II. ACTUAL OPERATION RESULTS FOR FY 2006

PART 1. DEVELOPMENT OF 2006 FISCAL YEAR PLAN

1. Development and Implementation of 2006 Fiscal Year Plan

- The Agency is required to develop the Mid-term plan in accordance with the Mid-term targets designated by the Minister of Health, Labour and Welfare, who must then approve the plan (the first period for the Mid-term targets is between April 2004 and March 2009). In order to achieve the Mid-term plan, the Agency is required to develop a plan for each fiscal year, submit these plans to the Minister and announce these plans to the public.

  The Agency has developed a 2006 fiscal year plan at the end of FY 2005, submitted this plan to the Minister, and has been implementing operations based on this plan in FY 2006.

  In addition, in response to the directive issued by the Minister of Health, Labour and Welfare dated March 31, 2006, the Agency sought and received approval for modifications to the Mid-term plan on the same day as the directive on aspects relating to “Optimization Plan for Operational Performance and Information Systems of Incorporated Administrative Agencies,” “Major Policies for Administrative Reform,” and “Handling of Income from One’s Own Resources in the Calculation of Grants for Operating Expenditures.”

  The 2006 fiscal year plan was developed based on the modified Mid-term targets and Mid-term plan, as well as operational performance from FY 2005 as 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.

- The Agency has implemented various approaches, such as through making efforts to further reinforce development and management of an organizational structure so that a performance level that meets the public’s expectations can be realized.

  In the same way as for FY 2005, the Agency announced its three priority issues for FY 2006 at the 1st Advisory Council Meeting held on June 22, 2006. The priority issues are as follows.

  i) Enhancement of review operations
  ii) Enhancement of safety measures
  iii) Improvement of relief fund operations

  In addition, to steadily promote the Mid-term plan, fiscal plan and priority issues for FY 2006, the Agency organized the issues that should be implemented within FY 2006 and announced these issues as “Priority Issues for Operations in the Second Half of FY 2006” at the 2nd Advisory Council Meeting held on October 3, 2006.

2. Evaluation Results of Operational Performance in FY 2005

- It is stipulated that the each ministry in charge of an independent administrative agency should establish an “Evaluation Committee for Incorporated Administrative Agencies” to conduct administrative processing of the agencies under its control (Article 12 of the Law on General Rules of Incorporated Administrative Agencies).

The Agency received results from an evaluation on its performance in FY 2005 on August 17, 2006 by the Evaluation Committee for Incorporated Administrative Agencies of the MHLW, which is responsible for conducting evaluations on the Agency. The overall evaluation results consisted of 17 As and 3 Bs, out of 20 evaluation items (the 3 Bs were for “Prompt relief benefit services,” “Consultations regarding clinical study” and “Budget, income and expenditure plan, and financial planning” (due to discrepancies between the budget and closing in the user fee income for accounts for reviews, etc.)).

The Agency posted these evaluation results on the PMDA website and reported the results to the Advisory Council that was held on October 3, 2006 as well.

Note: Five-level grading of S, A, B, C and D with S being the highest
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

Performance evaluation of the Agency by the "Evaluation Committee on Incorporated Administrative Agencies", MHLW

Classification in the Midterm and fiscal year plan		Evaluation items		Evaluation Result FY2004 Performance	Evaluation Result FY2005 Performance
Part 1	Improvement in overall operations and quality in services of the Agency eg. services to the public				
	(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 reduction by increased efficiency of operations	3	Expense savings	A	A
		4	Collection and management of contributions	A	A
	(3) Improvement of services to the public	5	Strengthening of the consultation system and disclosure of the work of the Agency	A	A
Part 2	Improvement in operation 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 consultation 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	C	B
	(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 those patients infected with HIV from blood preparations	9	Conduct of relief services for SMON patients and those patients infected with HIV from blood preparations	A	A
2	Reviews and related operations/ post-marketing safety measures				
	(1) Faster access to leading-edge pharmaceuticals and medical devices	10	Expeditious operation and improvement of the system (drugs)	A	A
		11	Expeditious operation and improvement of the system (medical devices)	B	A
		12	Expeditious operation and improvement of the system (clinical trial consultations)	C	B
	(2) Improvement in reliability of reviews and related operations/post-marketing safety measures	13	Improvement in quality of review and related operations/ post-marketing safety measures	A	A
		14	Promotion of appropriate clinical trials	A	A
		15	Promotion of transparency of review and related operations/ post-marketing safety measures	A	A
	(3) Reinforcement of information management and emergency 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	B
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 determined by orders from the competent ministry				
	(1) Personnel matters (2) Ensuring security	20	Personal 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	17	17
	B	Somewhat exceeding the level prescribed in the midterm-plan	1	3
	C	Slightly below the level prescribed in the midterm-plan	2	0
	D	Below the level prescribed in the midterm-plan, therefore requiring drastic improvements	0	0

- On November 27, 2006, the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications expressed opinions on the results of the evaluations regarding the Agency by the Evaluation Committee for Incorporated Administrative Agencies of the MHLW. The evaluation of the Agency suggested that “as for the approval reviews, the Agency should expedite the process to enhance the international competitiveness of the pharmaceutical and medical device industries, increase the quality of approval reviews, and set specific, quantitative goals for approaches that include the development of a structure to accelerate and streamline such procedures; furthermore, the Evaluation Committee for Incorporated Administrative Agencies of the MHLW should request the Agency and the competent minister to conduct appropriate reviews of measures and evaluate the achievement status of these targets.”

3. Modifications in the Mid-term Plan (Approved on March 30, 2007)

- It has been pointed out that more time is required in Japan than in Europe and the U.S. for new drugs to be placed on the market, and that there is problem where effective pharmaceuticals already approved in Europe and the U.S. are not available in Japan (otherwise known as “drug lag”).

Since its establishment in April 2004, the Agency has been working towards enhancing the review system, but the review personnel are still weak as compared to Europe and the U.S.; thus, further enhancement and reinforcement of the review system is desired in order to comply with the increasing number of reviews at the Agency, as well as with the upgrading of approval reviews following the development of science and technology.

In “Institutional Reform for Promoting Science and Technology and Passing on Its Benefits to Society” (Dec. 25, 2006. Hereinafter referred to as “Proposal from Council for Science and Technology Policy”), in which opinions from the Council for Science and Technology Policy are presented, suggestions are made to double the number of reviewers within approximately 3 years in order to resolve delays in consultations regarding clinical study and approval reviews at the Agency.

Considering this situation, in accordance with the directive by the Minister of Health, Labour and Welfare dated March 29, 2007, the Agency sought the Minister’s approval to revise the Mid-term plan on the same day as the directive, and received approval for modifications on March 30, 2007 (Main revisions made to the Mid-term plan include: (a) addition of statements regarding cost control with improved efficiency of the operations; (b) addition of statements regarding the acceleration of the approval reviews; (c) modification of the budget for the Mid-term plan (in accordance with hiring more reviewers); and (d) modification of statements regarding personnel matters (in accordance with hiring more reviewers)).

Countermeasures for Drug Lag

- To reduce the "drug lag" by a total of 2.5 years by 2011 through 1.5-year and 1.0-year reductions in the development and approval times respectively;
and to cut down the marketing lag to 500 days in line with the U.S.

Counter-measures

•Improving consultation in quantity and quality

-Advice on overall development strategy to improve development time and cost

-Avoid delay in starting CT due to losing a drawing for CT consultations and reapplication

-Expedite decision-making in applicant company by actively giving advice to interpret CT results

-Shorten pre-application time by improving pre-application consultations

▪Giving advice and instruction on pharmacovigilance from CT consultation stage

•Clarifying review policy

•Promoting global CTs

-More guidance on the rate of Japanese subjects to include and trial design

-Give active Face-to-face advice for participation in global CTs

•Issuing guidance to introduce microdosing study

•Strengthening capability to respond to cutting-edge technologies eg. pharmacogenomics and regeneration medicine

•Introduce prior assessment of toxicity, pharmacology, etc. into consultation at development stage for more efficiency after filing

•Giving advice on pharmacovigilance from review stage

•Standardizing and streamlining review process, improving project management, further utilizing IT, upskilling reviewers — to increase productivity of reviewers

-Approx. doubling the number of reviewers (introducing two-track system?)

-Introducing project manager for each review team

-Further improvement and streamlining of the operation

-Upskilling reviewers by upgrading training programs

▪Expanding interaction with foreign regulatory authorities eg. FDA

Targets to achieve by FY 2011

To reduce pre-application time lag* between Japan and US/ EU by 1.5 years

*Median difference of application dates for new active ingredients between Japan and US/EU

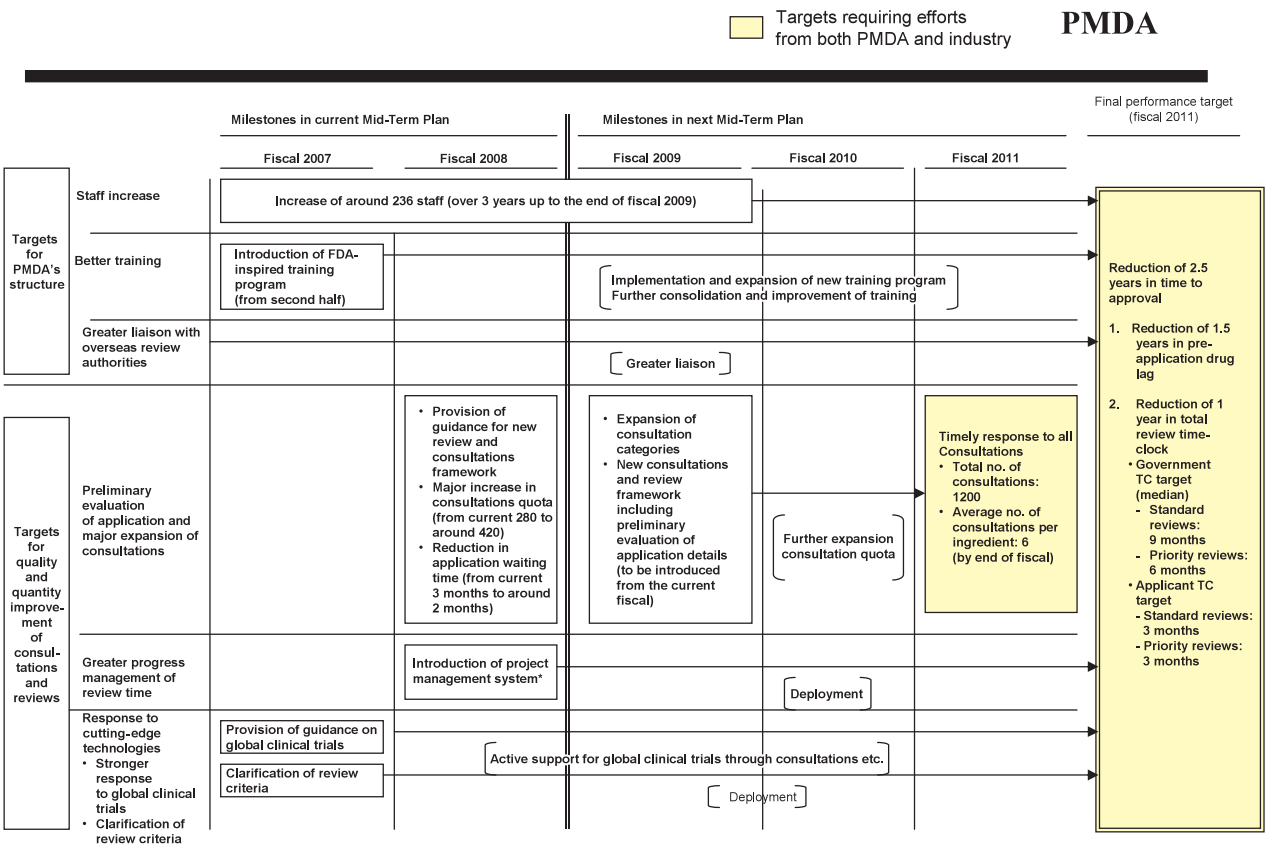
To reduce total review time for standard products by 1.0 year

Targets for products applied after FY 2004 (median):

-Standard products: total 12 mths (regulator: 9 mths + applicant: 3 mths)

-Priority products: total 9 mths (regulator: 6 mths + applicant 3 mths)

Milestones for each fiscal year



* Setting progress target for each review step and sharing it with the applicant.

PART 2. IMPROVEMENT IN OVERALL MANAGEMENT OF OPERATIONS AND SERVICE QUALITY OF THE AGENCY

1. Efficient and Flexible Management of Operations

1. (1) Operation through Management by Objectives

- In managing operations, the Agency clarifies the objectives and responsibilities of operations for each department, in addition to striving to identify and remedy problems through managing its operational progress on a daily basis.

- In order to do so, the Agency has managed operations based on management of objectives by creating operating plans based on the responsibilities for each responsible office and division in conjunction with the creation of the PMDA's annual plan for FY 2006.

- To comprehend the progress of operating plans in each office, in November 2006, the Agency conducted a hearing with its directors about the actual operating performance from the first half of FY 2006 in light of the operating plans, and the issues that were pointed out by the directors during this hearing were reported in the Board of Directors Meeting that was held on December 19, 2006. In another hearing with directors conducted in February 2007 in preparation for the development of the FY 2007 plan, the Agency also reported to the directors on the progress of FY 2006 operations.

1. (2) Reinforcement of Operational Management System and Top Management

- The Agency considers it necessary to reinforce its function to develop overall strategies for operations, as well as the system for managing operations such as for risk management and check functions. In addition, the Agency also plans to build an organizational system where management decisions by the Chief Executive are speedily reflected in operations.

- To this end, since FY 2005, the Agency 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.

  Concretely, the Agency has regularly (in principle, once a week) held Board of Directors meetings, attended by the Chief Executive and management personnel who are division heads or hold a higher position, since FY 2004.

- In meetings (held 4 times in FY 2006) for "Headquarters for PMDA Reform," which is headed by the Chief Executive, discussions on the direction of the PMDA reform were conducted, taking into consideration the results of operation and system diagnoses using external consultants as well as reports on the results of operational reform carried out by each division, starting with the review divisions. In addition, the "Committee on Clinical Trial Issues" established under the

Headquarters for PMDA Reform developed its interim report in October 2006.

- To comprehend the progress status of reviews and consultations regarding clinical studies of pharmaceuticals and medical devices, meetings for the “Committee for Progress Management of Review Operations” headed by the Chief Executive have been regularly held (11 times in FY 2006), and in addition, relevant documents were drastically revised in August 2006 so that the progress can be grasped more accurately.

- To reinforce the management structure for the Agency’s information system, the “Optimization Plan for Operations and Systems” has been discussed in the “Management Committee on Information Systems” led by the PMDA’s Chief Executive in cooperation with the “Information Systems Division” established in April 2006 (which became independent from Office of Planning and Coordination in December 2006, subsequently becoming reorganized as “Information Technology Promotion Group” and directly controlled by the Chief Information Officer (hereinafter referred to as “CIO”)) and external Deputy CIO (5 meetings were held during FY 2006).

  In this Management Committee, a “Committee on Investment for Information Systems” was also formed not only to comprehensively examine the reasonability of investments towards new developments and modifications for the information system, including from the aspects of cost-effectiveness and technical feasibility, but also to conduct systematic and effective investments under the management judgment of the Chief Executive (3 meetings were held during FY 2006).

- In order to maintain sound financial performance and adequate operations, the “Financial Management Committee,” headed by the Chief Executive, was established, and has been holding regular meetings (11 meetings in FY 2006), during which reports on the monthly application status for user fees according to each review division, reports on the monthly cash flow analysis, and reports on the declared amount of contributions are made.

- Moreover, starting with the 2006 fiscal year plan, reviews have been conducted on future improvements in operations by using external consultants, taking the changes in conditions surrounding the Agency and the status of management of operations since its establishment into consideration.

- A final report was issued on February 6, 2007 regarding the results of reviews by the Task Force created in compliance with the decision taken at the discussion meeting with the Japan Pharmaceutical Manufacturers Association (JPMA).

  Furthermore, another Task Force has been created for matters relating to medical devices and in vitro diagnostics, and working groups, which have been established separately for each issue, have also started to conduct reviews.

- The Agency is continuing with reviews for preparing the second-stage Mid-term plan based on the Proposal from Council for Science and Technology Policy, revisions made to the current Mid-

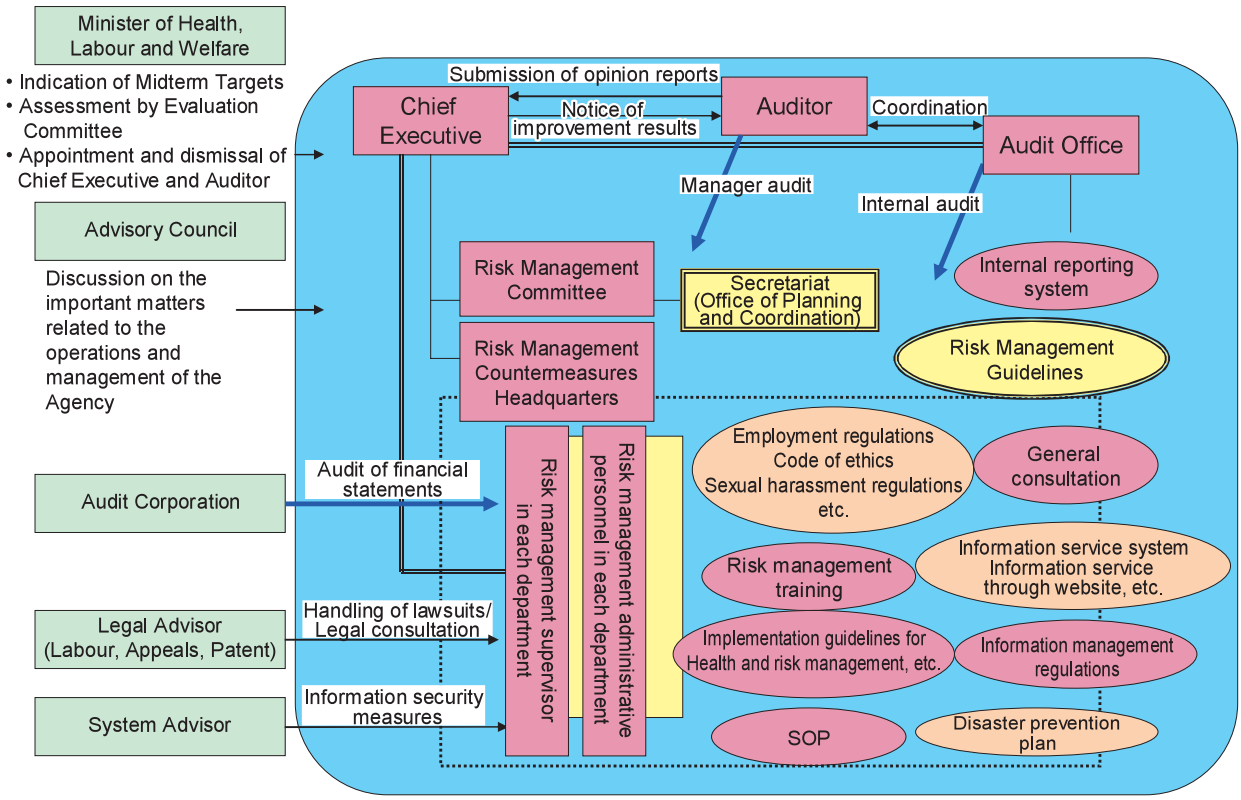
term plan, and results of operational diagnoses made by external consultants (refer to “II-Part1-3 Modification in the Mid-term Plan (Approved on March 30, 2007)”).

- To conduct risk management for the overall Agency, the PMDA has established the “Risk Management Committee.” In FY 2006, the Board of Directors, which includes members of the Risk Management Committee, convened weekly and discussed issues that should be prioritized and promptly addressed. The Agency staff have also continued to be familiarized with the risk management manual.

The Chief of the Audit Office, which is structured directly under the Chief Executive, has continued to conduct management of internal audit and internal reporting systems.

- To respond to disaster risks resulting from fires and earthquakes, the Agency informed all employees of the disaster prevention plan.

PMDA Risk Management System



★Risks the Agency may face:

a. Risks to the organization

・Possibility of an event that damages or threatens the reputation of the Agency in society

・Possibility of an event that significantly hinders or threatens the Agency's execution of operations

・Possibility of an event that financially damages or threatens the Agency

b. Risks that the Agency should address as part of its tasks

・Risks relating to the Agency's operations and that have the possibility of causing or expanding critical adverse health effects due to pharmaceuticals, medical devices, etc. (pharmaceuticals, medical devices, quasi-drugs and cosmetics, as well as agents and equipments subject to clinical trials).

1. (3) Advisory Council Meetings

- To create opportunities for exchanges of opinions between academic experts of diverse fields, the Agency established the "Advisory Council" (chaired by Masaaki Hirobe, Professor Emeritus at the University of Tokyo) consisting of academic experts, people involved in the medical field, representatives from relevant industries, consumer representatives and representatives of people who have suffered from adverse drug reactions caused by pharmaceuticals, etc. By seeking recommendations and improvement measures for operations and the management system, the Council is working to secure fairness and transparency of the Agency's operations, in addition to contributing to the streamlining of operations. Under the Advisory Council, the "Committee on Relief Services" (chaired by Hideaki Mizoguchi, Director of the Saitama Prefecture Red Cross Blood Center) and the "Committee on Reviews and Safety Operations" (chaired by Masaaki Hirobe, Professor Emeritus at the University of Tokyo) were also formed to discuss specialized issues relating to operations, and the dates of the meetings and specific agendas for FY 2006 are shown below.

In FY 2006, upon the expiration of the terms of members involved in the "Advisory Council," "Committee on Relief Services" and "Committee on Review and Safety Operations," new members were elected (including outside experts selected for the "Committee on Relief Services" through open recruitment). The new members have attended meetings for these Committees since the 2nd Advisory Committee Meeting held on October 3, 2006.

[Advisory Council – FY 2006]

Agenda for 1st Meeting (June 22, 2006)

(1) PMDA Operating Report for FY 2005

(2) Financial Report for FY 2005

Agenda for 2nd Meeting (October 3, 2006)

(1) Election of the Chairperson

(2) Appointment of Acting Chairperson

(3) Results of evaluation on actual operating performance in FY 2005

(4) Report on progress of major operations until the end of August 2006 and major issues

regarding operations in the second half of FY 2006
(5) Interim report by the Committee on Clinical Trial Issues
(6) Others
a. Handling of job restrictions of employees
b. Training for clinical trial coordinators

Agenda for 3rd Meeting (March 6, 2007)
(1) Modification of Mid-term plan (draft)
(2) Future organization of PMDA
(3) 2007 fiscal plan (draft)
(4) Financial plan for FY 2007 (draft)
(5) Report on employment status of personnel from the private sector
(6) Others

[Committee on Relief Services – FY 2006]

Agenda for 1st Meeting (June 2, 2006)
(1) Operating Report for FY 2005
(2) Others

Agenda for 2nd Meeting (December 5, 2006)
(1) Election of Chairperson
(2) Appointment of Acting Chairperson
(3) Actual operating performance for first half of FY 2006 and future perspectives
(4) Others

[Committee on Review and Safety Operations – FY 2006]

Agenda for 1st Meeting (June 1, 2006)
(1) Operating Report for FY 2005
(2) 2006 fiscal plan
(3) Others

Agenda for 2nd Meeting (December 4, 2006)
(1) Election of Chairperson
(2) Appointment of Acting Chairperson
(3) Actual operating performance for first half of FY 2006 and future perspectives
(4) Enhancement of consultations regarding clinical trials relating to medical devices
(5) Handling of job restrictions of employees
(6) Results of the APEC Network Symposium
(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, in principle, open to the public and the minutes, materials, etc., relating to the meetings are disclosed on the PMDA website.

- It was determined that “Handling of job restrictions of employees” would be discussed starting with the 2nd Advisory Council Meeting on October 3, 2006, and that “Job assignment status of personnel from the private sector,” “Work status of personnel from the private sector with regard to approval reviews of pharmaceuticals/devices and GMP conformity audits,” and “Total number of non-regular and administrative support personnel” would be reported on at meetings for the Advisory Council and the Committee on Review and Safety Operations after the 2nd meeting for the Committee on Review and Safety Operations held on December 4, 2006.

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

1. (4) Approaches for an Efficient Operation System

- The Agency is aiming 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 required flexible approaches in particular, the Agency successively adopted a structure where, in addition to adopting a group system, Review Directors are placed underneath the division head, and the Review Directors are in charge of each review team.

  The Agency also invites commissioned outside experts to ask for their professional opinions relating to scientifically significant matters at specialized discussions on reviews and safety measures (873 such commissioned external experts as of March 31, 2007).

  Similarly, the Agency invites commissioned external experts to ask for their opinions on adverse drug reactions from pharmaceuticals and adverse health effects caused by infections from biological products (50 such commissioned outside experts as of March 31, 2007 (11 of which are also commissioned as external experts for reviews and safety measures as described above)).

- The names of the commissioned outside experts are listed on the PMDA website.

- In progressing with operations, the Agency has also commissioned lawyers and accountants as advisors in order to handle operations that require specialized knowledge of laws and taxes. In addition, upon undertaking operational management of information systems and introducing a personnel evaluation system, the Agency made use of private companies to minimize increasing the number of permanent staff in the Agency. Feasibility studies for information system reform and assistance for operational reforms that were implemented in preparation for development of “Optimization Plan for Operations and Systems” were also commissioned to private companies.

- The Agency 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.

1. (5) Standardization of Operating Procedures

- In order to effectively utilize part-time staff and limit the number of permanent staff through standardizing various operating procedures, the Agency has developed Standard Operating Procedures (SOPs) for its major tasks. The contents of these SOPs have been confirmed and inspected, and revisions have been made as necessary. The Agency also used part-time employees for routine operations.

1. (6) Development of Databases

- In FY 2006, meetings for the “Management Committee on Information Systems” and “Committee on Investment for Information Systems” and 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 the Agency, and improvements in the security of the e-mail system were carried out.

  Also, the Agency promoted establishment of databases in order to systematically organize and store documents, as well as to enable for easy gathering and analysis of compiled information. This effort includes creating a database that compiles inquiries from the general public regarding the Agency’s relief fund operations. The Agency has also upgraded existing databases on information relating to new drugs, adverse drug reactions, and malfunctions in order to apply such information widely to its operations.

- From among the notifications issued by the MHLW and the Agency, those 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

1. (7) Approaches to Developing the Optimization Plan for Operations and Systems

- Incorporated administrative agencies in Japan are required to develop an Optimization Plan for Operations and Systems as soon as possible by the end of FY 2007, in accordance with national efforts. For this purpose, the Agency conducted operation and system diagnoses by using external consultants.

- In the first half of FY 2006, diagnoses of operations by review divisions were conducted, and in the second half of FY 2006, a diagnosis of operations by the Agency overall was carried out. Based on the results of these diagnoses, each division launched operational reforms.

- With the assistance of the Deputy CIO, who is an external expert, the Agency used external consultants to conduct surveys on the status of its information system resources, operating conditions and network configuration, as well as a feasibility study for information system reform.

2. Cost Control by Increased Efficiency of Operations

2. (1) Retrenchment of General Administrative Expenses

- In addition to improving operations and endeavoring to increase efficiency of management, the Agency is expected to make the following cutbacks for the budget in the Mid-term plan relating to general administrative expenses (excluding retirement allowance) at the end of the effective period for the Mid-term targets, through suppressing personnel expenses by reviewing wage levels and through the reduction of procurement costs.
  1) Approximately 15% cutback in comparison with FY 2003
  2) The general administrative expenses that are incurred starting in FY 2004 in connection with revisions to laws and systems, etc., are to be cut back by approximately 12% in comparison with FY 2004.
  3) The general administrative expenses that are incurred starting in FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 are to be cut back by approximately 9% in comparison with FY 2005.

  The budget in the Mid-term plan 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. The Agency is to develop a fiscal budget plan based on the Mid-term plan and achieve the Mid-term targets by appropriately operating within the planned budget.

- In order to efficiently enforce the fiscal budget plan, the periodic salary increase for the Agency's permanent staff has been continuously halted since FY 2006 based on the fiscal year plan. In addition, the Agency made efforts to reduce procurement costs, such as by developing information disclosure standards for negotiated contracts and introducing an open competitive bidding system for external outsourcing such as of English language training based on the "Notice to Optimize Contract Procedures" issued by the Committee of Chief Executives from Agencies under the MHLW held in June 2006. As a result, general administrative expenses were reduced by 2.8% with respect to the budget, even when excluding unnecessary expenditures due to personnel vacancies.

2. (2) Cost Control of Project Expenses

- By increasing efficiency of operations through promoting computerization, the Agency is expected to make the following cutbacks with regard to the budget in the Mid-term plan relating to project expenses (excluding expenses related to payment of benefits and single-year expenses due to new project launches) at the end of the effective period for the Mid-term targets.
  1) Approximately 5% cutback in comparison with FY 2003
  2) The project expenses that are incurred starting in FY 2004 in connection with revisions to laws and systems are to be cut back by approximately 4% in comparison with FY 2004.
  3) The project expenses that are incurred starting in FY 2005 in connection with the enforcement of the revised Pharmaceutical Affairs Law in FY 2005 are to be cut back by approximately 3% in comparison with FY 2005.

