hyaluronate, chondroitin sulfate sodium	A drug in a new dosage form indicated for adjunctive treatment for crystalline lens reconstruction.
3-2	Jan. 20, 2010	27	Bridion Intravenous 200 mg Bridion Intravenous 500 mg (Schering-Plough K.K.)	Approval Approval	Sugammadex sodium	Drugs with a new active ingredient indicated for the recovery from neuromuscular blockade induced by rocuronium bromide or vecuronium bromide.
3-2	Jan. 20, 2010	28	Xalacom Combination Eye Drops (Pfizer Japan Inc.)	Approval	Latanoprost/timolol maleate	A new combination drug indicated for the treatment of glaucoma and ocular hypertension.
3-2	Jan. 20, 2010	29	Durotep MT Patch 2.1 mg Durotep MT Patch 4.2 mg Durotep MT Patch 8.4 mg Durotep MT Patch 12.6 mg Durotep MT Patch 16.8 mg (Janssen Pharmaceutical K.K.)	Change Change Change Change Change	Fentanyl	Drugs with a new indication for analgesia of moderate to severe chronic pain which cannot be managed by treatments with non-opioid analgesics and weak opioid analgesics (for use only in patients who switch from an opioid analgesic).
3-2	Mar. 12, 2010	30	Dormicum Injection 10 mg (Astellas Pharma Inc.)	Change	Midazolam	A drug with a new additional pediatric dosage indicated for anesthetic premedication and for sedation during artificial respiration in patients under intensive care.
4	Apr. 22, 2009	31	Orapenem Fine Granules 10% for Pediatric (Meiji Seika Kaisha, Ltd.)	Approval	Tebipenem pivoxil	A drug with a new active ingredient indicated for the treatment of pneumonia, otitis media, and sinusitis.
4	Apr. 22, 2009	32	Cravit Tablets 250 mg Cravit Tablets 500 mg (Daiichi Sankyo Co., Ltd.)	Approval Approval	Levofloxacin hydrate	Drugs in an additional dosage form and with a revised dosage of once-daily administration for conventional indications.
		33	Cravit Fine Granules 10% (Daiichi Sankyo Co., Ltd.)	Approval		

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	May 20, 2009	34	Valixa Tablets 450 mg (Mitsubishi Tanabe Pharma Corporation)	Change	Valganciclovir hydrochloride	A drug with a new additional indication for the treatment of cytomegalovirus infection in organ transplantation (including hematogenic stem cell transplantation), malignant tumor, etc.
4	Jun. 17, 2009	35	AmBisome 50 mg for Intravenous Drip Infusion (Dainippon Sumitomo Pharma Co., Ltd.)	Change	Amphotericin B	A drug with new additional indications and a new dosage for the treatment of fungal infections caused by Mucor species, Absidia species, Rhizopus species, Rhizomucor species, Cladosporium species, Cladophialophora species, Fonsecaea species, Phialophora species, Exophiala species, Coccidioides species, Histoplasma species, and Blastomyces species and visceral leishmaniasis.
4	Oct. 16, 2009	36	Vancomycin Ophthalmic Ointment 1% (Toa Pharmaceutical Co., Ltd.)	Approval	Vancomycin hydrochloride	A drug with a new route of administration indicated for the treatment of conjunctivitis, blepharitis, meibomianitis, and dacryocystitis caused by vancomycin-sensitive methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus epidermidis (MRSE).
4	Oct. 16, 2009	37	Ozex Fine Granules 15% for Pediatric (Toyama Chemical Co., Ltd.)	Approval	Tosufloxacin tosilate hydrate	A drug with new additional indications and a new dosage and in a new dosage form for the treatment of pneumonia, cholera, otitis media, and anthrax in children.
4	Dec. 18, 2009	38	Tamiflu Dry Syrup 3% Tamiflu Capsule 75 (Chugai Pharmaceutical Co., Ltd.)	Change Change	Oseltamivir phosphate	Drugs with a new additional indication and a new dosage for prophylaxis of influenza A or B virus infections.
4	Jan. 13, 2010	39	Rapiacta 300 mg Bag for Intravenous Drip Infusion Rapiacta 150 mg Vial for Intravenous Drip Infusion (Shionogi & Co., Ltd.)	Approval Approval	Peramivir hydrate	Drugs with a new active ingredient indicated for the treatment of influenza A or B virus infections.
4	Jan. 20, 2010	40	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 additional indication and a new dosage for the treatment of febrile neutropenia.
5	Jul. 7, 2009	41	Avolve Capsules 0.5 mg (GlaxoSmithKline K.K.)	Approval	Dutasteride	A drug with a new active ingredient indicated for the treatment of benign prostatic hyperplasia.
5	Jul. 7, 2009	42	Gonalef 75 Gonalef Pen 300 Gonalef Pen 450 Gonalef Pen 900 (Merck Serono Co., Ltd.)	Change Change Change Change	Follitropin alfa (genetical recombination)	Drugs with a new additional indication and a new dosage for induction of ovulation in patients with anovulation and infrequent ovulation associated with hypothalamic-pituitary dysfunction or polycystic ovarian syndrome.
5	Nov. 6, 2009	43	Rinderon Injection 2 mg (0.4%) Rinderon Injection 4 mg (0.4%) (Shionogi & Co., Ltd.)	Change Change	Betamethasone sodium phosphate	Drugs with a new additional indication and a new dosage for prevention of neonatal respiratory distress syndrome by way of enhancing fetal lung maturation by maternal administration for use in cases where premature birth is expected.
5	Dec. 18, 2009	44	Uritos Tablets 0.1 mg (Kyorin Pharmaceutical Co., Ltd.) Staybla Tablets 0.1 mg (Ono Pharmaceutical Co., Ltd.)	Change Change	Imidafenacin	Drugs with a new dosage indicated for the treatment of urgency of urination, pollakiuria, and urge urinary incontinence associated with overactive bladder.
5	Dec. 18, 2009	45	Bup-4 Tablet 10 Bup-4 Tablet 20 Bup-4 Fine Granule 2% (Taiho Pharmaceutical Co., Ltd.)	Change Change Change	Propiverine hydrochloride	Drugs with a new additional indication for the treatment of urgency of urination, pollakiuria, and urge urinary incontinence associated with overactive bladder.
6-1	Apr. 22, 2009	46	Allermist 27.5 μg 56 metered Nasal Spray (GlaxoSmithKline K.K.)	Approval	Fluticasone furoate	A drug with a new active ingredient indicated for the treatment of allergic rhinitis.
6-1	Apr. 22, 2009	47	Zyrtec Dry Syrup 1.25% Zyrtec Tablet 5 (UCB Japan Co., Ltd.)	Change Change	Cetirizine 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	Jun. 17, 2009	48	Celecox Tablets 100 mg Celecox Tablets 200 mg (Astellas Pharma Inc.)	Change Change	Celecoxib	Drugs with new additional indications for the treatment of lumbago, scapulohumeral periarthritis, cervico-omo-brachial syndrome, and tendinitis/tenosynovitis.

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Jul. 7, 2009	49	Enbrel 25 mg for S.C. Injection (Wyeth K.K.)	Change	Etanercept (genetical recombination)	A drug with a new indication and a new dosage for the treatment of polyarticular-course juvenile idiopathic arthritis (for use only in patients who have not sufficiently responded to conventional treatments).
6-1	Jul. 7, 2009	50	Asmanex Twisthaler 100 µg 60 doses Asmanex Twisthaler 200 µg 60 doses (Schering-Plough K.K.)	Approval Approval	Mometasone furoate	Drugs with a new route of administration indicated for the treatment of bronchial asthma.
6-1	Jul. 7, 2009	51	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new indication and a new dosage for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not sufficiently responded to conventional treatments. [Expedited review]
6-1	Oct. 16, 2009	52	Erizas Capsule for Nasal Spray 400 µg (Nippon Shinyaku Co., Ltd.)	Approval	Dexamethasone cipecilate	A drug with a new active ingredient indicated for the treatment of allergic rhinitis.
6-1	Oct. 16, 2009	53	Symbicort Turbuhaler 30 doses Symbicort Turbuhaler 60 doses (AstraZeneca K.K.)	Approval Approval	Budesonide/formoterol fumarate hydrate	New combination drugs indicated for the treatment of bronchial asthma (when a combination treatment of an inhaled steroid and a long-acting beta-$_2$ agonist is needed).
6-1	Nov. 6, 2009	54	Mohrus Tape 20 mg Mohrus Tape L 40 mg (Hisamitsu Pharmaceutical Co., Inc.)	Change Change	Ketoprofen	Drugs with a new additional indication for relief of local pain associated with rheumatoid arthritis.
6-1	Jan. 20, 2010	55	Spiriva 2.5 µg Respimat 60 puffs (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Tiotropium bromide hydrate	A drug in a new dosage form and with a new dosage as a kit product consisting of Respimat inhaler and a cartridge (solution).
6-1	Jan. 20, 2010	56	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with new additional indications and a new dosage for the treatment of plaque psoriasis, psoriatic arthritis, pustular psoriasis, and erythrodermic psoriasis in patients who have not responded sufficiently to conventional treatments.
6-1	Jan. 20, 2010	57	Humira 40 mg 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 treatment of plaque psoriasis and psoriatic arthritis in patients who have not responded sufficiently to conventional treatments.
6-1	Feb. 5, 2010	58	Enbrel 10 mg for S.C. Injection Enbrel 25 mg Syringe 0.5 mL for S.C. Injection (Wyeth K.K.)	Change Change	Etanercept (genetical recombination)	Drugs with a new dosage indicated for the treatment of rheumatoid arthritis (for use only in patients who have not sufficiently responded to conventional treatments).
		59	Enbrel 25 mg for S.C. Injection Enbrel 50 mg Syringe 1.0 mL for S.C. Injection (Wyeth K.K.)	Change Approval		
6-2	Apr. 22, 2009	60	Norditropin S Injection 5 mg Norditropin S Injection 10 mg Norditropin NordiFlex Injection 5 mg Norditropin NordiFlex Injection 10 mg Norditropin NordiFlex Injection 15 mg (Novo Nordisk Pharma Ltd.)	Change Change Change Change Change	Somatropin (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of adult growth hormone deficiency (for use only in severe cases).
6-2	Apr. 22, 2009	61	Apidra Inj. Cart Apidra Inj. OptiClik Apidra Inj. SoloStar Apidra Inj. 100 U/mL （Sanofi-Aventis K.K.）	Approval Approval Approval Approval	Insulin glulisine (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	May 20, 2009	62	Melbin Tablets 250 mg (Dainippon Sumitomo Pharma Co., Ltd.) Glycoran Tablets 250 mg (Nippon Shinyaku Co., Ltd.)	Change Change	Metformin hydrochloride	Drugs with a new indication and a new dosage for the treatment of type 2 diabetes mellitus in patients who have not responded sufficiently to either (1) diet and exercise therapies alone or (2) sulfonylurea along with diet and exercise therapies.
6-2	Jun. 17, 2009	63	Norditropin S Injection 5 mg Norditropin S Injection 10 mg Norditropin NordiFlex Injection 5 mg Norditropin NordiFlex Injection 10 mg Norditropin NordiFlex Injection 15 mg (Novo Nordisk Pharma Ltd.)	Change Change Change Change Change	Somatropin (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of dwarfism with no epiphyseal closure in patients born small for gestational age (SGA).
6-2	Jul. 7, 2009	64	Growject for Injection 1.33 mg Growject for Injection 8 mg Growject BC for Injection 8 mg (JCR Pharmaceuticals Co., Ltd.)	Change Change Change	Somatropin (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of adult growth hormone deficiency (for use only in severe cases).

