ANNUAL REPORT FY 2007

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I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

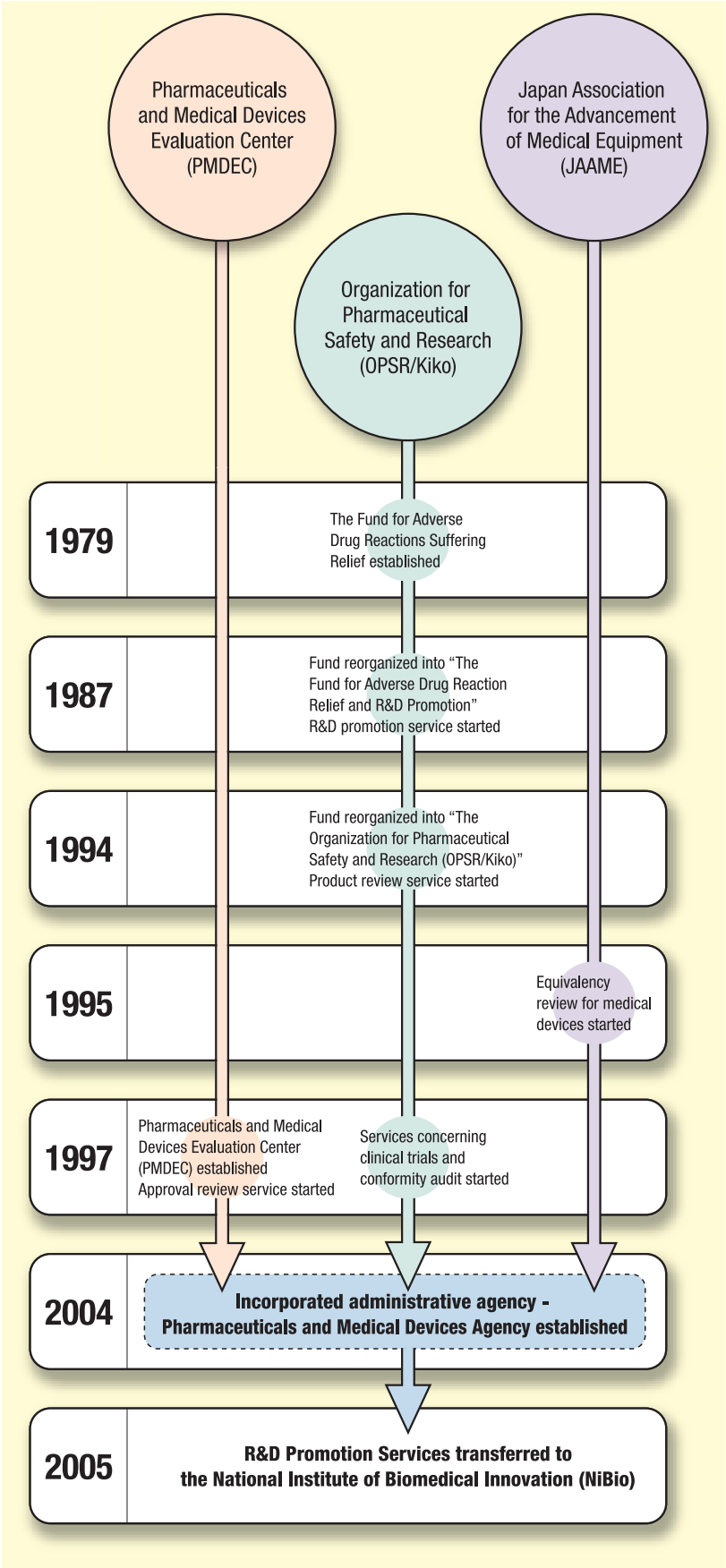
PART 1 History and Objective of PMDA

- As lessons learned from diseases caused by pharmaceuticals such as thalidomide-induced fetal malformations and subacute myelo-optical neuropathy (SMON), the Fund for Adverse Drug Reactions Suffering Relief was established in October 1979 based on stipulations in the Adverse Drug Reaction Suffering Relief Fund Law (Law No. 55 of 1979), for the purpose of providing prompt relief to patients suffering from adverse drug reactions (ADRs). In 1987, the Fund started R&D-promoting operations under the name of the Fund for Adverse Drug Reaction Relief and R&D Promotion and was then reorganized into the Organization for Pharmaceutical Safety and Research (OPSR/Kiko) in 1994 to play a role in equivalency reviews of generic drugs. Later, in 1997, the organization started to provide advice on clinical trials and conduct conformity audits on applications for approval of pharmaceuticals.

- In 1997, the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) was established at the National Institute of Health Sciences (NIHS) in order to develop a full-scale approval review system and to make the contents of the review more advanced. It was decided that at the Center, reviews should be conducted by teams consisting of experts specializing in pharmaceutical science, medical science, biostatistics, etc. In addition, the Japan Association for the Advancement of Medical Equipment (JAAME) began operations in 1995 to conduct equivalency reviews of medical devices as a designated investigative body under the Pharmaceutical Affairs Law.

- From 1997 to 1999, there was a systematic and drastic increase in the number of the staff engaging in reviews and post-marketing safety measures at the former Ministry of Health and Welfare and the three organizations above (from 121 staff members in 1996 to 241 in 1999). However, there was a limit to further increasing the number of staff and developing the structure as governmental organizations.
  In the midst of these situations, the Cabinet adopted the Special Service Agency Restructuring Plan in December 2001, in which it was decided that the OPSR/Kiko should be dissolved and that the Pharmaceutical and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to PMDEC, OPSR/Kiko, and JAAME in order to further enhance reviews and safety measures. In 2002, a legislative bill for the Law for the Pharmaceuticals and Medical Devices Agency was discussed and passed at the 155th extraordinary session of the Diet, resulting in the establishment of PMDA on April 1, 2004 in accordance with the Law for the Pharmaceuticals and Medical Devices Agency (Law No.192 of 2002).

- The objective of PMDA is to contribute to improvement in public health by providing prompt relief services for sufferers of adverse health effects resulting from infections derived from biological products in addition to adverse drug reactions (Relief for Adverse Health Effects); providing guidance and reviews regarding the quality, efficacy, and safety of pharmaceuticals and medical devices through a system that is consistent from pre-clinical research to approval (Reviews); and collecting, analyzing, and providing information on post-marketing safety (Safety Measures).
  Previously, one of the objectives of the Agency was to promote basic research and development of pharmaceuticals and medical devices that contribute to maintaining and improving the health of the nation (Promotion of R&D). However, the Regulatory Division and the Research Promotion Division were separated, and services for promotion of R&D were transferred to the National Institute of Biomedical Innovation (NiBio) in April 2005, in order to allow the Agency to focus specifically on reviews, safety measures, and relief services for adverse health effects.


Pharmaceuticals and Medical Devices Evaluation Center (PMDEC)
Japan Association for the Advancement of Medical Equipment (JAAME)
Organization for Pharmaceutical Safety and Research (OPSR/Kiko)
1979
The Fund for Adverse Drug Reactions Suffering Relief established
1987
Fund reorganized into "The Fund for Adverse Drug Reaction Relief and R&D Promotion" R&D promotion service started
1994
Fund reorganized into "The Organization for Pharmaceutical Safety and Research (OPSR/Kiko)" Product review service started
1995
Equivalency review for medical devices started
1997
Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) established Approval review service started
Services concerning clinical trials and conformity audit started
2004
Incorporated administrative agency - Pharmaceuticals and Medical Devices Agency established
2005
R&D Promotion Services transferred to the National Institute of Biomedical Innovation (NiBio)

PART 2 Outline of Operations

2.1 Relief Services for Adverse Health Effects

- As a service inherited from the OPSR/Kiko, the Agency provides benefits for medical expenses, disability pensions, and bereaved family pensions to the sufferers of illnesses or disabilities caused by adverse drug reactions (Adverse Drug Reaction Relief Service).

- In April 2004, the Agency started to provide benefits to sufferers of adverse health effects caused by infections from pharmaceuticals and medical devices manufactured by using ingredients and materials derived from biological entities (Relief Service for Infections Derived from Biological Products).

- In January 2008, the Agency also started the service of providing benefits to individuals affected by hepatitis C according to the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus (Specific Relief Service).

- The Agency is also commissioned by the government and pharmaceutical companies to provide healthcare allowances and nursing care expenses to SMON patients (Service for Healthcare Allowances). In addition, the Agency works under the commission of the Yu-ai Welfare Foundation to make payments for healthcare expenses for HIV-positive and AIDS patients (Service for Healthcare Allowances).

2.2 Review Services

- In accordance with the Pharmaceutical Affairs Law, the Agency reviews the efficacy, safety, and quality of pharmaceuticals and medical devices for which applications for approval have been submitted, based on the current scientific and technological standards. In addition, the Agency conducts re-examinations/re-evaluations of pharmaceuticals and medical devices and reviews of applications for pre-clinical assurance of products processed with cell tissue as well as reviews of applications for genetically modified biological entities in accordance with the Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Law No. 97 of 2003) (Approval Review Services).

- In response to requests from clinical trial sponsors, the Agency provides face-to-face guidance and consultations on clinical trials of new drugs and medical devices as well as on clinical trials for re-examinations/re-evaluations of approved products (Face-to-face Consultation Service).

- For items for which applications were made for approval reviews and re-examinations/re-evaluations, on-site and document inspections are implemented to determine whether documents attached to approval applications conform to Good Laboratory Practice (GLP), Good Clinical Practice (GCP), and conformity standards for application documents (Conformity Audit Services).

- In addition, on-site and document inspections are conducted to determine whether manufacturing equipment and manufacturing control methods for new drugs and medical devices, etc., conform with ministry ordinances relating to standards for manufacturing control and quality control, and whether there is a system for manufacturing products of appropriate quality (GMP/QMS Conformity Audits Services).

2.3 Safety Measures

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

  (i) Services for centrally collecting and organizing information on the safety of pharmaceuticals and medical devices from a broad range of sources, such as reports from the private sector, information from medical institutions, information from foreign regulatory agencies, and conference papers, relating to adverse drug reactions, malfunctions, and infections (Collection and Organization of Information).