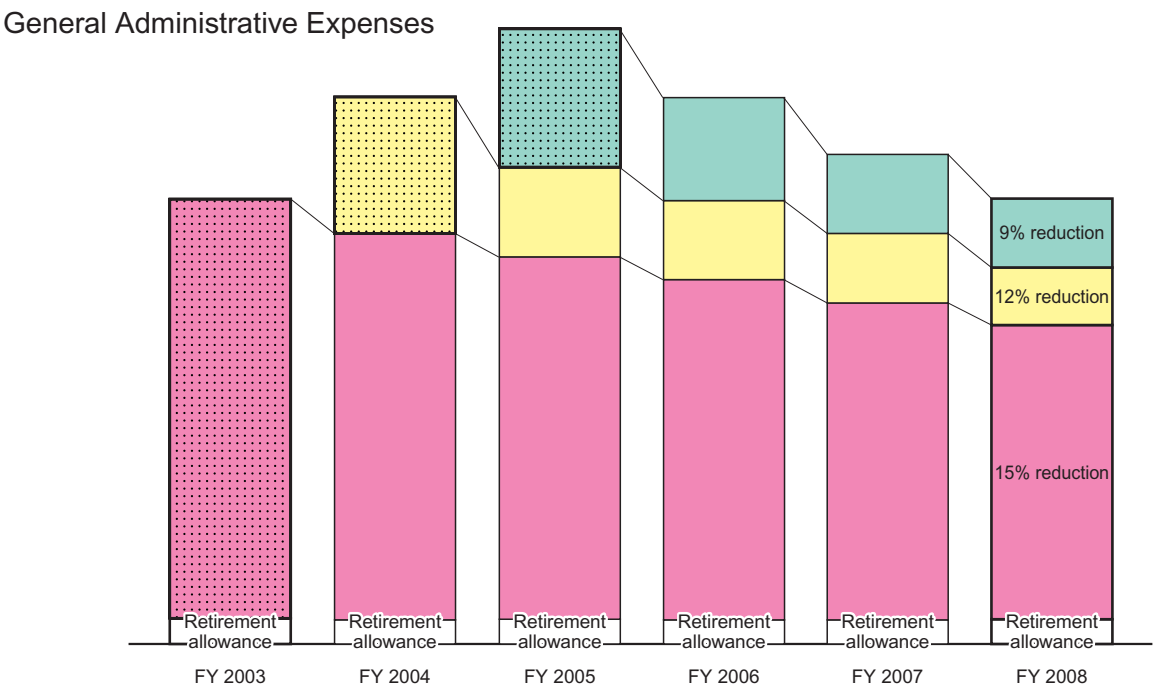
The budget in the Mid-term plan relating to project expenses is based on the Mid-term targets for cost control as directed by the Minister of Health, Labour and Welfare. The Agency is to develop a fiscal budget plan based on the Mid-term plan and achieve the Mid-term targets by appropriately operating within the planned budget.

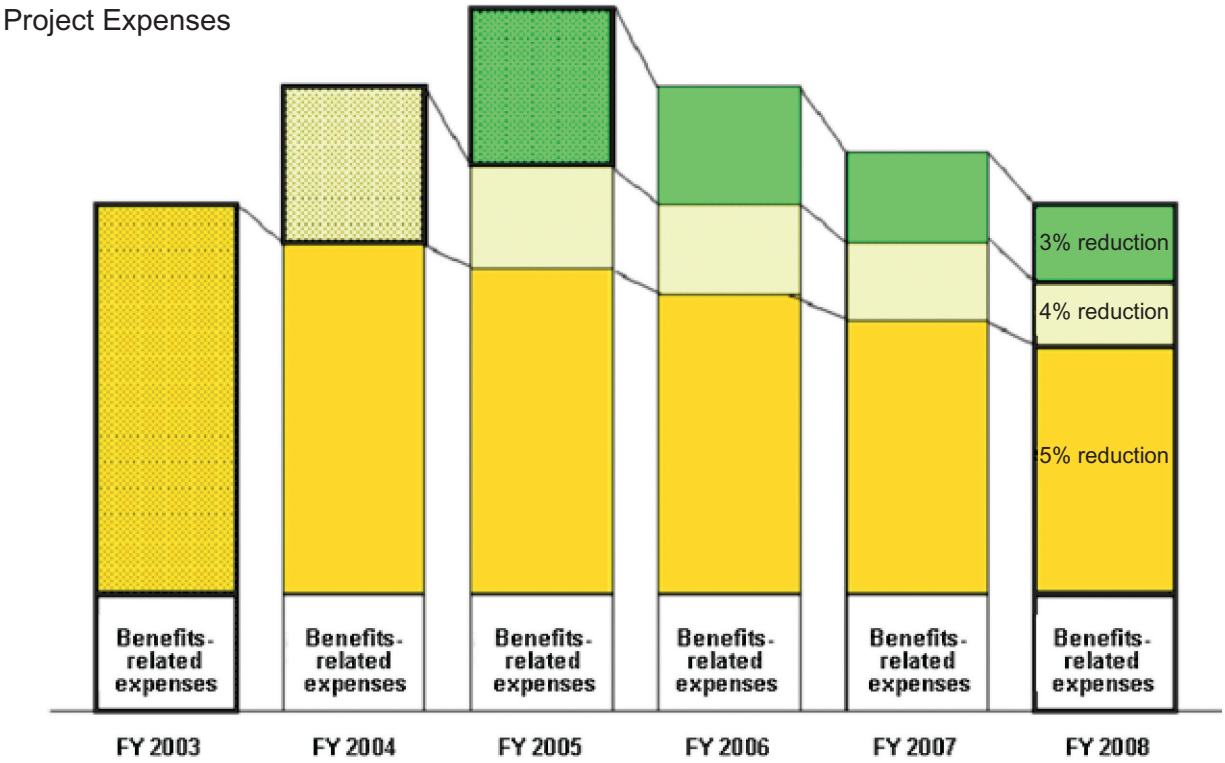
- In FY 2006, the Agency reviewed its expenditures taking the financial results from FY 2005 into consideration, and made efforts to increase efficiency such as by promoting computerization. In calculating various system development costs, cost reductions were planned such as by commissioning external system experts to conduct detailed audits and using an open competitive bidding system for procurement of foreign magazines and data processing service. The Agency also carried out sound operational management and reviewed unnecessary expenses, while observing profit-making trends from incomes consisting of user fees and contributions, which serve as the financial resources of various operations. As a result, the project expenses were reduced by 6.0% with respect to the budget.

Number of General Competitive Bids Based on Disclosure Standards

FY 2006: 21 bids (of which 5 were regarding general administrative expenses)
FY 2005: 18 bids (of which 7 were regarding general administrative expenses)
FY 2004: 9 bids (of which 6 were regarding general administrative expenses)

Reduction in General Administrative Expense and Project Expenses (Simplified graph)





2. (3) Collection and Management of Contributions

- Contributions from marketing authorization holders of the industry enable the Agency to secure financial resources for adverse drug reaction relief for adverse health effects, consisting of adverse drug reactions caused by pharmaceuticals and infections derived from biological products, and other operations to improve the quality, efficacy and safety of pharmaceuticals and medical devices. Specifically, contributions for the adverse drug reaction fund are declared and made by marketing authorization holders of approved drugs, contributions for relief for infections derived from biological products 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 pharmaceuticals and medical devices.

- The Agency upgraded its contribution collection management system that manages all collections of contributions for the adverse drug reaction fund, contributions for relief for infections derived from biological products and contributions to safety measures, so that basic data, such as those concerning newly approved items (pharmaceuticals and medical devices), money transfer information, etc., can be automatically processed. This upgrade aims at streamlining management of contribution collection operations, which include calculation of basic trading amounts of marketing authorization holders and processing of data on unpaid contributions. The Agency 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.

- the Mid-term plan, the Agency sets the contribution collection rate for the adverse drug reaction

fund and infection contributions to be no less than 99% by the end of effective period for the Mid-term targets. In FY 2006, the resulting contribution collection rate for the adverse drug reaction fund was 99.7%, and the rate for infection contributions was 100%.

- Similarly, the Agency sets the contribution collection rate for contributions to safety measures to be no less than 99% by the end of effective period of the Mid-term targets in the Mid-term plan. In FY 2006, the resulting contribution collection rate for contributions to safety measures was 98.3%.

FY 2006 contribution collection results

Category		Subjects (cases)	Number of payers who made contributions (cases)	Collection rate	Contribution amount
ADR Contributions	MAH	778	778	100%	3,240
	Pharmacy	9,002	8,968	99.6%	9
	Total	9,780	9,746	99.7%	3,249
Infectious disease contributions	MAH	101	101	100%	556
Safety measures contributions	MAH	3,344	3,180	95.1%	1,211
	Pharmacy	9,002	8,960	99.5%	9
	Total	12,346	12,140	98.3%	1,220

MAH : Marketing Authorization Holder

- To efficiently improve contribution collection rates,
  1) The Agency continued to commission the Japan Pharmaceutical Association to collect contributions from marketing authorization holders of pharmacy-compounded drugs.
  2) The Agency continued to call for requests to declare and make contributions to safety measures through industry associations and lectures, as well as through advertisements on websites and relevant trade journals. The Agency 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.

2. (3).1. Collected contributions for adverse drug reaction fund and shifts in the liability reserve

a. Adverse drug reaction fund

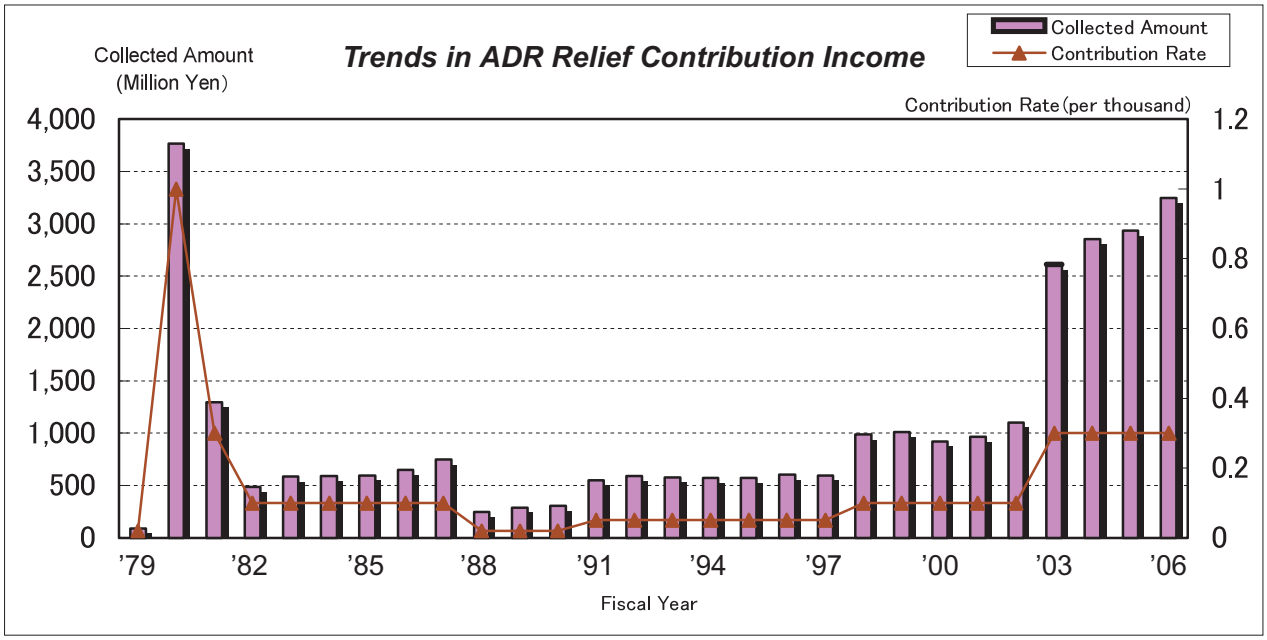
- To fund the adverse drug reaction relief service, the Agency has collected adverse drug reaction funds from marketing authorization holders of approved drugs. In FY 2006, the contribution rate applied toward such marketing authorization holders was 0.3/1000 and the

collected amount was 3,249 million yen.

(Million yen)

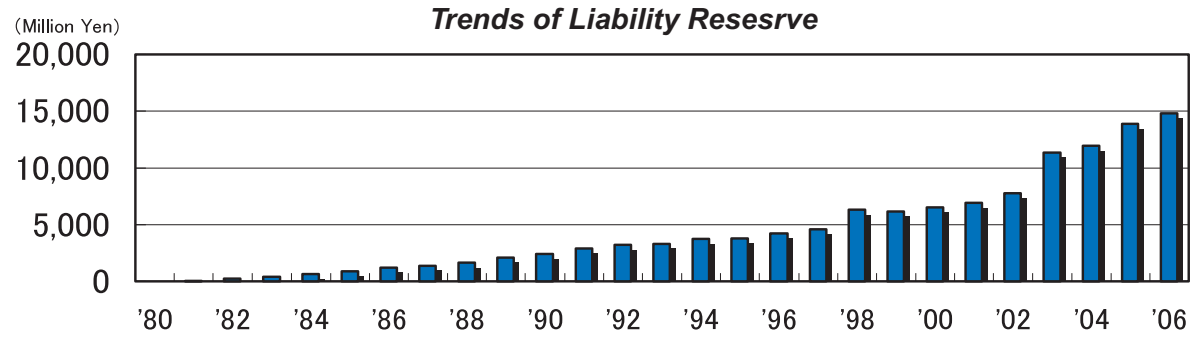
Fiscal year	FY2003 (number of MAHs)	FY2004 (number of MAHs)	FY2005 (number of MAHs)	FY2006 (number of MAHs)
MAH of approved drugs	2,596 (842)	2,844 (833)	2,923 (787)	3,240 (778)
MAH of pharmacy-compounded drugs	11 (11,175)	11 (10,550)	10 (9,993)	9 (8,968)
Total amount	2,607	2,855	2,933	3,249
Contribution rate	0.3/1000	0.3/1000	0.3/1000	0.3/1000

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



b. Liability reserve

- To cover the estimated relief benefit service costs that eligible persons will receive in the future, the Agency calculates the amount that they should possess at the end of every fiscal year and accumulates funds accordingly. The liability reserve at the end of FY 2006 was 14,825 million yen.



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

2. (3).2. Collected contributions for relief for infections derived from biological products

- To fund the relief service for infections derived from biological products, the Agency has collected infection contributions from marketing authorization holders of approved biological products. In FY 2006, the contribution rate applied toward such marketing authorization holders was 1/1000 and the collected amount was 556 million yen.

(Million yen)

Fiscal year	FY 2004	FY 2005	FY 2006
MAH of approved biological products	554 (108 companies)	553 (105 companies)	556 (101 companies)
Contribution rate	1/1000	1/1000	1/1000

2. (3).3. Collected contributions for safety measures

- To fund services for improvements in quality, efficacy and safety of pharmaceuticals, etc., the Agency has collected contributions to safety measures from marketing authorization holders of pharmaceuticals and medical devices. In FY 2006, the contribution rate applied towards such marketing authorization holders was 0.11/1000 and the collected amount was 1,220 million yen.

(Million yen)

Fiscal year	FY 2004 (number of MAHs)	FY 2005 (number of MAHs)	FY 2006 (number of MAHs)
MAH of drugs/medical devices	1,091 (3,076)	1,143 (2,982)	1,211 (3,180)
MAH of pharmacy-compounded drugs	10 (10,541)	10 (9,987)	9 (8,960)
Total amount	1,101	1,153	1,220
Contribution rate	0.11/1000	0.11/1000	0.11/1000

2. (4) Reduction in Personnel Expenses and Overhaul of the Pay System

- In line with the policy stating that “fundamentally, personnel expenses should be reduced by at least 5% within the next 5 years, in accordance with the Mid-term targets. In addition, the pay system for Agency staff should be reconsidered taking the structural reform of the civil servant wage system into account,” which is included in the “Major Policies of Administrative Reform” (approved in a Cabinet meeting on December 24, 2005), and based on the directive by the MHLW dated March 31, 2006, the Mid-term plan was revised to specify that within the 5 years after FY 2006, the Agency will reduce personnel expenses by at least 5%, and that by FY 2008, which is the final year of the primary period for the Mid-term targets, the Agency will reduce personnel expenses by at least 3%.

- In FY 2006, the Agency was able to reduce personnel expenses by approximately 2.7%, even when excluding reductions resulting from personnel vacancies, by suspending periodic salary increases for permanent staff who met certain criteria and by hiring young people.

- Together with the implementation of a new personnel evaluation system starting in April 2007, the Agency also developed a new salary system based on structural reforms in the civil servant wage system, and made necessary revisions to the salary regulations, etc.

3. Improvement of Services to the Public

3. (1) General Consultation Service

- Based on the “General Consultation Guidelines” that specifies how to handle inquiries directed towards the Agency and how to reflect comments and opinions to improve operations, the Agency is managing a general consultation service and makes questionnaires available at its reception counter, enabling for comments and opinions of visiting customers regarding the Agency’s overall operations to be gathered. In gathering opinions, etc., the Agency started enabling for visitors to send opinions, requests, complaints, etc., via fax in November 2006. To provide increased convenience to visitors, the Agency is also implementing the consultation service all day, including during lunch breaks.

- Among the 2,394 inquiries that the Agency received in FY 2006, 1,452, or approximately 60% of the total inquiries received, were those relating to applications and consultations for pharmaceuticals and medical devices.

FY 2006	Inquiry / consultation	Complaint	Opinion / request	Others	Total
Total # of consultations	2,387 (1,446)	3 (3)	4 (3)	0 (0)	2,394 (1,452)

1. The numbers in parentheses indicate the cases related to consultations and applications for drugs and medical devices approval. They are included in the total numbers above.
2. The Office of Review Administration also accepts inquiries on consultations and applications for drugs and medical devices approval, separately from this general consultation service.

3. (2) Responses to Consultations, Complaints and Claims of Dissatisfaction from the Private Sector regarding Reviews and Safety Operations

- In addition to responding to consultations and complaints from general consumers, the Agency also handles complaints from the private sector regarding reviews and safety operations.

- For inquiries relating to progress on reviews for new drugs, new medical devices and improved medical devices, meetings are set up with the office director of the Agency in charge of the applicable review case. During these meetings, the office director explains the estimated time required to reach the next review stage. In FY 2006, the Agency handled consultations in such a way for 87 cases regarding new drugs and 3 cases each for new medical devices and improved medical devices.

Number of inquiries from companies on review progress of new drugs

Division	Therapeutic category		Total cases
Office of New Drug I	Category 1	Gastrointestinal drugs, dermatologic medicines	2
	Category 4	Antibacterial agents, vermifuge, antifungal agents, antiviral agents except anti-HIV agents	1
	Oncology drugs	Anti-cancer drugs	6
	Anti-AIDS drugs	Anti-HIV agents	0
Office of New Drug II	Category 2	Cardiovascular drugs, anti-Parkinson's disease drugs, antithrombotics, anti-Alzheimer's disease drugs	12
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs	12
	Radio-pharmaceuticals	Radiopharmaceuticals	0
	In vivo diagnostics	Contrast medium	0
Office of New Drug III	Category 3	Central/peripheral nervous system drugs, sensory organ drugs (except drugs classified in category 6-1), narcotics	10
	Category 6-1	Respiratory tract drugs, anti-allergy drugs, sensory organ drugs for inflammatory diseases	27
	Category 6-2	Hormone drugs, drugs for metabolic disorders (excluding combination drugs)	10
Office of Biologics	Biological products	Vaccines, antitoxic serum	2
	Blood products	Serum globulin, blood coagulation factors	4
	Cellular and tissue-derived products	Products for cell therapy	1
Total			87

- In FY 2004, the Agency has established a system where, if an applicant files claims of dissatisfaction, etc., regarding reviews and safety measures, the 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. In FY 2006, there were no claims of dissatisfaction regarding reviews and safety measures.

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

3. (3) Development of the PMDA Website

- The Agency compiled “Operating Report for FY 2005” regarding actual operating performance in FY 2005 and “Report for First Half of FY 2006” on operations from April to September 2007, and have posted them on the PMDA website.

- In addition, materials used in Advisory Council meetings were also posted on the website sequentially.

- On March 30, 2007, the Agency upgraded the main PMDA Web page and the Information Pages of the PMDA website, which had gained more pages and contents, to reorganize the structure and contents. On the same day, the English version of the PMDA website was also upgraded and reorganized to provide information in an easier and more user-friendly manner.

- In accordance with the “Implementation Guidance on Face-to-face Consultations and Examination for Issuing Certificates by the PMDA” (Notification No. 0330004 of the Chief Executive of the PMDA, dated March 30, 2007), the Agency integrated contents relating to face-to-face consultations (consultations regarding clinical studies and simple consultations) with those of preliminary consultations, making them more easy to understand for those seeking consultations.

3. (4) National Forum on Pharmaceuticals and Medical Devices

- The Agency held the “National Forum on Pharmaceuticals and Medical Devices” at the Yurakucho Asahi Hall on Saturday, December 2, 2006, in order to widely inform the public of the Agency’s operations and activities for these operations, as well as to educate the public on the significance and appropriate use of pharmaceuticals and medical devices.

  The forum, which had the theme of “Learning More about Pharmaceuticals and Medical Devices — for Reliable Medical Care,” focused on pharmaceuticals as well as medical devices and consisted of keynote lectures, a mini seminar and a panel discussion.

  Part I of the forum consisted of keynote lectures by two experts: Dr. Yasufumi Sawada, professor

of Laboratory of Drug Informatics, Graduate School of Pharmaceutical Sciences at the University of Tokyo, and Dr. Kunihiko Fukuda, professor at the Jikei University School of Medicine.

For the mini seminar, the theme was “Correct Knowledge on Pharmaceuticals and Medical Devices: How to Make Best Use of the PMDA Website,” and PMDA staff members made a presentation.

Part II of the forum consisted of a panel discussion led by Ms. Megumi Yoshimoto, a former NHK announcer, who served as the coordinator.

Over 300 participants attended the forum, including people involved in the medical field, students and the general public.

Part I

Keynote Lectures

Lecture 1: “Becoming More Familiar with Pharmaceuticals”

Dr. Yasufumi Sawada (Professor of Laboratory of Drug Informatics, Graduate School of Pharmaceutical Sciences, University of Tokyo)

Lecture 2: “Looking Deeply into Your Body”

Dr. Kunihiko Fukuda (Professor, Jikei University School of Medicine)

Mini Seminar: “Correct Knowledge on Pharmaceuticals and Medical Devices: How to Make Best Use of the PMDA Website”

Part 2

Panel Discussion “For Reliable Medical Care”

▶Panelists

Dr. Hatsuo Aoki (President of Japan Pharmaceutical Manufacturers Association)
Yoko Kishimoto (Writer)
Dr. Yasufumi Sawada (Professor of Laboratory of Drug Informatics, Graduate School of Pharmaceutical Sciences, University of Tokyo)
Dr. Kunihiko Fukuda (Professor at Jikei University School of Medicine)
Kiyoshi Mamiya (Deputy Chief Caretaker, Japan Confederation of Drug-induced Sufferers Organizations)
Takashi Wachi (Chairman, Japan Federation of Medical Devices Associations)
Akira Miyajima (Chief Executive, Pharmaceuticals and Medical Devices Agency)

▶Coordinator

Megumi Yoshimoto (Former NHK announcer)

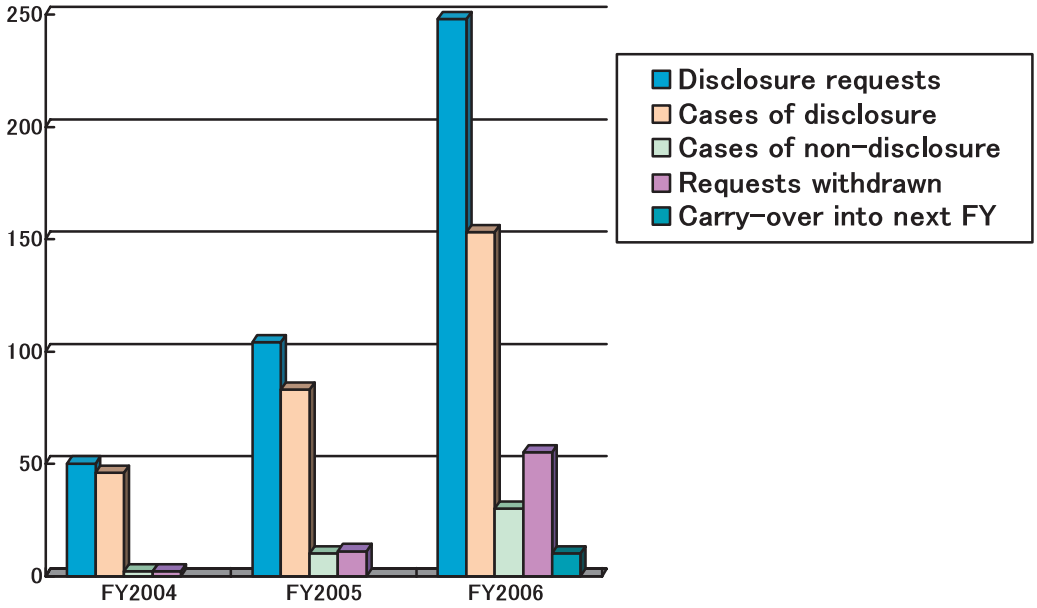
3. (5) Disclosure Request for Corporate Documents

- The table below shows the numbers of requests for disclosure of information. There were no requests for disclosure of personal information based on the Personal Information Protection Law.

- In FY 2006, there 6 objections regarding requests for disclosure of corporate documents. Consultations and deliberations on these objections are planned on being held with the Committee on Information Disclosure and Personal Information Protection.

Number of disclosure requests of corporate documents

	Total requests	Requests withdrawn	Decisions					Objections	Carry-over into next FY
			Full disclosure	Partial disclosure	Non-disclosure	Documents not existing	Refusal to answer on existence/ non-existence of the document		
FY 2004	50	2	9	37	0	2	0	0	0
FY 2005	104	11	13	70	4	6	0	4	0
FY 2006	248	55	15	138	9	21	0	6	10
Total	402	68	37	245	13	29	0	10	10



1. The number of cases of disclosure includes full and partial disclosure.
2. The number of cases of non-disclosure includes cases of non-existing documents.

Number of disclosure requests of corporate documents by requester

Requester/fiscal year	FY 2004	FY 2005	FY 2006	Sum total
Individuals	35	74	113	222
Corporates (e.g., Drug manufacturers)	14	25	132	171
Press	1	5	3	9
Total	50	104	248	402

"Individuals" include requests made under an individual name, even if it substantially represents a corporation.

Number of disclosure requests of corporate documents by operational category

	FY 2004	FY 2005	FY 2006	Examples
Approval review	8	22	90	Marketing authorization application for drugs not subject to approval
GLP/GCP/GMP/ QMS etc. conformity audits	32	69	117	Notice of GCP audit results
Post-marketing safety	8	13	40	ADR report
Others	2	—	1	Business trip order forms
Total	50	104	248	

The numbers include requests that were withdrawn or decided not to be disclosed, and those for non-existing documents.

3. (6) 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, the Agency 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 of the Agency's management and operations.

- In FY 2006, the Agency conducted internal audits on the management of the corporate documents and personal information that it possesses.

3. (7) Report on Financial Standing

- To ensure transparency of its expenditures, the Agency disclosed its financial standing, including the use of contributions and user fees from reviews, in government gazettes and on the PMDA website.

4. Personnel Issues

4. (1) Review of a Personnel Evaluation System

- The Mid-term targets for the Agency require that personnel evaluation that takes work performance of the staff into consideration be implemented appropriately. In the Mid-term plan, the Agency aims to establish such a personnel evaluation system that motivates the staff and that appropriately reflects the evaluations and achievements of the staff through remunerations, salary increases and promotions.

- For this purpose, the Agency experimentally implemented an evaluation system that was

developed at the Panel on Personnel Evaluation System from April to September 2006 in anticipation of the full-fledged implementation of the system starting in April 2007. The entire staff was evaluated through this trial system in order to detect and review problems.

- Also, the Agency formed a working team to adopt opinions from personnel involved in various operations, and to consider individual issues regarding the personnel evaluation system (grade system, evaluation system and salary system). Based on discussions conducted by this working team, the Agency developed necessary rules, such as those for personnel evaluation.

4. (2) Systematic Implementation of Staff Training

- In the operations for reviews, post-marketing safety measures and relief conducted by the Agency, an extremely high level of expertise is required. In addition, rapid strides are constantly in the advancement of scientific technology for developing pharmaceuticals and medical devices. Under such circumstances, it is necessary for the Agency to appropriately implement capacity development to enhance the level of expertise of the staff. Therefore, in FY 2006, the Agency systematically implemented various staff training programs in accordance with different types of operations and targets. To enable for efficient and effective training adapted to the qualifications and skills of each staff member, external institutions and experts were used to strive for enriched training. In addition, the Agency has had its staff actively participate in academic conferences in both Japan and overseas, to enable them to absorb new knowledge and improve their skills.

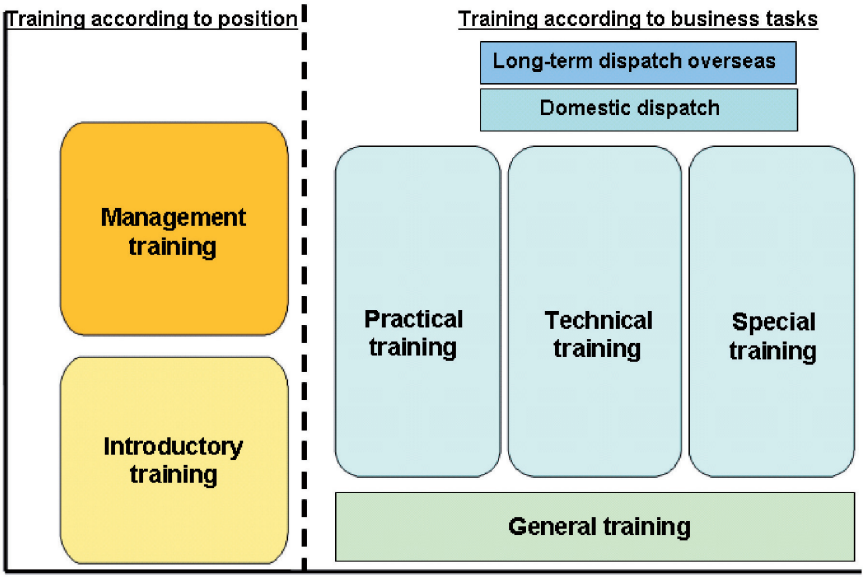
- Specifically, the Training Committee devised plans for introductory training, internal training and external training based on the needs of each division. Various training programs, as introduced below, were implemented.
    1) In addition to conducting introductory training and training for management personnel in April and October of 2006, the Agency dispatched a total number of 58 staff members to universities in Japan and overseas, as well as to foreign pharmaceutical regulatory authorities for training.
    2) As special training programs, the Agency also held 13 training sessions on technical issues, inviting experts who belong to domestic or foreign regulatory authorities, corporations and universities.
    3) As practical training programs, the Agency held courtesy training sessions twice in April 2006, as well as a training session by external institutions for book-keeping and for financial matters trainings once each, which were open to administrative employees.
    4) In May and June of 2006, the Agency conducted the “Test of English for International Communication (TOEIC)” as training for the English language. The Agency also provided an English conversation training program from November 2006 to March 2007, the contents of which had been considered by the Training Committee.
    5) In addition to conducting general training on pharmaceutical affairs (implemented once) for administrative staff who are aiming to learn basic knowledge relating to pharmaceutical affairs, the Agency also held another training session (implemented once) where lecturers from organizations for sufferers of drug-induced diseases and

patient organizations speak on what is desired of the PMDA from the perspectives of sufferers and patients.