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Aug. 20, 2009	65	NovoRapid 70 Mix Penfill NovoRapid 70 Mix FlexPen (Novo Nordisk Pharma Ltd.)	Approval Approval	Insulin aspart (genetical recombination)	Drugs with a new dosage indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	Aug. 20, 2009	66	Humalog Mix 50 Cart Humalog Mix 50 Kit Humalog Mix 50 MirioPen (Eli Lilly Japan K.K.)	Change Change Change	Insulin lispro (genetical recombination)	Drugs with a new dosage indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	Sep. 18, 2009	67	NovoRapid 50 Mix Penfill NovoRapid 50 Mix FlexPen (Novo Nordisk Pharma Ltd.)	Approval Approval	Insulin aspart (genetical recombination)	Drugs with a new dosage and in an additional dosage form indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	Oct. 16, 2009	68	Januvia Tablets 25 mg Januvia Tablets 50 mg Januvia Tablets 100 mg (Banyu Pharmaceutical Co., Ltd.) Glactiv Tablets 25 mg Glactiv Tablets 50 mg Glactiv Tablets 100 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval Approval Approval	Sitagliptin phosphate hydrate	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus (for use only in patients who do not sufficiently respond to any one of the following treatments): 1. Dietary therapy and/or exercise therapy only 2. Use of sulfonylureas in addition to dietary therapy and/or exercise therapy 3. Use of thiazolidinediones in addition to dietary therapy and/or exercise therapy 4. Use of biguanides in addition to dietary therapy and/or exercise therapy
6-2	Oct. 16, 2009	69	Basen Tablets 0.2 Basen OD Tablets 0.2 (Takeda Pharmaceutical Company Limited)	Change Change	Voglibose	Drugs with a new additional indication and a new dosage for prevention of type 2 diabetes mellitus in patients with impaired glucose tolerance (only for whom glycemic control is not sufficient by diet and/or exercise).
6-2	Nov. 6, 2009	70	Seibule Tablets 25 mg Seibule Tablets 50 mg Seibule Tablets 75 mg (Sanwa Kagaku Kenkyusho Co., Ltd.)	Change Change Change	Miglitol	Drugs with a new additional indication for improvement of postprandial hyperglycemia in patients with diabetes mellitus (for use only in patients who have not responded sufficiently to treatment with biguanides in conjunction with dietary and exercise regimens).
6-2	Jan. 20, 2010	71	Equa Tablets 50 mg (Novartis Pharma K.K.)	Approval	Vildagliptin	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to either [1] diet and exercise therapies alone or [2] sulfonylurea along with diet and exercise therapies).
6-2	Jan. 20, 2010	72	Metgluco Tablets 250 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Metformin hydrochloride	A drug with a new dosage exceeding the maximum dosage (750 mg/day) of the conventional formulation indicated for the treatment of type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to either [1] diet and exercise therapies alone or [2] sulfonylurea along with diet and exercise therapies).
6-2	Jan. 20, 2010	73	Victoza Subcutaneous Injection 18 mg (Novo Nordisk Pharma Ltd.)	Approval	Liraglutide (genetical recombination)	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus (for use only in patients who have not responded sufficiently to either [1] diet and exercise therapies alone or [2] sulfonylurea along with diet and exercise therapies).
AIDS drugs	Aug. 20, 2009	74	Prezistanaive Tablets 400 mg (Janssen Pharmaceutical K.K.)	Approval	Darunavir ethanolate	A drug with a new dosage indicated for the treatment of HIV infection. [Orphan drug]
Blood products	Oct. 16, 2009	75	BeneFIX Intravenous 250 BeneFIX Intravenous 500 BeneFIX Intravenous 1000 BeneFIX Intravenous 2000 (Wyeth K.K.)	Approval Approval Approval Approval	Nonacog alfa (genetical recombination)	Drugs with a new active ingredient indicated for inhibition of bleeding tendency in patients with hemophilia B (congenital blood coagulation factor IX deficiency). [Orphan drug]
Blood products	Mar. 12, 2010	76	NovoSeven for Injection 1.2 mg NovoSeven for Injection 4.8 mg (Novo Nordisk Pharma Ltd.)	Change Change	Eptacog alfa (activated) (genetical recombination)	Drugs with a new additional indication and a new dosage for inhibition of bleeding tendency in patients with congenital factor VII deficiency.
		77	NovoSeven HI for Intravenous Injection 1 mg NovoSeven HI for Intravenous Injection 2 mg NovoSeven HI for Intravenous Injection 5 mg (Novo Nordisk Pharma Ltd.)	Change Change Change		
Oncology drugs	Apr. 22, 2009	78	Doxil Injection 20 mg (Janssen Pharmaceutical K.K.)	Change	Doxorubicin hydrochloride	A drug with a new indication and a new dosage for the treatment of ovarian cancer which has progressed after cancer chemotherapy. [Expedited review]
Oncology drugs	Apr. 22, 2009	79	Tykerb Tablets 250 mg (GlaxoSmithKline K.K.)	Approval	Lapatinib tosilate hydrate	A drug with a new active ingredient indicated for the treatment of inoperable or recurrent breast cancer with HER2 overexpression. [Priority review]
Oncology drugs	May 20, 2009	80	Nexavar Tablets 200 mg (Bayer Yakuhin, Ltd.)	Change	Sorafenib tosilate	A drug with a new additional indication for the treatment of unresectable hepatocellular carcinoma.
Oncology drugs	May 20, 2009	81	Alimta Injection 100 mg Alimta Injection 500 mg (Eli Lilly Japan K.K.)	Approval Change	Pemetrexed sodium hydrate	Drugs with a new additional indication and a new dosage in an additional dosage form (Alimta Injection 100 mg) indicated for the treatment of unresectable advanced or recurrent non-small cell lung cancer.