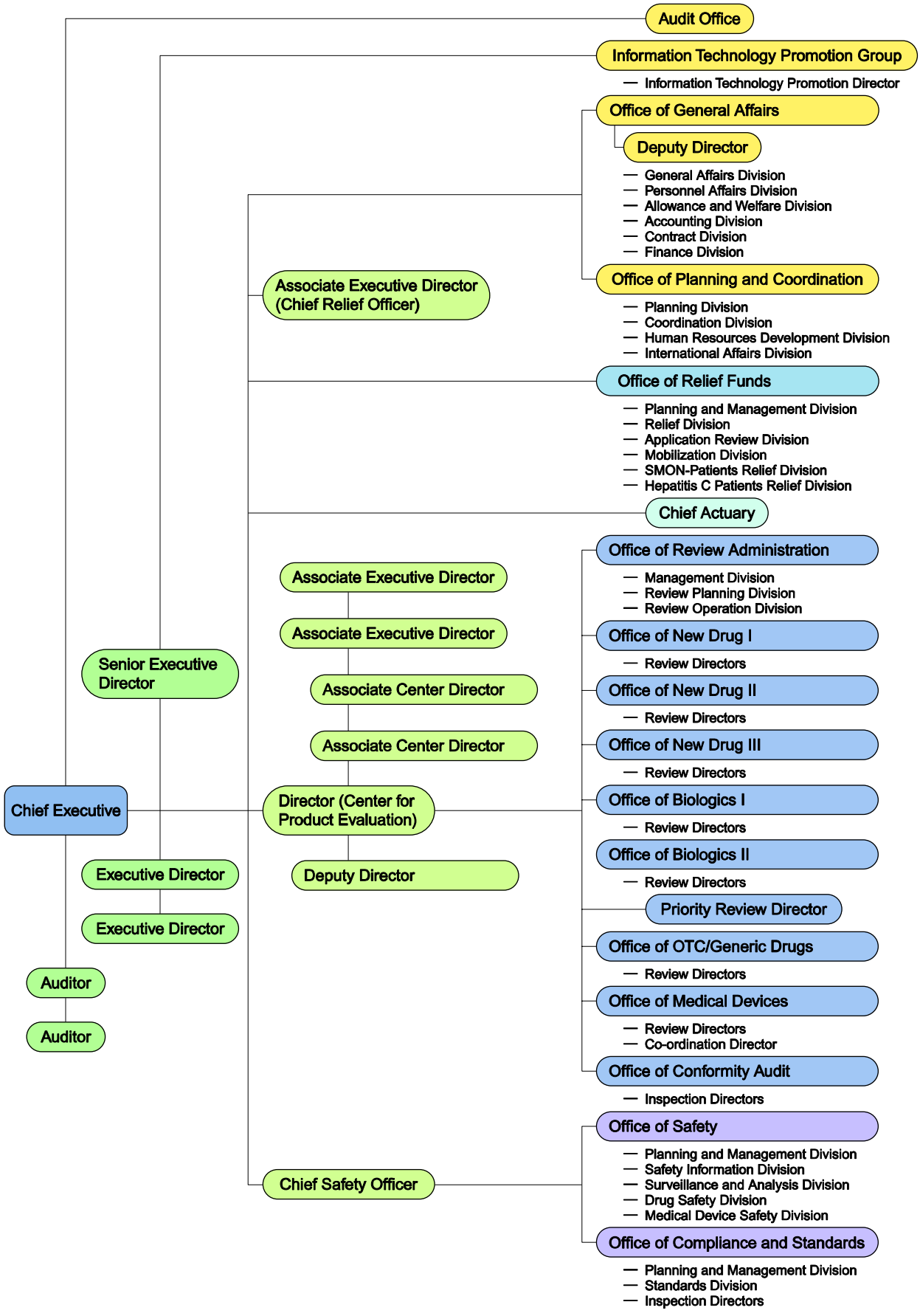
  (ii) Services for conducting research and reviews relating to safety measures based on the information collected in (i) above (Research and Review Services).

  (iii) Services for giving guidance and advice to marketing authorization holders (MAHs) as well as providing advice in response to consultations from consumers (Consultation Services).

  (iv) Services to provide information on the safety of pharmaceuticals and medical devices widely to healthcare professionals, patients, private companies, etc., in a timely manner (Information Provision Services).

  (v) Surveys related to developing various standards, such as the Japanese Pharmacopoeia (JP) that is stipulated in the Pharmaceutical Affairs Law (Standards Development-related Survey Services)

Structure of the PMDA (FY 2007)



II. ACTUAL OPERATION RESULTS FOR FY 2007

PART 1 The Reorganization and Rationalization Plan for Independent Administrative Institutions and the Review of the Overall Organization/Services

1.1 Establishment of the Reorganization and Rationalization Plan for Independent Administrative Institutions

- The Basic Guidelines for Economic and Fiscal Reform in FY 2007 (approved at the cabinet meeting held on June 19, 2007) lays down that all 101 independent administrative institutions should be reviewed for their organizations/services in line with the principles of shift from public to private sector, competition, and consistency, and on the basis of the results of the review, a Reorganization and Rationalization Plan for Independent Administrative Institutions should be formulated toward the end of FY 2007. In this regard, the Basic Policy for the Establishment of the Reorganization and Rationalization Plan for Independent Administrative Institutions was approved at the cabinet meeting held on August 10, 2007.

  After that, the Council of advisers on downsizing/streamlining public administration played a central role in scrutinizing the reorganization and rationalization plan formulated by each independent administrative institution in line with the above basic policy, and the Reorganization and Rationalization Plan for Independent Administrative Institutions was approved at the cabinet meeting held on December 24, 2007.

Reference: Items Relating to PMDA Highlighted in the Reorganization and Rationalization Plan for Independent Administrative Institutions

(1) Review of Services and Operations

- **New drug reviews**

  In order to achieve the target of clearing up 2.5 years of drug lag in FY 2011, the Agency shall set an annual target for each year and formulate action plans for expediting the procedures and improving the quality of reviews, assess/verify its progress each year, and make necessary revisions on the basis of the progress status.

  As for the action plans, the achievements shall be evaluated without delay after the end of the target fiscal year for clearing up the drug lag that falls in the period of the next Mid-term plan.

- **New medical device reviews**

  The Agency shall understand the current status of the device lag and analyze the causes behind it. On the basis of the results of the analysis, the Agency shall expedite reviews by taking necessary measures such as the standardization of the review process, strengthening of management, and improvement in the efficiency of services.

- **Safety measures**

  With regard to safety measures, including the swift and timely collection, analysis, and provision of safety information on pharmaceuticals and medical devices, in the next Mid-term plan, the Agency shall set an indicator, which will facilitate a more suitable evaluation of the achievements

of each service, so that the safety measures are implemented more efficiently and steadily.

(2) Review of the Organization

- **Streamlining of the organization**

  The Agency shall review the organization, including the feasibility of relocating the head office, and take the necessary measures during the period of the next Mid-term plan.

(3) Improvement in the Efficiency and Promotion of Autonomy of Overall Operations

- **Streamlining the structure of the operation of services**

  Taking into account the fluctuations in the number of staff, the Agency shall make comprehensive efforts to ensure the effective and efficient operation of services.

1.2 Implementation of the Review of Overall Organization/Services

- With respect to the review of the overall organization/services upon the expiration of the Mid-term plan, the Basic Guidelines for Economic and Fiscal Reform in FY 2007 laid down that along with formulating the Reorganization and Rationalization Plan for Independent Administrative Institutions, the institutions that were originally scheduled to conduct reviews in FY 2008 shall conduct their reviews ahead of schedule in FY 2007 together with the institutions that were already scheduled to conduct reviews in FY 2007. Because of this decision, the Agency was required to review the overall organization/services one year ahead of schedule.

  In line with the above decision, the chairman of the Committee for the Evaluation of Policy/Independent Administrative Institutions notified the Minister of Health, Labour and Welfare of the direction of recommendation for the improvement or elimination of principal operations/services in independent administrative institutions. On the basis of the above notification, the Ministry of Health, Labour and Welfare drafted a proposal of review taking into account the issues pointed out in the direction of recommendation for the improvement or elimination of principal operations/services at the Pharmaceuticals and Medical Devices Agency and submitted it to the Administrative Reform Promotion Office. The proposal was finally approved by the Administrative Reform Promotion Office on December 24, 2007.

Reference: Outline of the Proposal of Review Taking into Account the Issues Pointed out in the Direction of Recommendation for the Improvement or Elimination of Principal Operations/Services at PMDA

(1) Review of Services/Operations

During the period of the next Mid-term plan, the Agency shall endeavor to make reviews expeditious, improve the quality of services, and steadily implement safety measures, while simultaneously reviewing services and trying to improve their efficiency. These measures will be taken so that the Agency can cope with an increase in the workload of reviews/safety measures as well as with a higher level of expertise and it assumes an international role along with the U.S. and Europe as a

member of a tripolar structure. The following are the measures in this regard:

(i) Reviewing drug evaluation-related services to clear up the drug lag
(ii) Reviewing medical device evaluation-related services to clear up the device lag
(iii) Steady implementation of safety measures
(iv) Exhaustive efforts toward improvement in efficiency in overall services

(2) Review of Other Services

In addition to (1) above, the Agency shall tackle the following tasks:

(i) Setting the target for improvement in efficiency
(ii) Realizing the reasonable pay standard, etc.
(iii) Reviewing the practice of optional contracts

PART 2 Development of Fiscal Year 2007 Plan

2.1 Development and Implementation of Fiscal Year 2007 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, and to obtain the Minister's approval for 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 developed a fiscal year 2007 plan and submitted this plan to the Minister at the end of FY 2006 and is implementing operations based on this plan in FY 2007.

  In addition, on January 15, 2008, the agency submitted an application to the Minister of Health, Labour and Welfare for approval for the modification of the Mid-term plan necessitated by the launch of the payment of benefits pursuant to the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus, and obtained the approval on the same day.

  The fiscal year 2007 plan was developed based on the modified Mid-term targets and Mid-term plan as well as operational performance for FY 2006 as evaluated by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour, and Welfare 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 improve the organizational structure and reinforce management so that a performance level that meets the public's expectations can be realized.

  In the same way as for FY 2006, the Agency announced its three priority issues for FY 2007 at the 1st Advisory Council Meeting held on June 22, 2007. The priority issues are as follows:

  (i) Enhancement of review services
  (ii) Enhancement of safety measures services
  (iii) Improvement of adverse health effects relief services

  In addition, to steadily promote the Mid-term plan, fiscal year plan, and priority issues for FY 2007, the Agency organized the issues that should be implemented within FY 2007 and announced these issues as Priority Issues for Operations in the Second Half of FY 2007 at the 3rd Advisory Council Meeting held on December 26, 2007.

2.2 Evaluation Results of Operational Performance in FY 2006

- 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 of an evaluation on its performance in FY 2006 on August 17, 2007 by the Evaluation Committee for Incorporated Administrative Agencies of MHLW, which is responsible for conducting evaluations on the Agency. The overall evaluation results consisted of 1 S, 17 As and 2 Bs

out of 20 evaluation items (the S was for expeditious provision of relief benefits, the 2 Bs were for improvement in the provision of services to citizens [e.g., publication of the agency's services] and clinical trial consultations).

The Agency posted these evaluation results on PMDA website and reported the results at the meeting of the Advisory Council that was held on September 18, 2007.

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

- As for the results of the evaluations conducted by the Committee on the Evaluation of Independent Administrative Institutions at the Ministry of Health, Labour and Welfare, the Committee on the Evaluation of Policies/Independent Administrative Institutions at the Ministry of Internal Affaires and Communications submitted its conclusions on January 31, 2008, in which it highlighted the following issues concerning the evaluation results for the Agency.

(1) "In the adverse drug reactions relief account and infection relief account of FY 2006, the current gross income of about ¥520 million and about ¥480 million, respectively, as well as the year-end surplus of about ¥3,150 million and about ¥1,520 million, respectively, are credited. Although it is explained in the Actual Operation Results of FY 2006 that such surplus is attributable to the fact that the payment of benefits was below the estimates, there is no convincing explanation for the appropriateness of the operation which supposedly contributed to such surplus. In view of the fact that the bulk of the income in these accounts is contributed by private companies, the appropriateness of operation contributing to the surplus should be evaluated in the future."