- For newly appointed members, the Agency also provided facility tours (at 3 pharmaceuticals manufacturing plants, 3 medical device manufacturing plants, 6 medical institutions and 2 research institutes) from May to December of 2006.

- In addition, the extent of participation in academic societies from each division were tracked and checked every fiscal quarter (664 participants in total as of the end of March 2007).

Various training systems



4. (3) Appropriate Personnel Allocation

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

- To achieve this target, the Agency conducted personnel allocation taking the knowledge and work experience of staff members into consideration. The Agency fundamentally avoids short-term rotation of personnel with the exception of cases such as health-related issues and special reasons related to operations.

4. (4) Securing Human Resources through Open Recruitment

- In order to ensure smooth enforcement of the revised Pharmaceutical Affairs Law from 2005 and to execute rapid and proper reviews and safety measures, it is an important issue for the Agency to recruit competent human resources with high levels of expertise, while paying due consideration to the neutrality and fairness of the Agency.

- The Mid-term plan specifies that the Agency is to have 317 permanent executive and regular

employees at the beginning of the Mid-term period (April, 2004), and 346 such employees by the end of the Mid-term period (March, 2009) (these numbers were set before the revision of the Mid-term plan at the end of FY 2006). However, the Agency started with 256 permanent executive and regular employees at the beginning of the effective period of the Mid-term plan, which was significantly lower than expected in the plan.

- Therefore, the Agency has made efforts to increase competent human resources for the understaffed areas through open recruitment, which resulted in 319 permanent executives and regular employees as of April 1, 2006. Even afterwards, the Agency has subsequently recruited employees through announcements on the PMDA website and in specialized magazines, constituting 7 instances of open recruitment for permanent staff and 9 instances of open recruitment for non-regular personnel. The numbers of employed and informally appointed staff are shown below.

Employment through open recruitment in fiscal 2006 - as of April 1, 2007

1) Technical staff (Open recruitment, 5 times)	
Number of applicants	About 320
Number of the employed	28
Number of the persons scheduled to be employed	16
2) Administrative staff (Open recruitment, twice)	
Number of applicants	About 150
Number of the employed	6
3) Non-regular experts (Open recruitment, 9 times)	
Number of applicants	About 60
Number of the employed	15
Number of the persons scheduled to be employed	3

- As a result of open recruitment in FY 2006, the Agency was able to increase the number of personnel by 50. However, due to a substantial decrease of personnel sent from affiliated organizations, the total permanent staff number was 341 as of April 1, 2007.

  As the goal is to increase the number of staff by 236 in the three years from FY 2007 to FY 2009 (58 employees in FY 2007, 80 in FY 2008 and 98 in FY 2009), the Agency is to continuing with further efforts for open recruitment to secure sufficient competent human resources for the understaffed fields.

- The Agency is making efforts to recruit competent human resources for GMP audits and biostatistics, areas for which it is particularly difficult to secure personnel, by provisionally establishing special measures regarding restrictions prescribed in work regulations, taking neutrality and fairness of the Agency into consideration, so that recruitment from the private sector can be facilitated. However, in FY 2006, no employees were recruited through these special measures.

Numbers of the Agency's permanent staff members

	April 1, 2004	April 1, 2005	April 1, 2006	April 1, 2007	Numbers expected at the end of FY 2008 (in Mid-term plan)
Total	256	291	319	341	484
Review section	154	178	197	206	—
Safety section	29	43	49	57	—

1. *The expected number of the staff including executives at the beginning of effective Mid-term period when the Agency was established, April 2004, was 317 (The number includes 11 staff members engaged in the R&D promotion service of the Agency).*
2. *The "Total Staff # in Agency" includes 6 executives, except for April 1, 2006, which includes 5 executives.*
3. *The "Total Staff # in Agency" as of April 1, 2004 includes 11 staff members engaged in the R&D promotion service. Before the service were transferred to the National Institute of Biomedical Innovation (NIBIO) in FY 2005, the planned total number at the end of the Mid-term plan (at the end of FY 2008), was 357. Before the Mid-term plan was revised at the end of FY 2006, the planned total number at the end of the Mid-term plan (at the end of FY 2008) was 346.*
4. *The Review Section consists of Director of the Center for Product Evaluation, Associate Center Directors, Office of Review Administration, Office of New Drug I, II, and III, Office of Biologics, Priority Review Director, Office of OTC/Generic Drugs, Office of Medical Devices and Office of Conformity Audit.*
5. *The Safety Section consists of Chief Safety Officer, Office of Safety and Office of Compliance and Standards.*

4. (5) Appropriate Personnel Management Based on Work Regulations

- The Agency is careful in conducting appropriate personnel management so that suspicions of inappropriate ties with the pharmaceutical companies do not arise, by imposing certain restraints on recruitment and allocation of executives and regular employees as well as on reemployment after retirement from the Agency.

- For this purpose, the Agency is conducting appropriate personnel management by prescribing, in the work regulations, restrictions for newly-employed staff members regarding the submission of a written oath, personnel allocation and reemployment after retirement, as well as work restrictions for staff members whose family members work in the pharmaceutical industry. The Agency also strives to keep its staff members informed of these regulations.

- More specifically, (1) the Agency revised its work regulations to require its staff members to submit a written oath relating to compliance with the work regulations, and (2) revised its ethical standards that prescribe ethical behavior criteria and the prohibition of particular interactions between the staff members and stakeholders, such as pharmaceutical companies. The Agency also created summaries and a Q&A list concerning relevant regulations, and is making sure to keep staff members informed through the internal website and during introductory training.

- In addition, from the perspective of further informing the staff about service-related regulations, the Agency has created a handbook that includes service disciplines that should be followed by the staff and a Q&A list, and has distributed this handbook to all of the staff members.

5. Ensuring Security

5. (1) Management of Entries and Exits

- To ensure security and protect confidential information, the Agency has installed entrance/exit control equipment for each office and is reinforcing the internal security control system.

- By introducing a security 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 or leaves each office, outsiders are not able to enter the rooms unaccompanied.

- In order to ensure further strict access control, the Agency has also prescribed restrictions on the entrance/exit control relating to operational management of the security control system, and has made maximum efforts to inform staff members about these restrictions through the internal website and during introductory training.

5. (2) Security Measures for Information Systems

- Based on the 2006 fiscal plan, the Agency has strived to ensure security of the information relating to information systems.

- In FY 2006, the Agency considered backup methods for data to be sent to remote external consignees, for the purpose of enhancing the backup functions for information and data. To prevent leaks of information and data through operations, the Agency also started making revisions to various rules, including those for management and use of information systems, in conjunction with revisions to rules for document management.

- The Agency has developed a new e-mail system (Secure Mail) to achieve smooth and prompt information exchange between applicants and Agency representatives regarding reviews, etc. In January 2006, the Agency started accepting registration from the private sector for trial operation of this system, and the trial was conducted from April to June 2006, followed by full operation starting in July 2006.

- To further improve security, the Agency expanded the usage scope of Secure Mail, which once had been limited to correspondence with applicant companies on reviews of new drugs, face-to-face consultations regarding new drugs and surveys on investigational new drug applications, to include issues relating to conformity audits starting in March 2007.

Number of users/issued certificates using the secure e-mail system by the end of March 2007

	Number of registered companies	Number of issued certificates
Outside the Agency	33	96
Within the Agency		85

PART 3. IMPROVEMENT IN MANAGEMENT OF OPERATIONS AND QUALITY OF SERVICES IN EACH DIVISION

1.Relief Fund Services

To widely inform the public on the Adverse Drug Reaction Relief System and the Relief System for Infections derived from Biological Products (hereinafter referred to as “relief systems”), and to operate these relief systems appropriately, the Agency, through relief fund services, is taking the following measures to provide adequate and prompt relief for those suffering from adverse drug reactions caused by pharmaceuticals and infections derived from biological products.

1. (1) Expansion and Reconsideration of the Provision of Information

1. (1). 1. Disclosure of cases of payment of benefits on the Website

- To enrich the contents of the provision of information relating to the relief systems and making the administration of the systems more transparent, the Agency plans on disclosing information about actual performance of operations achieved in FY 2006 on the PMDA website. In addition, the Agency has finished posting cases judged for approval/rejection up until the third quarter of FY 2005 on the website with due consideration to protecting personal information. The Agency is also planning on providing information on cases judged after FY 2006 successively on the website.

  Cases of approval/rejection: http://pmda.go.jp/hkenkouhigai/help/information2.html

1. (1). 2. Improvement of pamphlets, etc.

- Improvements were made to pamphlets and instruction manuals about applying for relief benefit payments, so that the contents can be easily used and understood by doctors and patients.

- To reduce the amount of time required for administrative processing due to incomplete applications, and to make operations more efficient, the Agency carried out the following.
  a) Created and distributed brochures describing the relief systems in an understandable manner, and in addition, posted the brochures on the PMDA website (in PDF format) together with animations summarizing the brochure.
  b) Created an application sample and made improvements so that patients, etc., can fill out the forms more easily.
  c) Applications, which used to be mailed upon request, are now available for download on the PMDA website, and the URL from which applications can be downloaded are included in pamphlets, enabling for easier use.

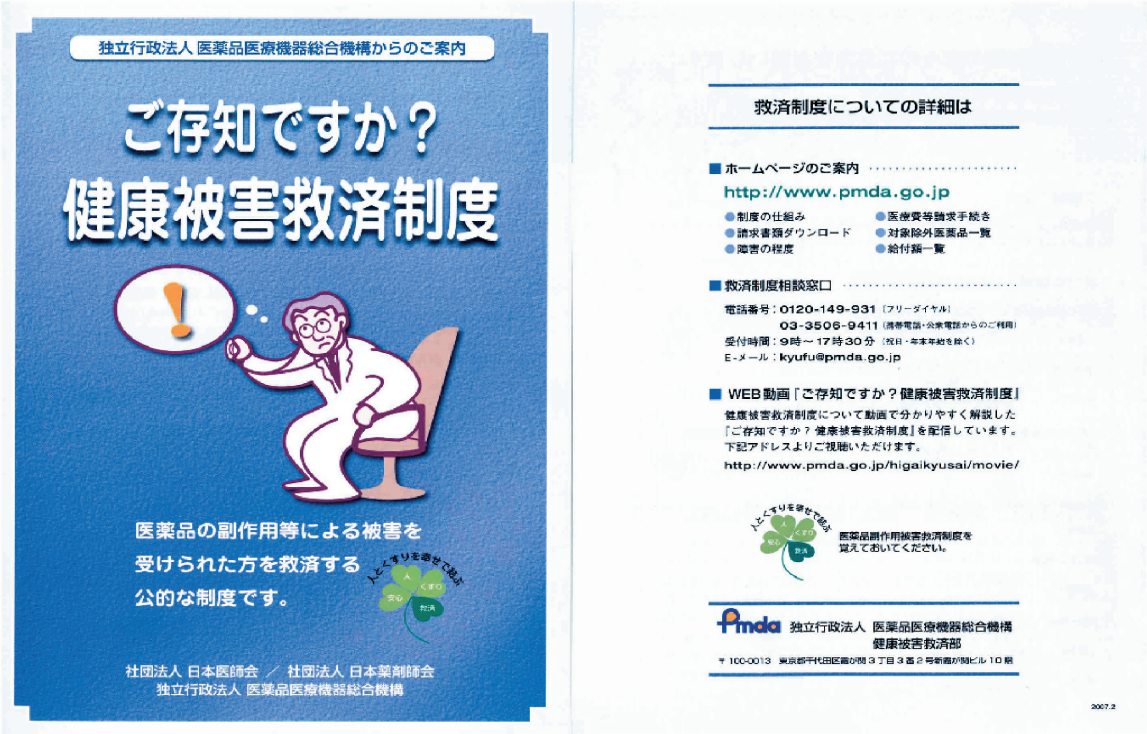
  Application forms are available at: http://search.pmda.go.jp/fukusayo_dl/

1. (2) Active Implementation of Public Relations Activities

- To widely inform the public of the relief systems, the Agency reviewed methods for effective publicity and carried out the following :
  1) Publicity through a brochure entitled “Do you know about Relief Services?” explaining the relief systems in an easily understandable manner (this brochure is included in magazines published by the Japanese Association of Medical Sciences and the Japan Pharmaceutical Association; the contents of this brochure have also been summarized into animations and posted on the PMDA website, along with a PDF version of the brochure), publicity via the Internet (banner advertisement on 2 websites directed exclusively towards medical professionals, keyword-linked advertisement on 7 general websites, promotion on “So-net M3,” a site directed towards doctors), and publicity through *yakutai*, or paper bags in which hospitals, pharmacies, etc., give prescription medication to patients).
  2) Publicity on the infection relief system in 6 specialized magazines, and publicity on commissioned payment services for HIV positive patients, etc., in 5 specialized magazines.
  3) Introduction of the relief systems in the Abstract Journal of Japan Municipal Hospital Association.
  4) Participation in medical conventions (Annual Meeting of Japanese Society of Pharmaceutical Health Care and Sciences, Japan Pharmaceutical Association Congress of Pharmacy and Pharmaceutical Science, and Annual Meeting of the Pharmaceutical Society of Japan) and lectures on the relief systems at 8 different events.
  5) Explanations on the relief systems at 6 different medical institutions in Japan.
  6) Implementation of publicity for the “20th Annual Meeting of the Japanese Society for AIDS Research,” such as through poster displays, articles in journals and distribution of materials relating to the relief systems overall.

- With help from concerned bodies, the following were carried out as individual PR activities :
  1) Publicity in a magazine on drug safety updates (DSU) published by the Federation of Pharmaceutical Manufacturers’ Associations of Japan; the magazines were distributed to all medical institutions.
  2) With help from Japan Pharmaceutical Association, pamphlets introducing the relief systems were distributed to pharmacies.
  3) With help from the Japanese Red Cross Society Blood Center, pamphlets introducing the relief systems were distributed to medical institutions.
  4) Introduction of the relief systems in “Drug Handbook,” published by the Japan Pharmaceuticals Association, etc.

Publicity through brochures



- To convey the concepts of the relief systems in an understandable manner to people involved in the medical field, the Agency consigned professionals to create the layout, print and distribute the “Do you know about Relief Services?” brochure (consisting of a total of 8 pages, including the cover). These brochures were enclosed with magazines published by the Japan Medical Association (approximately 170 thousand copies) as well as the February issue of a magazine published by Japan Pharmaceutical Association (approximately 100 thousand copies of magazines), and distributed.

  In addition, animations summarizing the brochure (14 minutes) and the brochure itself (in PDF format) were made available on the PMDA website.

Publicity on the back of drug envelopes (yakutai)

- Since it is possible to directly inform patients taking pharmaceuticals about the relief systems by using the back of *yakutai*, which are paper bags used for prescription medication, as publicity space, the Agency consigned professionals to create the layout, print, and select distribution destinations for these *yakutai*. Ultimately, approximately 4.45 million of these bags were distributed to 419 health insurance pharmacies across Japan.

1. (3) Expansion of the Consultation Service

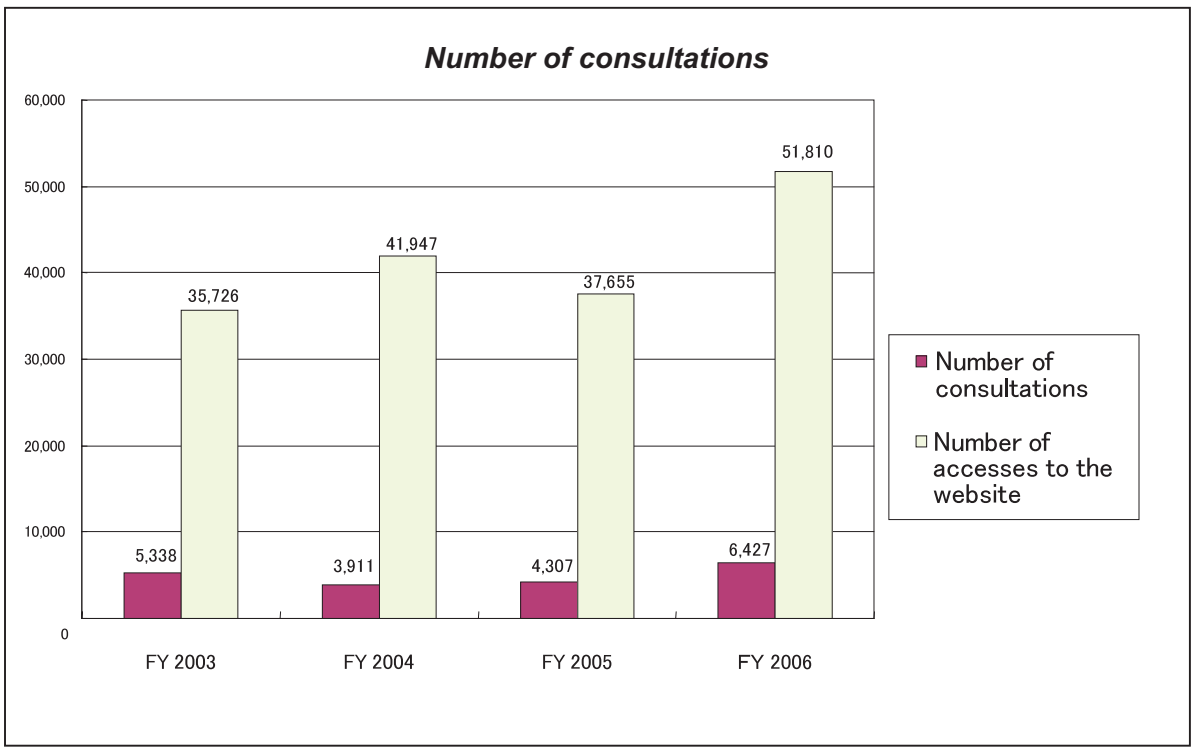
- In the 2006 fiscal plan, the Agency's goal is to increase the number of consultations and accesses to the PMDA website, both by 15% in comparison to FY 2003, but the actual number of consultations in FY 2006 increased by 20% as compared to FY 2003. This was due to the creation of brochures understandably explaining the relief systems, publicity from enclosing the brochures with magazines published by Japan Medical Association and Japan Pharmaceutical Association, publication of animations summarizing this brochure on the PMDA website, publicity via the Internet, and publicity through *yakutai*.

  Also, the number of accesses to the PMDA website in FY 2006 increased by 45% as compared to FY 2003.

  Moreover, upon implementing publicity through the Internet for a period of 5 months, there were 74,564 accesses to the Web pages used exclusively for publicity containing overviews of the relief system.

Fiscal Year	FY 2003	FY 2004	FY 2005	FY 2006	Compared with FY 2003
Number of consultations	5,338	3,911	4,307	6,427	20% increase
Number of web accesses	35,726	41,947	37,655	51,810	45% increase

Toll Free Number: 0120-149-931
Phone: 03-3506-9411
E-mail address of the relief consultation service: kyufu@pmda.go.jp



1. (4) Uniform Management of Information through Databases

- To make operations more efficient, the Agency plans on newly developing an “Integration and Analysis System for Databases on Relief Benefit Services” that can analyze various information relating to adverse drug reaction relief benefit services and relief benefit services for infections (information of offending drugs and names of illnesses from adverse drug reactions in particular) and detect trends in pathogeny of adverse drug reactions and their correlations, etc., through statistical analysis. The Agency launched the first phase of developments by concluding a multiple-year contract with professionals for a delivery period from November 2006 to August 2007.

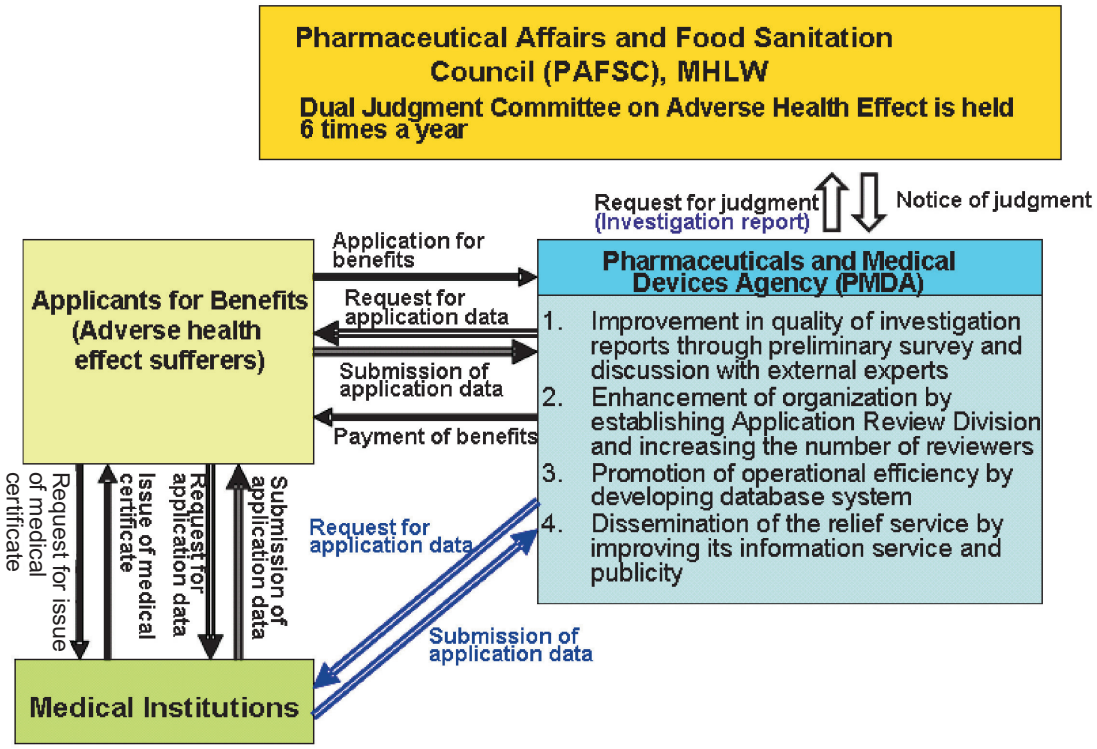
1. (5) Prompt Processing of Relief Applications

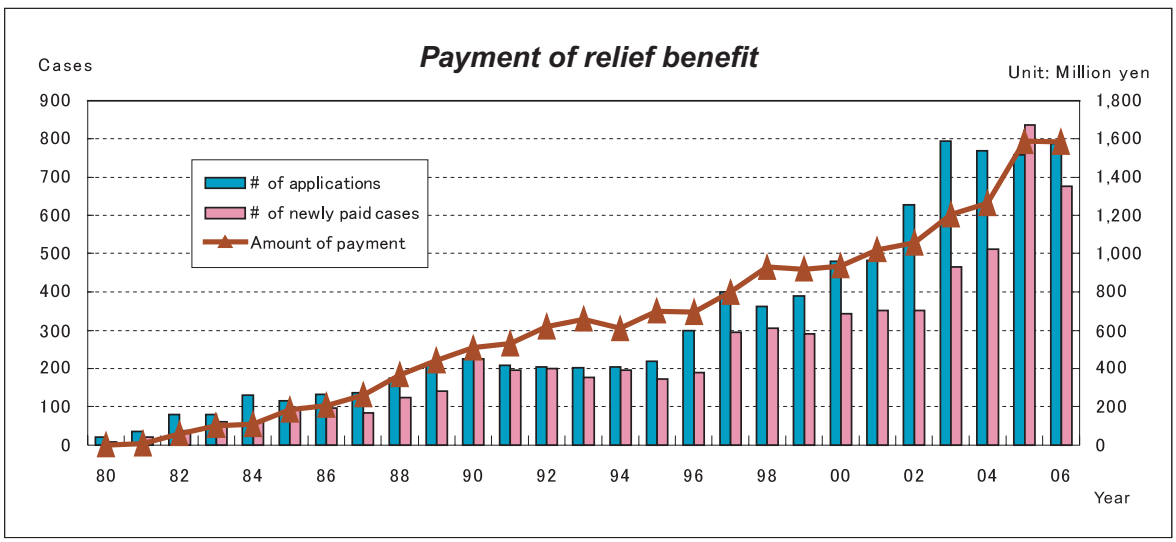
- In order to conduct prompt administrative processing of relief benefit services, the Agency investigates and organizes the facts given in the contents of applications upon receiving an

application for relief benefit services, and requests the Minister of Health, Labour and Welfare to make a medical and pharmaceutical judgment on the application. For this purpose, the following operations are conducted :

1) Fact-finding investigations, etc., of the relevant incident included in the application
2) Creation of a summary chart tracing the case over time
3) Creation of investigation reports.

Improvement of Adverse Health Effect Relief Services





[FY 2006]

▶Relief services for adverse drug reactions

Number of applications: 788

Number of judged cases for approval / rejection: 845 (of which 676 were judged for approval)

▶Relief services for infections

Number of applications: 6

Number of judged cases for approval / rejection: 7 (of which 7 were judged for approval)

- The Agency is also setting the time period for standard administrative processing of applications from when they are submitted until judgments on approval or rejection are made (including the time required for a medical and pharmaceutical judgment to be made by MHLW) to 8 months. Through collaborations with MHLW, the Agency is planning on processing applications for benefits smoothly and completing judgments within the standard administrative processing time for 60% or more of the cases filed in FY 2008, which is the last year of the effective period for the Mid-term targets.

- Therefore, in addition to cooperating with MHLW, which makes medical and pharmaceutical judgments during processing, to review the time allocated to administrative processing, and allocating 2 months of the process to the Ministry and 6 months to the Agency (excluding time periods where administrative processing is not possible due to additional/supplementary documents and investigations being required of applicants, medical institutions, etc.), the Agency established a system for making a list of cases being processed on a routine basis to enable for appropriate management of processing time for paperwork.

- The achievement rate during FY 2006 was 65.3%, a 52.6 point increase as compared to FY 2005, for which the achievement rate was 12.7%. This is a successful result of reinforced operational structures and intensive processing of paperwork that includes items that had not yet been processed in the past (or “accumulated items”).

1. (5). 1. Adverse drug reaction relief services

The Agency is implementing payment of benefits consisting of medical expenses, medical allowances, disability pensions, pensions for raising handicapped children, bereaved family pensions, lump-sum benefits for bereaved family and funeral expenses for illnesses, disabilities and deaths that occurred on or after May 1, 1980, caused by ADRs even though pharmaceuticals were used properly.

a. Actual performance of adverse drug reaction relief

Actual performance of FY 2006 is shown below.

Fiscal Year		FY2003	FY2004	FY2005	FY2006
Number of applications		793	769	760	788
Number of judged cases		566	633	1,035	845
	Approved	465	513	836	676
	Refused	99	119	195	169
	Withdrawn	2	1	4	0
Cases in progress*		820	956	681	624
Achievement rate**		17.6%	14.5%	12.7%	65.3%
Processing Time (median)		10.6 mths	12.4 mths	11.2 mths	6.6 mths

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

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

b. Number of applications according to types of benefits

The numbers of applications in FY 2006 according to types of benefits are shown below.

(Unit: cases)

Fiscal Year		FY2003	FY2004	FY2005	FY 2006
Number of applications		793	769	760	788
Types of benefit	Medical expenses	640	613	602	643
	Medical allowances	683	650	659	694
	Disability pensions	68	73	78	60
	Pension for raising handicapped children	9	14	5	14
	Bereaved family pensions	56	54	41	31
	Lump-sum benefits for bereaved family	42	47	48	51
	Funeral expenses	98	101	84	88

An application could include more than one kind of benefits.

c. Judgment status according to types of benefits

The status of judgments in FY 2006 according to types of benefits is shown below.

(Unit: thousand yen)

Types	FY2003		FY2004		FY2005		FY2006	
	Number of cases	Amount of payment	Number of cases	Amount of payment	Number of cases	Amount of payment	Number of cases	Amount of payment
Medical expenses	367	34,813	448	51,722	717	78,527	572	67,502
Medical allowances	408	35,388	472	42,711	757	70,073	624	60,034
Disability pensions	22	552,869	24	592,028	33	653,143	35	692,446
Pension for raising handicapped children	2	16,991	4	17,810	17	40,639	6	30,131
Bereaved family pensions	32	335,829	31	412,167	44	502,468	22	493,010
Lump-sum benefits for bereaved family	30	217,148	19	137,041	32	228,708	34	229,446
Funeral expenses	61	11,205	48	9,167	74	14,010	53	10,386
Total	922	1,204,243	1,046	1,262,647	1,674	1,587,567	1,346	1,582,956

"Number of cases" means judged cases. "Amount of payment" means benefits paid for both new and continuing cases.

1. (5). 2. Infections derived from biological products relief

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

* *Biological products refer to pharmaceuticals, 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 Minister of Health and Labour and Welfare upon hearing opinions from the Pharmaceutical Affairs and Food Sanitation Council.*

a. Actual performance of relief for infections

Actual performance of FY 2006 is shown below.