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Aug. 20, 2009	82	Elplat I.V. Infusion Solution 50 mg Elplat I.V. Infusion Solution 100 mg Elplat for Injection 50 mg Elplat for Injection 100 mg (Yakult Honsha Co., Ltd.)	Approval Approval Change Change	Oxaliplatin	Drugs with a new additional indication and a new dosage in an additional dosage form (Elplat I.V. Infusion Solution 50 mg and Elplat I.V. Infusion Solution 100 mg) for post-operative adjuvant chemotherapy for colon cancer. [Priority review]
Oncology drugs	Aug. 20, 2009	83	Miripla Suspension Vehicle 4 mL (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Iodine addition products of the ethyl esters of the fatty acids obtained from poppyseed oil	A drug with a new indication for suspending Miripla for intra-arterial injection 70 mg.
Oncology drugs	Sep. 18, 2009	84	Xeloda Tablet 300 (Chugai Pharmaceutical Co., Ltd.)	Change	Capecitabine	A drug with a new additional indication and a new additional dosage and administration for combination therapy with other anticancer drugs (XELOX + BV regimen) for advanced or recurrent colorectal cancer not suited for curative resection.
Oncology drugs	Sep. 18, 2009	85	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication and a new additional dosage and administration for combination therapy with other anticancer drugs (XELOX + BV regimen) for advanced or recurrent colorectal cancer not suited for curative resection.
Oncology drugs	Sep. 18, 2009	86	Elplat for Injection 100 mg Elplat I.V. Infusion Solution 50 mg Elplat I.V. Infusion Solution 100 mg (Yakult Honsha Co., Ltd.)	Change Change Change	Oxaliplatin	Drugs with a new additional indication and a new additional dosage and administration for combination therapy with other anticancer drugs (XELOX + BV regimen) for advanced or recurrent colorectal cancer not suited for curative resection.
		87	Elplat for Injection 50 mg (Yakult Honsha Co., Ltd.)	Change		
Oncology drugs	Oct. 16, 2009	88	Miripla for Intra-arterial Injection 70 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Miriplatin hydrate	A drug with a new active ingredient indicated for lipiodolization in hepatocellular carcinoma.
Oncology drugs	Oct. 16, 2009	89	Rasuritek 1.5 mg for I.V. Injection Rasuritek 7.5 mg for I.V. Injection (Sanofi-Aventis K.K.)	Approval Approval	Rasburicase (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of hyperuricemia in patients receiving cancer chemotherapy.
Oncology drugs	Nov. 6, 2009	90	Fludara Tab. 10 mg (Bayer Yakuhin, Ltd.)	Change	Fludarabine phosphate	A drug with a new additional indication for the treatment of chronic lymphocytic leukemia with anemia or thrombocytopenia.
Oncology drugs	Nov. 6, 2009	91	Fludara for IV Inj. 50 mg (Bayer Yakuhin, Ltd.)	Change	Fludarabine phosphate	A drug with new additional indications and a new dosage for the treatment of recurrent or refractory low-grade B-cell non-Hodgkin's lymphoma and mantle cell lymphoma.
Oncology drugs	Nov. 6, 2009	92	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of unresectable advanced or recurrent non-squamous non-small cell lung cancer. [Priority review]
Oncology drugs	Jan. 20, 2010	93	Temodal Injection 100 mg (Schering-Plough K.K.)	Approval	Temozolomide	A drug with a new route of administration indicated for the treatment of malignant glioma.
Oncology drugs	Jan. 20, 2010	94	Afinitor Tablets 5 mg (Novartis Pharma K.K.)	Approval	Everolimus	A drug with a new additional indication and a new dosage for the treatment of renal cell carcinoma which is metastatic or not suitable for curative resection. [Priority review]
Oncology drugs	Feb. 5, 2010	95	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 inoperable or recurrent breast cancer.
Biologicals	Oct. 16, 2009	96	Cervarix (GlaxoSmithKline K.K.)	Approval	HPV-16 L1 VLP and HPV-18 L1 VLP	A drug with a new active ingredient indicated for prevention of cervical cancer (squamous-cell carcinoma and adenocarcinoma) and its precursor lesions (cervical intraepithelial neoplasia [CIN] 2 and 3) associated with human papillomavirus (HPV) types 16 and 18 infection. [Priority review]
Biologicals	Oct. 16, 2009	97	Prevenar Suspension Liquid for S.C. Injection (Wyeth K.K.)	Approval	Pneumococcal polysaccharide (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F)-	A drug with a new active ingredient indicated for prophylaxis of pneumococcal invasive infections (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F). [Priority review]
Biologicals	Jan. 20, 2010	98	Arepanrix (H1N1) Intramuscular Injection (GlaxoSmithKline K.K.)	Emergency approval	Inactivated split-virus influenza A (A/California/7/2009 [H1N1])	A drug with a new active ingredient indicated for prophylaxis of pandemic (H1N1) influenza. [Emergency approval]
Biologicals	Jan. 20, 2010	99	Cell-culture Derived Influenza A (H1N1) Emulsion HA Vaccine "Novartis" for Intramuscular Injection (Novartis Pharma K.K.)	Emergency approval	Pandemic influenza virus surface antigens of A/California/7/2009 (H1N1) like strain	A drug with a new active ingredient indicated for prophylaxis of pandemic (H1N1) influenza. [Emergency approval]
In vivo Diagnostics	Sep. 18, 2009	100	Indigocarmine Injection 20 mg "Daiichi Sankyo" (Daiichi Sankyo Co., Ltd.)	Change	Indigocarmine	A drug with a new route of administration, a new indication, and a new dosage for sentinel lymph node mapping in breast cancer and malignant melanoma. [Expedited review]

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
In vivo Diagnostics	Sep. 18, 2009	101	Diagnogreen for Injection 25 mg (Daiichi Sankyo Co., Ltd.)	Change	Indocyanine green	A drug with a new route of administration, a new indication, and a new dosage for sentinel lymph node mapping in breast cancer and malignant melanoma. [Expedited review]
In vivo Diagnostics	Mar. 12, 2010	102	FerriSeltz Powder 20% (Otsuka Pharmaceutical Co., Ltd.)	Change	Ferric ammonium citrate	A drug with a new additional indication and a new dosage for negative contrast of digestive tract in cholangiopancreatography.
Bio-CMC	Jun. 22, 2009	103	Somatropin BS S.C. Injection 5 mg [Sandoz］ Somatropin BS S.C. Injection 10 mg [Sandoz] (Sandoz K.K.)	Approval Approval	Somatropin (genetical recombination)	Follow-on biologics indicated for the treatment of growth disturbance due to growth hormone deficiency before epiphyseal closure and growth disturbance associated with Turner syndrome or chronic renal insufficiency before epiphyseal closure.
Radio-pharmaceuticals	Sep. 18, 2009	104	Tin Colloid Tc-99m Kit (Nihon Medi-Physics Co., Ltd.)	Change	Technetium (^{99m}Tc) stannous colloid	A drug with a new route of administration and a new indication for sentinel lymph node mapping in breast cancer and malignant melanoma. [Expedited review]
Radio-pharmaceuticals	Sep. 18, 2009	105	Techne Phytate Kit (Fujifilm RI Pharma Co., Ltd.)	Change	Technetium (^{99m}Tc) phytate	A drug with a new route of administration and a new indication for sentinel lymph node mapping in breast cancer and malignant melanoma. [Expedited review]
Radio-pharmaceuticals	Nov. 6, 2009	106	MyoMIBG-I^{123} Injection (Fujifilm RI Pharma Co., Ltd.)	Change	3-iodobenzylguanidine (^{123}I) injection	A drug with a new additional indication and a new dosage for diagnosis of neuroblastoma in tumor scintigraphy.
Radio-pharmaceuticals	Feb. 5, 2010	107	Cardiolite Injection Daiichi Cardiolite Daiichi (Fujifilm RI Pharma Co., Ltd.)	Change Change	Technetium (^{99m}Tc) hexakis (2-methoxy-isobutyl isonitrile) Tetrakis (2-methoxy-isobutyl isonitrile) copper (I) tetrafluoroborate	Drugs with a new additional indication for diagnostic localization of hyperparathyroidism in parathyroid scintigraphy.

Table 2. Products Approved in FY 2009: New Medical Devices

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Apr. 28, 2009 Total review time: 876 days Regulatory review time: 621 days	- Domestic clinical study results	1	Ortho-K (Alpha Corporation Inc.)	Approval	Instrument & apparatus 72 Orthokeratology contact lens	The first orthokeratology contact lens in Japan for patients with myopia and myopic astigmatism to reshape the corneal anterior surface by wearing it during sleep and correct unaided vision after removal of the lens.
1	May 22, 2009 Total review time: 1669 days Regulatory review time: 615 days	Oct. 17, 2003 Overseas clinical study results	2	Allegretto Wave (Wavelight Laser Technologie AG)	Approval	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism by laser ablation of corneal tissue. (The original product is in a reexamination period)
1	Jul. 1, 2009 Total review time: 96 days Regulatory review time: 91 days	May 23, 2003 No clinical study results	3	VISX Excimer Laser System (AMO Japan K.K.)	Approval	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism and remove corneal opacities by laser ablation of corneal tissue. (Application for change from a foreign exceptional approval to a regular marketing approval in the reexamination period)
1	Jul. 3, 2009 Total review time: 51 days Regulatory review time: 50 days	- No clinical study results	4	Ortho-K (Alpha Corporation Inc.)	Change	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 to correct unaided vision after removal. The addition of a manufacturing site. (A partial change in the reexamination period)
1	Jul. 24, 2009 Total review time: 186 days Regulatory review time: 131 days	Nov. 8, 2006 Overseas clinical study results	5	Excimer Laser Corneal Surgery System EC-5000CXIII (Nidek Co., Ltd.)	Change	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia, hyperopia or astigmatism, remove corneal surface opacities, or smooth corneal irregularities by laser ablation of corneal tissue. A partial change for the objectives including the addition of correction of hyperopia to the indications. (A partial change in the reexamination period)
1	Aug. 13, 2009 Total review time: 394 days Regulatory review time: 142 days	Oct. 1, 2001 No clinical study results	6	O_2 Optics (Ciba Vision K.K.)	Change	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	A silicone hydrogel contact lens indicated for daily or up to 1 month extended wear. Addition of a supplementary fluid and a manufacturing site. (A partial change in the reexamination period)
1	Dec. 17, 2009 Total review time: 28 days Regulatory review time: 20 days	- No clinical study results	7	α Ortho-K (Alpha Corporation Inc.)	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. (Addition of a brand name to Ortho-K in the reexamination period) (The original product is in a reexamination period)
1	Feb. 2, 2010 Total review time: 1771 days Regulatory review time: 524 days	Dec. 22, 2005 Domestic clinical study results	8	ICL (STAAR Japan Inc.)	Approval	Instrument & apparatus 72 Phakic posterior chamber intraocular lens	An intraocular lens to be implanted in the posterior chamber of the phakic eye (in front of the human crystalline lens) to correct refractive errors in the eye (myopia).
3-1	April 27, 2009 Total review time: 55 days Regulatory review time: 48 days	Sep. 22, 2006 No clinical study results	9	Angioguard XP (Johnson & Johnson K.K.)	Change	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	The first device in Japan to prevent distal emboli with a polyurethane filter to capture and remove embolic substances including thrombi released while a stent is placed in the carotid artery. Application for a partial change to alter the materials. (A partial change in the reexamination period)
3-1	Aug. 25, 2009 Total review time: 265 days Regulatory review time: 251 days	Jul. 12, 2007 No clinical study results	10	Precise for Carotid Artery (Johnson & Johnson K.K.)	Change	Instrument & apparatus 7 Stent for the carotid artery	The first stent for the carotid artery in Japan to dilate carotid stenosis and prevent restenosis. Change for addition of RX type. (A partial change in the reexamination period)
3-1	Jan. 8, 2010 Total review time: 589 days Regulatory review time: 229 days	Jul. 2, 2008 Domestic and overseas clinical study results	11	XIENCE V Drug Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with everolimus coating used for dilating and holding a stenotic site of the coronary artery in symptomatic ischemic heart disease.
3-1	Jan. 8, 2010 Total review time: 589 days Regulatory review time: 229 days	Jul. 2, 2008 Domestic and overseas clinical study results	12	PROMUS Drug-Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with everolimus coating used for dilating and holding a stenotic site of the coronary artery in symptomatic ischemic heart disease.
3-1	Jan. 8, 2010 Total review time: 283 days Regulatory review time: 236 days	Oct. 2, 2008 Overseas clinical study results	13	Endeavor Sprint Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with zotarolimus coating used for dilating and maintaining the stenotic site of the coronary artery in symptomatic ischemic heart diseases, with a different delivery catheter from the original product. (The original product is in a reexamination period)
3-1	Jan. 25, 2010 Total review time: 285 days Regulatory review time: 73 days	Oct. 10, 2008 No clinical study results	14	TAXUS Liberté Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with paclitaxel coating used for dilating and holding a stenotic site of the coronary artery in ischemic heart disease. Application for a partial change to alter the test method for raw materials. (A partial change in the reexamination period)
3-1	Jan. 25, 2010 Total review time: 285 days Regulatory review time: 73 days	Mar. 4, 2004 No clinical study results	15	TAXUS Express2 Stent (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with paclitaxel coating used for dilating and holding a stenotic site of the coronary artery in ischemic heart disease. Application for a partial change to alter the test method for raw materials. (A partial change in the reexamination period)