(2) "According to the important policies for administrative reform, the Committee on the Evaluation of Independent Administrative Institutions established at each ministry is required to conduct stringent ex post evaluations of the suitability of the pay standard at independent administrative institutions in the case where their pay standard is higher than that of the national government employees. Despite the fact that the Agency's pay standard was 1.211 times that of national government employees (clerical/technical employees) in FY 2006, thereby far exceeded the national government employees' pay standard, there is no reference to the suitability of the pay standard in the evaluation results. In the future, rigorous evaluation of the suitability of the pay standard should be conducted from the citizen's perspective and take into account III-1-(4) of the Reorganization and Rationalization Plan, that is, 'Realizing a Reasonable Pay Standard, etc.'"

(3) "Regarding the proper management of optional contracts, the Proper Management of Optional Contracts at Independent Administrative Institutions instructs every ministry to conduct ex post evaluations along with annual evaluations by taking into account the issues pointed out by the committee in November 2006. However, there is no reference to the proper management of optional contracts in the evaluation results. In the future, rigorous evaluation of the progress of the optional contract review plan should be conducted by taking into account III-1-(1) of the Reorganization and Rationalization Plan, that is, 'Review of the Practice of Optional Contracts.'"

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

Classification in the mid-term and fiscal year plan		Evaluation items		Evaluation result FY2005 performance	Evaluation result FY2006 performance
Part 1	Improvement in overall operations and quality in services of the Agnecy eg. Services to the publilc				
(1) Efficient and Flexible Operations		1	Operation through target management/top management	A	A
		2	Ensuring of transparency by establishing deliberative bodies	A	A
(2) Cost 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	B
Part 2	Improvement in operations of each department, and quality of other services eg. services to the public				
1	Adverse health effect relief services				
(1) Expansion and review of dissemination of information regarding the System		6	Provision of information on the System and strengthening of the consulatation system	A	A
(2) Proactive public relations activity toward familiarity with the System					
(3) Expansion of the scale of the consultation office					
(4) Unified management of information through the database		7	Expeditious processing of applications and improvement of the system	B	S
(5) Expeditious processing of relief applications through fact-finding study and other measures					
(6) Promotion of appropriate communication of information through cross-functional collaboration		8	Conduct of cross-functional collaboration and surveys on adverse health effects	A	A
(7) Consideration of conducting surveys on adverse health effects, etc.					
(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)	A	A
		12	Expeditious operation and improvement of the system (clinical trial consultations)	B	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	B	A
Part 4	Limit of short-term borrowing				
Part 5	Plan for transferring or mortgaging				
Part 6	Use of surplus funds				
Part 7	Other operational issues determined by orders from the competent ministry				
(1) Personnel matters		20	Personal issues and establishment of security	A	A
(2) Ensuring security					

Evaluation scale on performance of Incorporated Administrative Agency of MHLW			FY2005 performance	FY2006 performance
	S	Significantly exceeding the level prescribed in the midterm-plan	0	1
	A	Exceeding the level prescribed in the midterm-plan	17	17
	B	Somew hat exceeding the level prescribed in the midterm-plan	3	2
	C	Slightly below the level prescribed in the midterm-plan	0	0
	D	Below the level prescribed in the midterm-plan, therefore requiring drastic improvements	0	0

2.3 Modifications in the Mid-term Plan (Approved on January 15, 2008)

- Pursuant to the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus, the Agency is in charge of the payment of benefits to individuals infected with hepatitis C though specified products. In order to carry out this task, the Agency was required to modify the Mid-term plan. Therefore, the Agency submitted the application for approval for the modification of the Mid-term plan to the Minister of Health, Labour and Welfare on January 15, 2008 and obtained the approval on the same day.

  (Major modifications to the Mid-term plan: (i) inclusion of the description concerning the payment of benefits to individuals infected with hepatitis C by the administration of specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus and (ii) amendment of the Mid-term budget, including the creation of a new account that is necessary for the commencement of the payment of benefits to individuals infected with hepatitis C by the administration of specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus.)

1. Outline of the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

(1) Persons Eligible for Benefits

Persons who meet both the criteria given below are eligible for benefits:

(i) Persons who have been infected with hepatitis C virus by administration of a specified fibrinogen product or blood coagulation factor IX product contaminated by hepatitis C virus

(ii) Persons who, through the process of settlement/arbitration in court or by definitive judgment, are recognized as persons described above (i) or are their successors (inclusive of those who have been cured as well as those who have been infected by the mother-to-child transmission).

Note: The fact of the administration of the virus and the existence of causal relations and symptoms shall be determined by the court.

(2) Details of the Benefits

(i) Benefits are classified into three levels according to symptoms:

a. Persons who have suffered from cirrhosis or liver cancer due to the progress of chronic hepatitis C ..... ¥40 million

b. Persons who have suffered from chronic hepatitis C..... ¥20 million

c. Asymptomatic carriers ..... ¥12 million

(ii) Additional benefits

Additional benefits shall be paid in case where the symptoms progress within ten years after the benefits are received.

In this case, the amount payable is the difference between the amount corresponding to progression of symptoms and the amount paid earlier.

(3) Period for Claims

(i) Claims for seeking benefits shall be made within five years after the law comes into effect (hereinafter referred to as expiration date).

Notwithstanding the above, in the case where litigation or application for settlement/arbitration is filed on the expiration date and the final decision thereof is made or a settlement/arbitration is reached/established after the expiration date, the period for claims shall be within one month after the day of the final decision or the day of the settlement/arbitration.

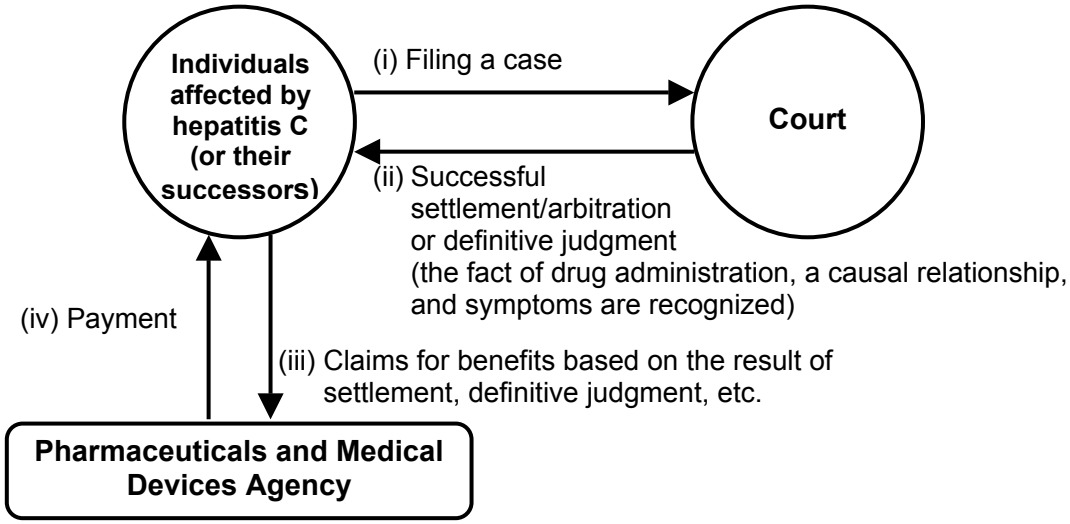
(ii) Claims for additional benefits shall be made within three years after diagnosis of the progression of symptoms.

(4) Clerical Job Pertaining to Payment

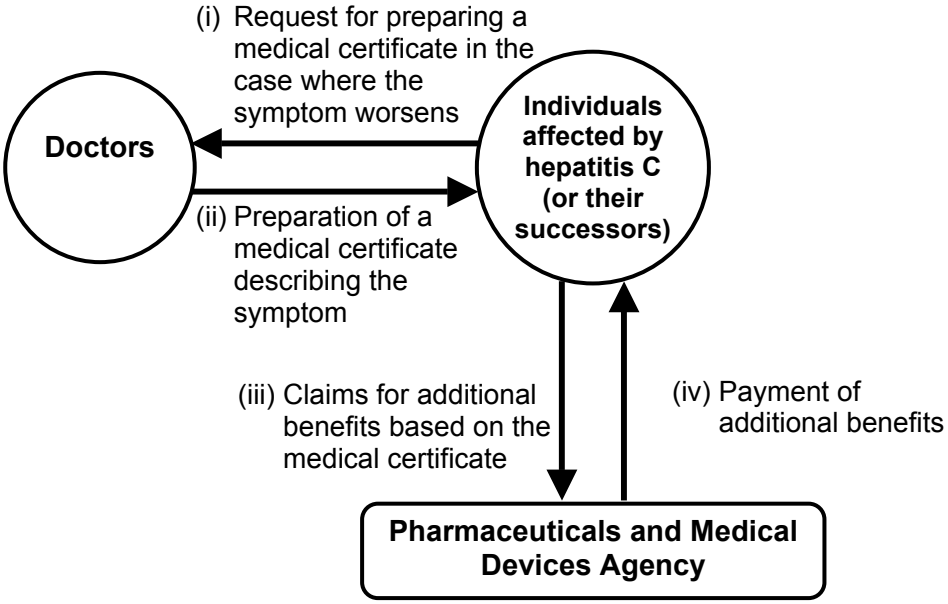
The clerical job pertaining to the payment of benefits shall be handled by the Pharmaceuticals and Medical Devices Agency, an independent administrative institution, and the fund for this purpose shall be established by the Agency.

2. Claim for Benefits and Additional Benefits

(1) Claim for Benefits - Flowchart



(2) Claim for additional benefits



PART 3 Improvement in Overall Management of Operations and Service Quality of the Agency

3.1 Efficient and Flexible Management of Operations

3.1.(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 resolve problems through managing its operational progress on a daily basis.

- In order to do so, the Agency has managed operations through management of objectives by developing operating plans based on the duties for each responsible office and division in conjunction with the development of PMDA's annual plan for FY 2007.

- To comprehend the progress of operating plans in each office, in November 2007, the Agency conducted a hearing with its directors about the actual operating performance up to the end of October 2007 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 Feburuary 5, 2008.

3.1.(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 2006, 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.

  Specifically, the Agency has regularly (usually 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.

- In meetings (held 4 times in FY 2007) for the Headquarters for PMDA Reform, which is headed by the Chief Executive, the results of operations reform at each office, including the ones in charge of reviews, as well as the status of studies concerning basic principles for reviews (reviews policy) were reported.

- In order to appraise the reviews of pharmaceuticals/medical devices and clinical trial consultations, the Agency regularly (12 times in FY 2007) held meetings of the Committee for Progress Management of Reviews Operations, headed by the Chief Executive, which facilitated a thorough management of the progress of reviews.

- The Headquarters of Information Systems Management was established with the aim of reinforcing the structure of information systems management and was headed by the Chief Executive. The basic approach to the review concerning the optimization of operations and systems, which constitutes the premise for the formulation of an Optimization Plan for Operations and Systems, has been studied in

cooperation with the deputy CIO. In the course of the study, we engaged in comprehensive discussions, taking into consideration the opinions expressed by offices in charge of operations, with regard to the optimization of operations and systems, and tried to build consensus within the Agency. The establishment of the Optimization Plan for Operations and Systems and its publication was approved at the Headquarters of Information Systems Management (held twice in FY 2007), and the Optimization Plan for Operations and Systems was publicized on March 28, 2008.