Fiscal Year		FY 2004	FY 2005	FY 2006
Number of applications		5	5	6
Number of judgments		2	6	7
	Approved	2	3	7
	Refused	0	3	0
	Withdrawn	0	0	0
Cases in progress*		3	2	1
Achievement rate**		100.0%	50.0%	100.0%
Processing Time (median)		3.0 mths	5.6 mths	3.8 mths

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

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

b. Number of applications according to types of benefits

The numbers of applications in FY 2006 according to types of benefits are shown below.

(Unit : cases)

Fiscal Year		FY 2004	FY 2005	FY 2006
Number of applications		5	5	6
Types of benefits	Medical expenses	5	5	5
	Medical allowances	5	5	5
	Disability pensions	0	0	0
	Pension for raising handicapped children	0	0	0
	Bereaved family pensions	0	0	1
	Lump-sum benefits for bereaved family	1	0	0
	Funeral expenses	1	0	1

An application could include the payment of more than one benefit.

c. Judgment status according to types of benefits

The status of judgments in FY 2006 according to types of benefits is shown below.

(Unit: thousand yen)

Types of benefits	FY2004		FY2005		FY 2006	
	Number of cases	Amount of payment	Number of cases	Amount of payment	Number of cases	Amount of payment
Medical expenses	2	161	3	475	6	473
Medical allowances	2	142	3	249	6	497
Disability pensions	—	—	—	—	—	—
Pension for raising handicapped children	—	—	—	—	—	—
Bereaved family pensions	—	—	—	—	1	1,387
Lump-sum benefits for bereaved family	—	—	—	—	—	—
Funeral expenses	—	—	—	—	1	199
Total	4	302	6	724	14	2,556

1. (6) Promotion of Appropriate Communication of Information through Collaboration between Divisions

- To plan for collaboration between divisions within the Agency, information of judged cases relating to eligibility for adverse drug reaction relief benefits in FY 2006 was provided to the Office of Safety, after excluding personal information.

Information relating to relief benefits for infections in FY 2006, consisting of 6 applications and 7 judged cases, was also provided to the Office of Safety.

1. (7) Surveys on Actual Status of Effects from Adverse Drug Reactions Caused by Pharmaceuticals (Investigative Researches as a Part of Health and Welfare Services)

- As it is deemed necessary for operations other than payments for relief benefits to be conducted in order to plan for prompt relief of adverse health effects stemming from adverse health reactions caused by pharmaceuticals, the Agency is implementing health and welfare services for sufferers of adverse health effects (Article 15, Paragraph 1, Item 1-2 of the Law for the Pharmaceuticals and Medical Devices Agency).

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

As part of health and welfare services, the Agency established "Investigative Researches for Improvements in Quality Of Life of Sufferers of Severe and Rare Adverse Health Effects Caused by Pharmaceuticals" in April 2006 based on the results of a survey on the actual conditions of adverse health effects stemming from adverse health reactions caused by pharmaceuticals implemented in FY 2005, and initiated investigative researches to obtain materials for reviewing the ideal way to provide required services and measures for improving the QOL of sufferers of severe and rare adverse health effects for which general measures for disabled people do not necessarily provide sufficient support.

[Contents of Researches]

The Agency collects, analyzes and evaluates reports, such as survey slips, etc., from sufferers of adverse health effects regarding the conditions of various efforts in their daily life (63 volunteers in FY 2006).

[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	Independent Administrative Agency National Center for Persons with Severe Intellectual Disabilities, Nozominosono Senior Researcher

1.(8) Appropriate Implementation of Healthcare Allowances for SMON Patients and HIV Positive Patients Infected through Blood Products

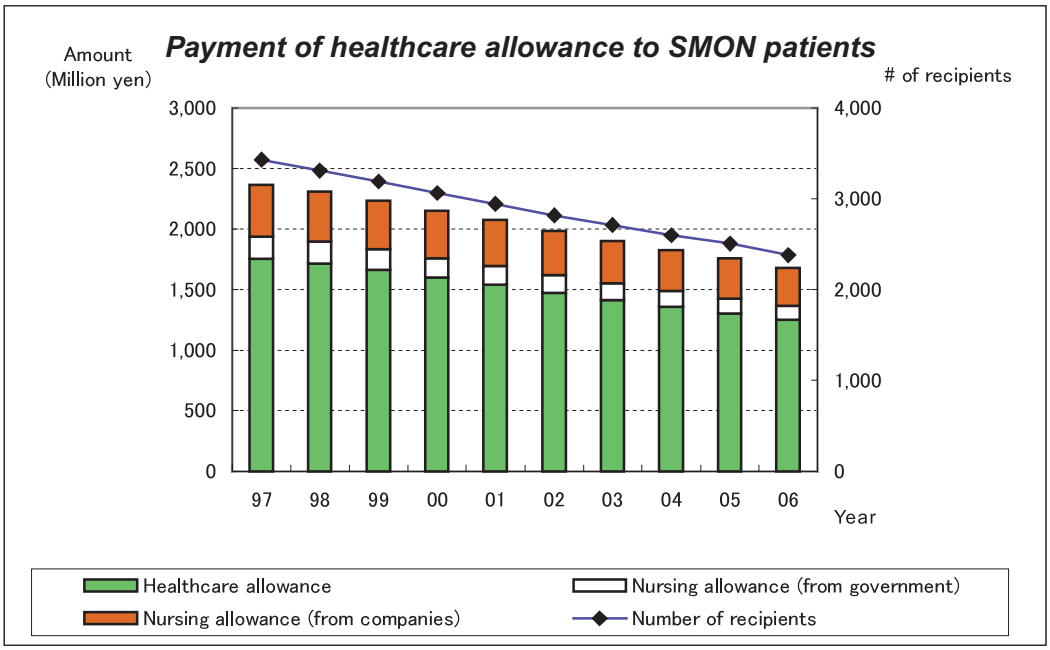
In order to appropriately provide healthcare allowances, etc., for SMON patients and HIV positive patients infected through blood products, the Agency implemented appropriate operations based on the contents of consignment contracts, giving due consideration to the confidentiality of personal information.

1. (8). 1. Services for SMON-patients (healthcare allowances)

- The Agency provides healthcare allowances and nursing care allowances for SMON patients for whom a settlement has been reached in the courts. In FY 2006, the number of patients receiving such allowances was 2,381 and total amount of payments was 1.684 billion yen.

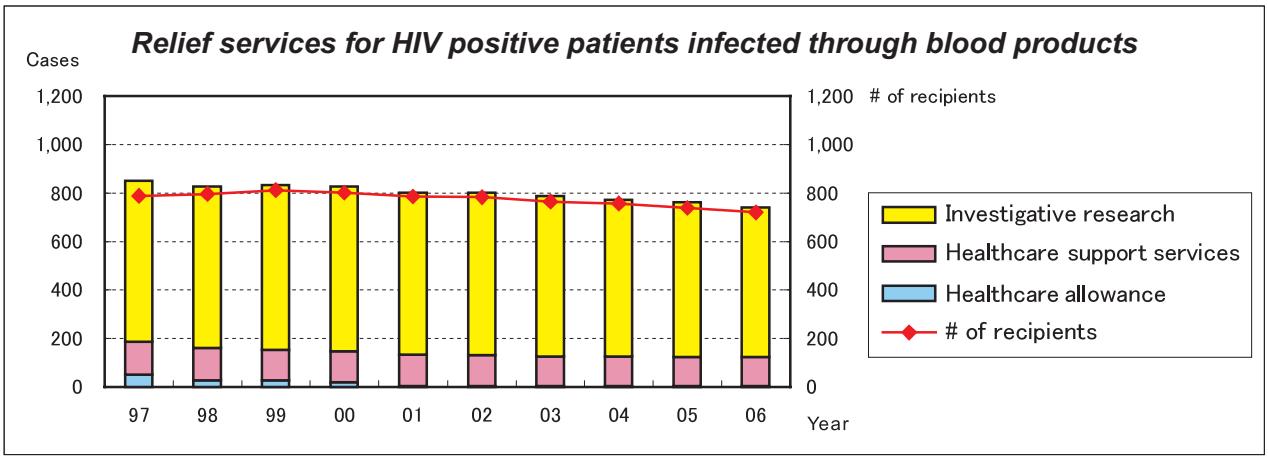
Fiscal Year		FY 2003	FY 2004	FY 2005	FY 2006
Number of recipients		2,713	2,598	2,504	2,381
Amount paid (thousand yen)		1,901,829	1,829,332	1,757,774	1,683,500
Break-down	Healthcare allowance	1,417,469	1,359,056	1,305,168	1,251,622
	Nursing allowance (from companies)	349,933	342,357	330,086	315,027
	Nursing allowance (from government)	134,427	127,920	122,520	116,850

Since the numbers are rounded off to the nearest thousand yen, the amount paid does not always match the sum of each breakdown category.



1. (8). 2. AIDS-related services (healthcare allowances)

- The Agency provides the 3 services below for HIV positive patients infected through blood products. From among the HIV positive patients who received benefits in FY 2006, 618 patients received allowances relating to investigative researches, 120 patients received allowances for healthcare support services and 3 patients received healthcare allowances. The total number of patients receiving allowances was 741 patients, and the total amount of payments was 553 million yen.
  a. Payment of healthcare allowances for HIV positive patients, as services for investigative researches.
  b. Payment of healthcare allowances for AIDS patients for whom a settlement has been reached in the courts, as healthcare support services.
  c. Payment of special allowances, etc., for AIDS patients for whom a settlement has not been reached in the courts, as healthcare allowances.



Fiscal Year	FY 2003		FY 2004		FY 2005		FY 2006	
	Number of recipi-ents	Amount of payment (Thousand yen)	Number of recipi-ents	Amount of payment (Thousand yen)	Number of recipi-ents	Amount of payment (Thousand yen)	Number of recipi-ents	Amount of payment (Thousand yen)
Investigative research	662	355,343	647	348,446	638	341,017	618	334,653
Healthcare support services	127	221,400	124	210,600	121	210,300	120	210,000
Healthcare allowance	3	8,733	3	8,706	3	8,706	3	8,678
Total	789	576,477	772	567,752	762	560,023	741	553,331

2. Reviews and Related Services / Safety Measures

To enable for the public to safely use pharmaceuticals and medical devices that have international standards, it is desired for the Agency, through reviews and related services and safety measures, to provide better pharmaceuticals and medical devices to clinical practice settings faster and with greater safety, ensure that pharmaceuticals and medical devices are used properly, prevent health hazards, and respond appropriately and promptly if hazards should occur, so that pharmaceuticals and medical devices can fulfill their purpose over a longer period of time. Therefore, the Agency 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 2006 fiscal year plan.

2. (1) Faster Access to the Latest Pharmaceuticals and Medical Devices

2. (1). 1. Ensuring the benefits of pharmaceuticals and medical devices for the public and healthcare professionals

- It is desired for the Agency to ensure that the public and healthcare professionals enjoy the benefits of the latest and safe pharmaceuticals and medical devices promptly and to the fullest extent, and to ensure that pharmaceutical companies are benefited from this prompter access.

a. Implementation structure for clinical trial consultations and reviews

- The review system for pharmaceuticals and medical devices has improved significantly since 1997. In 2004, the Pharmaceuticals and Medical Devices Agency (PMDA) was founded while leaving the authority for approval and final judgment on pharmaceuticals and medical devices to the Ministry of Health, Labour and Welfare (MHLW), enabling for consolidation of review functions. By taking the following kinds of measures, further improvements in the system were able to be planned.

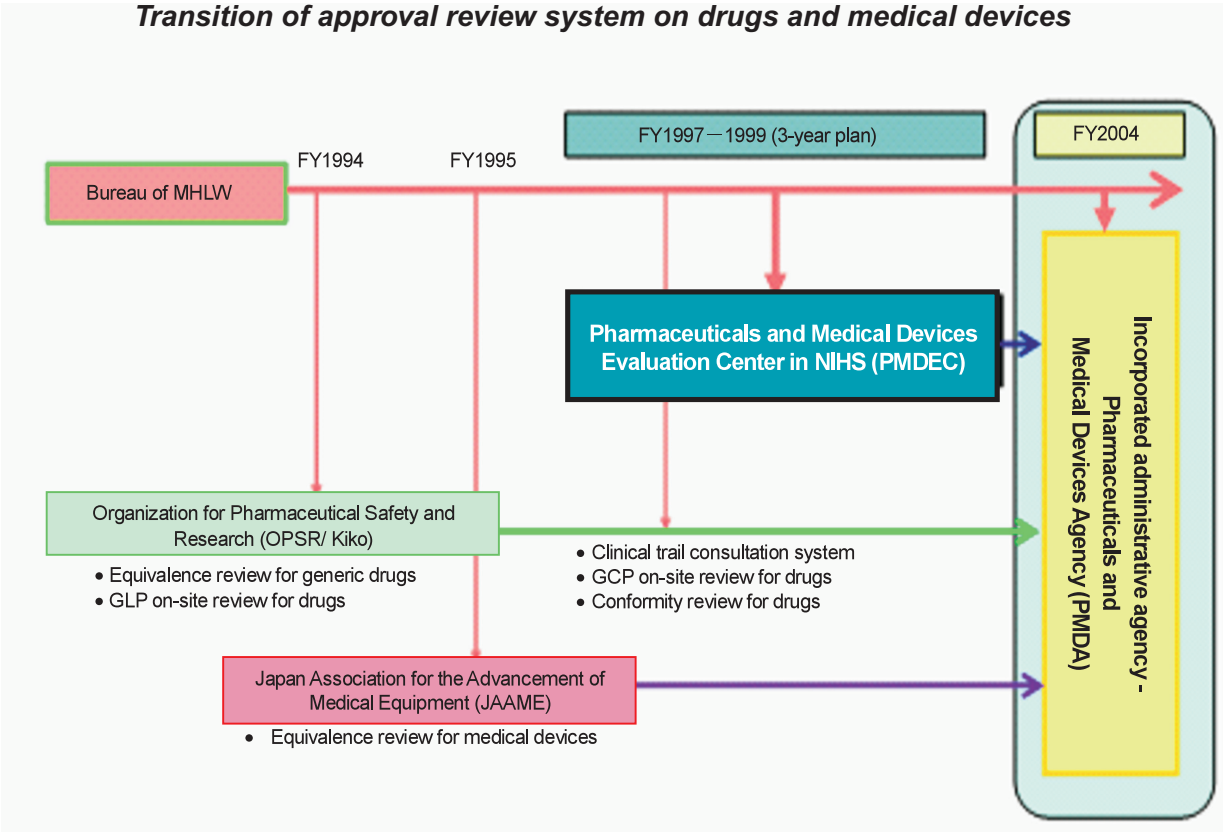
i) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency (PMDA), was established through the integration of 3 separate organizations responsible for review and related services.

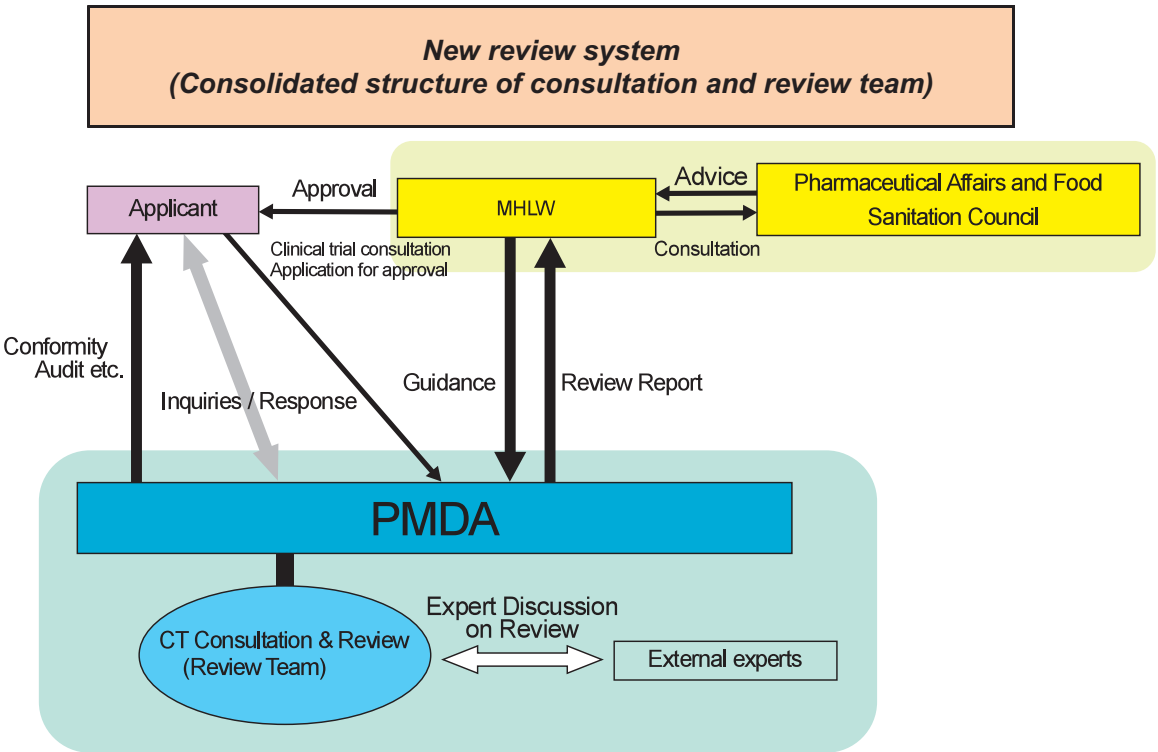
ii) The Agency decided to greatly increase in the number of its staff by about 100, including reviewers, within the effective period for the Mid-term targets.

iii) Under the new system of the Agency, the entire review process, from consultations regarding clinical study until review operations, is conducted by the same team with the same staff members for consistency and coordination. (As consultations regarding clinical study and review operations were done by different organizations and different staff members under the previous system, there were discrepancies in opinions and policies between the different parties.)

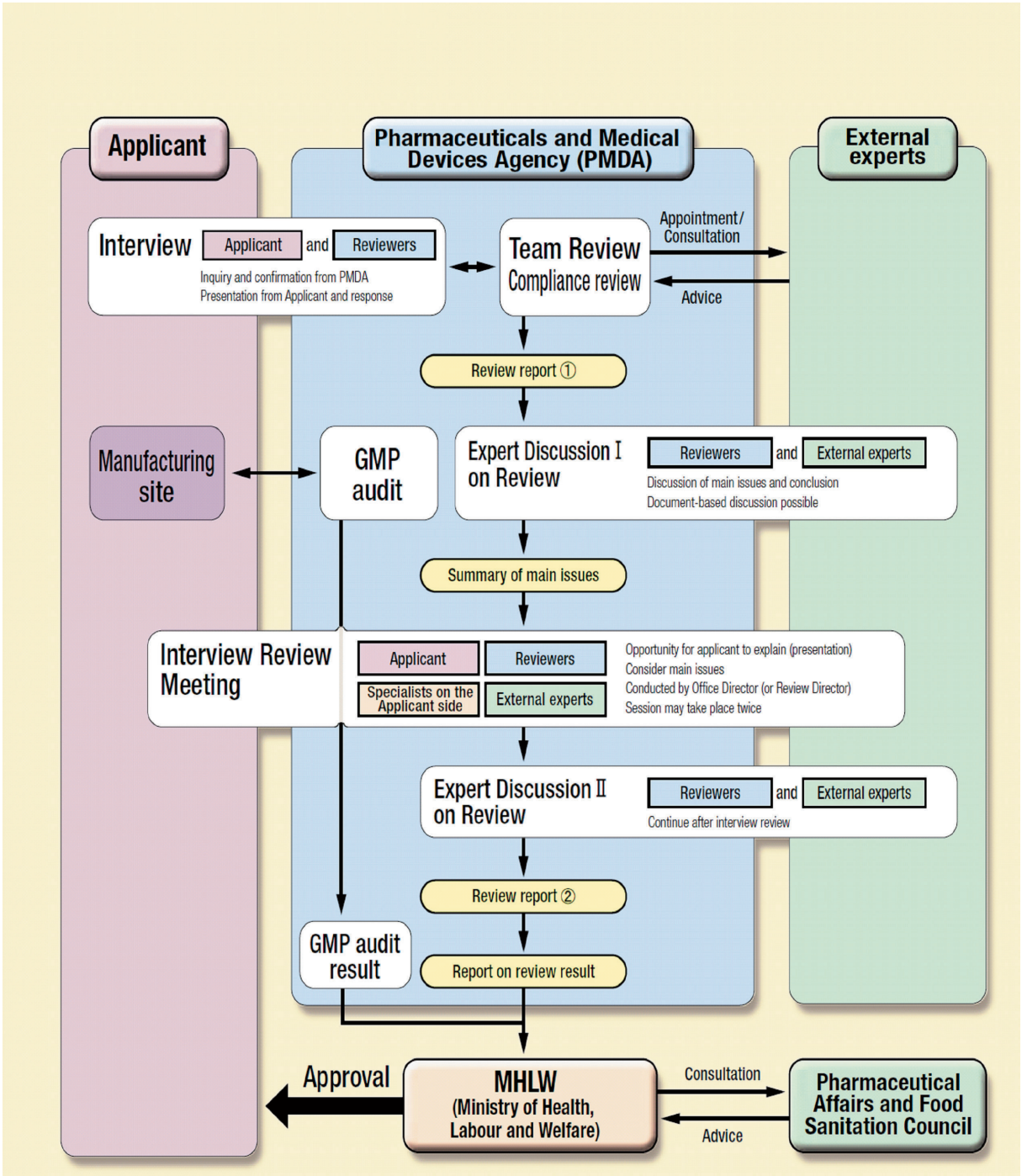
iv) To respond to new needs in the future, the Agency is reinforcing its functions for reviewing medical devices, as well as enhancing reviews of biological and biotechnology-derived products.

Transition of approval review system on drugs and medical devices





Flowchart of review process for approval



Actual results of review services in FY 2006

Reviews:

Pharmaceuticals

1) Number of expert discussions conducted: 170 (130 in written form, 40 through meetings)
2) Applications discussed at the Drug Committees (PAFSC): 60
   Review reports made to the Drug Committees (PAFSC): 17

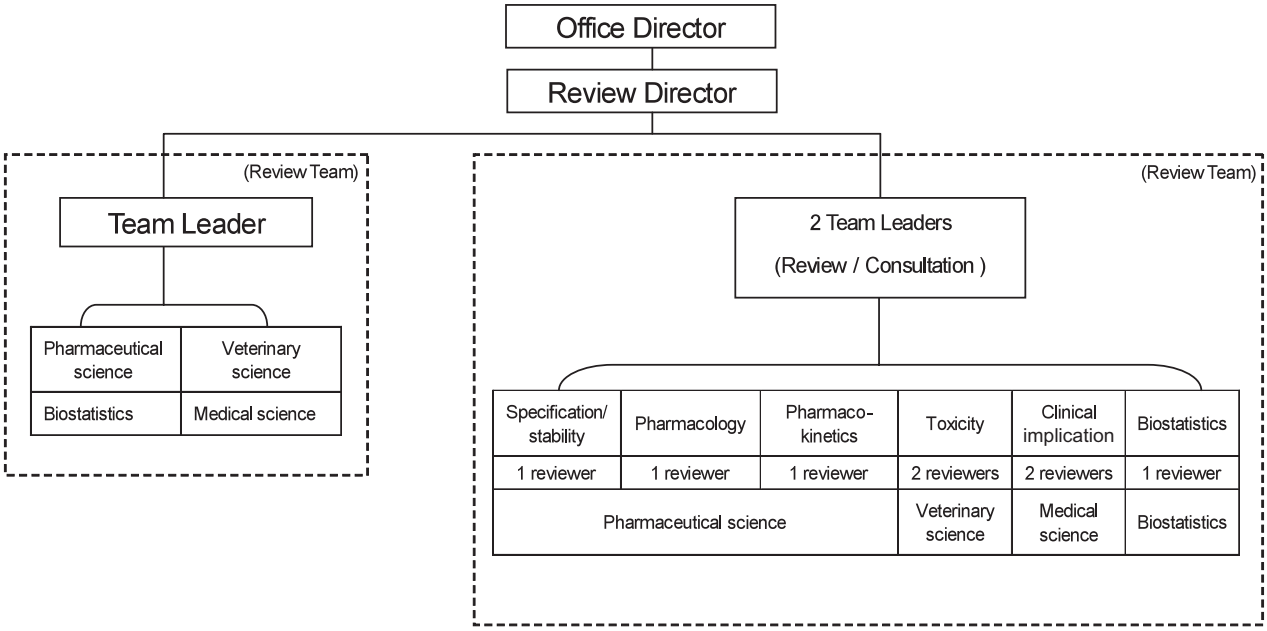
Medical devices and pharmaceuticals for *in-vitro* diagnostics

1) Number of expert discussions conducted: 150 (138 in written form, 12 through meetings)
2) Applications discussed at the Drug Committees (PAFSC): 8
   Review reports made to the Drug Committees (PAFSC): 107
   (90 cases for medical devices, 17 cases for pharmaceuticals for *in-vitro* diagnostics)

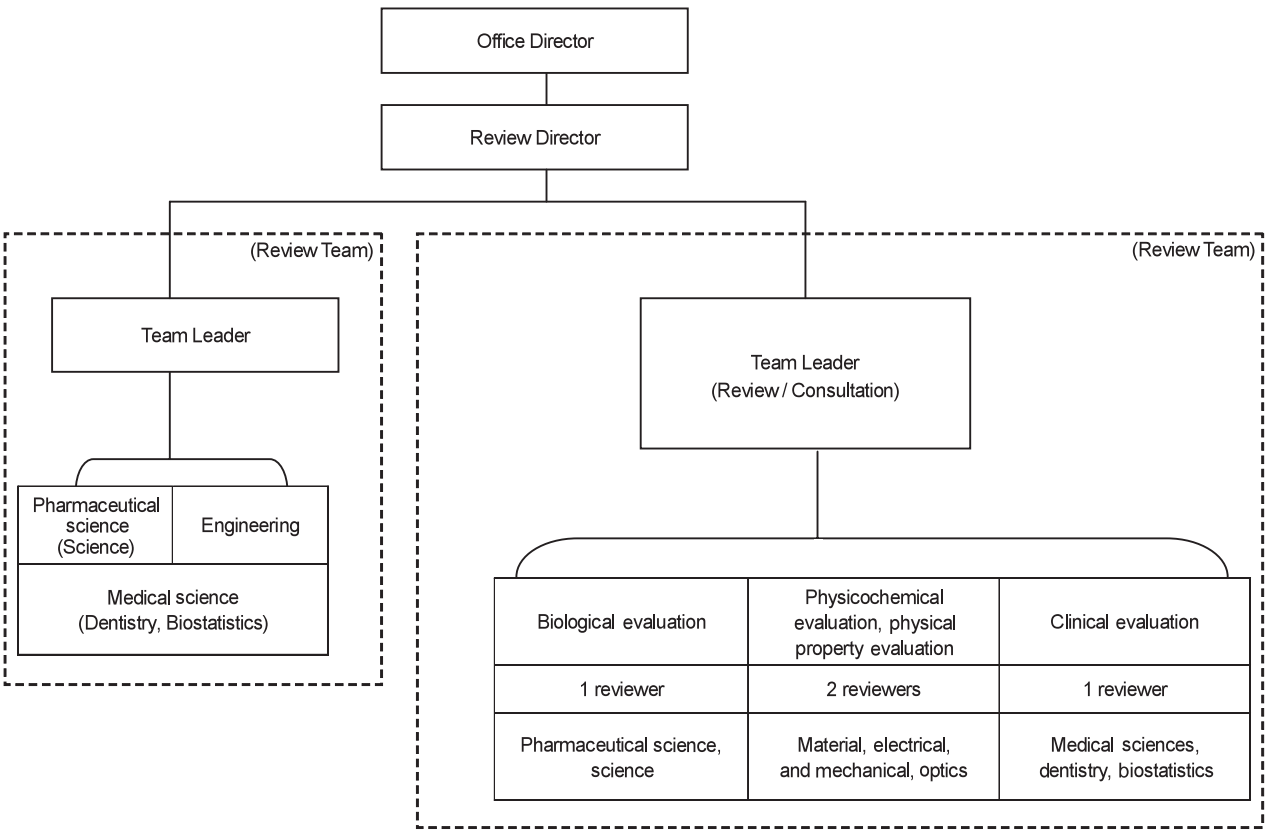
- As provided below, reviews of new drugs were conducted by review teams consisting of experts who, in principle, have academic degrees in pharmaceutical science, medical science, veterinary science, biostatistics, etc. The review team is fundamentally comprised of an office director, a review director, team leader(s), deputy team leader(s) and reviewers respectively specialized in quality, toxicity, pharmacology, pharmacokinetics, clinical implication and biostatistics.

- Similarly, reviews of new medical devices were conducted by review teams consisting of experts who, in principle, have academic degrees in engineering, pharmaceutical sciences, medical science, dentistry, veterinary science, statistics, etc. The review team is fundamentally comprised of an office director, a review director, team leader, and reviewers respectively specialized in biological evaluations, physicochemical/physical property evaluations and clinical evaluations.

Structure of review team for NDAs



Structure of review team for new medical devices



- Reviews on new drugs were implemented upon establishing a dedicated office and team to each therapeutic category as shown below.