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
3-2	Apr. 9, 2009 Total review time: 714 days Regulatory review time: 243 days	Jun. 5, 2008 Overseas clinical study results	18	TALENT Thoracic Stent Graft System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	A stent graft for thoracic aortic aneurysms used to prevent blood flow into the aneurysm and aneurysm rupture. (The original product is in a reexamination period)
3-2	May 1, 2009 Total review time: 56 days Regulatory review time: 52 days	- No clinical study results	19	Triplex (Terumo Corporation)	Change	Instrument & apparatus 7 Artificial blood vessel for the central circulation system	An artificial blood vessel consisting of a triple layer structure containing a non-porous layer held between 2 polyester stockinette layers; together these layers form a tubular body. This does not require sealing with biological materials. Application for a partial change to alter the materials. (A partial change in the reexamination period)
3-2	May 27, 2009 Total review time: 187 days Regulatory review time: 181 days	Jul. 21, 2005 No clinical study results	20	ONYX Liquid Embolic System LD (ev3 Inc.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	The first liquid embolic material in Japan used to occlude the flow of blood as pretreatment for surgical resection of arteriovenous malformations (bAVM's). A change of adding description concerning compatible catheters. (A partial change in the reexamination period)
3-2	Nov. 25, 2009 Total review time: 215 days Regulatory review time: 139 days	Nov. 7, 2008 No clinical study results	21	GORE TAG Thoracic Aortic Stent Graft System (Japan Gore-Tex Inc.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft for thoracic aortic aneurysm used to prevent blood flow into the aneurysm and its rupture. Application for a partial change to add a delivery system. (A partial change in the reexamination period)
3-2	Jan. 8, 2010 Total review time: 302 days Regulatory review time: 179 days	May 8, 2007 Domestic and overseas clinical study results	22	Codman Enterprise VRD (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A cylindrical, mesh-like vascular reconstruction device to be deployed in the parent artery in order to prevent the embolic coils from protrude and/or dropout into the parent artery during coil embolization of wide-neck intracranial aneurysms, which are difficult to treat with surgery. [Orphan device]
4	May 27, 2009 Total review time: 106 days Regulatory review time: 94 days	Dec. 9, 1997 (12Fr) Sep. 4, 1998 (14Fr/16Fr) Jan. 25, 2002 (16Fr SLSII) May 2, 2002 (12/14FrSLSII) No clinical study results	23	Excimer Laser Cardiac Lead Removal System (DVx Inc.)	Change	Instrument & apparatus 7 Pacemaker/defibrillator lead removal kit	The first extraction laser sheath in Japan used at removal of chronically implanted pacing or defibrillator leads to ablate binding tissue around the circumference of leads using the laser energy delivered from a dedicated excimer laser system. Addition of a manufacturing site. (A partial change in the reexamination period)
4	Nov. 18, 2009 Total review time: 2091 days Regulatory review time: 200 days	May 31, 2001 Domestic and overseas clinical study results	24	Implantable Ventricular Assist Device HeartMate XVE LVAS (Nipro Corporation)	Approval	Instrument & apparatus 7 Implantable ventricular assist device	An implantable diaphram left ventricular assist device intended for use to improve the circulation in patients with end-stage heart failure who are difficult to survive despite the conventional short-term, mechanically-assisted circulation and maximum medical management, and are considered to be difficult to be rescued without heart transplantation. The efficacy and safety of this product for the target patients were evaluated in the clinical studies using the previous model. [Orphan device]
4	Jan. 8, 2010 Total review time: 423 days Regulatory review time: 192 days	Jun. 16, 1997 Overseas clinical study results	25	Vagus Nerve Stimulation (VNS) System (Nihon Kohden Corporation)	Approval	Instrument & apparatus 12 Vagus nerve stimulation device with anti-seizure effects	An electrical stimulation device to stimulate vagus nerve as an adjuvant therapy for patients with drug-resistant epilepsy who have refractory epileptic seizures. Clinical studies were conducted to confirm the efficacy and safety of this product in the target patients. [Priority review]
5	Aug. 6, 2009 Total review time: 427 days Regulatory review time: 188 days	Jan. 15, 2002 No clinical study results	26	Dornier Epos Ultra (Dornier MedTech Japan Co. Ltd.)	Change	Instrument & apparatus 12 Extracorporeal shock wave pain therapy system	A low-energy extracorporeal shock wave therapy system for orthopedic use with reduced output of the conventional electromagnetic induction-type extracorporeal shock wave lithotripter applied for pain relief therapy. Application for a partial change for the objectives including for addition of the ultrasonic imaging device used to position the affected area. (A partial change in the reexamination period)
5	Sep. 1, 2009 Total review time: 679 days Regulatory review time: 413 days	Oct. 22, 2004 Overseas clinical study results	27	MR-Guided Focused Ultrasound Surgery System ExAblate 2000 (GE Healthcare Japan Corporation)	Approval	Instrument & apparatus 12 Ultrasound hyperthermia system	A focused ultrosonic surgery system used for treatment of symptomatic uterine fibroid while monitoring the tissue temperature with MR in order to improve the symptoms.

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas	No.	Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
5	Jan. 8, 2010 Total review time: 283 days Regulatory review time: 84 days	May 6, 2005 Domestic clinical study results	28	Cryosurgical Unit CryoHit (Hitachi Medical Corporation)	Approval	Instrument & apparatus 31 Versatile cryosurgical unit	A cryosurgical system used to kill renal tumor cells of small diameter by utilizing Joule-Thompson effect of high-pressure argon gas to cool the tip end of probe or needle (-100°C or lower) under Magnetic Resonance (MR) Image guidance.
5	Jan. 15, 2010 Total review time: 703 days Regulatory review time: 254 days	Sep. 24, 2001 Domestic clinical study results	29	Deflux (Q-Med AB)	Approval	Medical products 4 Filling material for the treatment of vesicoureteral reflux	A device with injectable material consisting of dextranomer microspheres which is a bulge forming material and solution of stabilized hyaluronate sodium in phosphate buffered saline filled in a disposable syringe equipped with a tip cap, used for treatment of patients with vesicoureteral reflux grade II - IV.
6	Nov. 2, 2009 Total review time: 584 days Regulatory review time: 273 days	Oct. 10, 2003 Domestic clinical study results	30	V.A.C. ATS Therapy System (KCI KK)	Approval	Medical products 4 Negative Pressure Wound Therapy System	A therapy system used for protection of the wounds, maintaining a healing environment, and promoting and shortening the time of wound healing in patients with intractable traumatic wounds or dehisced wounds, post-operative open wounds or skin defect wounds, post-operative wounds after dismemberment of extremities due to diabetics, etc. The novelty of this product is the capability of the system to control the treatment mechanically while the conventional simple suction therapy was performed by individual physicians using a prepared set of tools. A clinical study was conducted in Japan to evaluate its clinical efficacy and safety.
6	Dec. 24, 2009 Total review time: 462 days Regulatory review time: 142 days	May 25, 2004 Clinical evaluation report	31	Stryker SpinePlex Bone Cement (Stryker Japan K.K.)	Approval	Medical products 4 Orthopedic bone cement	An acrylic bone cement used for pain relief in percutaneous vertebroplasty for painful vertebral body fracture caused by malignant spine tumor such as metastatic bone tumor and myeloma which are not responsive to conventional therapies. A clinical evaluation report summarizing the Japanese clinical study results and the literature research data on the use results of this and similar products in foreign countries was submitted to verify the safety and efficacy. [Priority review]
6	Feb. 5, 2010 Total review time: 651 days Regulatory review time: 368 days	Jul. 2, 1998 Domestic and overseas clinical study results	32	KYPHON BKP System (Medtronic Sofamor Danek Co., Ltd.)	Approval	Instrument & apparatus 58 Single-use vertebral body restoration device	A treatment system to be used in percutaneous kyphosis correction performed for restoration of the height of fractured vertebral body, fixation of the vertebral body, and pain relief in spinal compression fracture. The novelty of this product is the capability to fill the bone cement safely after restoration of the physical vertebral height by forming a cavity in the fractured vertebral body in comparison with the conventional vertebroplasty. A clinical study was conducted in Japan to evaluate its efficacy and safety. In addition, results from overseas clinical studies were submitted.
6	Feb. 5, 2010 Total review time: 651 days Regulatory review time: 347 days	Apr. 1, 2004 Domestic and overseas clinical study results	33	KYPHON BKP Bone Cement HV-R (Medtronic Sofamor Danek Co., Ltd.)	Approval	Medical products 4 Orthopedic bone cement	A therapeutic spine bone cement used in percutaneous kyphosis correction in spinal compression fracture performed for restoration of the height of fractured vertebral body, fixation of the vertebral body, and pain relief. The novelty of this product is the capability to fill the bone cement safely after restoration of the physical vertebral height by forming a cavity in the fractured vertebral body in comparison with the conventional vertebroplasty. A clinical study was conducted in Japan to evaluate its efficacy and safety.In addition, results from overseas clinical studies were submitted.
8	Nov. 18, 2009 Total review time: 331 days Regulatory review time: 205 days	Apr. 29, 2005 Overseas clinical study results	34	da Vinci Surgical System (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 12 Surgical robot, operational unit	A device to assist a surgeon in controlling endoscopic instruments attached to three arms of the patient cart with master-slave control in order to perform cutting, coagulating and suturing the tissue by manipulating the master controller on the surgeon console.
8	Nov. 18, 2009 Total review time: 331 days Regulatory review time: 232 days	Apr. 29, 2005 Overseas clinical study results	35	EndoWrist Bipolar Instrument (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 25 Reusable active endotherapy device using radio frequency	An endoscopic instrument to be connected to "da Vinci Surgical System" to follow the movement of surgeon's hands and wrists by manipulating the master controller intended to work mechanically including grasping,suturing etc.and to cut and coagulate the tissue by using radiofrequency electrosurgery current under endoscopic visualization.
8	Nov. 18, 2009 Total review time: 331 days Regulatory review time: 232 days	Apr. 29, 2005 Overseas clinical study results	36	EndoWrist Monopolar Instrument (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 25 Reusable active endotherapy device using radio frequency	An endoscopic instrument to be connected to "da Vinci Surgical System" to follow the movement of surgeon's hands and wrists by manipulating the master controller intended to work mechanically including grasping etc. and to cut and coagulate the tissue by using radiofrequency electrosurgery current under endoscopic visualization.
8	Nov. 18, 2009 Total review time: 331 days Regulatory review time: 235 days	Apr. 29, 2005 Overseas clinical study results	37	EndoWrist Instrument (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 25 Reusable active endotherapy device	An endoscopic instrument to be connected to "da Vinci Surgical System" to follow the movement of surgeon's hands and wrists by manipulating the master controller intended to work mechanically including grasping, suturing, ligation etc. under endoscopic visualization.