Moreover, at the Committee on Investment in Information Systems, which is under the Headquarters, the Agency appraised the appropriateness of the investment in the development of new systems and the modification of existing systems from the perspectives of cost-benefit performance and technical difficulties and selected systematic and effective investment decisions according to the Chief Executive's business judgment (three meetings were held during FY 2007).

- 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 (12 meetings in FY 2007), during which reports on the monthly application status for user fees for each review division, reports on the monthly cash flow analysis, and reports on the declared amount of contributions were made.

- The Agency organized meetings with the Japan Pharmaceutical Manufacturers Association (JPMA), the Pharmaceutical Research and Manufacturers of America (PhRMA), and the European Federation of Pharmaceutical Industries and Associations (EFPIA) twice (in July and December).

  Further, the Agency convened task force meetings six times, starting in February 2007, concerning medical devices and *in vitro* diagnostics. The Agency also convened meetings of four working groups, established under the task force, a total of 63 times.

- The Agency continues a study that aims to formulate the second phase Mid-term plan on the basis of the issues indicated in the Reorganization and Rationalization Plan for Independent Administrative Institutions.

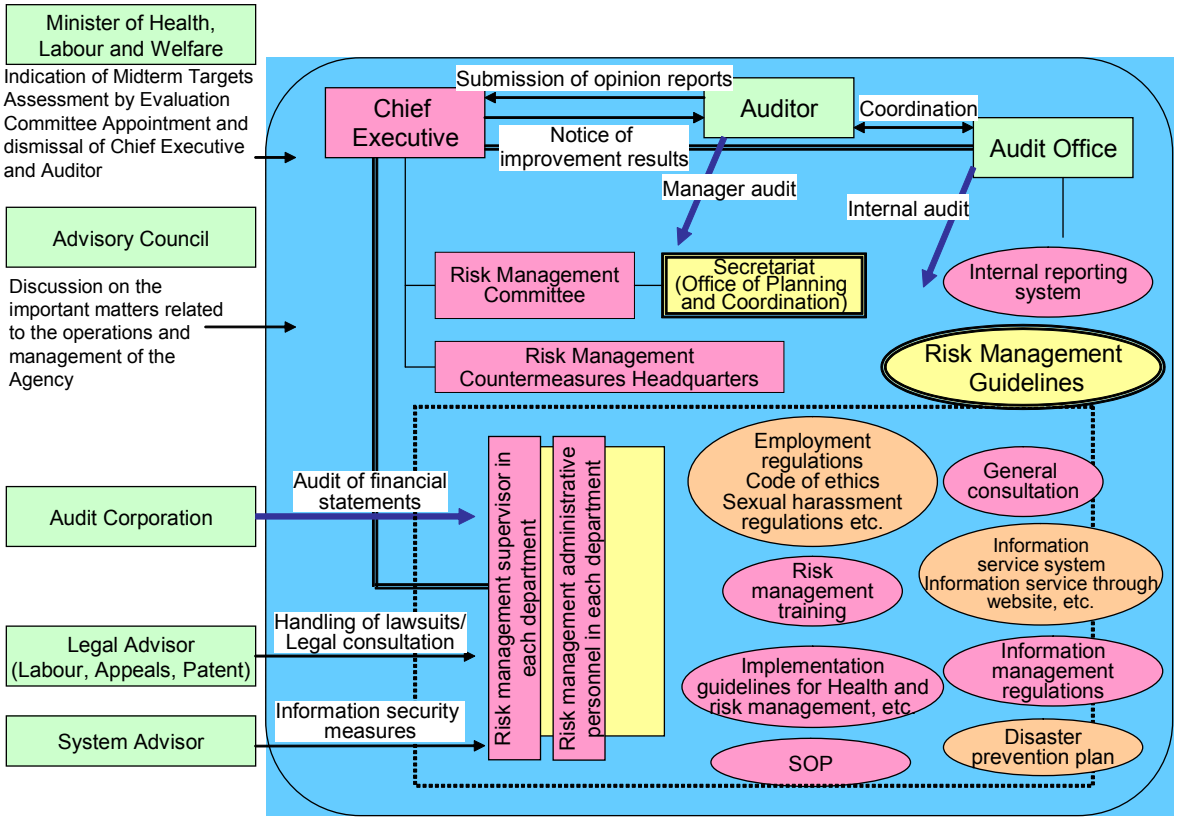
- In order to ensure proper risk management of the overall organization, the Agency has established and operated a Risk Management Committee pursuant to the Risk Management Policy. At the Committee meeting held in FY 2007, we discussed the rule concerning taking important documents out of the Agency and established necessary regulations. Moreover, the Agency revised the operation policy of the Committee and decided to hold the Committee meeting once a month in order to increase awareness of risk management at the Agency.

  The Agency executives and employees have also continued to be familiarized with the risk management manual.

  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 executives and employees of the disaster preparedness plan.

PMDA Risk Management System



Note: Risks the Agency may face:

a. Risks to the organization
   - Possibility of an event that damages or may damage the reputation of the Agency in society
   - Possibility of an event that significantly hinders or may damage the Agency's execution of operations
   - Possibility of an event that financially damages or may damage 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 equipment subject to clinical trials).

3.1.(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, healthcare professionals, representatives from relevant industries, consumer representatives, representatives of people who have suffered from adverse drug reactions caused by pharmaceuticals, etc. By providing recommendations and improvement measures for operations and the management system, the Council works 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 Post-marketing 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 2007 are shown below.

Advisory Council—FY 2007

Agenda for the 1st Meeting (June 22, 2007)

(1) PMDA Annual Report for FY 2006
(2) Financial Report for FY 2006
(3) Priority issues in FY 2007 operations
(4) Report on the employment status of personnel from the private sector
(5) Report on the status of problems caused by the anti-influenza drug Tamiflu
(6) Report on the measures against the problem of conflict of interests involving an outside expert
(7) Others

Agenda for the 2nd Meeting (September 18, 2007)

(1) Results of the evaluation of operations performance for FY 2006
(2) Original plan for the review of overall organization/services
(3) Restrictions with respect to employing personnel from the private sector
(4) Others

Agenda for the 3rd Meeting (December 26, 2007)

(1) Review of overall organization/services
(2) Principal achievements up to the end of October 2007 and priority issues in the latter half of FY 2007
(3) Restrictions with respect to employing personnel from the private sector
(4) Rate of contribution to the adverse drug reaction fund in FY 2008 and onward (draft)
(5) Others

Request for approval (January 11, 2008)

(1) Amendments to the Mid-term target and Mid-term plan of Pharmaceuticals and Medical Devices Agency
(2) Amendments to the FY 2007 Plan of the Pharmaceuticals and Medical Devices Agency
(3) Amendments to the operation manual concerning relief services of the Pharmaceuticals and Medical Devices Agency

Agenda for the 4th Meeting (March 13, 2008)

(1) Payment of benefits based on the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus
(2) Fiscal year 2008 plan (draft)
(3) Budget for FY 2008 (draft)
(4) Report on the employment status of personnel from the private sector
(5) Others

Committee on Review and Safety Operations—FY 2007

Agenda for the 1st Meeting (June 6, 2007)

(1) Operating Report for FY 2006
(2) Fiscal year 2007 plan
(3) Others

Agenda for 2nd Meeting (December 13, 2007)

(1) Principal achievements up to the end of October 2007 (between April and October) and the issues to be addressed hereafter.
(2) Rate of contribution to the adverse drug reaction fund in FY 2008 and onward (draft)
(3) Others

Request for approval (January 11, 2008)

(1) Amendment to the Mid-term target and Mid-term plan of the Pharmaceuticals and Medical Devices Agency
(2) Amendment to the FY 2007 Plan of the Pharmaceuticals and Medical Devices Agency
(3) Amendment to the operation manual concerning relief services of the Pharmaceuticals and Medical Devices Agency

Committee on Review and Safety Operations—FY 2007

Agenda for the 1st Meeting (June 8, 2007)

(1) Operating Report for FY 2006
(2) Amendment to the Mid-term plan
(3) Future structure of the Agency
(4) Fiscal year 2007 plan
(5) Report on the employment status of personnel from the private sector
(6) Report on the problems caused by the anti-influenza drug Tamiflu
(7) Report on the measures against the problem of conflict of interests involving an outside expert
(8) Others

Agenda for the 2nd Meeting (August 27, 2007)

(1) Review of services at the Pharmaceuticals and Medical Devices Agency
(2) Restrictions with respect to employing personnel from the private sector
(3) Others

Agenda for the 3rd meeting (December 11, 2007)

(1) Principal achievements up to the end of October 2007 and the issues to be addressed hereafter.
(2) Review of overall organization/services of the Pharmaceutical and Medical Devices Agency
(3) Restrictions with respect to employing personnel from the private sector
(4) 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 generally open to the public and the minutes, materials, etc. relating to the meetings are disclosed on PMDA website.

- At the second Advisory Council meeting organized on September 18, 2007, discussion was made on the subject of restrictions with respect to employing personnel from the private sector and it was decided to revise the rule concerning the restrictions on employment of personnel from the private sector on the condition that the following measures are implemented in addition to the existing ones in order to secure fairness/transparency.

(i) The scope of report to the Advisory Council with regard to the status of allocation of personnel recruited from the private sector shall be widened so that the report is produced on an office basis instead of a functional basis.
(ii) The audit office which is directly under the Chief Executive shall periodically check the status of compliance with the rule concerned and report the results to the Advisory Council semi-annually.
(iii) The status of compliance with the rule concerned shall be included in the subjects of the annual audit conducted by the Auditor.

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

3.1.(4) Approaches for an efficient operation system

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

  In review divisions that required flexible approaches in particular, the Agency continued to adopt 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 (896 such commissioned outside experts as of March 31, 2008).

  Similarly, the Agency invites commissioned outside experts to ask for their opinions on adverse drug reactions and adverse health effects caused by infections from biological products (63 such commissioned outside experts as of March 31, 2008 [14 of which are also commissioned as outside experts for reviews and safety measures as described above]).

- The names of the commissioned outside experts are listed on 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. Assistance services for the development of the 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.

3.1.(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 examined and inspected, and revisions have been made as necessary. The Agency also used part-time employees for routine operations.

3.1.(6) Development of databases

- In FY 2007 as well, meetings of the Management Committee on Information Systems and Committee on Investment in Information Systems were held. In addition, discussions regarding the operational status of each information system, upgrades for the shared LAN system that serves as the common infrastructure system of 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 easy collection and analysis of 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.

- The notifications issued by MHLW and the Agency 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

3.1.(7) Approaches to developing the optimization plan for operations and systems

- The Agency developed the Optimization Plan for Operations and Systems with the assistance of the deputy CIO, an outside expert, and publicized it on March 28, 2008. The plan was based on the Plan for the Development of e-Government (decided at the Liaison Meeting of the Chief Information Officers (CIO) of the Ministries and Agencies held on July 17, 2003) and the Measures for the Realization of Optimal Operations/Systems at Independent Administrative Institutions (decided at the Liaison Meeting of the Chief Information Officers of the Ministries and Agencies held on June 29, 2005). In the course of the above, the Agency deployed external consultants and maintained a close collaboration with relevant offices in charge of services.