Therapeutic categories assigned to each office of new drug

Name	Therapeutic Category	
Office of New Drug I	Category 1	Gastrointestinal drugs, dermatologic medicines
	Category 4	Antibacterial agents, vermifuge, antifungal agents, antiviral agents except anti-HIV agents
	Anti-cancer drugs	Anti-cancer drug
	Anti-AIDS drugs	Anti-HIV agents
Office of New Drug II	Category 2	Cardiovascular drugs, anti-Parkinson's disease drugs, antithrombotics, anti-Alzheimer's disease drugs
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs
	Radiopharmaceuticals	Radiopharmaceuticals
	In vivo diagnostics	Contrast medium
Office of New Drug III	Category 3	Central/peripheral nervous system drugs, sensory organ drugs (except drugs classified in Category 6-1), narcotics
	Category 6-1	Respiratory tract drugs, anti-allergy drugs, sensory organ drugs for inflammatory diseases
	Category 6-2	Hormone drugs, drugs for metabolic disorders (excluding combination drugs)
Office of Biologics	Biological products	Vaccines, antitoxic serum
	Blood products	Serum globulin, blood coagulation factors
	Cellular and Tissue-derived products*	Products for cell therapy

** Pharmaceuticals for gene therapy belong to Cellular and Tissue-derived products.*

- Review on new medical devices were implemented upon establishing a team to each therapeutic category as shown below.

Therapeutic categories in the office of medical devices

Therapeutic Category	
Category 1	Mainly for ophthalmology and otorhinolaryngology
Category 2	Mainly for dentistry
Category 3	Mainly for cerebral, cardiovascular, respiratory, psychoneurologic (materials)
Category 4	Mainly for cerebral, cardiovascular, respiratory, psychoneurologic (mechanical)
Category 5	Mainly for gastrointestinal and urinary systems, obstetrics and gynecology
Category 6	Mainly for orthopedic surgery, plastic surgery, dermatology
Category 7	Mainly for clinical test (*in-vitro* diagnostic)
Category 8	Mainly for multicategory medical devices, advanced electronic medical devices, other uncategorized medical devices

- PMDA conducted face-to-face consultations regarding clinical studies for new drugs based on guidance plan made by the Review Director, as well as the Chief Reviewer and the Deputy Reviewer in charge, who were appointed from a review team.

- PMDA conducted face-to-face consultations regarding new medical devices based on team reviewed guidance plan made by the Review Director, as well as the Chief Reviewer and the Deputy Reviewer in charge, who were appointed from a review team.

b. Comprehension of the needs of the public and healthcare professionals

- The Agency has actively exchanged opinions with healthcare professionals by participating in academic societies, etc., both in Japan and abroad, to comprehend their needs.
  **A total of 664 PMDA staff members participated in 296 domestic and international academic societies and seminars.*

- In order to periodically grasp the needs of academic societies and patients regarding pharmaceuticals approved in Europe and the U.S. but not yet in Japan, the “Investigative Panel Study Group on Use of the Problems Concerning Unapproved Drugs” (chaired by Dr. Tomomitsu Hotta, Director of National Hospital Organization Nagoya Medical Center Adjunct) has been conducting investigations ever since its establishment under the MHLW in January 2005. The Agency has applied results from investigations conducted by this panel when providing consultations regarding clinical studies and reviewing applications.

- Consultations regarding clinical studies of medical devices and pharmaceuticals for *in vitro* diagnostics are expected to contribute to the promotion of product development and more speedy approval reviews by responding in detail to various needs at each stage of development.

For pharmaceuticals that use cellular tissue and that were 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 approval application, as there are only a few precedents for development.

In order to respond to these needs, the Agency established new categories for consultations regarding clinical studies of medical devices and pharmaceuticals for *in vitro* diagnostics, as well as for consultations on preparation of documents for pharmaceuticals that use cellular tissue (Since April 1, 2007).

2. (1). 2. Efforts for efficient and prompt reviews

- It is desired for the Agency to improve its services by establishing an efficient review system and targets (for normal conditions excluding cases where there are significant changes in the review system or in social conditions) for the time required administratively process reviews (time that it takes for the MHLW and the PMDA to process items approved in the same fiscal year) for applications submitted after the PMDA was established on April 1, 2004.

- In order to achieve the target administrative processing time for reviews for each category of approval applications submitted on and after April 1, 2004, the Agency has been improving its operations such as through acceleration of reviews.

a. Approval reviews for new drugs

- For new drugs, the Agency aims to review 70% (80% in FY 2008) of all filed NDAs within the review processing time of 12 months. In order to attain this target, the Agency:
    - (i) reinforced the review system and improved its operational efficiency by increasing the number of reviewers for categories in which processing of applications was considered to be difficult due to bias of items in approval applications for new drugs;
    - (ii) regularly discussed its review policy with the MHLW and managed the review process through the Progress Management Committee for Review-Related Operations within the PMDA so that review operations can be conducted smoothly;
    - (iii) made efforts to properly manage the review process by observing guidelines for implementing reviews and investigations, keeping reviewers informed about review-related information and developing standard operating procedures.

- With regard to new drugs (pharmaceuticals that are clearly different from already-approved pharmaceuticals in terms of active ingredients, quantities, administration, dosage, indications, efficacy, etc.) for which approval applications have been submitted, approval reviews were conducted by review teams consisting of experts in pharmaceutical science, medical science, veterinary science, 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, the Agency developed the “Implementation Manual for Approval Reviews of New Drugs” regarding reviews and related procedures, and “Standard Operating Procedures” for various operations.

- In order to achieve the targets relating to time periods for administratively processing reviews as given in the Mid-term plan and to conduct review-related work promptly and appropriately, the Agency continued to have the “Progress Management Committee for Review-Related Operations” hold meetings to monitor and examine operational progress so that the Chief Executive and other executives of the Agency could accurately grasp the progress on approval review operations and plan for improvements in the progress. In order to comprehend progress more accurately, the Agency made fundamental revisions to documentation and materials in August 2006.

  In the review divisions, the directors of the review divisions comprehended the operational progress on a daily basis, and based on the reports from these directors, the Director of the Center for Product Evaluation and the Associate Center Director provided necessary guidance at liaison meetings for review-related divisions.

- The status of approval reviews for new drugs in FY 2006 is shown below.

Number of approved pharmaceuticals etc.

(cases)

Fiscal Year / Type of applications	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006
Ethical drugs	3,532	2,077	2,467	3,742	2,199	2,390
OTC drugs	4,865	2,956	1,934	1,781	1,570	1,030
In vitro diagnostics	873	404	368	502	281	136
Quasi-drugs	5,260	3,605	2,992	2,972	2,611	2,287
Cosmetics	0	0	0	0	0	0
Total	14,530	9,042	7,761	8,997	6,661	5,843
--Breakdown--						
New drugs	**75**	**48**	**51**	**49**	**60**	**77**
- Priority review applications out of NDAs above	**21**	**4**	**10**	**22**	**18**	**24**

The number of “Cases” is obtained based on the number of applications discussed at and the number of review reports made to the Drug Committees of Pharmaceutical Affairs and Food Sanitation Council (PAFSC).

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Number of approved NDAs

Top: number of approval, middle: () median review time, bottom: [ ] time clock achievement rate

	FY 2002*	FY 2003	FY 2004	FY 2005		FY 2006	
					Applications filed in and after FY 2004***		Applications filed in and after FY 2004***
New drugs (total)	52 (10.8 mths)	51 (11.3 mths)	49 (8.6 mths) [65%]**	60 (12.0 mths) [50%]**	24 (8.6 mths) [83%]	77 (13.7 mths) [39%]**	49 (10.5 mths) [59%]
Priority review items (included in total)	4	10 (3.8 mths)	22 (2.8 mths) [8.6%]**	18 (8.9 mths) [28%]**	9 (2.8 mths) [56%]	24 (7.3 mths) [42%]**	20 (6.4 mths) [50%]
Standard items (included in total)	48	41 (11.5 mths)	27 (12.3 mths) [41%]**	42 (14.2 mths) [41%]**	15 (10.3 mths) [73%]	53 (15.5 mths) [23%]**	29 (12.8 mths) [41%]

* *The data in 2002 is based on the calendar year.*

** *The percentage in [ ] indicates the ratio of the number of applications processed within 12 months (6 months for priority review items).*
The values for FY 2004 to FY 2006 include the NDAs filed before April 2004, which are excluded from targets in the Mid-term plan.

*** *The data indicate the number of applications filed in and after FY 2004, and approved in FY 2005 and FY 2006. These figures are breakdown of the result in FY 2005 and FY 2006.*

Review status of NDAs

	Cases*	Approved	Withdrawn	Under Review
Applications submitted by March 31, 2004	139	96 (28)	23 (6)	20 [-34]
Applications submitted in FY 2004	87 (-1)**	64 (27)	9 (1)	14 [-29]
Applications submitted in FY 2005	57	20 (16)	4 (4)	33 [-20]
Applications submitted in FY 2006	103	6 (6)	0	97 (97)
Total	386 (102)	186 (77)	36 (11)	164 [14]

* *The number of "Cases*" is obtained based on the scheduled number of review reports discussed at and reported to the Drug Committees of Pharmaceutical Affairs and Food Sanitation Council (PAFSC).*

** *The number of applications submitted in FY 2004 is one less than that shown in the previous annual report because the Agency integrated two separate applications for one ingredient as one application.*

1. Values in () indicate those processed in FY 2006 (included in values above).

2. Values in [ ] indicate difference from FY 2005.

Number of applications processed and time consumed 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 review result approval
FY 2005	Number of processed cases	58 cases	22 cases	25 cases	24 cases
	Review process time (median)	80 days	407 days	23 days	4.5 days
FY 2006	Number of processed cases	79 cases	54 cases	56 cases	49 cases
	Review process time (median)	83.0 days	397.5 days	44.5 days	25.0 days

* *The days shown in each review process are the median of total review process time (the sum of reviewers' and applicants' time clocks).*
Values are of applications filed in and after April 2004.

[Review status of new drugs overall]

- When looking at the approval status in FY 2006, the Agency attained an achievement level 59% for performance targets within 12 months by processing 29 out of 49 applications for new drug approvals submitted in or after April 2004. 20 out of the 49 approved applications, however, were priority review items, and when including the applications submitted before April 2004, the achievement rate was 39% (30 out of 77 applications).

- Compared to the 60 applications approved the previous year, the number of new drugs approved in FY 2006 increased somewhat due to progress in the development of the review system. However, when comparing the median for the review time, it is apparent that more time was required to conduct reviews in FY 2006 as compared to FY 2005. This is considered as being due to the processing of applications filed before the establishment of the PMDA.

- As for the 139 applications submitted before the establishment of the PMDA (in or before March 2004) and the 247 applications submitted after the establishment of the PMDA (in or after April 2004), the Agency processed reviews in the order of their submission, giving full consideration to the target time for processing reviews. However, the Agency has called for withdrawal of applications that were considered to be difficult to approve due to a lack of response by applicants to inquiries made by the Agency.

- As for the applications submitted before March 2004, the Agency was able to process 119 such applications through approvals or withdrawals by FY 2006. However, in order to achieve the target for the review processing time earlier, the Agency is progressing with reviews vigorously, and is striving to concentrate all resources on the applications submitted after its establishment.

[Status of priority reviews]

- With regard to priority reviews for pharmaceuticals specified by the Minister of Health, Labour and Welfare, the Agency is aiming to process 50% of all such reviews within a review processing time of 6 months by the end of the effective period for the Mid-term targets.

- Approval reviews for applications for orphan diseases and other pharmaceuticals that are regarded as having particularly high medical necessity (pharmaceuticals for severe diseases and with distinctly superior efficacy or safety as compared to existing pharmaceuticals or treatment methods) were conducted on a priority basis as priority review items. In FY 2006, there were 20 applications for priority reviews of pharmaceuticals that are regarded as having particularly high medical necessity, among which 9 were accepted as a priority review item, 3 were declined because they did not meet the requirements and 8 are currently being reviewed.

b. Approval reviews for new medical devices

- With regard to new medical devices, the Agency aimed for an achievement level of 70% for the target review processing time of 12 months in FY 2004 (80% in FY 2005 and FY 2006; 90% in FY 2007 and 2008). Similarly to measures taken for approval reviews of new drugs, in order to attain these goals the Agency took concrete measures to improve and accelerate reviews, such as by establishing operating procedures for reviews and examinations.

- Review teams consisting of reviewers with expertise in engineering, pharmaceutical science, medical science, dentistry, veterinary science, biostatistics, etc., conducted approval reviews of new medical devices (devices subject to re-examination (medical devices that have a clearly different structure, usage, indication, efficacy, performance, etc., as compared to existing approved medical devices or certified medical devices).

- To carry out reviews on new medical devices promptly and appropriately, the Agency established the “Implementation Manual for Approval Reviews of New Medical Devices” regarding reviews and review-related procedures, as well as standard operating procedures relating to various operations. The Agency also collected monthly data on the achievement level of the target review processing time and informed the review staff of the achievement status.

- With regard to the progress of reviews, etc., the Progress Management Committee for Review-Related Operations continued to monitor and examine operational progress. In order to comprehend the progress more accurately, the Agency made fundamental revisions to documentation and materials in August 2006.

  In the review divisions, Director of the Office of Medical Devices comprehends the operational progress on a daily basis, and at liaison conferences for review-related divisions, the Director of the Center for Product Evaluation and the Associate Center Director provide the necessary guidance.

- The status of approval reviews for new medical devices in FY 2006 is shown below.

Number of approved new medical devices

Top: number of approval, middle: () median review time, bottom: [ ] time clock achievement rate

	FY 2002*	FY 2003	FY 2004	FY 2005		FY 2006	
					Applications filed in and after FY 2004**		Applications filed in and after FY 2004**
New medical devices (total)	3 (2.9 mths)	14 (9.5 mths)	8 (12.7 mths) [50%]*	11 (7.7 mths) [82%]*	5 (1.8 mths) [100%]	23 (6.0 mths) [83%]*	15 (3.4 mths) [100%]
Priority review items (included in total)	3 (2.9 mths)	4 (9.4 mths)	2 (9.3 mths) [50%]*	0	0	1 (5.7 mths) [100%]*	1 (5.7 mths) [100%]
Standard items (included in total)	0	10 (9.6 mths)	6 (15.0 mths) [33%]*	11 (7.7 mths) [82%]*	5 (1.8 mths) [100%]	22 (6.3 mths) [82%]*	14 (3.2 mths) [100%]

* *The percentage in [ ] indicates the ratio of the number of applications processed within 12 months (9 months for priority review items).*
The values for FY 2004 to FY 2006 include the new medical devices filed before April 2004, which are excluded from targets in the Mid-term plan.

** *The data indicate the number of applications filed in and after FY 2004, and approved in FY 2005 and FY 2006. These figures are breakdown of the result in FY 2005 and FY 2006.*

Review status of new medical devices

	Cases*	Approved	Withdrawn	Under Review
Applications submitted by March 31, 2004	132	43 (13)	72 (8)	17 [-21]
Applications submitted in FY 2004	56	15 (10)	16 (2)	25 [-12]
Applications submitted in FY 2005	7 (-1)***	3 (2)	0	4 [-3]
Applications submitted in FY 2006	24	2 (2)	1 (1)	21 [21]
Total	219 (23)	63 (27)**	89 (11)	67 [-15]

* *The figures of "Cases applied" are the number of applications for new medical devices.*

** *Among 63 cases of the total of "Approved" were 29 approved as improved medical devices. Eight approved improved medical devices are included in total (27) of "Approved". In addition, one application which was applied as an improved medical device but approved as a new medical device, and 3 applications which were applied as a medical device that does not have approval standards and does not require clinical data, but approved as new medical device are excluded.*

*** *One application that did not fall under the category of medical devices was removed.*

1. Values in () indicate those processed in FY 2006 (included in values on their left).

2. Values in [ ] indicate difference from FY 2005.

Number of applications processed and time consumed 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 review result approval
FY 2005	Number of processed cases	31 cases	7 cases	2 cases	5 cases
	Review process time (median)*	57.0 days	294.0 days	262.0 days	12.0 days
FY 2006	Number of processed cases	14 cases	17 cases	10 cases	15 cases
	Review process time (median)*	46.5 days	484.0 days	101.0 days	9.0 days

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

1. Expert discussions were held several times as needed.

2. Values are of applications filed in and after April 2004.

[Review status of new medical devices overall]

- In FY 2006, the, the Agency approved all applications for new medical devices submitted in and after April 2004 (15 out of 15 cases) within 12 months, reaching an achievement level of 100% for the target review processing time. The median of the review processing time was 3.4 months. However, when applications submitted in and before March 2004 are included, the achievement ratio decreases to 83% (19 out of 23 applications), and the median of the review process time becomes 6.0 months.

- For the 132 applications submitted before the establishment of the PMDA (in and before 2004)

and the 87 applications submitted after the establishment of PMDA (in and after April 2004), the Agency processed reviews taking the target review processing time sufficiently into consideration. However, the Agency has called for withdrawal of applications that were considered difficult to approve due to a lack of response from applicants to inquiries made by the Agency.

- As to the applications submitted before April 2004, the Agency was able to process 115 such applications through approvals or withdrawals by FY 2006. However, in order to achieve the target for the review processing time earlier, the Agency is progressing with reviews vigorously, and is striving to concentrate all resources on the applications submitted after its establishment.

[Status of priority reviews]

- With regard to priority reviews for new medical devices specified by the Minister of Health, Labour and Welfare, the Agency is aiming to process 70% of all such reviews within a review processing time of 9 months by the end of the effective period for the Mid-term targets.

- Approval reviews for applications for orphan medical devices and other devices that are regarded as having particularly high medical necessity (medical devices for severe diseases and with distinctly superior efficacy or safety as compared to existing medical devices or treatment methods) were conducted on a priority basis as priority items. In FY 2006, there was one approval and no new applications for priority review.

[Status of development of approval standards]

- In order to support the MHLW in developing approval standards for medical devices, the Medical Device Approval Standards Committee held meetings twice in FY 2006, where 19 drafts for medical device approval standards were discussed, before reporting 6 of them to the MHLW. Also, in FY 2006, the Agency supported the development of 8 new medical device approval standards as well as 24 certification standards for designated controlled medical devices which are subject to certification by a registered certification body.

- The Agency established a database of medical device approval standards that can be accessed within the Agency.

Number of established approval standards and certification standards of medical devices and in vitro diagnostics

Established	FY 2004	FY 2005	FY 2006	Total
Approval standards	0	17	8	25
Certification standards	363	9	24	396

c. Document conformity audit of application materials, GLP conformity audits, GCP conformity audits and GPMSP conformity audits

- The Agency efficiently conducted on-site and document inspections on approval application materials for new drugs and medical devices as well as on the tests on which these application materials are based, to ensure that such materials comply with GLP (Good Laboratory Practice; standards indicated in ministerial ordinances relating to standards for implementing non-clinical tests relating to safety of pharmaceuticals), GCP (Good Clinical Practice; standards indicated in ministerial ordinances relating to standards for implementing clinical tests for pharmaceuticals), GPMSP (Good Post-Marketing Surveillance Practice; standards indicated in ministerial ordinances relating to standards for post-marketing surveys on pharmaceuticals) and to determine whether they were gathered in accordance with conformity standards for the application materials.

Number of conducted conformity audits

		FY 2002	FY 2003	FY 2004	FY 2005	FY 2006
Document conformity audits		189	173	161	136	426
	Pharmaceuticals	189	173	161	135	251
	Medical devices	-	-	-	1	175
GLP conformity audits		40	24	20	39	31
	Pharmaceuticals	40	24	20	37	23
	Medical devices	-	-	-	2	8
GCP conformity audits*		118	143	73	131	149
	New drugs	101	132	68	120	137
	Generic drugs	17	11	5	11	12
	Medical devices	-	-	-	0	0
GPSP conformity audits**		102	66	27	82	103

** Values for GCP and GPMSP conformity audits after FY 2004 are notification values after evaluation were conducted.*

*** All audits performed in and after FY 2005 were conducted as GPMSP conformity audits.*

1. GLP: Good Laboratory Practice

2. GCP: Good Clinical Practice

3. GPMSP: Good Post-Marketing Surveillance Practice

4. GPSP: Good Post-marketing Study Practice

- In order to efficiently carry out document conformity audits and on-site inspections for application materials, the Agency took the following measures.

1) Improvement of the consultation system/Making the interpretation of GCP operations be known

- The Agency made efforts to conduct consultations on GCP inspections for medical institutions within a possible range after the inspections were carried out, and made efforts to spread

knowledge on GCP operations by providing an enrichment of information such as Q&As and interpretations of case examples, as well as by exemplifying points to consider upon conducting clinical trials through the "Conformity Audit" page on the PMDA website. To deepen understanding regarding the GCP, the Agency held "GCP Workshops" in Tokyo and Osaka for people in charge of drug development and pharmaceutical affairs at pharmaceutical companies, auditors, site management organizations (SMOs) and healthcare professionals, and in addition, PMDA staff members made lectures at academic societies, etc., for healthcare professionals.

2) Enhancement and reinforcement of GCP on-site inspections

- The Agency increased the number of GCP on-site inspections for medical institutions while giving consideration to the allocation of PMDA staff servicing the division in charge.

- Although a standard administrative processing time for conformity audit services has not been set, the Agency made efforts so that the review processing time for approval reviews for relevant items were not affected, resulting in no delays in the approval reviews for these audit services in FY 2006.

d. Approval reviews for generic drugs, over-the-counter (OTC) drugs and quasi-drugs

- In accordance with "Standard Administrative Process Time for Approval Review," Notification No. 960 of the Director-General of the Pharmaceutical Affairs Bureau, Ministry of Health and Welfare dated October 1, 1985, the Agency set the standard administrative processing time of applications for generic drugs and other drugs submitted in and after April 2004 as follows.
  1) Generic drugs: 12 months
  2) OTC drugs: 10 months
  3) Quasi-drugs: 6 months

- With regard to reviews of generic drugs, etc., in order to carry out review operations promptly and accurately, the Agency developed the "Implementation Manual for Approval Review of Generic Drugs," "Implementation Manual for Approval Review of OTC Drugs," "Implementation Manual for Approval Review of Insecticides/Rodenticides" and "Implementation Manual for Approval Review of Quasi-drugs" as well as standard operating procedures for various operations. In addition to collecting data on the achievement level of the target review processing time each month and informing the review staff of these levels, monthly meetings of the Progress Management Committee for Review-Related Operations were continuously held to monitor and examine operational progress. In order to comprehend the progress more accurately, the Agency made fundamental revisions to documentation and materials in August 2006.

- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2006 are as follows.

Number of approved generic drugs and others

	FY 2002	FY 2003	FY 2004	FY 2005	**FY 2006**
Generic drugs	1,831	2,243	3,476	1,919	**2,152**
- Number of approved applications filed in and after April 2004 (breakdown)	—	—	1,468	1,782	**2,029**
- Median of review process time (for the applications filed in and after April 2004)	—	—	3.3 mths	7.3 mths	**4.0 mths**
- Achievement rates on target process time (for the applications filed in and after April 2004)	—	—	100%	98%	**93%**
OTC drugs	2,956	1,934	1,781	1,570	**1,030**
- Number of approved applications filed in and after April 2004 (breakdown)	—	—	270	1,163	**923**
- Median of review process time (for the applications filed in and after April 2004)	—	—	8.7 mths	7.8 mths	**6.3 mths**
- Achievement rates on target process time (for the applications filed in and after April 2004)	—	—	83%	84%	**85%**
Quasi-drugs	3,605	2,992	2,972	2,611	**2,287**
- Number of approved applications filed in and after April 2004 (breakdown)	—	—	1,431	2,575	**2,275**
- Median of review process time (for the applications filed in and after April 2004)	—	—	5.6 mths	5.3 mths	**5.5 mths**
- Achievement rates on target process time (for the applications filed in and after April 2004)	—	—	89%	86%	**67%**
Total	8,392	7,169	8,229	6,100	**5,469**
- Number of approved applications filed in and after April 2004 (breakdown)			3,169	5,520	**5,227**

Application and approval of OTC drugs and quasi-drugs by category of application

(OTC drugs)

Category of application	1	2	3	4-1	4-2	OTC test drugs	Insecticide, rodenticide	Total
Applied in FY 2006	1	29	30	126	1,002	-	48	1,236
Approved in FY 2006	0	24	33	74	845	-	54	1,030

(Quasi-drugs)

Category of application	1, 3	2	Insecticide 1, 2	Insecticide 3	Total
Applied in FY 2006	169	2,334	-	-	2,503
Approved in FY 2006	130	2,156	1	-	2,287

1. Categories of application

(OTC drugs)
1: Direct OTC drugs
2: Switch OTC drugs
3: Relatively innovative drugs excluding "1" and "2"
4-1: Relatively less innovative drugs
4-2: Drugs that are not innovative

(Quasi-drugs)
1: Products that include new active ingredient
2: Products that are not innovative
3: Innovative products excluding "1"
Insecticide 1: Products that include new active ingredient
Insecticide 2: Innovative products excluding "Insecticide 1"
Insecticide 3: Products that are not innovative

2. Each application belongs to the category for which it was submitted.
3. Each approval belongs to the category in which it was granted.

Status of generic and other drug reviews

	No. of Total Applications*	Approvals	Withdrawals**	Under Review
Generic drugs	4,790 (2,631)	2,152	173	2,465
OTC drugs	3,443 (1,236)	1,030	181	2,232
Quasi-drugs	3,998 (2,503)	2,287	96	1,615

** Values in ( ) show applications made in FY 2006 and are included in values above.*
*** Withdrawals include applications that were switched to another category during the review process.*

- With regard to achievement levels in FY 2006 of the target standard administrative processing time for applications submitted in and after April 1, 2004, the Agency attained an achievement level of 93% by reviewing 1,884 out of 2,029 applications for generic drugs within 12 months, 85% by reviewing 786 out of 923 applications for OTC drugs within 10 months and 67% by reviewing 1,533 out of 2,275 applications for quasi-drugs within 6 months. As a result, the Agency was able to adhere to the median for the administrative processing time indicated in the Ministry of Health and Welfare Notification No. 960 issued by Director-General of the

Pharmaceutical Affairs Bureau dated October 1, 1985.

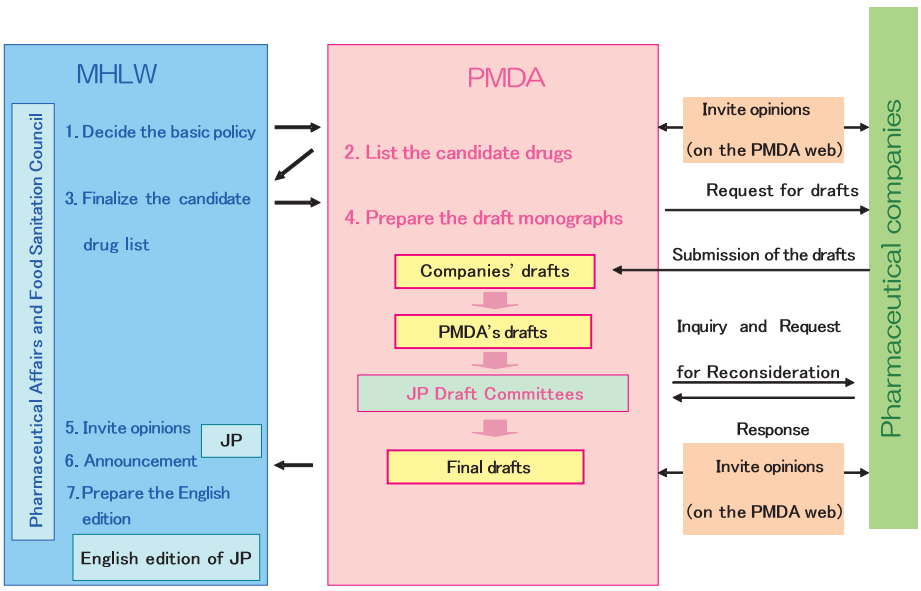
Document conformity audit conducted for generic drugs by fiscal year

	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006
Number of audits	1,228	1,425	1,090	941	628

- For generic drugs, the Agency implemented surveys to confirm the compliance with the conformity criteria for approval application materials, by collating them with raw data such as test records, experiment notes, case report forms.

- In FY 2006, the Japanese Pharmacopoeia Draft Committee held 92 meetings, and finalized 90 new monographs and 171 amendments for the first supplement of the 15th edition of the Japanese Pharmacopoeia (to be published in September 2007), while compiling a candidate drug list and reporting this list to the MHLW. In reviewing these items, a candidate drug list for Kampo extracts, and candidates for the first supplement of the 15th edition of the Japanese Pharmacopoeia were posted on the Agency's website for public comment. Also, the Agency developed guidelines for preparing the draft for the 16th edition of the Japanese Pharmacopoeia, distributed these guidelines to relevant industry groups and prefectural governments, and posted them on the PMDA website.

Flow of Revision of Japanese Pharmacopoeia



2. (1). 3. Improvement of clinical trial consultations

- In addition to improving pre-application consultations, it is desired for the Agency to give priority to conducting consultations regarding clinical studies for pharmaceuticals and medical devices expected to have high medical benefits, in order to shorten the time period for their approval.

a. Conducting priority clinical trial consultations

- With the priority clinical trial consultation system, the Agency succeeded in conducting clinical trial consultations in a prioritized manner as well as consultations on compliance with conformity

criteria, allowing an increase in opportunities to provide advice on approval applications before they are submitted.

- As for the priority clinical trial consultation system for pharmaceuticals considered to have particularly high medical necessity, the Agency received the applications for 9 ingredients in FY 2006 and designated 13 ingredients (including 4 ingredients for which an application was filed in FY 2005) out of 14 ingredients (including those for which an application was filed in FY 2005) as being applicable to priority clinical trial consultation, while rejecting one ingredient as it did not meet the requirements. For these designated ingredients, the Agency conducted a total of 16 clinical trial consultations.

  For medical devices, there were no applications for priority clinical trial consultations. For both pharmaceuticals and medical devices, there were no applications for face-to-face consultations regarding conformity for items designated as priority consultation items.

b. Acceleration of clinical trial consultations for pharmaceuticals

- The Agency worked to expedite clinical trial consultations for pharmaceuticals by shortening the duration from when application for a clinical trial consultation is submitted until a face-to-face consultation is conducted, as well as until the first face-to-face consultation for priority clinical trial consultations is conducted. This was made possible through properly managing operations by implementing appropriate improvement measures for such operations, and by developing an operational manual.