Note: Products submitted for application in 2003 and before are included.

Table 3. Products Approved in FY 2009: Improved Medical Devices (with Clinical Data)

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Jul. 24, 2009 Total review time: 401 days Regulatory review time: 161 days	Apr. 5, 2005 Clinical evaluation report	1	Relieva Sinus Balloon Catheter Set (Medico's Hirata Inc.)	Approval	Instrument & apparatus 51 Endoscopic dilatation catheter	A catheter set used to drain the pus by dilating narrowed natural openings of the frontal sinus, sphenoid sinus, and maxillary sinus with balloons for the treatment of sinusitis. A clinical evaluation report based on the overseas post-marketing clinical research was submitted to evaluate its efficacy and safety.
1	Dec. 9, 2009 Total review time: 588 days Regulatory review time: 384 days	- Domestic clinical study results	2	Menicon 1day Flat Pack (Menicon Co., Ltd.)	Approval	Instrument & apparatus 72 Single-use colored contact lenses for correcting visual acuity	A daily disposable soft contact lens for myopia and hyperopia. A copolymer of HEMA and GMA is used as lens materials. Clinical studies were conducted to evaluate the efficacy and safety.
1	Mar. 4, 2010 Total review time: 769 days Regulatory review time: 418 days	Mar. 3, 2008 Overseas clinical study results	3	1-Day Acuvue TruEye (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 72 Single-use colored contact lenses for correcting visual acuity	A daily disposable soft contact lens for myopia, hyperopia, astigmatism, or presbyopia. A copolymer of HEMA, OH-mPDMS, and DMA is used as lens materials. Clinical studies were conducted to evaluate the efficacy and safety.
2	Jan. 15, 2010 Total review time: 697 days Regulatory review time: 447 days	- Domestic clinical study results	4	Neobone (Covalent Materials Corporation)	Change	Medical products 4 Artificial bone implant	An artificial bone implant material consisting of granular and shaped (e.g. rectangular cuboid) products to be used for filling bone defect and for supporting bone regeneration. Application for a partial change to add spherical granular product and to add granular products for use in dental field to the indication in addition to its use in the orthopedic field. Clinical studies were conducted to evaluate its efficacy as bone filler for dental use.
3-1	Apr. 20, 2009 Total review time: 641 days Regulatory review time: 427 days	- Overseas clinical study results	5	Palmaz Genesis for Renal Artery (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 7 Stent for blood vessel	A stent used for dilating and holding a stenotic site in renal artery stenosis. Clinical studies were conducted to evaluate its clinical efficacy in renal artery stenosis.
3-1	Aug. 6, 2009 Total review time: 1989 days Regulatory review time: 859 days	Jul. 29, 2002 Clinical evaluation report	6	HydroCoil Embolic System (Terumo Corporation)	Approval	Instrument & apparatus 51 Sterilized tube and catheter for vascular treatment	A delivery pusher for platinum alloy coil intended to block the blood flow into brain aneurysm and for guiding the coil to the implanting site. The coil is coated with swellable hydrogel. Clinical evaluation data to evaluate its efficacy and safety were submitted.
3-1	Jan. 8, 2010 Total review time: 226 days Regulatory review time: 182 days	- Overseas clinical study results	7	Cypher Select+ Stent (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting stent coated with drugs to inhibit the neointimal proliferation and a delivery catheter. Clinical studies were conducted to evaluate its efficacy and safety.
3-2	Aug. 21, 2009 Total review time: 549 days Regulatory review time: 482 days	Apr. 7, 2005 Overseas clinical study results	8	DuraSeal Blue Spray (Tyco Healthcare Japan Inc.)	Approval	Medical products 4 Absorbable tissue reinforcement material	An absorbable prosthetic material for dura mater applied as an adjunct to suturing, on the dural gap, sutured site of dura mater, and the gap between the duraplasty material and dura mater. A clinical study was conducted to evaluate its efficacy and safety.
4	Apr. 16, 2009 Total review time: 533 days Regulatory review time: 195 days	May 7, 2007 Overseas clinical study results	9	Promote 36 (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 (treatment method to improve cardiac failure symptoms, which synchronizes ventricular contraction by stimulating cardiac muscles of both ventricles electrically for a long time), with the function of a defibrillator. The function to set the pacing timing was evaluated in the clinical study.
4	Apr. 16, 2009 Total review time: 533 days Regulatory review time: 243 days	Sep. 11, 2007 Overseas clinical study results	10	Promote RF 36 (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, with the function of a defibrillator. The function to set the pacing timing was evaluated in the clinical study.
4	Apr. 24, 2009 Total review time: 238 days Regulatory review time: 137 days	Sep. 11, 2007 Overseas clinical study results	11	Promote RF 30 (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, with the function of a defibrillator. The function to set the pacing timing was evaluated in the clinical study.
4	Jul. 7, 2009 Total review time: 439 days Regulatory review time: 335 days	Nov. 12, 2003 Overseas clinical study results	12	Endo-PAT2000 (CCI Corporation)	Approval	Instrument & apparatus 21 Regional body plethysmograph	A device to determine the vascular endothelium-mediated changes by measuring the volume pulse waves before and after 5-minute occlusion of the brachial artery with a cuff applied on the upper arm. Overseas clinical study results were used to evaluate the safety.
4	Aug. 5, 2009 Total review time: 383 days Regulatory review time: 299 days	Apr. 23, 2008 D970003/S096 Apr. 30, 2008 D970003/S097 Overseas clinical study results	13	Altrua 60DR (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. A clinical study was conducted to evaluate its Automatic Capture feature capability, which automatically adjusts the ventricular pacing output.
4	Aug. 5, 2009 Total review time: 352 days Regulatory review time: 268 days	Apr. 23, 2008 D970003/S096 Apr. 30, 2008 D970003/S097 Overseas clinical study results	14	Altrua 60SR (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	Dual-chamber implantable cardiac pacemaker. A clinical study was conducted to evaluate its Automatic Capture feature capability, which automatically adjusts the ventricular pacing output.
4	Aug. 10, 2009 Total review time: 510 days Regulatory review time: 290 days	Mar. 16, 2007 Overseas clinical study results	15	Cool Path Ablation System (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter used for the electrophysiological study of the heart and for creating endocardial lesions to treat typical atrial flutter with radiofrequency current. Clinical studies were conducted to evaluate the novel irrigation feature of this product that allows saline flushing from the tip electrode to avoid increasing tip electrode-tissue interface temperature.