- In FY 2007 as well, the Agency further promoted reform of services in accordance with the results of diagnosis of services conducted in the previous year.

3.2 Cost Control by Increased Efficiency of Operations

3.2.(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 in 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 the pay standard 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 amended Pharmaceutical Affairs Law in FY 2005 are to be cut back by approximately 9% in comparison with FY 2005.

4) The administrative expenses that are incurred starting in FY 2007 in connection with efforts aimed at expediting reviews, according to the report issued by the Council for Science and Technology Policy titled, “Revision of structures aimed at the promotion of science and technology and the return of achievement to society” (dated December 25, 2006; hereinafter, referred to as the “Report of the Council for Science and Technology Policy”) are to be cut back by approximately 3% in comparison with FY 2007.

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 FY 2007, in order to execute the annual plan budget efficiently, the Agency strived to curve personnel expenses by introducing a new pay policy based on the structural reform of the pay system of national government employees. Moreover, the Agency formulated and publicized the Plan for the Review of Optional Contracts in December 2007 as per the Basic Policy for the Establishment of Reorganization and Rationalization Plan for Independent Administrative Institutions, approved at the cabinet meeting in August 2007. On the basis of this Plan, the Agency promoted general competitive bids and strived to reduce procurement costs arising from the purchase of expendables such as copy papers, the outsourcing of printed materials and so on, and the purchase of additional office furniture as well as the rental contract of additional PCs necessitated by the increase in employees. Consequently, the Agency successfully reduced general administrative expenses, excluding unused personnel expenses for vacant positions by 3.3% of the size of the budget; this reflects the target of efficient execution.

3.2.(2) Cost control of operating expenses

- By increasing efficiency of operations through promoting computerization, the Agency is expected to make the following cutbacks in the budget in the Mid-term plan relating to operating 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 operating expenses that were incurred starting in FY 2004 in connection with revisions to laws and systems are to be cut back by approximately 4% in comparison with F Y2004
  3) The operating expenses that were 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
  4) The operating expenses that were incurred starting in FY 2007 in connection with the efforts to expedite reviews, in line with the Report of the Council for Science and Technology Policy, are to be cut back by approximately 1% in comparison with FY 2007

  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 2007, the Agency progressively promoted the introduction of open competitive bidding for the contract of the clinical trial coordinator development project as per the Plan for the Review of Optional Contracts, which constitutes the target of the review. Moreover, the Agency commissioned outside

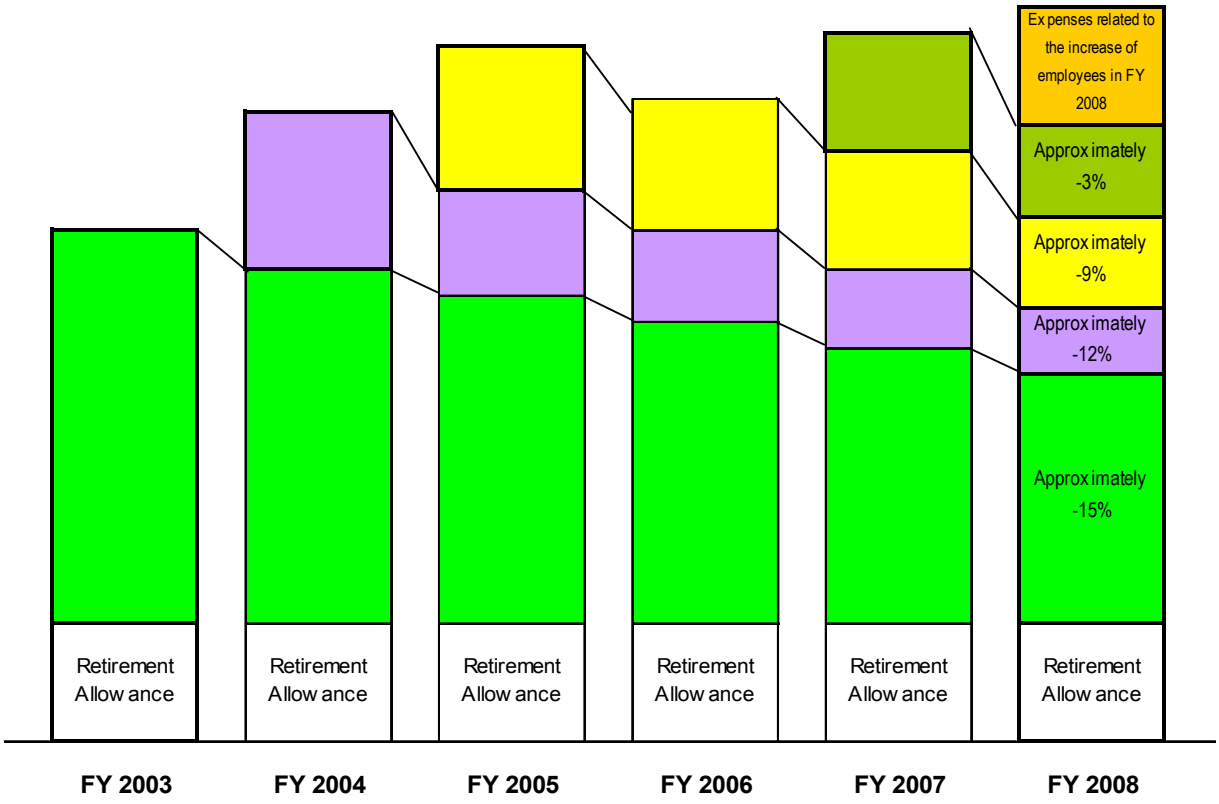
experts to assess expenses required for the development of various systems and tried to reduce cost. In the meantime, the Agency steadily managed the execution of operations, appraising the trend of commissions and contributions, which are the financial resources of operations, and securing necessary operations. Consequently, the Agency successfully reduced operating expenses, excluding the expenses for overseas GMP on-site inspections that were not used because the number of inspections was less than expected, by 13.1% compared with the budget amount, which is considered to be the target of efficient execution.

Number of Open Competitive Bids Based on Disclosure Standards

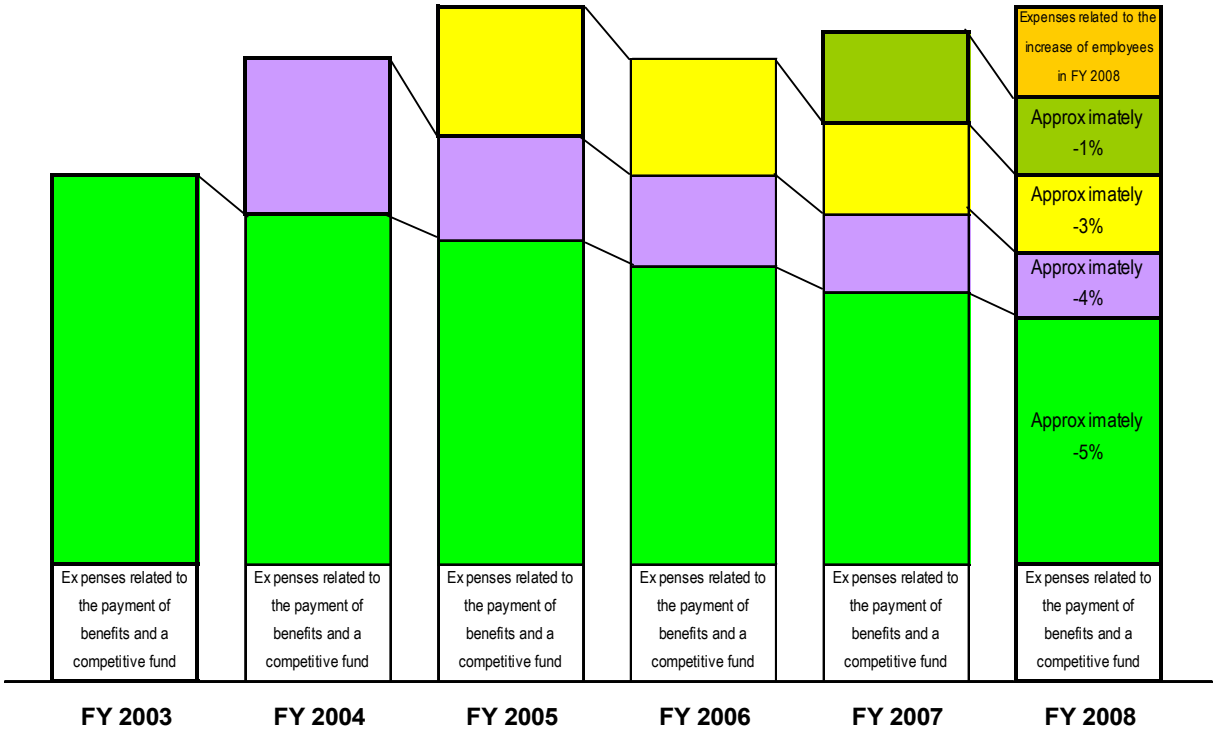
FY 2007: 55 bids (of which 21 were regarding general administrative expenses)
FY 2006: 21 bids (of which 5 were regarding general administrative expenses)
FY 2005: 18 bids (of which 7 were regarding general administrative expenses)
FY 2004: 9 bids (of which 6 were regarding general administrative expenses)

Reduction in General Administrative Expense and Operating Expenses in the Mid-term Plan (Expense Outlook Chart)

a. General Administrative Expenses



b. Operating Expenses



3.2.(3) Collection and management of contributions

- Contributions from marketing authorization holders of the industry enable the Agency to secure financial resources for relief for adverse health effects such as adverse drug reactions 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 automatically processed basic data such as those concerning newly approved items (pharmaceuticals and medical devices) and money transfer, using the contribution collection management system, which is able to manage contributions to the adverse drug reaction fund, infections fund, and safety measures fund in an integrated fashion. Consequently, the Agency efficiently conducted the operations of contribution collection management, such as the calculation of transaction value which constitutes the basis of the contribution amount and the management of the data concerning unpaid contributions. 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.

- In 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 the effective period for the Mid-term targets. In FY 2007, the resulting contribution collection rate for the adverse drug reaction fund was 99.6%, 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 the effective period of the Mid-term targets in the Mid-term plan. In FY 2007, the resulting contribution collection rate for contributions to safety measures was 97.6%.

FY 2007 Contribution Collection Results

Category		Subjects (cases)	Number of payers who made contributions (cases)	Collection rate (%)	Contribution amount (Million yen)
ADR contributions	MAH	762	762	100%	3,049
	Pharmacy	8,346	8,309	99.6%	8
	Total	9,108	9,071	99.6%	3,057
Infection contributions	MAH	98	98	100%	574
Safety measures contributions	Pharmaceutical manufacturers/traders	673	670	99.6%	529
	Medical device manufacturers/traders	2,454	2,226	90.7%	186
	Pharmaceutical & medical device manufacturers/traders	199	198	99.5%	504
	Pharmacy	8,346	8,297	99.4%	8
	Total	11,672	11,391	97.6%	1,227

- To efficiently improve contribution collection rates,

1) The Agency continued to commission the Japan Pharmaceutical Association (JPA) 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.