Clinical trial consultation for new drugs

	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006
Applications for CT consultation	246	185	334	339 (243)*	473 (327)*
Conducted CT consultations	225	206	193	218	288
Withdrawals	—	—	23	14	7
Total	225	206	216	232	295

** Values in ( ) do not include reapplications caused by rejection.*

- The Agency established goals so that for the period from when a face-to-face consultation is held until records are settled for 10% of all applications submitted is 30 business days, and the period until when the first face-to-face consultations is conducted for 50% of priority consultation applications is 30 business days. The number of clinical trial consultations for pharmaceuticals conducted in FY 2006 was 288 (excluding 7 withdrawn applications), and the number of consultations for which the period from when a face-to-face consultation was held until records were settled was 30 business days or less was 108 out of 320 cases (33.8%). The number of priority clinical trial consultations for which the period until the first face-to-face consultation was 30 business days or less was 12 out of 18 cases (66.7%), indicating that the goals for both

circumstances were achieved.

- In FY 2006, the Agency conducted 296 clinical trial consultations (including 7 withdrawals) in relation to a goal of 240 clinical trial consultations.

- The Agency promoted simple clinical trial consultations and support for joint international clinical trials. In FY 2006, it received 35 applications for consultations regarding joint international clinical trials for new active ingredients, of which 22 were carried out.

- In order to improve the quality of consultations, the Agency introduced a system in January 2007 in which the Agency's outlook regarding the consultation is presented to the applicant beforehand (PMDA preliminary outlook disclosure system).

Number of face-to-face clinical trial consultations conducted for drugs by category in FY 2006

	April	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	March	Total
Category 1 (Gastrointestinal drugs etc.)	3	1	4	3	3	3	3	3	3	3	3	1	33
Category 2 (Cardiovascular drugs)	3	2	4	3	3	3	3	4	6	2	3	4	40
In vivo diagnostics	0	1	0	0	0	0	1	0	0	0	0	1	3
Radiopharmaceuticals	0	0	0	1	1	1	0	0	0	0	0	0	3
Category 3 (Central/peripheral nervous system drugs etc.)	3	3	4	6	4	3	2	2	4	5	4	5	45
Category 4 (Antibacterial agents etc.)	1	2	2	3	1	1	3	1	3	3	2	2	24
Anti-AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 5 (Drugs for urogenital system etc.)	2	1	1	1	1	2	2	0	0	1	1	1	13
Category 6-1 (Respiratory tract drugs etc.)	1	1	3	2	2	3	4	1	3	3	1	0	24
Category 6-2 (Hormone drugs)	2	3	1	3	2	3	2	4	2	4	3	4	33
Anti-cancer drugs	5	3	3	5	3	5	3	5	4	4	4	3	47
Biologicals	1	1	0	1	1	1	0	1	2	1	1	1	11
Cellular and Tissue-derived products*	0	0	0	1	0	1	0	0	0	2	0	1	5
Blood products	0	1	1	1	1	0	1	1	1	0	0	0	7
Compliance to Conformity Criteria	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	21	19	23	30	22	26	24	22	28	28	22	23	288
Withdrawals	2	2	0	0	0	0	0	0	0	1	1	1	7
Grand Total	23	21	23	30	22	26	24	22	28	29	23	24	295

** Consultations on quality of biotechnology drugs fall into the category of "Cellular and Tissue-derived products."*

1. Consultation covering several categories was counted in terms of its main category.

2. Consultations on compliance with conformity criteria were all conducted by Office of Conformity Audit regardless of category.

Reference: Number of clinical trial consultations for new medical devices

	FY 2004	FY 2005	FY 2006
Applications for CT consultation*	9	33	46
(Medical devices)	7	32	43
(*In vitro* diagnostics)	2	1	3
Conducted CT consultations	8	30	42
(Medical devices)	6	29	39
(*In vitro* diagnostics)	2	1	3
Withdrawals	0	0	0
(Medical devices)	0	0	0
(*In vitro* diagnostics)	0	0	0
Total	8	30	42
(Medical devices)	6	29	39
(*In vitro* diagnostics)	2	1	3

** Applications submitted after arrangement of schedule.*

2. (1). 4. Promotion of international harmonization

- It is desired for the Agency to make efforts to accelerate the review process for new drug approvals, taking international trends into account, so that a target time for the total review process time (total of the processing time for the reviewer side and the processing time for the applicant side for items approved in a particular year) can also be established by the end of the effective period for the Mid-term targets.

a. Approaches towards international harmonization such as through the ICH

- In FY 2006, the Agency continued to actively participate in ICH Steering Committee Meetings and Expert Working Groups, and promoted further international harmonization by planning for consistency of Japanese standards with international standards such as for developing review data, which were agreed upon among Japan, the U.S. and the EU in ICH Meetings.

- Specifically, the Agency actively cooperated in efforts towards consistency and harmonization of international standards through participation in Steering Committee Meetings and Expert Working Groups of the ICH, GHTF, etc., as well as in the PDG.
  - ICH: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
  - GHTF: Global Harmonization Task Force for Medical Devices
  - PDG: Pharmacopoeial Discussion Group

International conferences on pharmaceuticals in which the PMDA participated (relating to reviews and safety measures)

- ICH Expert Working Groups
  - Electronic Standards for the Transfer of Regulatory Information (M2)
  - Non-Clinical Safety Studies for the Conduct of Human Clinical Trials (M3 (R3))
  - Data Elements for Transmission of Individual Case Safety Reports (E2B (R3))
  - Development Safety Update Report (E2F)
  - The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-antiarrhythmic Drugs (E14)
  - Terminology in Pharmacogenomics (E15)
  - Genotoxicity: A Standard Battery for Genotoxicity Testing of Pharmaceuticals (S2 (R1))
  - The Nonclinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Internal Prolongation) by Human Pharmaceuticals (S7B)
  - Immunotoxicity Studies for Human Pharmaceuticals (S8)
  - Pharmaceutical Development (addendum)(Q8 (R1))
  - Quality Risk Management (Q9)
  - GMP Quality Systems (Q10)
  - Regulatory Acceptance of Pharmacopoeial Interchangeability (Q4B)
  - Data Elements and Standards for Drug Dictionaries (M5)
- Pharmacopoeial Discussion Group (PDG)
- MedDRA (Medical Dictionary for Regulatory Activities) Steering Committee Meeting
- OECD Pharmacogenetics workshop
- WHO INN meeting
- WHO meeting on new influenza vaccine

- In order to build a concrete system for exchanging information, etc., relating to consultations, reviews and safety measures in cooperation with the U.S. and EU, the Agency held discussions with the FDA of the U.S. and the EMEA of the EU while collaborating with the MHLW.

International conferences on medical devices that the PMDA participated in (relating to reviews and safety measures)

ISO/TC/121
ISO/TC/150
ISO/TC/194
ISO/TC/210
ISO/TC/215
GHTF General meeting
GHTF SG1
GHTF SG2
GHTF SG3
GHTF SG4
GHTF SG5

b. Efforts to introduce the total review time

- In working towards introducing the concept of a total review time, the Agency is monitoring and managing the total review process time while taking international trends into account.

Number of approvals and review time of new drugs

	FY 2002*	FY 2003	FY 2004	FY 2005		FY 2006	
					Applied in and after April 2004**		Applied in and after April 2004**
Approved	52	51	49	60	24	77	49
PMDA review time (median)	(10.8 mths)	(11.3 mths)	(8.6 mths)	(12.0 mths)	(8.6 mths)	(13.7 mths)	(10.5 mths)
Total review time (median)	(15.8 mths)	(18.7 mths)	(13.5 mths)	(22.4 mths)	(16.2 mths)	(21.7 mths)	(19.2 mths)

* *The column of FY 2002 shows the data based on a calendar year.*

** *The figures show the breakdown on the applications approved in FY 2005 and FY 2006, which were applied in and after April 2004.*

- The number of new drugs that were approved in FY 2006 was 77, and the median of the review time (PMDA review time) for these applications was 13.7 months, whereas the median of the total review time was 21.7 months. Applications for 49 of these approved drugs were submitted in and after April 2004, of which the median of the review time (PMDA review time) was 10.5 months and the median of the total review time was 19.2 months.

Number of approvals and review time of new medical devices

	FY 2002*	FY 2003	FY 2004	FY 2005		FY 2006	
					Applied in and after April 2004*		Applied in and after April 2004*
Approved	3	14	8	11	5	23	15
PMDA review time (median)	(2.9 mths)	(9.5 mths)	(12.7 mths)	(7.7 mths)	(1.8 mths)	(6.0 mths)	(3.4 mths)
Total review time (median)	(5.9 mths)	(18.7 mths)	(35.8 mths)	(22.4 mths)	(10.3 mths)	(19.7 mths)	(15.3 mths)

* *The figures show the breakdown on the applications approved in FY 2005 and FY 2006, which were applied in and after April 2004.*

- The number of new medical devices that were approved in FY 2006 was 23, and the median of the review time (PMDA review time) for these applications was 6.0 months, whereas the median of the total review time was 19.7 months. Applications for 15 of these approved medical devices were submitted in and after April 2004, of which the median of the review time (PMDA review time) was 3.4 months and the median of the total review time was 15.3 months.

- As approaches directed towards implementing the total review time, the Agency continued to enrich clinical trial consultations and solve as many fundamental problems as possible before the submission of applications. In addition, for applications with reviews that were suspended due to reasons of the applicant, the Agency conducted consultations with the applicant and advised them to withdraw their application.

2. (2) Improvement in Reliability of Operations

2. (2).1. Planned recruitment of staff with advanced expertise and systematic provision of training opportunities

a. Staff recruitment

- In order to ensure smooth enforcement of the revised Pharmaceutical Affairs Law enacted in 2005, and to conduct operations for reviews and safety measures promptly and appropriately, the Agency recruited competent human resources with high expertise, mainly through open recruitment, while ensuring its neutrality and impartiality as an incorporated administrative agency (refer to “II-PART 2-4-(4) Securing Human Resources through Open Recruitment”).

b. Systematic training

- In order to implement systematic training adapted to the purpose of operations, as well as to provide training suited to the qualifications and capabilities of individual staff members, the Agency worked to improve the skills and knowledge of its staff members by providing them with training opportunities using external training organizations and outside experts (refer to “II-PART 2-4-(2). Systematic Implementation of Staff Training”).

2. (2). 2. Development of a GMP/QMS audit system

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

** GMP Ministerial Ordinance on Drugs and Quasi-drugs:*
"Standards for Manufacturing Control and Quality Control of Drugs and Quasi-drugs," MHLW Ministerial Ordinance No. 179 revised in December, 2004
** QMS Ministerial Ordinance on Medical Devices and In Vitro Diagnostics:*
"Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostics," MHLW Ministerial Ordinance No. 169 revised in December, 2004
** GMP: Good Manufacturing Practice. Standards for manufacturing control and quality control*
** QMS: Quality Management System*

- Therefore, the Agency continued to recruit GMP/QMS inspectors to form a system of 30 inspectors as of April 1, 2007. At the same time, the Agency is also promoting educational training for the GMP/QMS inspectors as well as training programs both domestic and abroad, including seminars hosted by PIC/S (Pharmaceutical Inspection Cooperation Scheme, a European-based international organization for GMP audits).

GMP/QMS audits conducted according to the revised Pharmaceutical Affairs Law

	FY 2005				FY 2006			
	Applied	Completed	With-drawn	In prog-ress	Applied	Completed	With-drawn	In prog-ress
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

** Excluding in vitro diagnostics*
Values in ( ) show the number of on-site audits.

- The actual performance of on-site inspections (including on-the-spot inspection of manufacturing sites abroad) that were initiated in FY 2005 is shown below.

On-site audit of overseas manufacturing sites of drugs by regions

	Europe	North, Central and South America	Asia	Africa	Total
FY 2005	2	10	2	0	14
FY 2006	15	21	2	1	39

	Europe	North, Central and South America	Asia	Africa	Total
FY 2005	1	1	0	0	2
FY 2006	5	12	0	0	17

- The administrative processing times of GMP/QMS inspections in FY 2006 are shown below.

Process time of GMP/QMS audit according to revised Pharmaceutical Affairs Law

	FY 2005		FY 2006	
	Total process time (median)	PMDA process time (median)	Total process time (median)	PMDA process time (median)
Drugs (excluding *in vitro* diagnostics)	78 days	59.5 days	161 days	117 days
In vitro diagnostics	101 days	101 days	149 days	100 days
Quasi-drugs	—	—	142 days	72 days
Medical dievices	131 days	104 days	161 days	110 days

- The processing status of audits for manufacturing facilities conducted in FY 2006 at domestic manufacturing sites under authorization by the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below.

Number of audit of buildings and facilities for domestic manufacturing sites

	FY 2005	FY 2006
Drugs*	12 (8)	30 (23)
In vitro diagnostics	1 (1)	6 (6)
Medical devices	2 (1)	1 (0)
Total	15 (10)	37 (29)

**) Excluding in vitro diagnostics*
Values include withdrawn cases. Values in () show the number of on-site audits.

- The processing status of audits for manufacturing facilities conducted in FY 2006 at overseas manufacturing sites under authorization by the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below.

Number of audit of buildings and facilities for overseas manufacturing sites

	FY 2005	FY 2006
Drugs*	69	614
In vitro diagnostics	9	85
Quasi-drugs	29	73
Medical devices	127	971
Total	234	1,743

** Excluding in vitro diagnostics*
Values include withdrawn cases. All cases were document inspections.

- The Agency conducts on-the-spot inspections, questioning and sampling with regard to manufacturers, etc., based on instructions from the MHLW. The number of on-the-spot inspections conducted in FY 2006 is shown below.

Number of on-site inspections

		FY 2005	FY 2006
Domestic manufacturers	Drug	15	11
	Medical devices	0	0
Foreign manufacturers	Drugs	2	3
	Medical devices	0	2
Total		17	16

2. (2).3. Use of external experts

- The Agency continued with procedures to commission external professionals as outside experts for the Agency in order to obtain specialized opinions relating to scientifically important matters during expert discussions, etc., for reviews and safety measures. (As of March 31, 2007, the number of commissioned experts is 873 (including outside experts commissioned for matters relating to safety measures).)

2. (2).4. System development for more efficient review services

- In addition to a new application/review system reviews used by the PMDA, Pharmaceutical and Food Safety Bureau in the MHLW, Regional Bureau of Health and Welfare, prefectural governments, pharmaceutical companies, etc, the system for review operations used by the Agency is comprised of the following individual systems necessary for executing reviews, surveys and management of commission: (i) Support system for surveys on pharmaceuticals, etc., (ii) New drug database system, (iii) Device system, (iv) Conformity audit support system, (v) Medical device survey 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).

- With this new application/review system, the Agency is able to manage the progress for the entire process, from acceptance of applications and notifications for marketing approval and business license on pharmaceuticals, quasi-drugs, cosmetics and medical devices, until their enforcement. In addition, the Agency uses this system for operations related to official licenses, such as the development of application data (application software), acceptance of the application data, data exchange among review and survey institutions, recording of review memorandums, preparation of approval certificates and management of approval registration list.

- In FY 2006, the Agency 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, the Agency conducted the following system developments to promptly and efficiently perform review and audit services.

    1) Addition of new functions to support system for eCTD review of new drugs
    - The Agency added a portal page, registration for draft versions of eCTD data and management functions to the system developed in FY 2005, and also newly developed a format check tool for applicants as well as data for browsing, equipped with a security management function for outside experts.

    2) Transportation of database systems such as of clinical trial plans, and upgrading of equipment
    - With regard to the clinical trial database system that had been used by OPSR (which is the predecessor to the PMDA), the Agency replaced the system since the maintenance period for equipment that had been used since December 2000 was close to expiring.

3) Development of support system for surveys on pharmaceuticals in conjunction with the establishment of new consultation categories for medical devices

- The Agency improved functions for the system so that it would be possible to receive and confirm the commission fees for new categories. It also improved the ledger management function of the system such as the aggregation function and ledger form output function for newly established categories.

2. (2).5. Reinforcement of partnerships with foreign regulatory authorities

- In order to reinforce the structure for international operations, the Agency appointed a full-time section chief in the International Affairs Division to collect and provide information. Also, the Agency promoted reinforcement of partnerships with regulatory authorities in the U.S. and Europe relating to operations for reviews and safety measures, as well as with those of Asian countries where more clinical trials are conducted, through dispatching and welcoming trainees.

- In order to promote reinforcement of partnerships with the regulatory authorities of the U.S. and Europe as well as with those of Asian countries where clinical trials are conducted, the Agency participated in international conferences such as for the ICH, GHTF and PDG, as well as in meetings of for the OECD and WHO, and promoted cooperation with relevant countries with regard to developing international guidelines. The Agency also provided lectures on its review services and safety measures at the DIA Annual Meeting in the U.S. and at the DIA EURO Meeting in Austria to improve international recognition of the Agency, while expanding the cooperative framework with Asian countries by visiting China, South Korea, Singapore, Hong Kong, etc. (refer to “II-Part 3-2-(1)-4.-a. Approaches towards international harmonization such as through the ICH”). The Agency also implemented the following measures to further strengthen its partnerships with foreign regulatory authorities.

1) The Agency collected information on the review system and safety measures at the FDA (Food and Drug Administration), EMEA (European Medicines Evaluation Agency), etc. The Agency also exchanged information with the FDA and EMEA on methods for conducting operations, etc. In addition, the Chief Executive and other members of the Agency were invited to the FDA’s 100th anniversary celebration, where they exchanged opinions with their counterparts in the FDA and other foreign regulatory agencies.

2) Based on the “Administrative Rules on Overseas Training on a Long-term Basis”, the Agency dispatched one employee each to FDA and OECD after recruiting personnel who were interested in being dispatched and screening the applicants.

3) The Agency accepted 2 trainees from Taiwan and 4 trainees from Indonesia.

2. (2).6. APEC network symposium

- The Agency hosted “The 2006 Symposium of APEC Network on Pharmaceutical Regulatory Science” under the theme of “Global Development of Drugs and Co-operation among Asian Economies” on October 12 and 13, 2006 at the Royal Park Hotel in Tokyo, where about 500 participants from regulatory agencies and industries in the U.S., Korea, Thailand, Taiwan,

Singapore, etc., gathered and held lively discussions through presentations and panel discussions. The presentation materials from this symposium have been made available on the English version of the PMDA website to inform people abroad of the symposium.

2. (2).7. Evaluation of the advanced technologies, such as biotechnology and genomics; cooperation in developing national guidelines

- As it is desired for the Agency to raise the standards for guidance and review techniques for the advanced technologies such as biotechnology and genomics, the Agency utilized outside experts with a high level of knowledge and cooperated in developing national guidelines for reviewing products to which new technology has been applied.

- The Agency cooperated in developing national evaluation standards for regenerative medicine to which new technology has been applied. At the same time, the Agency also compiled the points to consider when creating application materials, and provided information to the industry and academia such as through the academic societies in order to facilitate guidance and reviews.

- In order to expedite reviews relating to the new influenza vaccine using recombinant DNA technology, the Agency is making efforts for prompt reviews by offering necessary guidance to companies starting in the development stage.

- In order to study effects on the safety and efficacy of pharmaceuticals by genetic factors of individual patients, and to administer pharmaceuticals to each patient in more appropriate conditions, there are expectations for applications towards pharmaceutical development of pharmacogenomics. However, since there are still many aspects to be considered, such as how pharmagenomics should be used in clinical trials and approval reviews, the “Pharmacogenomics Discussion Group (PDG)” was established within the Agency to collect information from a scientific standpoint while cooperating with the MHLW and commencing reviews directed towards developing specific guidelines. In FY 2006, the PDG held 6 unofficial meetings with the private sector to share information on pharmacogenomics and exchange opinions.

- In order to conduct international exchange information relating to review items on biologics, such as central/peripheral nervous system drugs and genetically-modified protein, and to apply such information to consultations and review services, the Agency invited members responsible for reviews at the FDA, EMEA, etc., and hosted the “1st PMDA Biologics Symposium” on February 15, 2007.

  JAN : Japanese Accepted Names
  INN : International Non-proprietary Names

- The Agency held 4 meetings for expert discussions on pharmaceutical names and reported 27 Japanese Accepted Names (JAN) to the MHLW. The Agency also initiated application consultations for International Non-proprietary Names (INN) in August 2006 and participated in a conference on INN hosted by WHO in November of the same year.

2. (2).8. Promotion of appropriate clinical trials

- To improve the quality of clinical trials in Japan, the Agency informed and healthcare professionals and patients about appropriate clinical trials through its website and public relations, taking into consideration the results of on-site inspections at medical institutions, etc.

- For the purpose of contributing to promoting the development of clinical trial systems at medical institutions, from which trainees are dispatched, the Agency implemented “Training for Clinical Research Coordinators” (training through lectures in September 2006 and practical training from October 2006 to February 2007) to pharmacists and nurses from medical institutions.

- In addition, to facilitate an effective system for promoting clinical trials, the Agency granted subsidies to core medical institutions that implement clinical trials efficiently by gathering and accumulating clinical data and responding to severe adverse drug reactions from study drugs in cooperation with local core hospitals, clinics and SMOs (Site Management Organizations). (Clinical Trial Promotion Local Network Project)

  In FY 2006, which is the last year of the three-year plan period for activation of clinical trials nationwide (started on April 30, 2003 by the Ministry of Education, Culture, Sports, Science and Technology and the MHLW), the Agency continued to grant subsidies to the 2 facilities below.
  - Chiba University Hospital (Chiba city, Chiba prefecture)
  - Specified Medical Corporation Shouwakai, Brain Attack Center Ota Memorial Hospital (Fukuyama city, Hiroshima prefecture)

- On the PMDA website, the Agency disclosed case examples of GCP audits that it is implementing and for which there have been many suggestions.

2. (2).9. Prompt provision of information such as review reports

- In promoting appropriate use of pharmaceuticals and ensuring transparency of approval reviews, the Agency has, with the understanding and cooperation of related companies, and also with the cooperation of the MHLW, posted information on the approval of new drugs, etc., on the Information Page of the PMDA website as follows.

[Review reports on new drugs]

- Based on the contents of the submitted applications, new drugs are classified into two categories: those that are to be discussed in the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (hereinafter referred to as “discussion items”) and those that are to be reported to the Drug Committees of the PAFSC (hereinafter referred to as “reported items”). From among the information on newly approved drugs, “Review Reports” that describe the status and results of reviews, and “Summaries of Application Materials” that contain overviews of application materials, are subject to provision of information for discussion items, whereas “Review Reports” are considered subject to provision of information for reported items.

- Information provision is implemented upon conferring with the relevant companies regarding the

contents for disclosure for each item and based on the Notification from the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW.

- In FY 2006, the Agency finalized 77 review reports and 51 summaries of application materials to be officially disclosed.

[Review reports on new medical devices]

- The Agency sequentially disclosed review reports on new medical devices according to the procedures specified in the Notification of the Office of Medical Devices Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW dated September 22, 2005. In FY 2006, the Agency disclosed review reports for 7 applications.

[Review reports on OTC drugs and quasi-drugs]

- The Agency sequentially disclosed review reports on OTC drugs and quasi-drugs according to the procedures specified in the Notification of the Office of Medical Devices Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW dated March 31, 2006. In FY 2006, the Agency disclosed 14 review reports for OTC drugs and 10 for quasi-drugs.

2. (3) Enhancement of Safety Measures (Reinforcement of Information Management and Risk Management System)

2. (3).1. Basic direction of safety measures

- In order to improve the safety of marketed pharmaceuticals and medical devices, and to enable patients and healthcare professionals to use them properly, the Agency has been progressing with operations so that reviews and safety measures function in a way such that they are inseparable, by collecting and examining safety information efficiently, processing the information speedily and providing appropriate and accurate plans for safety measures and easily understandable safety information promptly.

- There are approximately 100,000 reports on adverse drug reactions caused by pharmaceuticals submitted to the PMDA from within and outside of Japan per year, and approximately 10,000 reports on malfunctions of medical devices from within and outside of Japan per year. The Agency organizes this information into a database and promotes the sharing of this information with the MHLW. In addition, the Agency is making efforts to take effective safety measures for pharmaceuticals and medical devices in the post-marketing stage by reinforcing cooperation between the review divisions and safety divisions, as well as between the relief divisions and safety divisions.

- In addition to reviewing such adverse reaction reports and malfunction reports with representatives from the MHLW every week based on daily reviews conducted by the supervising team in the PMDA, the Agency gathers opinions from professionals once every 5

weeks and proposes necessary safety measures, such as for revision of precautions in package inserts. Issues that require particular urgency are responded to immediately.

- The Agency distributes important safety information, such as on revision of precautions in package inserts, to people involved in the medical field and in the private sector 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 Information Page of the PMDA website: http://www.info.pmda.go.jp/.

- The Agency is in the process of implementing a method for detecting and analyzing new safety information by finding relevance with different kinds of information on adverse drug reactions (data mining method) during the effective period for the midterm-plan in order to establish measures to prevent adverse drug reactions from occurring.

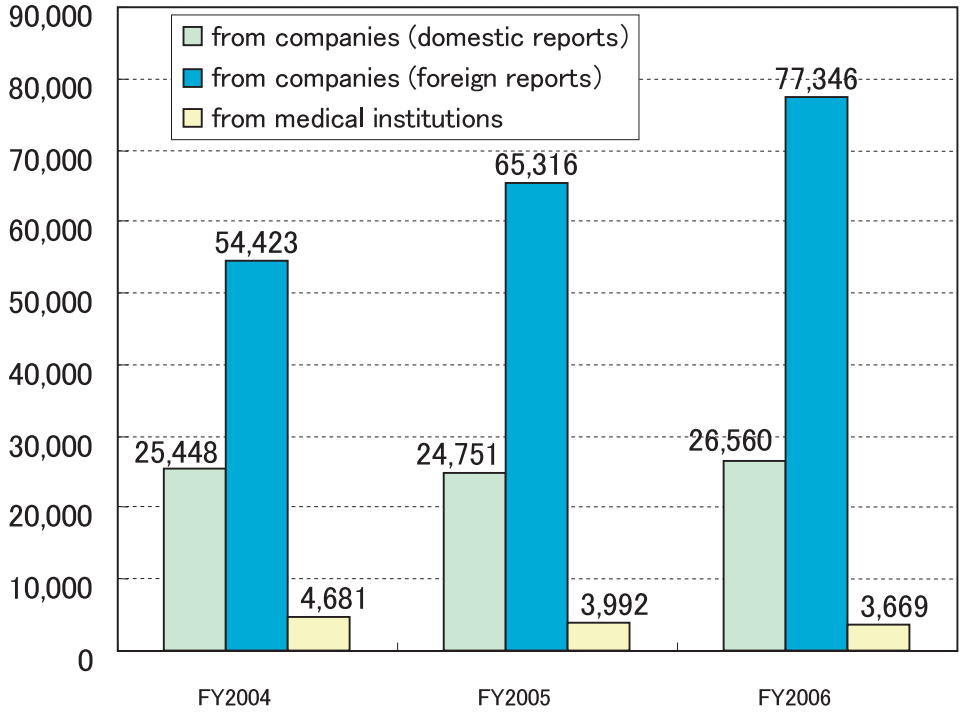
- In the future, the Agency plans on enhancing safety measures by working on those that are capable of “predicting and preventing” through active scientific evaluation and analysis, and by building a sentinel medical institution network, establishing a full-time department in which the data mining method is used and that extracts signals, etc.

[Collection of adverse reaction reports, etc.]