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Oct. 19, 2009 Total review time: 327 days Regulatory review time: 200 days	- Overseas clinical study results	16	Cool Path Duo Irrigation Catheter (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter used for the electrophysiological study of the heart and for creating endocardial lesions to treat typical atrial flutter with radiofrequency current. Clinical studies were conducted to evaluate the novel irrigation feature of this product that allows saline flushing from the tip electrode to avoid increasing tip electrode-tissue interface temperature.
4	Oct. 28, 2009 Total review time: 485 days Regulatory review time: 313 days	May 7, 2007 Overseas clinical study results	17	OptiSense S (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/pacemaker lead	A straight transvenous lead to be implanted in the right atrium, used for bradycardia pacing therapy (sensing and pacing). Clinical studies were conducted to evaluate the novel capability of this product to reduce far field sensing in order to inhibit inadequate actuation of the pulse generator (PG).
4	Oct. 28, 2009 Total review time: 485 days Regulatory review time: 313 days	Oct. 1, 2009 Overseas clinical study results	18	OptiSense Optim (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A straight transvenous lead to be implanted in the right atrium, used for bradycardia pacing therapy (sensing and pacing). Clinical studies were conducted to evaluate the novel capability of this product to reduce far field sensing in order to inhibit inadequate actuation of the PG.
4	Oct. 28, 2009 Total review time: 467 days Regulatory review time: 309 days	Oct. 1, 2009 Overseas clinical study results	19	OptiSense Optim Lead (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A straight transvenous lead to be implanted in the right atrium, used for bradycardia pacing therapy (sensing and pacing). Clinical studies were conducted to evaluate the novel capability of this product to reduce far field sensing in order to inhibit inadequate actuation of the PG.
4	Nov. 12, 2009 Total review time: 332 days Regulatory review time: 204 days	Nov. 21, 2001 Overseas clinical study results	20	Genesis Single 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	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. Clinical studies were conducted to evaluate the constant current stimulation that is generally used for electrical tissue stimulation and used in this product, while the constant voltage stimulation is used in conventional approved products.
4	Dec. 2, 2009 Total review time: 278 days Regulatory review time: 202 days	Mar. 28, 2008 Overseas clinical study results	21	EON Mini Dual 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	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. Clinical studies were conducted to evaluate the constant current stimulation that is generally used for electrical tissue stimulation and applied in this product.
4	Mar. 26, 2010 Total review time: 847 days Regulatory review time: 410 days	Feb. 4, 2005 Overseas clinical study results	22	ZOLL AED Pro Semi-Automatic Defibrillator (ZOLL Medical Corporation)	Approval	Instrument & apparatus 12 Semi-automatic defibrillator	A semi-automatic external defibrillator using biphasic defibrillator waveform dedicated for use by 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.
5	Jun. 2, 2009 Total review time: 736 days Regulatory review time: 303 days	Jun. 29, 2001 Domestic clinical study results	23	Monosyn (B. Braun Aesculap Japan Co., Ltd.)	Approval	Medical products 2 Polyglyconate suture	An absorbable synthetic monofilament suture made of glycolide/trimethylene carbonate/ε-caprolactone. A clinical trial was conducted to evaluate the efficacy and safety because the combination and amount of the polymers are different from the precedented approved product's.
5	Jun. 8, 2009 Total review time: 619 days Regulatory review time: 383 days	- Domestic clinical study results	24	Fuji IR (Fuji Latex Co., Ltd.)	Approval	Hygienic products 2 Contraceptive condom for males	A condom made chiefly from polyisoprene rubber used to cover the penis for the purpose of contraception and as an adjunct in the prevention of sexually transmitted diseases. A clinical study was conducted to compare its efficacy and safety with those of commercially available condoms (condom made from natural rubber latex).
5	Nov. 10, 2009 Total review time: 375 days Regulatory review time: 297 days	Dec. 4, 2006 Overseas clinical study results	25	WallFlex Duodenal Stent (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Gastroduodental stent	The device consists of a metal stent intended for dilatation and to maintain the patency in gastroduodenal obstructions produced by malignant neoplasms, and a delivery system for endoscopic implantation of the stent. Clinical studies were conducted to evaluate its efficacy for improvement of QOL for a certain period and the safety.

Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
5	Nov. 20, 2009 Total review time: 624 days Regulatory review time: 433 days	Jan. 8, 2002 Clinical evaluation report	26	Gynemesh (Johnson & Johnson K.K.)	Approval	Medical products 4 Nonabsorbable prosthetic material for hernia, chest wall, and abdominal wall	A mesh used for repair of pelvic organ prolapse, with limited intended use and shape and structure, while manufactured in the same way from the same materials as "Prolene Mesh (polypropylene)" (Approval No. 20400BZY00787000). A clinical evaluation report discussing the efficacy and safety through the defined algorithm for the literature survey was submitted.
5	Feb. 3, 2010 Total review time: 406 days Regulatory review time: 262 days	- Domestic clinical study results	27	Hemodialysis Monitoring Equipment TR-3000MA (Toray Medical Co., Ltd.)	Approval	Instrument & apparatus 7 Hemodialysis equipment	A hemodialysis monitoring equipment with additional functions to "TR-3000M (Approval No. 21500BZZ00045000),"of assisting priming, blood return, blood taking with diahysate, as well as rapid substitution and manual substitution. Clinical studies were performed in Japan to confirm its efficacy and safety.
6	May 8, 2009 Total review time: 2907 days Regulatory review time: 791 days	- Domestic clinical study results	28	Care Sheet "SS" (SSP Co., Ltd.)	Approval	Medical products 4 Hydrocolloid material	A wound dressing and protecting material using hydrogel in a form of poultice. A clinical study was conducted to evaluate its efficacy and safety.
6	Jun. 29, 2009 Total review time: 732 days Regulatory review time: 451 days	Aug. 5, 2004 Domestic clinical study results	29	OIC PEEK Interbody Cage (Stryker Japan K.K.)	Approval	Medical products 4 Spinal cage	A spinal cage made from a novel material polyetheretherketone (PEEK) resin. A pair of these products with bone graft packed inside are intervertebrally inserted and fixed by pressure using another intervertebral fixation system. Clinical studies were performed in Japan to confirm its efficacy and safety.
6	Aug. 6, 2009 Total review time: 934 days Regulatory review time: 487 days	- Domestic clinical study results	30	Blend-E (Nakashima Medical Co., Ltd.)	Approval	Medical products 4 Artificial knee joint, patellar and tibial component	A tibial insert and patellar component made from ultrahigh molecular weight polyethylene. The shape and structure are the same as the approved products of the company, but dl-α-Tocopherol, a kind of vitamin E, has been added to this product in order to give the antioxidative potential to the material and to improve the resistance to wear. Clinical studies were performed in Japan to confirm its efficacy and safety.
8	Oct. 30, 2009 Total review time: 1688 days Regulatory review time: 554 days	Jun. 15, 1999 Overseas clinical study results	31	Medtronic MiniMed CGMS-Gold (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 21 Glucose monitoring system	A glucose monitoring system to keep continuous record of glucose level in the interstitial fluid which is considered to change in parallel with the blood glucose level, intended for use to obtain information on the fluctuation pattern of blood glucose values necessary to optimize the diabetic treatment. A clinical trial was conducted to compare the correlation between the glucose level in blood and that in the interstitial fluid in order to confirm the clinical performance of this product.
8	Nov. 20, 2009 Total review time: 1169 days Regulatory review time: 677 days	- Domestic clinical study results	32	Ultrasound Bone Densitometer LD-100 (OYO Electric Co., Ltd.)	Approval	Instrument & apparatus 12 Ultrasound bone densitometer	A device to measure the bone density using ultrasound. This product calculates the bone density based on the measurement of arrival times and attenuations of fast wave and slow wave that propagate the radius and arrival times of the reflected waves, while conventional ultrasound bone densitometers measure the speed or attenuation of ultrasonic pulse that propagates the calcaneus. Clinical studies were performed in Japan to confirm its efficacy and safety.

Note: Products submitted for application in 2003 and before are included.

Table 4. Post-marketing Safety Measures Implemented and Revision of PRECAUTIONS for Drugs, etc. Instructed by MHLW in FY 2009

Post-marketing safety measures implemented by MHLW in FY 2009

	Drugs	Medical devices
Revision of PRECAUTIONS instructed	261	4
Information published on the Pharmaceuticals and Medical Devices Safety Information	29	5

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

Revision of PRECAUTIONS in the package inserts of drugs, instructed by MHLW in FY 2009

Date	Drug name
Apr. 24, 2009	1. Isoflurane 2. Toremifene citrate 3. Olmesartan medoxomil 4. Cellulose, oxidized 5. Sorafenib tosilate
May 8, 2009	1. Sertraline hydrochloride 2. Paroxetine hydrochloride hydrate 3. Fluvoxamine maleate Milnacipran hydrochloride
May 29, 2009	1. Monobasic sodium phosphate monohydrate/Anhydrous dibasic sodium phosphate 2. Blonanserin 3. Etanercept (genetical recombination) 4. Amrubicin hydrochloride 5. Erlotinib hydrochloride 6. Peginterferon alfa-2a (genetical recombination)
Jul. 3, 2009	1. Phenytoin Phenytoin/Phenobarbital Phenytoin/Phenobarbital/Caffeine and sodium benzoate Phenytoin sodium 2. Amitriptyline hydrochloride Amoxapine Imipramine hydrochloride Clomipramine hydrochloride (oral dosage form) Setiptiline maleate Dosulepin hydrochloride Trazodone hydrochloride Trimipramine maleate Nortriptyline hydrochloride Maprotiline hydrochloride Mianserin hydrochloride Lofepramine hydrochloride 3. Clomipramine hydrochloride (injectable dosage form) 4. Telmisartan 5. Potassium bromide Calcium bromide Sodium bromide Acetylpheneturide Ethosuximide Ethotoin Sultiame Trimethadione Saikokaryukotsuboreito (preparations with the indication of epilepsy) 6. Nitrazepam Phenobarbital Phenobarbital sodium (subcutaneous/intramuscular injection) Clonazepam Clobazam Phenytoin Phenytoin/Phenobarbital Phenytoin/Phenobarbital/Caffeine and sodium benzoate Phenytoin sodium Primidone