(i) Collected contributions for adverse drug reaction fund and shifts in the liability reserve

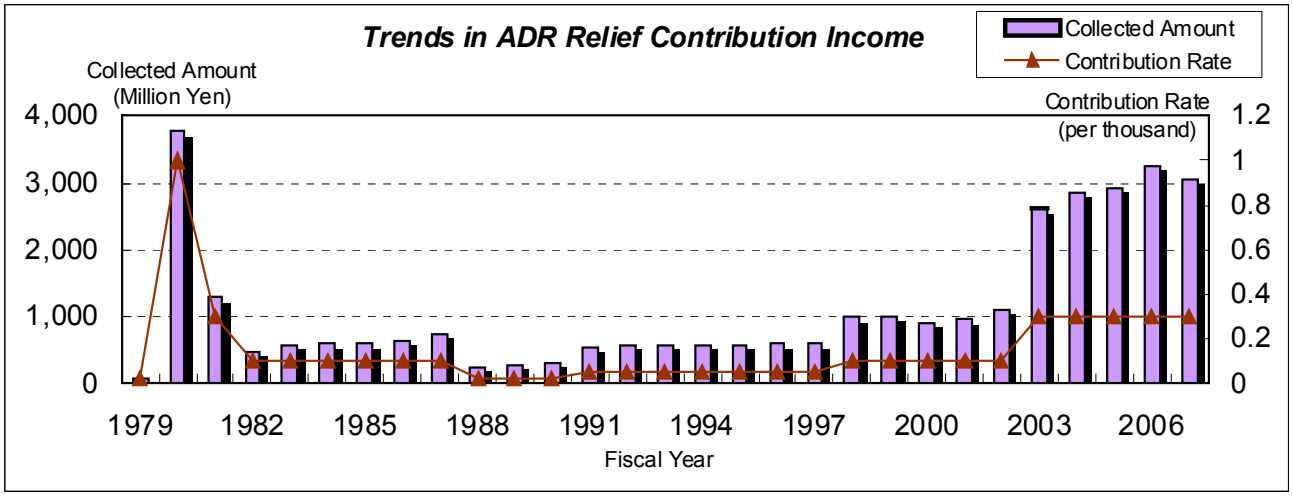
a. Adverse drug reaction fund

- 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 2007, the contribution rate applied to such marketing authorization holders was 0.3/1000 and the collected amount was 3,057 million yen.

(Million yen)

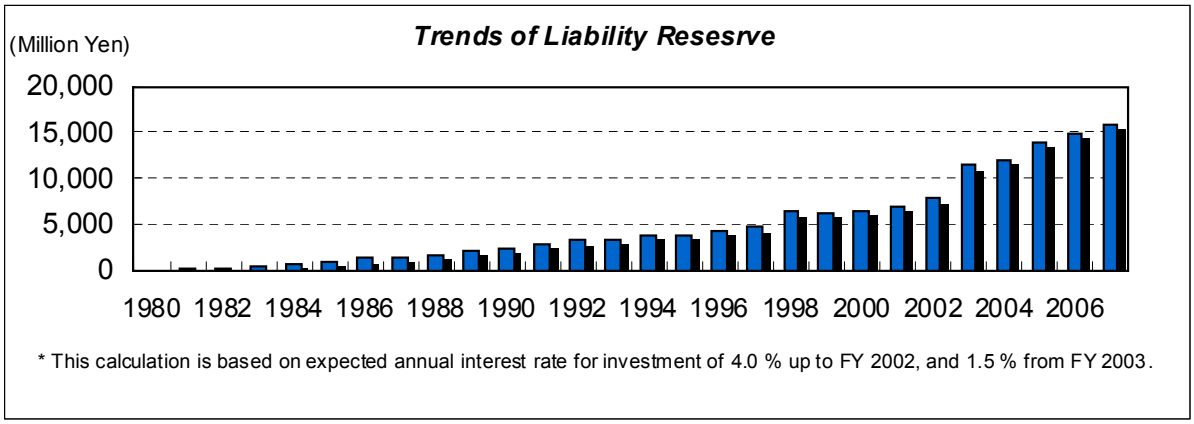
Fiscal year	FY 2003 (number of MAHs)	FY 2004 (number of MAHs)	FY 2005 (number of MAHs)	FY 2006 (number of MAHs)	FY 2007 (number of MAHs)
MAH of approved drugs	2,596 (842)	2,844 (833)	2,923 (787)	3,240 (778)	3,049 (762)
MAH of pharmacy-compounded drugs	11 (11,175)	11 (10,550)	10 (9,993)	9 (8,968)	8 (8,309)
Total amount	2,607	2,855	2,933	3,249	3,057
Contribution rate	0.3/1000	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 2007 was 15,912 million yen.



(ii) 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 2007, the contribution rate applied to such marketing authorization holders was 1/1000 and the collected amount was 574 million yen.

(Million yen)

Fiscal year	FY 2004	FY 2005	FY 2006	FY 2007
MAH of approved biological products	554 (108 companies)	553 (105 companies)	556 (101 companies)	574 (98 companies)
Contribution rate	1/1000	1/1000	1/1000	1/1000

(iii) 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 2007, the contribution rate applied to such marketing authorization holders was 0.11/1000 and the collected amount was ¥1,227 million.

(Million yen)

Fiscal year	FY 2004 (number of MAHs)	FY 2005 (number of MAHs)	FY 2006 (number of MAHs)	FY 2007 (number of MAHs)
MAH of drugs/medical devices	1,091 (3,076)	1,143 (2,982)	1,211 (3,180)	1,219 (3,094)
MAH of pharmacy-compounded drugs	10 (10,541)	10 (9,987)	9 (8,960)	8 (8,297)
Total amount	1,101	1,153	1,220	1,227
Contribution rate	0.11/1000	0.11/1000	0.11/1000	0.11/1000

3.2.(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 national civil servant pay system into account,” which is included in the Major Policies of Administrative Reform (approved at the Cabinet meeting on December 24, 2005), and based on the directive from 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%.

- Along with the introduction of the personnel evaluation system established in April 2007, the Agency introduced a new pay policy as per the reform of the pay structure of national government employees.

- The introduction of the new pay policy allowed the Agency to successfully reduce personnel expenses by approximately 3.3% (compared with the planned amount of FY 2005).

3.3 Improvement of Services to the Public

3.3.(1) General consultation service

- Based on the General Consultation Guidelines that specifies how to handle inquiries directed toward the Agency and how to reflect comments and opinions to improve operations, the Agency manages a general consultation service and makes questionnaires available at its reception counter, enabling the collection of comments and opinions of visiting customers regarding the Agency's overall operations. From June, 2007, the Agency has begun to receive comments and opinions via its website in addition to FAX so that citizens can transmit their opinions/requests more easily. Further, to provide increased convenience to visitors, the Agency is also implementing the consultation service all day, including during lunch breaks.

- Among the 2,821 inquiries that the Agency received in FY 2007, 1,402, or approximately 50% of the total inquiries received, were those relating to applications and consultations for pharmaceuticals and medical devices.

	Inquiry/consultation	Complaint	Opinion/request	Other	Total
FY 2007	2,711 (1,381)	56 (5)	45 (16)	9 (0)	2,821 (1,402)

Note 1: 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.

Note 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.

3.3.(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 of 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 2007, the Agency handled consultations in such a way for 114 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	5
	Category 4	Antibacterial agents, vermifuge, antifungal agents, antiviral agents except anti-HIV agents	1
	Oncology drugs	Antineoplastic agents	18
	Anti-AIDS drugs	Anti-HIV agents	0
Office of New Drug II	Category 2	Cardiovascular drugs, antiparkinsonian drugs, antithrombotics, anti-Alzheimer's drugs	9
	Category 5	Reproductive system drugs, genitourinary system drugs, combination drugs	4
	Radio-pharmaceuticals	Radiopharmaceuticals	0
	In vivo diagnostics	Contrast media	0
Office of New Drug III	Category 3	Central/peripheral nervous system drugs, sensory organ drugs (except drugs classified in category 6-1), narcotics	30
Office of New Drug IV	Category 6-1	Respiratory tract drugs, anti-allergy drugs, sensory organ drugs for inflammatory diseases	38
	Category 6-2	Hormone drugs, drugs for metabolic disorders (excluding combination drugs)	5
Office of Biologics I	Blood products	Blood coagulation factor products, confirmation of gene therapy, confirmation of Cartagena	1
	Bio-quality	Quality of antibody products	0
Office of Biologics II	Biological products	Vaccines, antitoxin	3
	Cellular and tissue-derived products	Cell therapy drugs	0
Total			114

- In FY 2004, the Agency 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. The Agency continues to operate the system in FY 2007 as well.

- In addition, the Agency developed a consultation manual 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.(3) Improvement in PMDA website

- The Agency has prepared and posted on its website the Annual Report in FY 2006, which concerns the operation results of FY 2006, and Principal Achievements up to the End of October 2007 (between April and October) and Future Undertakings, which concerns the operation results between April and October 2007.

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

- On the basis of the request from relevant offices, the Agency has posted on its website the procedures for and the flow of application for QMS audit, the document forms necessary for the application concerned, and the checklist concerning items required to be entered on the application form for approval for marketing.

- The Agency has posted information regarding information disclosure as a banner on the front page of our website so that it is more easily accessible.

- The Agency has revised the pages concerning recruitment information fundamentally and also considerably increased the information available to applicants.

3.3.(4) National forum on pharmaceuticals and medical devices

- The Agency held the National Forum on Pharmaceuticals and Medical Devices at the Enkei Hall of the Osaka Business Park on Saturday, October 20, 2007 with the aim of helping citizens understand the Agency's operations and activities as well as diffusing among citizens the significance of pharmaceuticals and medical devices and the necessity of proper use.

  The forum, the theme of which was "Correct understanding protects you. Talk of pharmaceuticals. Talk of medical devices," focused not only on pharmaceuticals but also medical devices as in the previous year and the keynote speeches and the panel discussions were conducted.

  In part I of the forum, Dr. Teruhiko Higuchi (President of National Center of Neurology and Psychiatry) and Dr. Yoshiyuki Taenaka (Deputy Director of the Research Institute, National Cardiovascular Center) made keynote speeches.

  Part II of the forum consisted of a panel discussion led by Ms. Rie Kouchi, a former NHK announcer, who served as the facilitator.

  Over 300 participants attended the forum, including healthcare professionals, students, and the general public.