1) Number of reports relating to pharmaceuticals

	FY2004	FY2005	FY2006
Reports from companies	82,624	92,678	106,285
(cases of adverse drug reactions: Japanese)	(25,142)	(24,523)	(26,309)
(cases of infections caused by drugs: Japanese)	(306)	(228)	(251)
(cases of adverse drug reactions: foreign)	(54,312)	(64,650)	(77,314)
(cases of infections caused by drugs: foreign)	(111)	(666)	(32)
(research reports)	(1,311)	(971)	(818)
(foreign corrective action reports)	(420)	(563)	(485)
(periodic infection reports)	(1,022)	(1,077)	(1,076)
Reports from medical professionals	4,594	3,992	3,669
Total	87,218	96,670	109,954

Changes in the number of reports on adverse drug reactions/infections

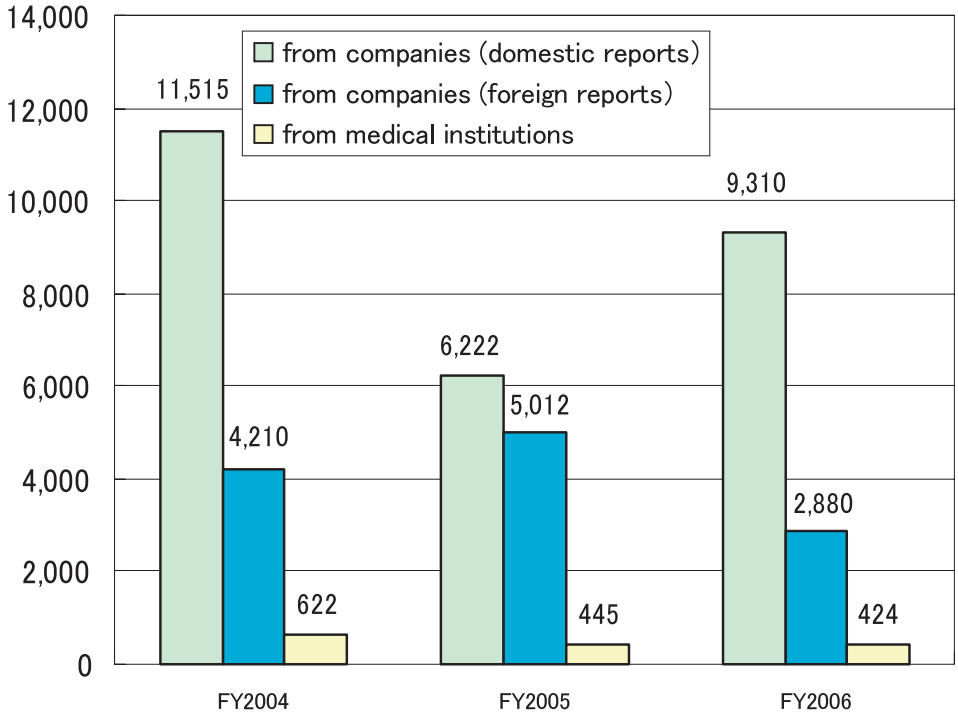


2) Number of reports relating to medical devices

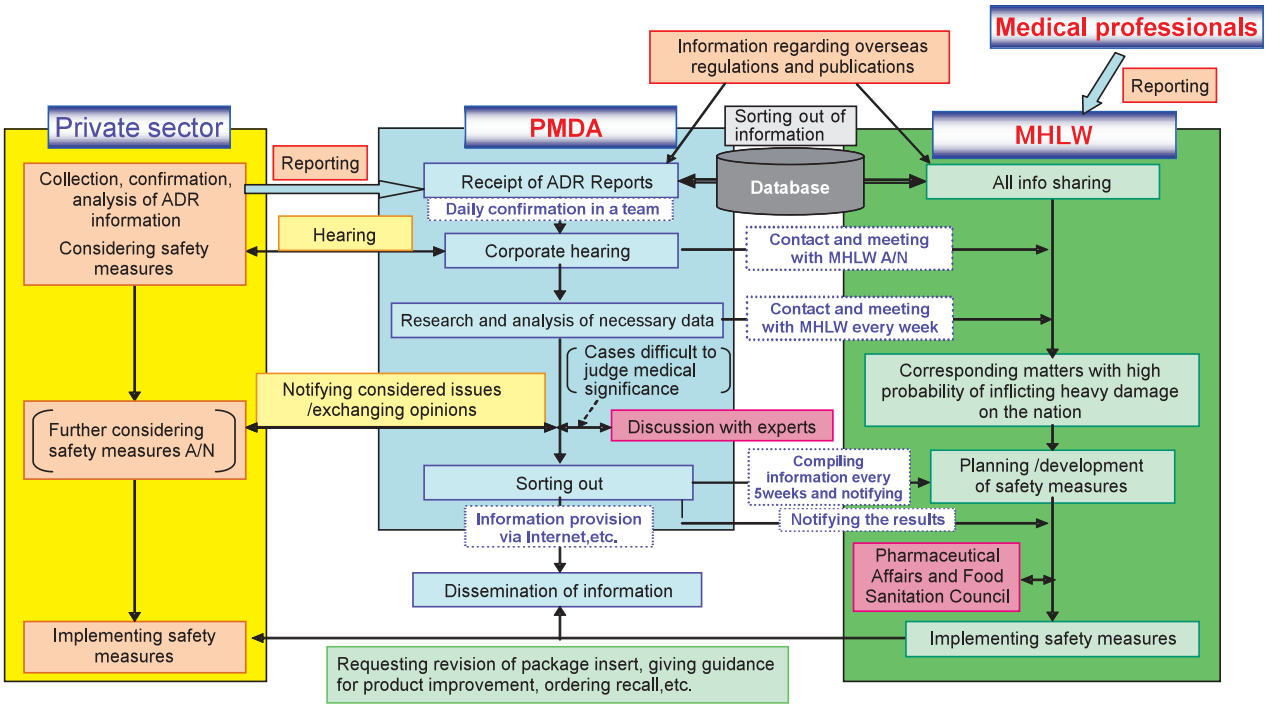
	FY2004	FY2005	FY2006
Reports from companies	16,264	11,802	12,770
(cases of malfunctions of medical devices: Japanese*)	(11,515)	(6,222)	(9,310)
(cases of malfunctions of medical devices: foreign*)	(4,210)	(5,012)	(2,880)
(research reports)	(157)	(37)	(36)
(foreign corrective action reports)	(287)	(436)	(482)
(periodic infection reports)	(95)	(95)	(62)
Reports from medical professionals	622	445	424
total	16,886	12,247	13,194

** There was no report of infection cases by medical devices.*

Changes in the number of reports on medical device malfunctions



Flowchart for processing adverse reaction reports



2. (3).2. Introduction of a new method (review of the data mining method)

- The Agency is aiming to implement a method for detecting and analyzing new safety information by finding relevancy in different kinds of information on adverse drug reactions (data mining method) in order to establish measures for preventing adverse drug reactions.

[Reference] What is 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 activity of retrieving, or “mining,” only useful information from the database.

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

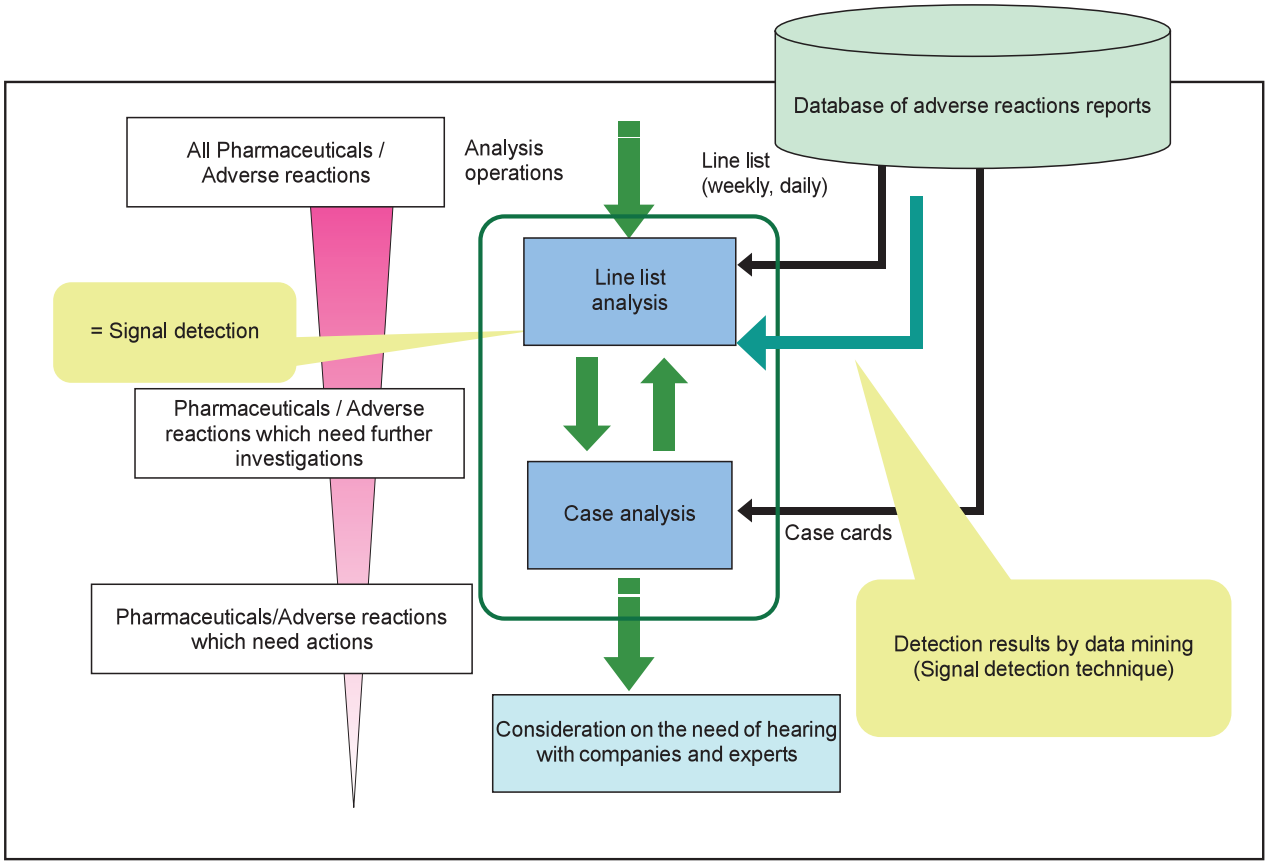
- In FY 2006, the Agency reviewed more advanced and appropriate signal detection techniques by incorporating the results of past reviews. In addition, the Agency established a signal detection technique by evaluating the accuracy of the technique through analyzing sensitivity and specificity, and by narrowing down the signal detection techniques to review in the future based on correlations between indicator values of signal detection techniques.

- In August 2006, the Agency also disclosed the state of implementation up until FY 2005 on the Information Page of the PMDA website.

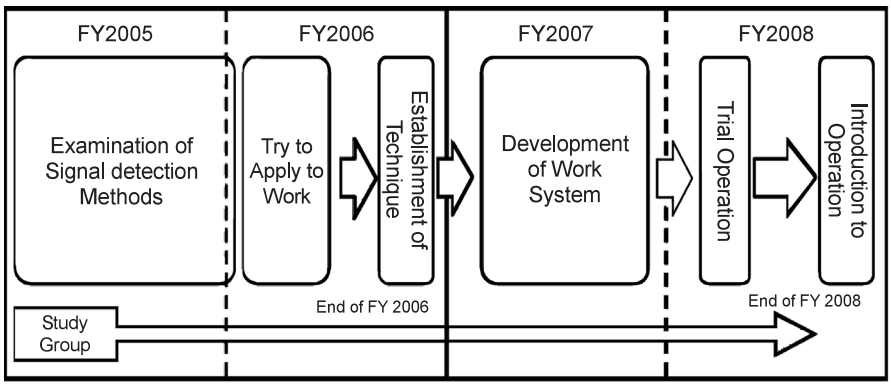
- In FY 2007, the Agency is planning on starting development of a system of operations as a support tool for current safety measures based on line lists and in accordance with review results obtained in FY 2006. Then, after conducting a trial operation, the Agency plans on introducing the system safety measures by FY 2008 (when the effective period for the midterm targets ends).

- The status of reviews relating to the implementation of safety measures for the data mining method is posted on the following website: http://www.info.pmda.go.jp/kyoten/dm.html

Introducing the data mining method into safety measures



Schedule for introducing the data mining method (planned)

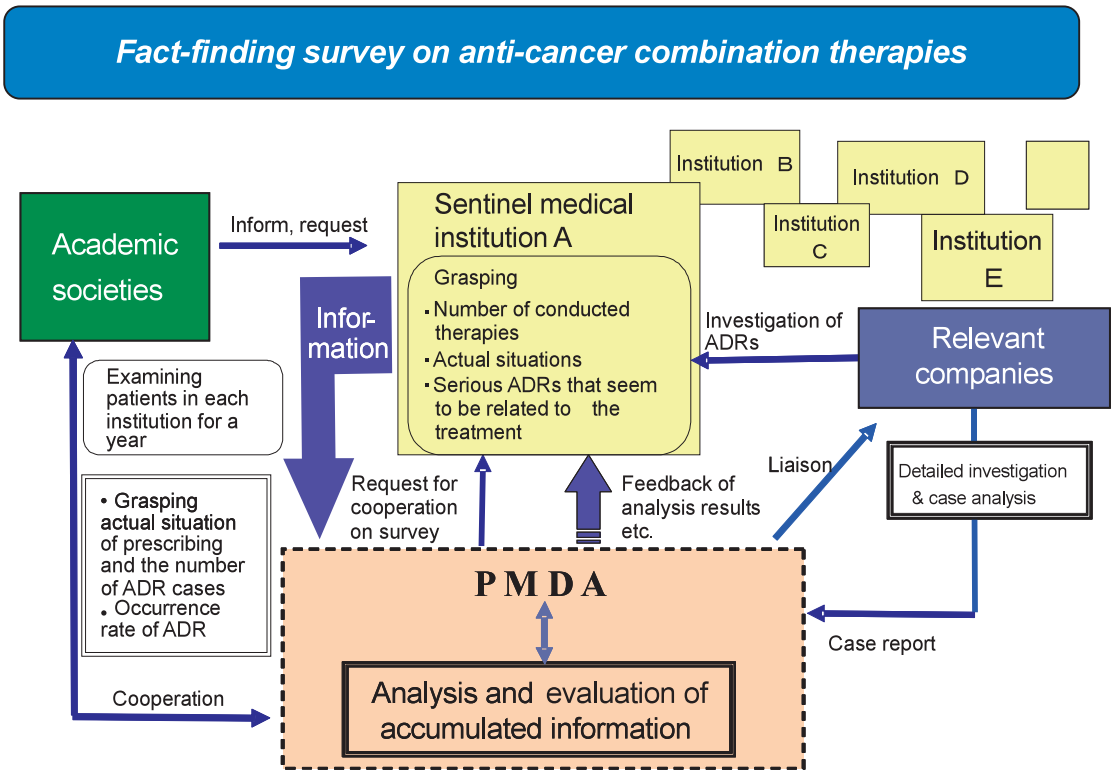


2. (3).3. Building a sentinel medical institution network

- As the Agency plans on emphasizing safety measures in the post-marketing stage in accordance with the midterm-plan, it is aiming to establish a sentinel medical institution network (a network of medical institutions organized according to specific therapeutic categories, products and diseases, of which the purpose is to collect information intensively within a certain period of time from the medical institutions in order to improve the accuracy of analysis of information on adverse drug reactions).

- The Agency has also continued to conduct fact-finding surveys on anti-cancer combination

therapies (22 therapies), and in FY 2006, the Agency disclosed preliminary results (using the data from up until March 2006) of 75 participating institutions, 2,926 registered patients and a total of 456 of reported incidents of adverse drug reactions on the PMDA website. Together with the preliminary results, the Agency also examined the methods for analysis and data entry for the final tabulation and evaluation that is to be conducted in FY 2007.



[Reference] Therapies subject to fact-finding survey on anti-cancer combination therapies (22 therapies*)

**The numbering for the 22 therapies is unique to the PMDA as therapies were categorized based on the implementation methods of the surveys.*

1. AC therapy (breast cancer)
2. Pamidronate Disodium (breast cancer)
3. (1) Ifosfamide single therapy (bone and soft tissue tumor)
   (2) Doxorubicin single therapy (bone and soft tissue tumor)
   (3) Ifosfamide and doxorubicin combination therapy (bone and soft tissue tumor)
4. (1) Ifosfamide (pediatric solid tumor)
   (2) Doxorubicin (pediatric solid tumor)
   (3) Etoposide (pediatric solid tumor)
5. AP therapy (uterin corpus cancer)
6. Cisplatin (malignant bone tumors)
7. VAD therapy (myeloma)
8. Fluorouracil (head and neck cancer)

9. Procarbazine/vincristine (brain tumor)
10. Fluorouracil/leucovorin (colon cancer)
11. (1) ESHAP (malignant lymphoma)
    (2) DHAP (malignant lymphoma)
12. (1) Cisplatin (pediatric solid tumor)
    (2) Carboplatin (pediatric solid tumor)
    (3) Cisplatin (medulloblastoma)
13. Actinomycin (Ewing's sarcoma family of tumors)
14. (1) EC therapy (breast cancer)
    (2) CEF therapy (breast cancer)

- The Agency conducted a survey for confirming the safety related to drug therapy for children, in order to comprehend the problems in collecting safety information in the pediatric field. This survey was conducted in conjunction with "Services for collecting supporting information on drug therapy for children" of the MHLW, and had the purpose of confirming the safety of pharmaceuticals regarded as items subject to being surveyed as part of these services. In addition, from among the pharmaceuticals with package inserts that state that "safety with regard to children has not been established," the Agency is aiming to conduct surveys for the purpose of confirming safety on those for which revisions have been requested from academic societies as well as those for which it is necessary to collect pediatric safety information from multiple companies.

- As a trial survey in the sentinel medical institution network, the Agency implemented "retrospective studies using an electronic medium on hyponatremia caused by the administration of maintenance fluid" in children in 3 different institutions in FY 2006. As a result, the Agency was able to obtain the data serum Na values before and after administration of the maintenance fluid from 1,291 cases in the 3 institutions.

- In FY 2007, the Agency plans on continuing to analyze this data.

- Furthermore, in order to conduct a survey on safety relating to "internal application of cromolyn sodium for atopic dermatitis based on food allergies in infants less than 6 months old," the Agency established a study team comprised of outside professionals and discussed safety.

- The Agency is planning on reconfirming the evidence that is necessary for revising package inserts together with the Ministry of Health, Labor and Welfare (MHLW), and re-reviewing the survey plans in FY 2007.

2. (3).4. Review of the system for comprehending and evaluating medical device malfunctions

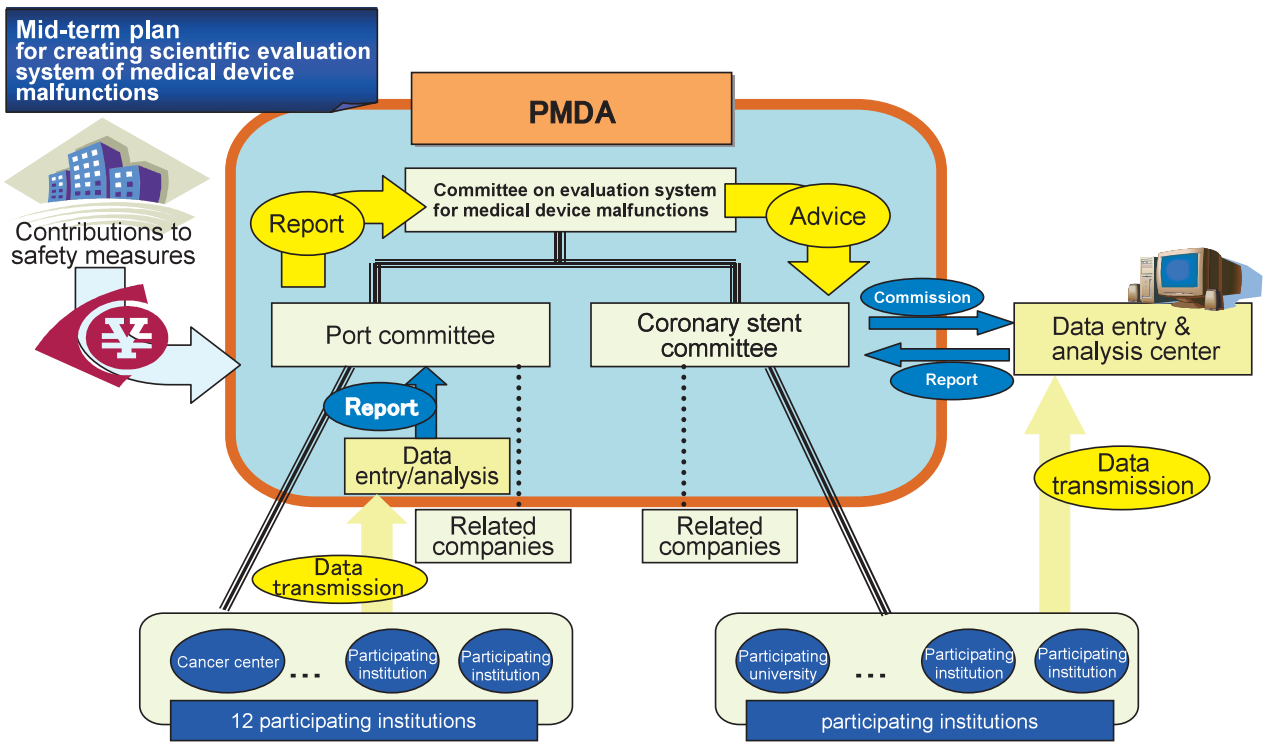
- Reports on the implementation status of surveys and the status of reviews in the sectional committee in charge in FY 2006 regarding coronary stents and implant-type infusion instruments (hereinafter referred to as "implant-type ports") were made to the "Discussion

Group for the System for Evaluating Medical Device Malfunctions."

The status of implementation in FY 2006 is as follows :

a) With regard to implant-type ports, in order to evaluate malfunctions that cannot be considered as resulting from structural defects, the Agency made classifications according to categories for malfunctions and conducted a survey for the purpose of evaluation. The Agency started registering patients in November 2006, and was able to register 113 patients from 12 participating institutions, exceeding the target of 100 registered patients. In FY 2007, the Agency plans on conducting a one-year follow-up study on registered patients and tabulating preliminary results during the course of the year.

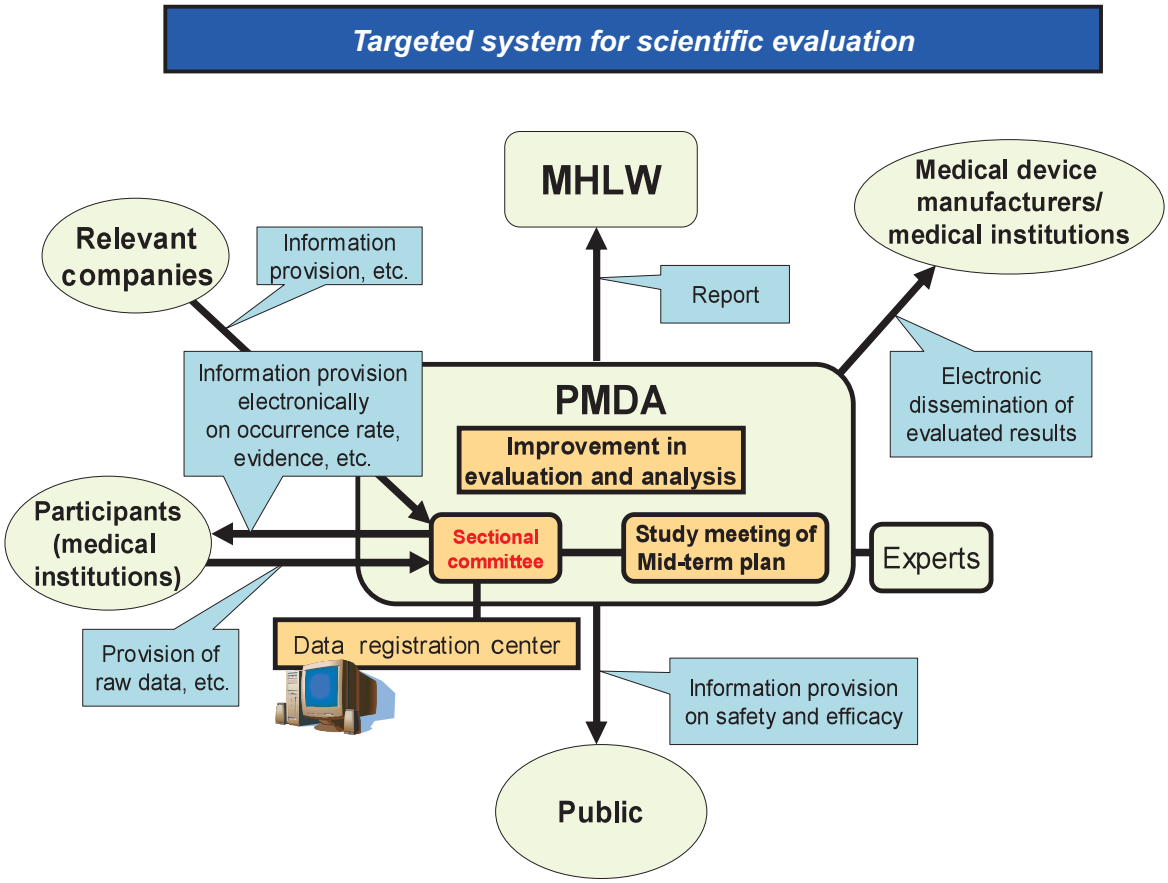
b) With regard to coronary stents, the Agency established a sectional committee comprised of professionals, etc., which discussed the survey objectives and methods for coronary stents, and conducted hearings with relevant companies. Based on the opinions, etc., obtained, the Agency created plans for implementing surveys and started selecting parties to which it commission the work, such as collection of survey slips, etc., in working towards conducting the coronary stent surveys.



- For surveys targeting medical devices that require tracking, such as cardiac pacemakers, the Agency conducted hearings with researchers and relevant companies, as well as reviews regarding the current status of tracking and needs of medical sites and of manufacturers. Based on the results obtained, the Agency developed an overview of the information collection system for medical devices requiring tracking that should be built by the Agency. The Agency also

reported the implementation status of these activities to the "Discussion Group for the System for Evaluating Medical Device Malfunctions." In FY 2007, the Agency plans to consider it further based on this overview and begin discussion to build the system.

[Reference] Medical devices that require tracking:
Medical devices for which it is obligatory for a marketing approval 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 Law, such devices are categorized as designated medical devices.



2. (3).5. Proper implementation of surveys for reports on adverse reaction and medical device malfunctions

- Adverse reaction reports, reports on medical device malfunctions, reports on infections, and research reports etc., from marketing approval holders of pharmaceuticals and medical devices based on the Pharmaceutical Affairs Law have been required to be submitted directly to the PMDA starting in April 2004. These reports are input into the PMDA database and managed so that information can be shared with the MHLW.

- In addition, adverse reaction reports, reports on infections, etc., that are submitted by medical professionals (doctors, pharmacists, etc.) to the MHLW are input into the PMDA database and

managed so that information can be shared with the MHLW.

- In conducting surveys on reports on adverse reaction and medical device malfunctions, the Agency has been closely working with the Safety Division of the Pharmaceutical and Food Safety Bureau at the MHLW to hold weekly reviews on both pharmaceuticals and medical devices, gather 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. Issues that require particular urgency are responded to immediately

- The number of reports made to the MHLW regarding items for which measures are necessary, such as for revision of package inserts, is as follows.

(Reports)

	FY2004	FY2005	FY2006
Pharmaceuticals	133	240	131
Medical Devices	15	18	4
Medical Safety*	2	2	2

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

- Safety measures taken by the MHLW in FY 2006 based on reports from the PMDA are as follows (including overlapping measures).

		FY2004	FY2005	FY 2006
Pharmaceuticals	Instructions for revision to precautions in package insert	149	212	131
	Posting articles and cases on Pharmaceuticals and Medical Devices Safety Information	33	26	24
Medical Devices	Instructions for revision to precautions in package insert or notifications to instruct self-inspection	7	7	0
	Posting articles on Pharmaceuticals and Medical Devices Safety Information	6	7	0

These numbers indicates those of safety measures taken by MHLW based on the report from PMDA.

- With regard to cooperation with review divisions within PMDA, approaches such as participation of personnel from Office of Safety in the review process (expert discussions, etc.) of new drugs and new medical devices, and cooperation in adverse drug reaction case evaluations for early

post-marketing stage vigilance (EPPV) are being implemented. As for cooperation with the Office of Relief Fund, information such as names of pharmaceuticals and adverse drug reactions in judged cases for payment/rejection of payment of benefits has been provided and is reflected in safety measures.

- In FY 2006, the Agency took the following approaches to appropriately collect, organize and examine the adverse reaction reports and reports on medical device malfunctions submitted by the private sector and medical institutions.

a) Raised the online reporting rate (to 90.4% for the full year) by holding consultations with companies that had not yet introduced an online reporting system for adverse drug reactions
b) Improved the efficiency in receiving adverse reaction reports by using data input tools
c) Enriched the staff members specialized in data input
d) Updated the master files consisting of pharmaceutical and company names
e) Encouraged staff members to attend academic societies (total of 55 participants) and gathered information through the academic societies that they participated in
f) Cooperated smoothly with the MHLW
g) Created standard operating procedures
h) Regularly held liaison meetings on both pharmaceuticals and medical devices every week with the MHLW

2. (3).6. Digitization of adverse reaction reports and reports on medical device malfunctions

- In FY 2006, as part of effectively and efficiently collecting safety information through utilizing IT, the Agency developed an environment that enables for easy online reporting system in order to promote transmission of information on adverse drug reactions, infections, etc., caused by pharmaceuticals through the Internet. In addition, the Agency requested for cooperation from the private sector and aimed to secure an online reporting rate of 80%.

- For this purpose, in addition to releasing data input tools on the Web and developing an environment that enables for easy transmission of data, the Agency monitored the electronic reporting rate monthly and directly asked major companies that had not yet implemented online reporting to implement such a system. The Agency also made efforts to encourage implementation of online reporting by making use of opportunities such as lectures at academic conferences. As a result, a reporting rate of 90.4 % on a full-year basis was achieved in FY 2006, exceeding the target of 80%.

Status of online reporting system for adverse reaction reports, etc.

	FY 2004	FY2005	FY2006
Electronic reporting rate (full year)	69.1%	86.4%	90.4%

Online reporting system started from October, 2003.
As of April 2004, the electronic reporting rate was 50%.
The target of the Mid-term plan: more than 80 % of average annual electronic reporting rate by the end of effective period of the Mid-term target
The target of FY2006 plan: ensuring the 80% of electronic reporting rate

2. (3).7. Establishment of post-marketing safety system based on feedback of information

a. Feedback to the private sector

1) Access to information on adverse drug reactions relating to a company's own product

- In order to contribute to enhancing the risk management system in the private sector, the Agency is building and enhancing a system that enables for a company to access information relating to its own products from among the information on adverse drug reactions reported by medical institutions and other companies. In FY 2005, the Agency disclosed all of the information on adverse drug reactions reported by the private sector after FY 2004, and subsequently started to release information as line lists in January 2006.

- At the end of March 2007, the agency disclosed 48,584 adverse reaction reports and 17,345 reports on medical device malfunctions that had been submitted up to the end of March 2006.

2) Responses to consultations from the private sector

- In order to contribute to the improvement of safety measures in the private sector, the Agency responded to various consultations (concerning pharmaceuticals, medical devices and medical safety) from the private sector. Specifically, these consultations related to revisions of package inserts, risk management plans for marketed products, creation of the Drug Guide for Patients and improvement of products to prevent medical accidents based on analyses of near-incident cases.

The numbers of consultations in FY 2006 are shown below.

(cases)

	FY2004	FY2005	FY2006
Pharmaceuticals	513	557	567
Medical Devices	722	553	292
Medical Safety	46	46	44

b. Feedback to healthcare professionals

- During FY 2006, the Agency took the following approaches to provide safety information on pharmaceuticals and medical devices to the public as well as healthcare professionals by using the Internet.

1) Prompt posting of information on the PMDA website

- The Agency posted information regarding revisions of package inserts for ethical drugs, etc., on the PMDA website within 2 days of receiving such information.