Date	Drug name
	Acetazolamide Acetazolamide sodium 7. Gabapentin Carbamazepine Zonisamide (preparations with the indication of epilepsy) 8. Topiramate Sodium valproate 9. Lamotrigine 10. Tosufloxacin tosilate hydrate (ophthalmic solution) 11. Azelnidipine 12. Levonorgestrel 13. Dalteparin sodium 14. Moxifloxacin hydrochloride (oral dosage form)
Aug. 7, 2009	1. Varenicline tartrate 2. Cibenzoline succinate (oral dosage form) 3. Cibenzoline succinate (injectable dosage form) 4. Estriol (preparations for vaginal application) 5. Cilostazol 6. Mycophenolate mofetil 7. Imatinib mesilate 8. Garenoxacin mesilate hydrate 9. Over-the-counter Drugs External preparations containing testosterone External preparations containing methyltestosterone
Sep. 28, 2009	1. Potassium canrenoate 2. Rosuvastatin calcium 3. Everolimus Gusperimus hydrochloride Ciclosporin (oral dosage form, injectable dosage form) Tacrolimus hydrate (oral dosage form, injectable dosage form) Mycophenolate mofetil Muromonab-CD3 4. Tegafur/Gimeracil/Oteracil potassium 5. Sunitinib malate 6. Sorafenib tosilate 7. Bevacizumab (genetical recombination) 8. Ciprofloxacin Ciprofloxacin hydrochloride 9. Basiliximab (genetical recombination) 10. Ivermectin 11. Pancuronium bromide Vecuronium bromide Rocuronium bromide 12. Amiodarone hydrochloride (oral dosage form) 13. Amiodarone hydrochloride (injectable dosage form) 14. Reviparin sodium 15. Buformin hydrochloride 16. Doripenem hydrate
Oct. 19, 2009	1. Influenza HA vaccine Influenza A (H1N1) HA vaccine
Oct. 27, 2009	1. Salazosulfapyridine 2. Pethidine hydrochloride

Date	Drug name
	Pethidine hydrochloride/Levallorphan tartrate 3. Indomethacin (oral dosage form) 4. Indomethacin (suppository) 5. Indometacin farnesil 6. Proglumetacin maleate 7. Lisinopril hydrate 8. Lanthanum carbonate hydrate 9. Parnaparin sodium 10. Zanamivir hydrate
Nov. 18, 2009	1. Sorafenib tosilate
Dec. 1, 2009	1. Tandospirone citrate 2. Aripiprazole Spiperone Sulpiride Zotepine Nemonapride Pipamperone hydrochloride Pimozide Moperone hydrochloride 3. Olanzapine Risperidone (oral dosage form) 4. Quetiapine fumarate 5. Risperidone (injectable dosage form) 6. Acemetacin 7. Oxypertine Carpipramine hydrochloride hydrate Carpipramine maleate Clocapramine hydrochloride hydrate Sultopride hydrochloride Timiperone Trifluoperazine maleate Fluphenazine decanoate Fluphenazine maleate Bromperidol Perphenazine Perphenazine hydrochloride Perphenazine fendizoate Perphenazine maleate Mosapramine hydrochloride 8. Chlorpromazine hydrochloride Chlorpromazine hibenzate Chlorpromazine phenolphthalinate 9. Chlorpromazine hydrochloride/Promethazine hydrochloride/Phenobarbital 10. Haloperidol 11. Haloperidol decanoate 12. Prochlorperazine maleate Prochlorperazine mesilate Propericiazine 13. Perospirone hydrochloride hydrate 14. Levomepromazine hydrochloride Levomepromazine maleate 15. Dihydrocodeine phosphate/*dl*-methylephedrine hydrochloride/Chlorpheniramine maleate Dihydrocodeine phosphate/Ephedrine hydrochloride/Ammonium chloride Platycodon fluid extract/Glycyrrhiza extract/Plantago herb extract/Peony root

Date	Drug name
	extract/Dihydrocodeine phosphate 16. Diprophylline/Dihydrocodeine phosphate/*dl*-methylephedrine hydrochloride/Diphenhydramine salicylate/Acetaminophen/Bromovalerylurea 17. Codeine phosphate hydrate Cherry bark extract/Codeine phosphate hydrate 18. Dihydrocodeine phosphate 19. Over-the-counter Drugs Preparations containing codeine phosphate hydrate Preparations containing dihydrocodeine phosphate Preparations containing hydrocodeine phosphate sekisanol 20. Etravirine
Jan. 12, 2010	1. Fludarabine phosphate 2. Bicalutamide 3. Amoxapine 4. Infliximab (genetical recombination) 5. Aluminum potassium sulfate hydrate/Tannic acid 6. Flurbiprofen (external dosage form) 7. Cinacalcet hydrochloride 8. Letrozole 9. Ribavirin (tablets) 10. Ribavirin (capsules) 11. Freeze-dried BCG vaccine 12. Interferon alfa (BALL-1) Interferon alfa (NAMALWA) Interferon alfa-2b (genetical recombination) Interferon alfacon-1 (genetical recombination) Interferon beta (not for administration in combination with ribavirin) Interferon beta-1a (genetical recombination) Interferon beta-1b (genetical recombination) Peginterferon alfa-2a (genetical recombination) Peginterferon alfa-2b (genetical recombination) 13. Interferon beta (for administration in combination with ribavirin) 14. Interferon gamma-1a (genetical recombination) Interferon gamma-n1
Feb. 16, 2010	1. Warfarin potassium 2. Methotrexate (tablet 2 mg, capsule) 3. Methotrexate (tablet 2.5 mg) 4. Methotrexate (injectable dosage form) 5. Bortezomib 6. Nalfurafine hydrochloride 7. Bethanechol chloride 8. Dorzolamide hydrochloride 9. Candesartan cilexetil/Hydrochlorothiazide Telmisartan/Hydrochlorothiazide Valsartan/Hydrochlorothiazide 10. Montelukast sodium 11. Recombinant adsorbed bivalent human papillomavirus-like particle vaccine (derived from Trichoplusia ni cells) 12. Over-the-counter Drugs Preparations containing bromhexine hydrochloride 13. Over-the-counter Drugs Preparations containing ketoprofen (dermatologic preparation)
Mar. 23, 2010	1. Aripiprazole

Date	Drug name
	Oxypertine Olanzapine Carpipramine hydrochloride hydrate Carpipramine maleate Quetiapine fumarate Clocapramine hydrochloride hydrate Chlorpromazine hydrochloride Chlorpromazine hydrochloride/Promethazine hydrochloride/Phenobarbital Chlorpromazine hibenzate Chlorpromazine phenolphthalinate Spiperone Sultopride hydrochloride Sulpiride Zotepine Timiperone Trifluoperazine maleate Nemonapride Haloperidol Haloperidol decanoate 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 Levomepromazine hydrochloride Levomepromazine maleate 2. Clozapine 3. Risperidone 4. Atorvastatin calcium hydrate Simvastatin Pitavastatin calcium Pravastatin sodium Fluvastatin sodium Rosuvastatin calcium 5. Amlodipine besilate/Atorvastatin calcium hydrate 6. Cetuximab (genetical recombination) 7. Zafirlukast 8. Pranlukast hydrate 9. Montelukast sodium
Mar. 29, 2010	1. Thalidomide

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 2009

Revision of PRECAUTIONS for medical devices instructed in FY 2009

Date	Title
Sep. 24, 2009	Instructions, etc. for revision of PRECAUTIONS on interactions between X-ray diagnostic equipment, etc. and implantable cardiac pacemakers
Sep. 24, 2009	Instructions, etc. for revision of package inserts of blood circuits used for haemodialysis therapy

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 2009

Date	Title
Aug. 25, 2009	Self-check of package inserts regarding tubes for airway pressure monitoring in a ventilator circuit
Mar. 1, 2010	Self-check of package inserts of lancing devices for capillary blood sampling

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

Table 6. FY 2009 Pharmaceuticals and Medical Devices Safety Information (No. 257-267)