Part I

Keynote Lectures

Speech I "Let's understand correctly. Efficacy and risk associated with pharmaceuticals"
Dr. Teruhiko Higuchi (President of National Center of Neurology and Psychiatry)

Speech II "Let's learn more about latest medical devices"
Dr. Yoshiyuki Taenaka (Deputy Director of Research Institute, National Cardiovascular Center)

Part II

Panel Discussion "Let's deal with pharmaceuticals and medical devices cleverly"

Panelists

Dr. Hatsuo Aoki (President of Japan Pharmaceutical Manufacturers Association)
Ms. Kuruyo Ima (manzai comedian)
Dr. Yoshiyuki Taenaka (Deputy Director of Research Institute, National Cardiovascular Center)
Dr. Teruhiko Higuchi (President of National Center of Neurology and Psychiatry)
Mr. Kiyoshi Mamiya (Deputy Chief Caretaker, Japan Confederation of Drug-induced Sufferers Organizations)
Mr. Takashi Wachi (Chairman, Japan Federation of Medical Devices Associations)
Mr. Akira Miyajima (Chief Executive, Pharmaceuticals and Medical Devices Agency)

Facilitator

Ms. Rie Kouchi (former NHK announcer)

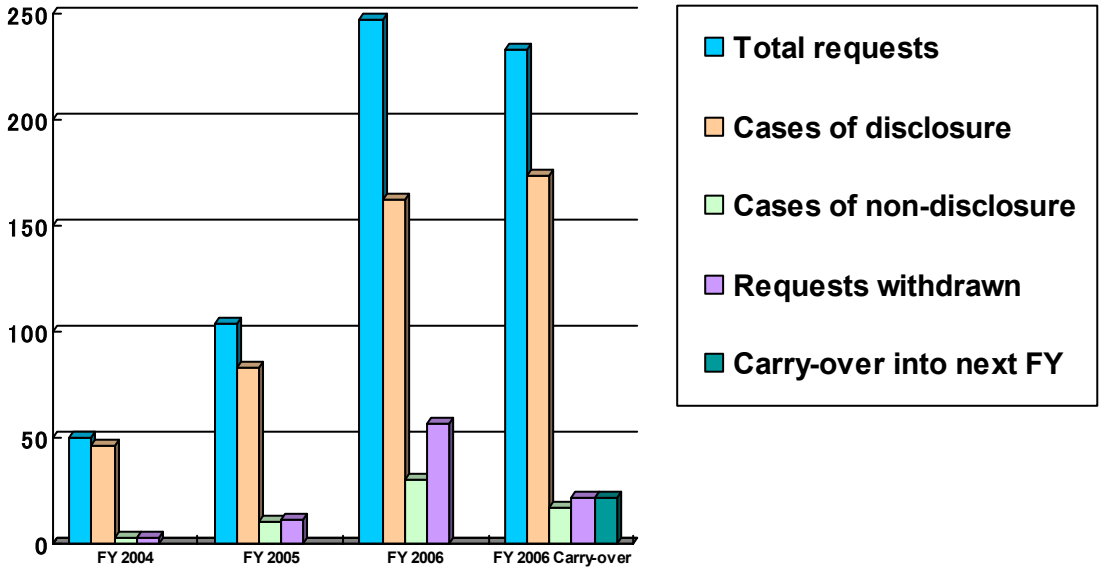
3.3.(5) Disclosure request for corporate documents

- The status of requests for information disclosure is shown below. The petition of objection concerning requests for disclosure of corporate documents was filed twice in FY 2007. These petitions are expected to be discussed at the Information Disclosure and Personal Information Protection Review

Board.

Number of Requests for Disclosure 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	56	15	147	9	21	0	6	0
FY 2007	233	21	7	167	0	17	0	2	21
Total	635	90	44	421	13	46	0	12	21



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

Number of Requests for Disclosure of Corporate Documents by Requester

Requester	FY 2004	FY 2005	FY 2006	FY 2007	Aggregate
Individuals	35	74	113	86	308
Corporates (e.g., drug manufacturers)	14	25	132	143	314
Press			3	4	13
Total	50	104	248	233	635

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

Number of Requests for Disclosure of Corporate Documents by Operational Category

Operational category	FY 2004	FY 2005	FY 2006	FY 2007	Examples
Approval review	8	22	90	115	Marketing authorization application for drugs not subject to approval
GLP/GCP/GMP/QMS etc. conformity audits	32	69	117	74	Notice of GCP audit results
Post-marketing safety	8	13	40	44	ADR report
Others	2	—	1	—	Business trip order forms
Total	50	104	248	233	

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

3.3.(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 in the Agency's management and operations.

- In FY 2007, the Agency conducted internal audits on the management status of corporate documents in possession of the Agency, the status of bids and contracts, and the status of compliance with the rule restricting the employment of personnel from the private sector.

3.3.(7) Report on the financial standing

- To ensure the 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 PMDA website.

3.3.(8) Official announcement of the plan for the review of optional contracts

- The Agency devised the Plan for the Review of Optional Contracts and publicized it on our website in December, 2007.

3.4 Personnel Issues

3.4.(1) Review of a personnel evaluation system

- According to the Mid-term target of the Agency, it is required to conduct proper personnel evaluation taking individual performance of full-time employees into consideration, and the Mid-term Plan of the Agency requests it to introduce a personnel evaluation system which enhances the morale of employees so that the results of the evaluation and the attainment of individual goals are properly reflected in remuneration, pay raise, and promotion.

- In line with the above, the Agency introduced the personnel evaluation system in April 2007 after conducting trials targeting at all full-time employees between April 2006 and September 2006.

  In order to ensure proper implementation of the personnel evaluation system, the Agency provided training courses for all employees, taking advantage of the personnel evaluation system as a subject of the training course for new recruits.

3.4.(2) Systematic implementation of staff training

- In the operations for reviews, post-marketing safety measures, and relief service 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 2007, the Agency revised the training policy on October 1, 2007 and reorganized the existing training course into two training courses: the general training course and the specialized training course. Consequently, employees can attend programs systematically. Furthermore, in order to provide efficient and effective training tailored to the abilities and standards of individual employees, the Agency actively deployed external institutions and experts, striving to reinforce training. The Agency also facilitated the participation of employees in academic conferences both at home and overseas to improve their knowledge and technological expertise.

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

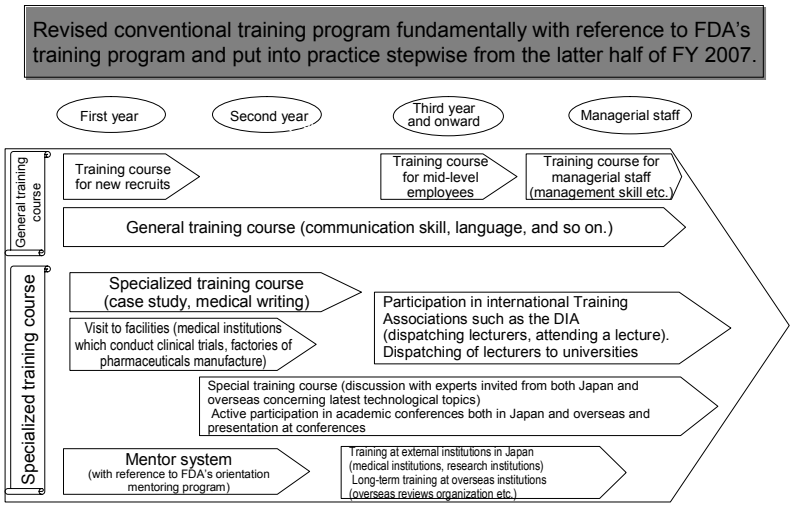
  (i) The Agency conducted a training course for new recruits in April and October of 2007 and fully implemented new programs, which were referred to those of FDA, in October, 2007 after introducing the programs from April 2007 on a trial basis.
  (ii) The Agency dispatched an aggregate of 57 employees to universities both at home and overseas as well as foreign drug regulatory authorities for the purpose of training.
  (iii) As special training programs, the Agency also held 20 training sessions on technical issues, inviting experts belonging to domestic or foreign regulatory authorities, corporations, and universities.
  (iv) As general training, the Agency conducted basic business communication training in April and September 2007 and advanced business communication training in October, which was focused on addressing complaints. Moreover, the Agency also conducted e-learning training in IT literacy, communication training, business writing training, and finance training for career-track employees, deploying external institutions once for each training.
  (v) As general training, the Agency conducted English conversation training between August and December 2007. The Agency also conducted TOEIC examinations in May and June 2007 and January 2008, for the purpose of assessing the effect of English conversation training as well as improving the linguistic ability of employees.
  (vi) The Agency conducted one training program aimed at acquiring basic knowledge on the protection of personal information. The Agency also conducted one training program, inviting lecturers from organizations of adverse drug reaction sufferers and organizations of patients. The training was intended to provide employees with the opportunity to listen to the requests to the Agency from respective standpoints.
  (vii) The Agency dispatched employees to technical training courses conducted by external institutions (e.g., training course for experts of pharmaceutical affairs, a visit to Showa University IRB)

- The Agency provided new recruits with the opportunity to visit various facilities between June 2007 and January 2008: five plants where pharmaceuticals are manufactured, five where medical devices are manufactured, six medical institutions, one research institution, and the Japanese Red Cross Society.

- In addition, the status of participation in academic societies from each division were tracked and

checked every fiscal quarter (1,023 participants in total as of the end of March 2008).

Human resource training and development



3.4.(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.

3.4.(4) Securing human resources through open recruitment

- At the Agency, it is an important task to recruit, while paying due attention to the neutrality and fairness of the Agency, capable persons with professional expertise so that the Agency can conduct its operation of reviews and safety measures expeditiously and properly.

- According to the Mid-term plan before the revision made at the end of FY 2006, it was decided that although the number of permanent employees at the start of the Mid-term plan (April 2004) was 317, by the end of the Mid-term plan (March, 2009), it would be 346. The number of permanent employees in April 2007 was 341, and the number of permanent employees was almost reached as planned.

- On the other hand, as the Mid-term plan after the revision made at the end of FY 2006 set the number of permanent employees at the end of Mid-term plan is 484, the Agency was required to recruit capable persons based on the recruitment plan for each job category. Under such circumstances, the Agency conducted four times of open recruitment of technical permanent employees, in 2007, by utilizing our website as well as job information website and decided to recruit, formally or informally, as shown below.

Note: Due to the revision of the Mid-term plan made at the end of FY 2006, the Agency plans to recruit 236 persons during the period of three years between FY 2007 and FY 2009 (58 persons in FY 2007, 80 persons in FY 2008, and 98 persons in FY 2009).

Recruitment Activities (FY 2007)

- **Schedule of briefing sessions on the Agency**
  June: Two sessions in Tokyo (total participants, 131 persons)
  September: Two sessions in Tokyo and one in Osaka (total participants, 273 persons)
  December: Two sessions in Tokyo and one session in Osaka (total participants, 175 persons)
  March: One session in Tokyo and one session in Osaka (total participants, 51 persons)

- **In-person visits to universities/hospitals by directors/employees and active approachs making use of opportunities at academic conferences**
  The academic societies to be approached:
  The Japan Pediatric Society, the Japan College of Rheumatology, the Japanese Diabetes Society, the Pharmaceutical Society of Japan, the Japanese Joint Statistical Meeting, the Joint Medical Meeting of National Hospitals; requests to dispatch employees to the Agency from national centers, the National Hospital Organization, and core hospitals engaging in clinical trials; briefing at conferences for deans of medical faculties of national/public/private universities, university visits, lectures, and so on.