2) Provision of information relating to package inserts of OTC drugs

- Upon revision of the Pharmaceutical Affairs Law in June 2006, the Agency began posting package inserts of OTC drugs on the PMDA website in March 2007 in order to develop information provision and consultation systems adapted to the degree of the risk, ensure the qualifications of experts engaged in selling pharmaceuticals and develop an environment to appropriately respond to consultations and provide information.

- On the PMDA website, package inserts can be searched using keywords such as the commercial name, company name, dosage form, ingredient name and added substances. This service enables a patient who is allergic to specific ingredients to narrow down their search.

3) Provision of manuals for countermeasures according to serious adverse drug reaction diseases

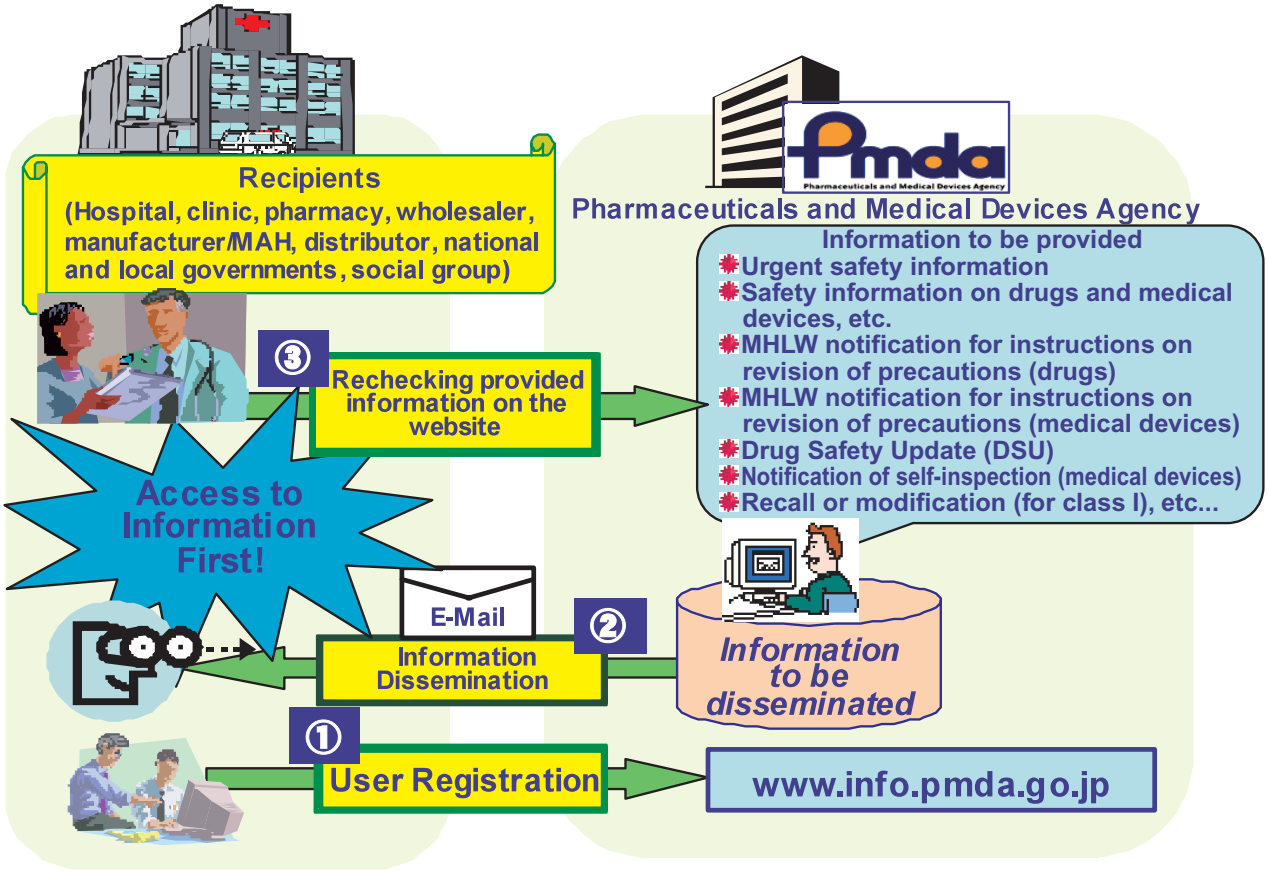
- Starting in November 2006, the Agency has been proving manuals created by the MHLW on countermeasures for the following 9 serious adverse drug reaction diseases: Stevens-Johnson syndrome, toxic epidermal nercosis, interstitial lung disease, acute lung injury/acute respiratory distress syndrome, asthma attacks caused by a nonsteroidal anti-inflammatory agent, drug-induced parkinsonism, rhabdomyolysis, leukoencephalopathy and pseudoaldosteronism.

  These manuals contain information for patients and families so that they can detect serious adverse reactions earlier based on subjective symptoms as well as diagnostic approaches and coping strategies for medical professionals.

4) E-mail Service for Information on Pharmaceuticals and Medical Devices

- In August 2005, the Agency launched the “E-mail Service for Information on Pharmaceuticals and Medical Devices” where safety information such as information regarding revisions of package inserts and class I recalls is sent by e-mail to people involved in the medical field who request to receive such information. By the end of March 2007, 6,762 delivery destinations were registered.

E-mail Service for Information on Pharmaceuticals and Medical Devices



Number of subscribers and issues of the E-mail service

(cases)

	By the end of FY2005	By the end of FY2006
Number of subscribers	2,892	6,762
Issued E-mails*	92	93

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

5) Disclosure of adverse drug reaction cases

- From among the contents of all adverse reaction reports submitted by the private sector since April 2004, the Agency has been disclosing information on “reported year,” “sex,” “age,” “primary disease,” “suspected drug,” “adverse event,” “suspected concomitant drug” and “outcome” on the Information Page of the PMDA website since January 2006. By the end of March 2007, the Agency was able to post reports submitted until March 2006.

[Reference] For cases with a fatal outcome, evaluations on the causality between the suspected drug and death is classified into the following 3 categories and disclosed on the website.

A: “Cases for which causality between the suspected drug and death cannot be denied”
Cases for which it is undeniable that the adverse event alleged to be associated with the suspected drug caused the death, after comprehensive judgment from medical and pharmaceutical perspectives and in view of various factors such as the relationship between the primary disease and the death, its pharmacological viewpoint and the time that had elapsed.

B: “Cases for which causality between the suspected drug and death cannot be found”
Cases for which it is not recognized that the adverse event alleged to be associated with the suspected drug caused the death, after comprehensive judgment from medical and pharmaceutical perspectives and in view of various factors such as the relationship between the primary disease and the death, its pharmacological viewpoint and the time that had elapsed.

C: “Cases for which causality between the suspected drug and death cannot be evaluated due to lack of information”
Cases for which the causality between the suspected drug and death cannot be evaluated because of insufficient information or inappropriateness of the usage purpose or usage method of the drug, etc.

6) Disclosure of medical device malfunction cases

- From among the contents of all reports on medical device malfunctions submitted by the private sector since April 2004, the Agency has been disclosing information on “reported year,” “sex,” “age,” “outcome,” “generic name,” “condition of the medical device” and “adverse effect on patient, etc.” on the Information Page of the PMDA website since March 2006. By the end of March 2007, the Agency was able to post reports submitted until March 2006.

[Reference] For cases with a fatal outcome, evaluations on the causality between the medical device used and death is classified into the following 3 categories and disclosed on the website.

A: “Cases for which causality between the medical device used and death cannot be denied”
Cases for which it is undeniable that the adverse event alleged to be associated with the medical device used caused the death, after comprehensive judgment from medical, pharmaceutical and engineering perspectives and in view of various factors such as the relationship between the primary disease and the death, the circumstances when the malfunction occurred, the status of maintenance inspections and the time that had elapsed.

B: “Cases for which causality between the medical device used and death cannot be found.”
Cases for which it is not recognized that the adverse event alleged to be associated with the medical device used caused the death, after comprehensive judgment from medical, pharmaceutical and engineering perspectives and in view of various factors such as the relationship between the primary cause and the death, the circumstances when the malfunction occurred, the status of maintenance inspections and the time that had elapsed.

C: “Cases for which causality between the medical device used and death cannot be evaluated due to lack of information”
Cases for which the causality between the medical device used and death cannot be evaluated because of insufficient information or inappropriateness of the usage purpose or usage method of the device, etc.

C. Provision of information to general consumers and patients

1) Implementation of consultations on drugs / medical devices

- In order for general consumers and patients to be able to use pharmaceuticals and medical devices safely and securely, the Agency is implementing a telephone consultation services for consumers.

- Consultation services for consumers regarding drugs have been carried out since July 1994. Starting in February 2005, however, consultation services have been available even during lunch breaks. Counseling services for consumers regarding medical devices were launched in July 2005.

- In FY 2006, there were 11,696 consultation requests for drugs and 581 requests for medical devices.

Number of consultations on drugs with consumers

	FY2001	FY2002	FY2003	FY2004	FY2005	FY2006
Number of phone calls*	6,370 (26.0 cases/day)	6,465 (26.4 cases/day)	7,641 (31.1 cases/day)	7,137 (29.6 cases/day)	7,741 (30.0 cases/day)	8,479 (34.5 cases/day)
Number of consultations*	8,085 (33.0 cases/day)	8,770 (35.8 cases/day)	9,906 (40.4 cases/day)	8,790 (36.5 cases/day)	10,505 (43.4 cases/day)	11,596 (47.7 cases/day)

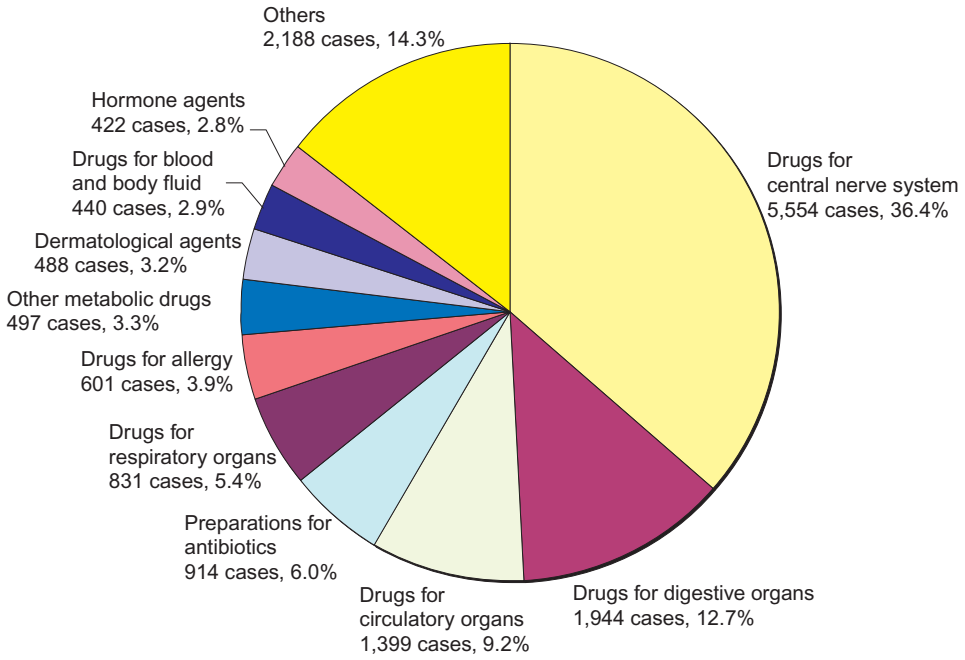
** One call can include multiple categories of consultation.*

Contents of consultations on drugs with consumers

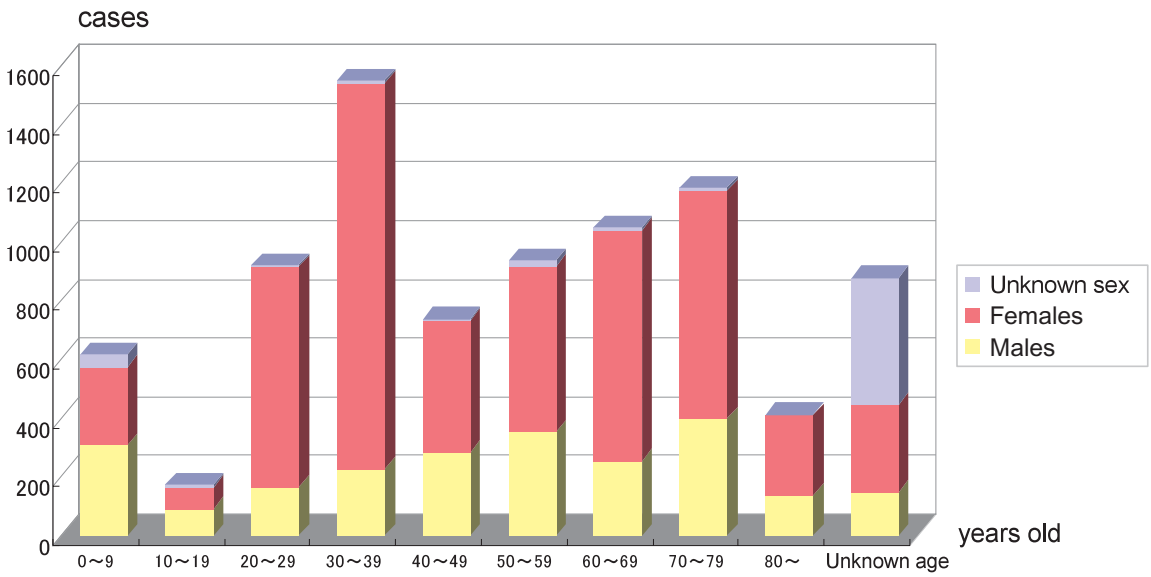
(cases)

Contents of consultation	FY2004	FY2005	FY2006
1. Safety	4,211 (47.9%)	5,968 (56.8%)	5,697 (48.7%)
2. Indications	1,194 (13.6%)	1,132 (10.8%)	1,175 (10.0%)
3. Administration and Dosage	669 (7.6%)	771 (7.3%)	828 (7.1%)
4. Interaction	611 (7.0%)	628 (6.0%)	691 (5.9%)
5. Active ingredients	205 (2.3%)	161 (1.5%)	219 (1.9%)
Others	1,900 (21.6%)	1,845 (17.6%)	3,086 (26.4%)
Total	8,790 (100.0%)	10,505 (100.0%)	11,696 (100.0%)

Number of consultations according to major classifications of therapeutic category (total of top 10 categories) in FY 2006



Number of patients (receiving counseling) according to age (FY 2006)



Number of consultations on medical devices with consumers

	FY 2005	FY 2006
Number of phone calls	166 (1.0 case/day)	376 (1.5 cases/day)
Number of consultations	323 (1.9 cases/day)	581 (2.4 cases/day)

The consultation service has been provided since July 2005.

Contents of consultations on medical devices with consumers

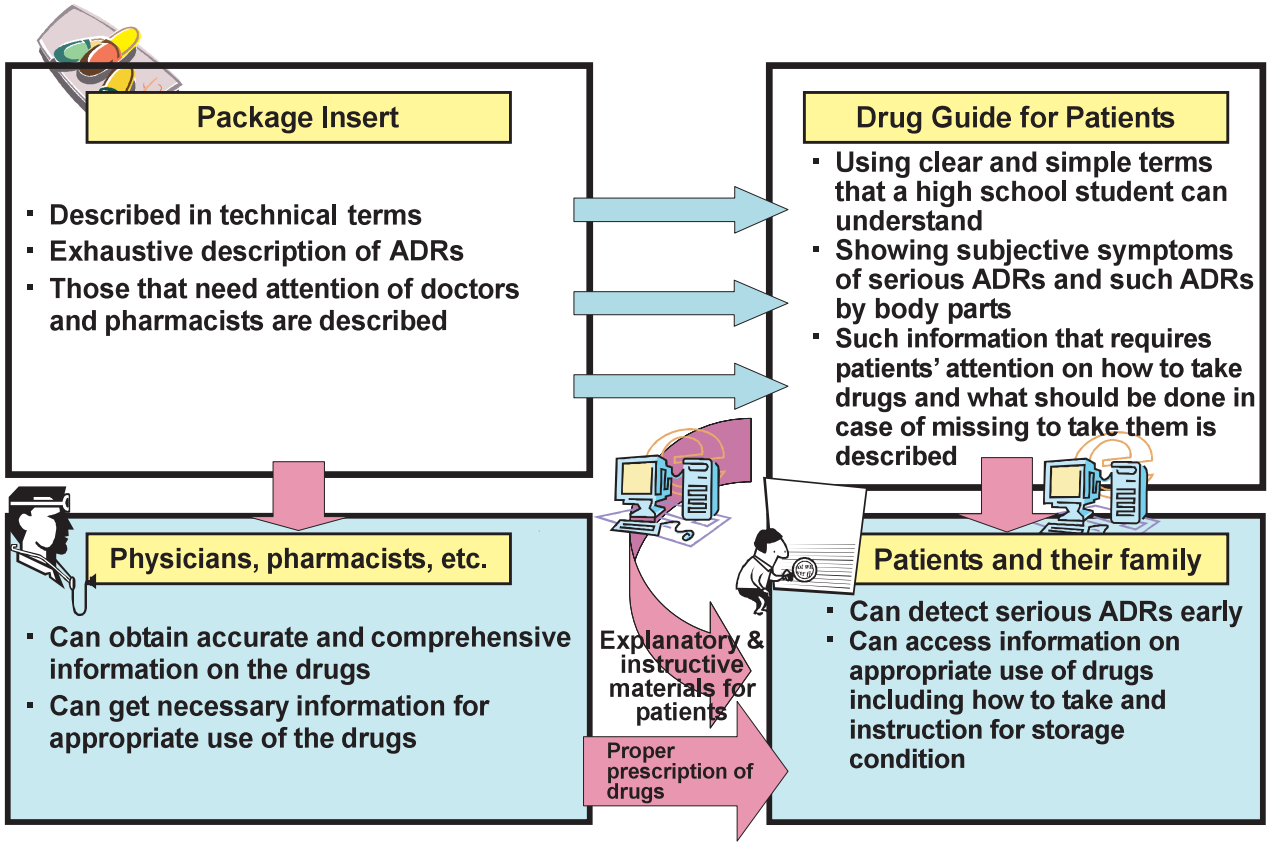
Contents of consultation	FY 2005	FY 2006
1. Safety	32 (9.9%)	62 (9.9%)
2. Indications	64 (19.8%)	101 (17.4%)
3. Performance	25 (7.7%)	45 (7.7%)
4. Directions for use	12 (3.7%)	16 (2.8%)
Others	190 (58.8%)	357 (61.4%)
Total	323 (100.0%)	581 (100.0%)

2) Publication of Drug Guide for Patients

- The “Drug Guide for Patients,” which has the purpose of making it possible for patients to properly understand ethical drugs and enabling them to detect serious adverse reactions earlier, has been posted on the PMDA website since January 2006. By the end of March 2007, the Agency posted 1,240 items.

- In accordance with “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), the Agency has reviewed and revised the Drug Guide for Patients by continuing to obtain advice from experts (scientific research by the MHLW (research on how to provide patients and people with drug safety information)).

Package insert for ethical drugs and Drug Guide for Patients



Number of Drug Guide for Patients published

Group of target Pharmaceuticals	Will be posted by	Number of component	Number of package insert	Number of item
Antidiabetic agents *	Jan. FY 2006	10	48	60
Antirheumatic drug *	Mar. FY 2006	2	9	11
Anticoagulant and antiplatelet agent *	Mar. FY 2006	3	46	72
Antiasthmatic drug *	Mar. FY 2006	8	14	21
The 100s to 200s of Classification of drugs by efficacy *	Jul. FY 2006	71	260	380
The 300s to 400s of Classification of drugs by efficacy *	Oct. FY 2007	50	220	295
The 500s, 600s, 700s, 800s of Classification of drugs by efficacy *	Jan. FY 2007	73	302	328
Injectable solution	Mar. FY 2007	20	38	73
	Total	237	937	1240

** The numbers of items with asterisk are figures that have been published as of the end of March 2007. (By PMDA)*

3) Upgrading of the Information Page of the PMDA website

- In FY 2006, the Agency upgraded the PMDA website based on the opinions of users accessing the website in order to strengthen functions to make it easier for users to find necessary information, such as by relocating information and adding a zoom function for the text.

- As information for the general public, the Agency posted the Drug Guide for Patients, the manual for countermeasures according to severe adverse drug reaction diseases and information on package inserts for OTC drugs, as well as information regarding the telephone consultation system for drugs and medical devices and a Q&A list in response to questions from general consumers regarding the drug consultation service, of which there were a relatively large number, on the upgraded PMDA website.

Upgraded Information Page of PMDA website

独立行政法人
医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

文字サイズ変更 − ＋
サイト内検索 検索

医薬品医療機器情報提供 ホームページ
www.info.pmda.go.jp

医薬品・医療機器等の安全な使用に役立てていただくため、
医薬品・医療機器等に関する最新の情報を提供しています。

緊急安全性情報(ドクターレター)等 発出のお知らせ

厚生労働省より、リン酸オセルタミビルについて緊急安全性情報等が発出されました。詳細につきましては以下のリンク先をご覧ください。
・緊急安全性情報(ドクターレター)
・厚生労働省発表資料(4月4日追加)
・使用上の注意改訂情報(4月16日追加) New

新着情報

- [平成19年4月13日] 医薬品
  使用上の注意の改訂指示(医薬品関連情報)
  厚生労働省より発出。
- [平成19年4月10日] 医療機器
  クラス I 回収(訂正)
  該当回収品目「MTI ハイドロフィリック ガイドワイヤー」
- [平成19年3月23日] 一般向け 医薬品 医療機器
  情報提供ホームページをリニューアルしました。新規コンテンツとして「一般用医薬品添付文書情報」(医薬品関連情報、一般の皆様向け)、「おくすりQ&A」(一般の皆様向け)の掲載を開始しました。

その他の新着情報はこちら >

お知らせ

- [平成19年3月23日] 一般向け 医薬品 医療機器
  情報提供ホームページをリニューアルしました。新規コンテンツとして「一般用医薬品添付文書情報」、「おくすりQ&A」の掲載を開始しました。
- [平成19年2月13日] 一般向け 医薬品
  「患者向医薬品ガイド」に注射剤(自己注射に用いられるものに限る)について順次情報を追加しました。
- [平成19年1月17日] 医薬品
  「維持液投与後の低Na血症発生に関する電子媒体を用いた遡及的調査」の情報提供を開始しました。

その他のお知らせはこちら >

一般の皆様向け

一般の皆様へ
ホームページで提供している情報をご利用される前に必ずお読み下さい。

おくすりQ&A
比較的多く寄せられた消費者からの質問及びその回答や医薬品に関して守っていただきたい一般的情報を掲載しています。

おくすり相談・医療機器相談窓口のご案内
電話でお答えする、おくすり相談・医療機器相談のご案内や、都道府県のおくすり相談窓口の情報を掲載しています。

患者向医薬品ガイド
医療用医薬品の正しい理解と、重大な副作用の早期発見などに役立てていただくために提供するものです。

重篤副作用疾患別対応マニュアル
重篤度などから判断して必要性の高い副作用について、患者さんや医療関係者などが活用する初期症状、治療法、判別法などを包括的にまとめたものです。

くすりの説明文書検索
(一般用医薬品添付文書検索)
消費者が、医師の処方によらず、個人の判断で薬局・薬店で買うことができる一般用医薬品の説明書(添付文書情報)の検索のページです。

医療関係者向け　医薬品・医療機器関連情報

医薬品関連情報
- 添付文書情報(医療用医薬品)
- 添付文書情報(一般用医薬品)
- 副作用が疑われる症例報告に関する情報
- 緊急安全性情報(ドクターレター)
- 医薬品・医療機器等安全性情報(厚生労働省発行)
- 医薬品安全対策通知
- 使用上の注意の改訂情報
- 厚生労働省発表資料(医薬品等関連)
- DSU(医薬品安全対策情報)
- 患者向医薬品ガイド
- 重篤副作用疾患別対応マニュアル
- 承認情報(医薬品)
- 医療用医薬品　品質情報
- 回収情報
- 医療安全情報
- 新たな安全対策の取り組み

医療機器関連情報
- 添付文書情報(医療機器)
- 不具合が疑われる症例情報
- 医薬品・医療機器等安全性情報(厚生労働省発行)
- 機器安全対策通知
- 厚生労働省発表資料(医療機器関連)
- 承認情報(医療機器)
- 回収情報
- 医療安全情報

- 医療機関報告のお願い
- 企業の皆様へ

医薬品医療機器総合機構 ホームページ
医薬品医療機器 情報配信サービス
健康被害救済制度

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独立行政法人 医薬品医療機器総合機構
〒100-0013 東京都千代田区霞が関3-3-2 新霞が関ビル


Q1 医師が処方するくすりと市販のくすりはどのようにちがうのですか？ | 医薬品医療機器情報提供ホームページ - Microsoft Internet Explorer
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一般の皆様向け
医薬品関連情報
医療機器関連情報
ホーム > 一般の皆様向け > おくすりQ&A > 知っておきたい薬のはなし > Q1 医師が処方するくすりと市販のくすりはどのようにちがうのですか。
Q1 医師が処方するくすりと市販のくすりはどのようにちがうのですか？
医師・歯科医師の処方せんや指示により使われるくすりを医療用医薬品、市販のくすりを一般用医薬品といいます。
解 説
医療用医薬品は、作用や使用方法などの点で医師や薬剤師などの専門家による管理が必要であり、大部分に保険が適用されています。あなたが医療機関や保険薬局で調剤を経て受け取るくすりは、診察した時点でのあなたの病状にあわせて種類や量が決められた医療用医薬品です。医師の指示通りに使用しましょう。医師から指示を受けずに保管して自分の判断で使用したり、他の人に譲ったりしてはいけません。
一般用医薬品は、一般の人が薬剤師などのアドバイスのもとに薬局やドラッグストアなどで購入し、自分の判断で使用するくすりです。市販薬、大衆薬、OTC(over-the-counter drug)などとも呼ばれます。成分の種類や含有量などの観点から、指示されている用量の範囲では比較的安全とされ、また、誰にでも使いやすいように工夫されたものなどがあります。また、効能・効果は、熱、鼻水、せき、胃痛、など症状からくすりが選択できるようになっているものが多く、使用量や使用方法などをわかりやすく記載した説明書(添付文書)がついています。説明書(添付文書)は必ず読むようにしましょう。
医療用医薬品と一般用医薬品で同じ効果を表示している場合でも、成分が異なったり、含量が異なったり、効き方や効き目が異なることがあります。医療用医薬品の効能・効果を知っているからといって、自分の判断で一般用医薬品の代わりに使うようなことは絶対にやめましょう。
リストに戻る
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Number of posted items on the "Information Page" of the PMDA website as of March 2007

Types of provided information	Number of posted information					
	FY2001	FY2002	FY2003	FY2004	FY2005	FY2006
Package insert information *						
Ethical drugs	11,045 sheets	11,380 sheets	11,516 sheets		11,819 sheets	12,341 sheets
Medical devices	—	—	—	—	1,524 sheets	3,995 sheets
OTC drugs	—	—	—	—	—	3,306 sheets
Drug Guide for Patients *	—	—	—	—	23 ingredients (150 items)	237 ingredients (1,240 items)
Safety information issued by MHLW - Instruction of revisions of package inserts - Pharmaceuticals and Medical Devices Safety Information - Press release	114 cases	153 cases	192 cases	231 cases	267 cases	294 cases
Urgent safety information (by pharmaceutical companies)	13 cases	20 cases	23 cases	23 cases	23 cases	24 cases
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ))	—	—	1 cases	11 cases	21 cases	31 cases
Notification of safety measures for medical devices						
Notification of self-assessment	—	—	—	42 cases	45 cases	45 cases
Notification of revisions of labeling	—	—	—	10 cases	20 cases	21 cases
Notification related to medical devices	—	—	—	29 cases	33 cases	35 cases
Information about case reports on suspected ADR (provided in new form)	—	—	—	—	3,884 cases	48,584 cases
Information about case reports on suspected ADR (provided in old form)						
A list of reported ADRs (a list by drugs)	3,909 cases	5,473 cases	7,098 cases	8,494 cases	10,136 cases	10,136 cases
Cases with unknown ADRs	3,078 cases	5,977 cases	10,999 cases	12,819 cases	17,317 cases	17,317 cases
Cases with known ADRs (including detailed information)	575 cases	808 cases	959 cases	1,011 cases	1,125 cases	1,125 cases
Information about case reports on suspected malfunction	—	—	—	—	1,750 cases	17,345 cases
Notification related to preventive measures for medical accidents	1 case	1 case	11 cases	14 cases	18 cases	21 cases
Information about approved new drugs - Review reports, summary of application materials	119 ingredients	127 ingredients	114 ingredients	137 ingredients	203 ingredients	261 ingredients
	(291 items)	(311 items)	(268 items)	(308 items)	(435 items)	(559 items)
Results of re-evaluation of ethical drugs	—	—	—	187 ingredients (606 items)	187 ingredients (606 items)	187 Ingredients (606 items)
A list of ethical drugs on which Quality Information Package (Orange Book) was published	158 ingredients/ formulation	190 ingredients/ formulation	358 ingredients/ formulation	427 ingredients/ formulation	481 ingredients/ formulation	481 ingredients/ formulation
	(1,780 items)	(1,971 items)	(3,083 items)	(3,513 items)	(3,737 items)	(3,737 items)
Information about withdrawals of pharmaceuticals or medical devices **	1,378 cases	2,150 cases	1,329 cases	1,295 cases	1,453 cases	2,128 cases
E-mail Service for Information on Pharmaceuticals and Medical Devices						
E-mails issued ***	—	—	—	—	92	93
Subscribers	—	—	—	—	2,892	6,762
Access count ****	76 million	87 million	107 million	233 million	289 million	391 million

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

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

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

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