Date	No.	Contents
May 28, 2009	257	1. Implementation of appropriate management/maintenance of automated external defibrillators (AEDs) 2. Revision of PRECAUTIONS (No. 205) Naproxen (and 7 others) 3. List of products subject to Early Post-marketing Phase Vigilance
Jun. 24, 2009	258	1. Selective serotonin reuptake inhibitors (SSRIs) and aggression 2. Important safety information (1) Isoflurane 3. Revision of PRECAUTIONS (No. 206) Olmesartan medoxomil (and 3 others) 4. List of products subject to Early Post-marketing Phase Vigilance (Reference Material) 1. Project for promoting safe use of drugs 2. Manuals for management of Individual Serious Adverse Drug Reactions 3. Extension of cooperating hospitals in the project for "Japan Drug Information Institute in Pregnancy"
Jul. 30, 2009	259	1. Important safety information (1) Monobasic sodium phosphate monohydrate and anhydrous dibasic sodium phosphate 2. Revision of PRECAUTIONS (No. 207) Blonanserin (and 4 others) 3. List of products subject to Early Post-marketing Phase Vigilance (Reference Material) 1. About oseltamivir phosphate (Tamiflu) [The brief summary of the review results of the investigation by the Subcommittee on Drug Safety (held on June 16, 2009)]
Aug. 26, 2009	260	1. Tricyclic and tetracyclic antidepressants, associated with aggression 2. Important safety information (1) Telmisartan (2) Phenytoin, phenytoin/phenobarbital, phenytoin/phenobarbital/caffeine and sodium benzoate, phenytoin Sodium 3. Revision of PRECAUTIONS (No. 208) Lamotrigine (and 9 others) 4. List of products subject to Early Post-marketing Phase Vigilance
Sep. 29, 2009	261	1. Drug-induced serious skin disorders 2. SSRIs/SNRIs and harmful behavior to others 3. Important safety information (1) Varenicline tartrate 4. Revision of PRECAUTIONS (No. 209) Cibenzoline succinate (oral dosage form) (and 7 others) 5. List of products subject to Early Post-marketing Phase Vigilance (Reference Material) 1. Reports on adverse reactions associated with influenza vaccines in FY 2008 (Conclusion of the Vaccine Adverse Reaction Review Committee)
Oct. 28, 2009	262	1. PMDA Medical Safety Information 2. The Relief System for Sufferers from Adverse Drug Reactions and Disease Infected from Biological Products 3. List of products subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
Nov. 27, 2009	263	1. Association between use of human insulin and insulin analogues and risk of cancer 2. Important safety information (1) Ivermectin (2) Everolimus, gusperimus hydrochloride, ciclosporin (oral dosage form, injectable dosage form), tacrolimus hydrate (oral dosage form, injectable dosage form), basiliximab (genetical recombination), mycophenolate mofetil, muromonab-CD3 (3) Ciprofloxacin, ciprofloxacin hydrochloride (4) Sunitinib malate (5) Sorafenib tosilate (6) Tegafur/gimeracil/oteracil potassium (7) Bevacizumab (genetical recombination) (8) Rosuvastatin calcium 3. Revision of PRECAUTIONS (No. 210) 4. (1) Pancuronium bromide, vecuronium bromide, rocuronium bromide (and 7 others) (2) Blood circuits (and 3 others) 5. List of products subject to Early Post-marketing Phase Vigilance
Dec. 25, 2009	264	1. Safety measures for anaphylaxis and anaphylactoid symptoms associated with injectable antibiotics 2. Important safety information (1) Salazosulfapyridine (2) Pethidine hydrochloride, pethidine hydrochloride/levallorphan tartrate 3. Revision of PRECAUTIONS (No. 211) Indomethacin (oral dosage form) (and 7 others) 4. List of products subject to Early Post-marketing Phase Vigilance
Jan. 27, 2010	265	1. Handling of fire during Long-term Oxygen Therapy 2. Important safety information (1) Sorafenib tosilate (2) Aripiprazole, spiperone, sulpiride, zotepine, nemonapride, pipamperone hydrochloride, pimozide, moperone hydrochloride (3) Olanzapine, risperidone (oral dosage form), risperidone (injectable dosage form) (4) Quetiapine fumarate (5) Tandospirone citrate 3. Revision of PRECAUTIONS (No. 212) Acemetacin (and 14 others) 4. List of products subject to Early Post-marketing Phase Vigilance
Feb. 24, 2010	266	1. Proper procedures for soft contact lens care 2. Important safety information (1) Bicalutamide (2) Fludarabine phosphate 3. Revision of PRECAUTIONS (No. 213) Amoxapine (and 11 others) 4. List of products subject to Early Post-marketing Phase Vigilance
Mar. 31, 2010	267	1. Precautions on handling of lancing devices for capillary blood sampling 2. Important safety information (1) Bortezomib (2) Methotrexate 3. Revision of PRECAUTIONS (No. 214) Warfarin potassium (and 9 others) 4. 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. PMDA Medical Safety Information

No.	Date published	Title
10	May 2009	Good management & maintenance of automated external defibrillators (AEDs)
11	Aug. 2009	Precautions in artificial respiration (No. 2)
12	Sep. 2009	Misconnection of tourniquet cuff
13	Oct. 2009	Medical gas mix-ups
14	Feb. 2010	Precautions in handling electric scalpels (Part 1)
15	Mar. 2010	Precautions in handling electric scalpels (Part 2)

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

Table 8. List of User Fees (partially revised on April 1, 2009)

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 articles on user fees to MHLW in 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		
Review for approval of drugs (approval for partial changes to approved matters)					

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 Article 17 (4) 1-b (1)	739,800
				Overseas		933,500 + travel expenses Article 17 (4) 1-b (2)	933,500 + travel expenses
		Biological drugs/Radiopharmaceuticals		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 drugs/Sterilized quasi-drugs		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 drugs/quasi-drugs		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 drugs/ Radiopharmaceuticals	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 drugs/ Sterilized quasi-drugs	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 drugs/ quasi-drugs	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

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 articles on user fees to MHLW in 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 manufacturing 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		
Review for approval of medical devices (approval of partial changes to approved matters)						

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

Classification			User fees		
			Review	Inspection	Total
GLP inspection of medical devices					
	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 medical devices					
	GCP	Domestic		635,300	635,300
				Article 17 (3) 3-a	
		Overseas		918,400 + travel expenses	918,400 + travel expenses
				Article 17 (3) 3-b	
Re-examination of medical devices					
	New medical devices		502,600	624,600	1,127,200
			Article 17 (8) 2-a	Article 17 (9) 1-c	
	Medical devices other than new ones		51,600		51,600
			Article 17 (8) 2-b		
	GPSP	Domestic		610,700	610,700
				Article 17 (9) 2-b (5)	
		Overseas		949,000 + travel expenses	949,000 + travel expenses
				Article 17 (9) 2-b (6)	

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 application after arrangement of the date of the consultation
	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 the 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/biomarker		3,028,400 yen per consultation	
	Pre-application consultation for new OTC drugs		445,100 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 devices)		822,100 yen per consultation	
	Safety consultation for biological medical devices		910,100 yen per consultation	
	Quality consultation for medical devices (excluding biological 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	
	Clinical trial/pre-application consultation for *in vitro* diagnostics		1,594,700 yen per consultation	
	Application procedure consultation for medical devices		135,200 yen per consultation	
	Application procedure consultation for *in vitro* diagnostics		135,200 yen per consultation	
	Additional consultation for medical devices		1,130,100 yen per consultation	
	Additional consultation for *in vitro* diagnostics		927,500 yen per consultation	
	Consultation on GLP/GCP compliance for medical devices		772,900 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	
	Writing applications for new drugs		21,000 yen per consultation	
	GMP/QMS inspection		24,700 yen per consultation	
Review for designation of priority consultation				
Review for designation of priority consultation on drugs			818,800 yen per application	Request to PMDA after advance payment
Reviews for designation of priority consultation on medical devices or *in vitro* diagnostics			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

Summary of the Final Recommendations for Improvement of Drug Regulatory Administration to Prevent Similar Drug-induced Sufferings

(Committee for Investigation of Drug-induced Hepatitis Cases and
Appropriate Regulatory Administration to Prevent Similar Sufferings)

Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

[Text in boldface: Newly added items after First Recommendations (*: main items)]

Part 1 Introduction

- The Committee was set up for the purpose of investigating the drug-induced hepatitis cases and of providing recommendations for improvement of the drug regulatory administration to prevent similar sufferings.
- The Committee held 23 meetings from May 2008 to March 2010.
- The results of deliberation in FY 2009 were added to the First Recommendations.

Part 2 Problems Identified from the History of Drug-induced Hepatitis Cases

- The problems identified from the history of drug-induced hepatitis cases were sorted and organized from the viewpoint of future prevention of recurrence. [*Same as in the First Recommendations]
  (1) History relating to fibrinogen products
  (2) History relating to coagulation factor IX products
  (3) Underlying facts concerning the above products
- **In FY 2009, the following investigations were newly conducted and then problems were sorted and organized (*)**
  (1) Hearing from persons in charge of handling this incident in the regulatory authority and pharmaceutical companies at the time when incidence cases came out
  (2) Awareness survey in healthcare professionals (questionnaires replied by doctors, interviews with doctors)
  (3) Actual status survey in sufferers (patient survey, survey in bereaved family)

Part 3 History of Major Revisions of Regulatory Systems to Date [*Same as in the First Recommendations]

- Past major revisions of regulatory systems related to drug regulatory administration were sorted and organized.
  - History of revisions of Pharmaceutical Affairs Act
  - History of changes in the structure of drug regulatory administration

Part 4 Reviews of Drug Regulatory Administration to Prevent Drug-Induced Sufferings

- Thorough review of drug regulatory administration aiming to prevent similar drug-induced sufferings was recommended.
  (1) Basic concepts
    (i) Review of laws and regulations, and basic attitudes required for persons who are engaged in drug administration,
    (ii) Review of the structure of the drug regulatory bodies, and development of the human resources,
    (iii) Education concerning drug-induced sufferings and drugs evaluation, and

(iv) Establishment of a resource center for research on drug-induced sufferings,
(v) Fostering of experts and promotion of pharmacoepidemiological research (*)

(2) Clinical studies/trials

(3) Review for approval

(i) Safety/efficacy evaluation, **(ii) Neutrality, transparency, etc. of review procedures and deliberations (*)**, (iii) Package inserts, and (iv) Re-evaluations

(4) Post-marketing safety measures, etc.

(i) Reinforcement of system of collecting information, **(ii) Evaluation of obtained information (introduction of new risk management methods (*), etc.), (iii) Proactive and smooth provision of information to improve risk communication & involvement of patients and consumers (*)**, (iv) Ways of transmitting ADR information to the primarily affected individuals and disclosing information, (v) Proper use of drug products via appropriate provision of information and publicity, (vi) GMP inspections, (vii) GVP/GQP inspections, and (viii) Personal import of drugs

(5) Safety measures at medical institutions

(6) Relief system for adverse health effects

(7) Measures to effectively utilize expertise

(8) Basic attitudes required as pharmaceutical companies, etc. (*)

Part 5 Future Stance of Drug Regulatory Bodies

- **Organizing the discussions on drug regulatory bodies (*)**
  - Discussion was held focusing on issues such as centralized management (by government or incorporated administrative agency) of drug regulatory bodies. In this fiscal year, questionnaire survey was given to employees.
  - Basic factors are proposed for appropriate structures of drug regulatory bodies, regardless of the form of organization, such as a system that allows the ultimate responsibility to be left to the government.
- **Establishment of a third-party monitoring/evaluation organization (*)**
  - In order to prevent the occurrence and expansion of drug-induced sufferings, it is necessary to establish a third-party organization that monitors and evaluates drug regulatory bodies and makes proposals for taking appropriate actions.

Part 6 Closing Comment

- There is an opinion that in order to realize the recommendations, it is necessary to **consider the development of a comprehensive basic law** regarding drug regulatory administration. This should also be taken into consideration.