- **Tools for recruitment activities**
  Brochures for recruitment have been sent out to approximately 900 institutions including medical faculties of universities, medical institutions such as university hospitals, pharmacy faculties of universities, pharmacy departments of hospitals, faculties relevant to biostatistics and veterinary science, and research institutions. The brochures were also utilized at briefing sessions on the Agency.
  Renewal of websites and the production of a DVD introducing the Agency
  Posters for recruitment sent out to medical faculties of universities (80), distributed individually, and used in conjunction with other tools

- **Information to be posted on job information websites**
  (the websites NIKKEI NAVI and NIKKEI CAREER NET were chosen via a planning competition)
  Information to be posted on the following:
  Website presenting job offers for 2008 graduates (NIKKEI NAVI 2008)
  Pre-website presenting job offers for 2009 graduates (NIKKEI NAVI 2009—Special feature of pharmaceuticals/biotech industry)
  Website presenting job offers for 2009 new graduates (NIKKEI NAVI 2009)
  Website presenting job information for those seeking a career change (NIKKEI CAREER NET. For 1 month from September 7 and for 1 month from December 7)

- **Recruitment advertising via academic journals**
  The Japanese Biochemical Society (website), the Japanese Pharmacological Society (website), the Academy of Pharmaceutical Science and Technology, Japan (Journal of Pharmaceutical Science and Technology, Japan), the Japanese Society for the Study of Xenobiotics (Website), the Japanese Society of Clinical Pharmacology and Therapeutics (Clinical Pharmacology), the Japanese Society of Toxicology (website), the Pharmaceutical Society Japan (FARUMASHIA), the Journal of Japanese Society of Hospital Pharmacists, the Japan Medical Journal, the Nikkei Medical, Thorough study on Pharmaceuticals/biotech industry (job information journal for the post-graduates of pharmacy), the Japanese Joint Statistical Meeting (collected report of lectures), the Journal of Japanese Society of Pharmaceutical HealthCare and Sciences, Nature, and the 128th conference of the Pharmaceutical Society Japan (display advertising)

- **Advertising via booth displays at academic conferences**
  The 61st Joint Medical Conference of National Hospitals and the 128th conference of the Pharmaceutical Society Japan

Employment through Open Recruitment in FY 2007—as of April 1, 2008

1)	Technical employees (4 times of public recruitment)	
	Number of applicants	About 1,070
	Number of employment	77
	Number of prospective staff	74
2)	Administrative employees (twice of public recruitment)	
	Number of applicants	190
	Number of employment	14

- Under extremely difficult circumstances for the recruitment of personnel who are qualified for GMP conformity audits and biostatistics, the Agency had set, with paying due attention to the fairness and transparency of the Agency, temporary exception to the Rule for operation concerning the restriction of employee's engagement in jobs. However, since April 1, 2007, there was no recruit based on this exception until the revised Rule for operation concerning the restriction of employee's engagement in jobs took effect (October 1, 2007).

Numbers of the Agency's Permanent Staff

	April 1, 2004	April 1, 2005	April 1, 2006	April 1, 2007	April 1, 2008	Numbers at the end of FY 2008 (in the Mid-term plan)
Total	256	291	319	341	426	484
Review divisions	154	178	197	206	277	
Safety divisions	29	43	49	57	65	

Notes 1. The expected number of the staff including executives at the beginning of the 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" includes 6 executives, except for April 1, 2006, which includes 5 executives.

3. The "Total" as of April 1, 2004 includes 11 staff members engaged in the R&D promotion service. Before the service was 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 divisions include the Director (Center for Product Evaluation), Associate Executive Director, Deputy Director, Associate Center Director, Office of Review Administration, Officse of New Drug I to IV, Office of Biologics I and II, Priority Reviews Director, Office of OTC/Generic Drugs, Office of Medical Devices, and Office of Conformity Audit (Office of New Drug IV was established on July 1, 2007 and the former Office of Biologics were divided into two on October 1, 2007).

5. The safety divisions consist of the Chief Safety Officer, Office of Safety, and Office of Compliance and Standards.

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

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

- For this purpose, the Agency conducts 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 employees whose family members work in the pharmaceutical industry. The Agency also strives to keep its staff

members informed of these regulations.

- More specifically, the Agency created summaries and a Q & A list concerning relevant regulations, and makes sure to keep the staff informed through the intranet and during beginner 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.

3.5 Ensuring Security

3.5.(1) Management of entries and exits

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

- Specifically, 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 intranet and during beginner training.

3.5.(2) Security measures for information systems

- Based on the FY 2007 plan, the Agency has strived to ensure the security of the information relating to information systems.

- By abolishing the Information Security Policy and amending the Information Management/Use Policy, the Agency established a security structure headed by CIO and consisted of owners of each system.

- In order to reinforce the backup function of information data, the Agency selected a storing company through competitive bids and commenced storing back-up data of information systems at remote locations in January 2008.

- In order to spread the use of secure e-mail to the services of medical device reviews, clinical trial consultations, and quality management, the Agency revised relevant policies and notified relevant institutions to that effect on March 31, 2008 so that the use of secure e-mail in relation to those services became available from FY 2008.

Numbers of Users/Issued Certificates Using the Secure e-mail System as of the End of March 2008

	Number of registered companies	Number of issued certificates
Outside the Agency	43	218
Within the Agency		223

Note: The numbers of registered companies and issued certificates as of the end of March 2008.

PART 4 Improvement in Management of Operations and Quality of Services in Each Division

4.1 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 collectively referred to as “relief systems”), and to operate these relief systems appropriately, the Agency, through relief fund services, takes the following measures to provide adequate and prompt relief for those suffering from adverse drug reactions and infections derived from biological products.

4.1.(1) Expansion and reconsideration of the provision of Information

(iv) 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 to make the administration of the systems more transparent, the Agency plans to disclose information about actual performance of operations achieved in FY 2007 on PMDA website. In addition, the Agency has finished posting cases of approval/rejection up to the fourth quarter of FY 2006 on the website with due consideration to protecting personal information. The Agency also plans to provide information on cases in and after FY 2007 successively on the website.

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

(v) Improvement of brochures, etc.

- Improvements were made to brochures 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 because of incomplete applications, and to make operations more efficient, the Agency carried out the following:
  a) Prepared and distributed brochures describing the relief systems in an understandable manner, and also posted the brochures on PMDA website (in PDF format) together with animations summarizing the brochure.
  b) Prepared an application sample and made improvements so that patients, etc., could fill out the forms more easily.
  c) Applications, which used to be mailed upon request, are now available for download on PMDA website, and the URL from which applications can be downloaded are included in brochures for easier use.

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

4.1.(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:

(i) Publicity through a brochure entitled “Do You Know about Relief Systems?” explaining the relief systems in an understandable manner (this brochure is included in magazines published by the Japan Medical Association and the Japan Pharmaceutical Association; the brochure is also distributed on PMDA website in the form of an abridged animation version and a full-text PDF version), publicity via the Internet (banner advertisement on four websites aimed exclusively at

medical professionals, keyword-linked advertisements on seven general websites, and promotion on So-net m3, a site aimed at doctors), and publicity by Prefectural Governments.

(ii) Publicity on the infection relief system in six specialized magazines and publicity on commissioned payment services for HIV-positive patients, etc., in five specialized magazines

(iii) Introduction of the relief systems in four programs and abstract journals of the Japan Municipal Hospital Association and other associations

(iv) Participation in medical conventions (e.g., General Assembly of the Japanese Dermatological Association, the Spring Meeting of the Japanese Society of Allergology, the general assembly of the East Japan Branch of the Japan Society of Chemotherapy) and distribution of brochures about and presentations on the relief systems at 10 different events

(v) Explanation of the relief systems at seven different domestic medical institutions, workshops for vaccination specialists, the general assembly of the Society of National Hospital Pharmacists, and the Tokyo Transfusion Therapy Workshop

(vi) Implementation of publicity for the 21st 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 the help of concerned bodies, the following were carried out as individual PR activities:

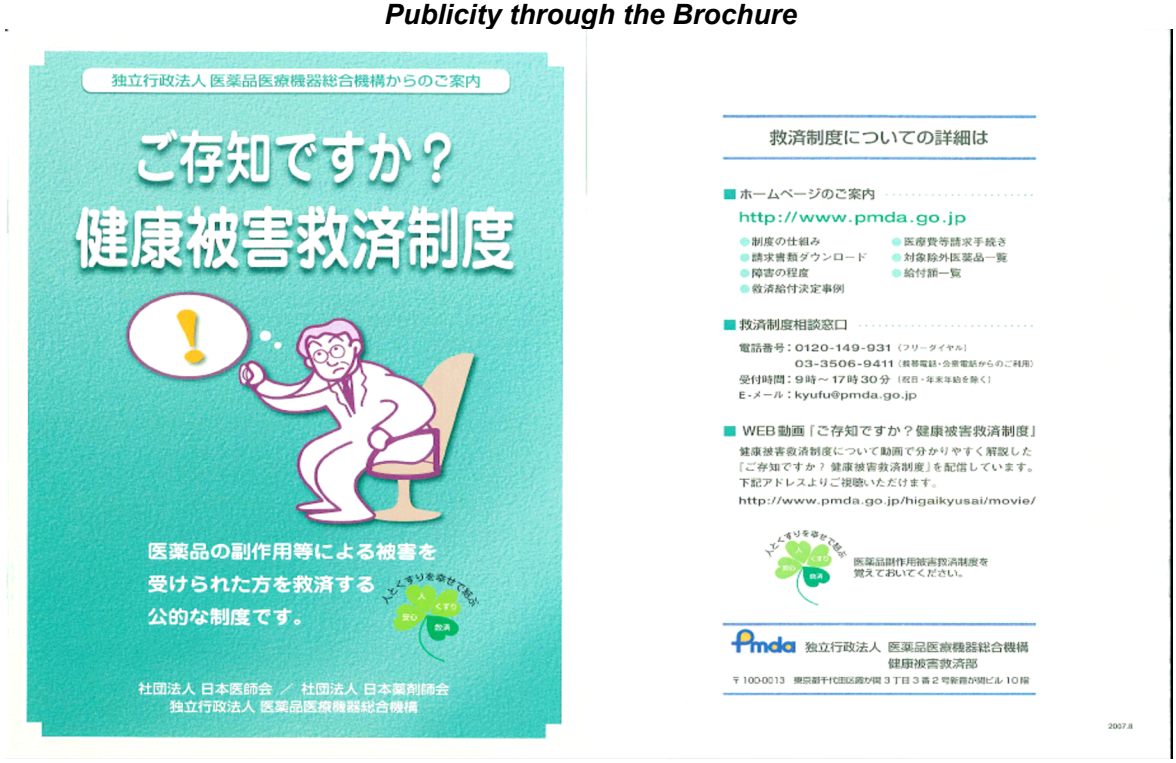
(i) Publicity in a magazine on drug safety updates (DSU) published by the Federation of Pharmaceutical Manufacturers' Association of Japan and distribution of these magazines to all medical institutions

(ii) Distribution of the brochure introducing the system to pharmacies by the Japan Pharmaceutical Association

(iii) Distribution of the brochures introducing the relief systems to medical institutions by the Japanese Red Cross Society Blood Center

(iv) Introduction of the relief systems in the drug handbook published by the Japan Pharmaceuticals Association.

Publicity through the Brochure



- To convey the concepts of the relief systems in an understandable manner to healthcare professionals, the brochure titled “Do You Know about Relief Systems?” (8 pages in total including the cover) and posters were distributed as attachments to the Japan Medical Association (about 150,000 copies) and Japan Pharmaceutical Association journals (about 100,000 copies).

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

4.1.(3) Expansion of the consultation service

- In the FY 2007 plan, the Agency’s goal is to increase the number of consultations and accesses to PMDA website, both by 20% in comparison to FY 2003, but the actual number of consultations in FY 2007 increased by 36% as compared to FY 2003.

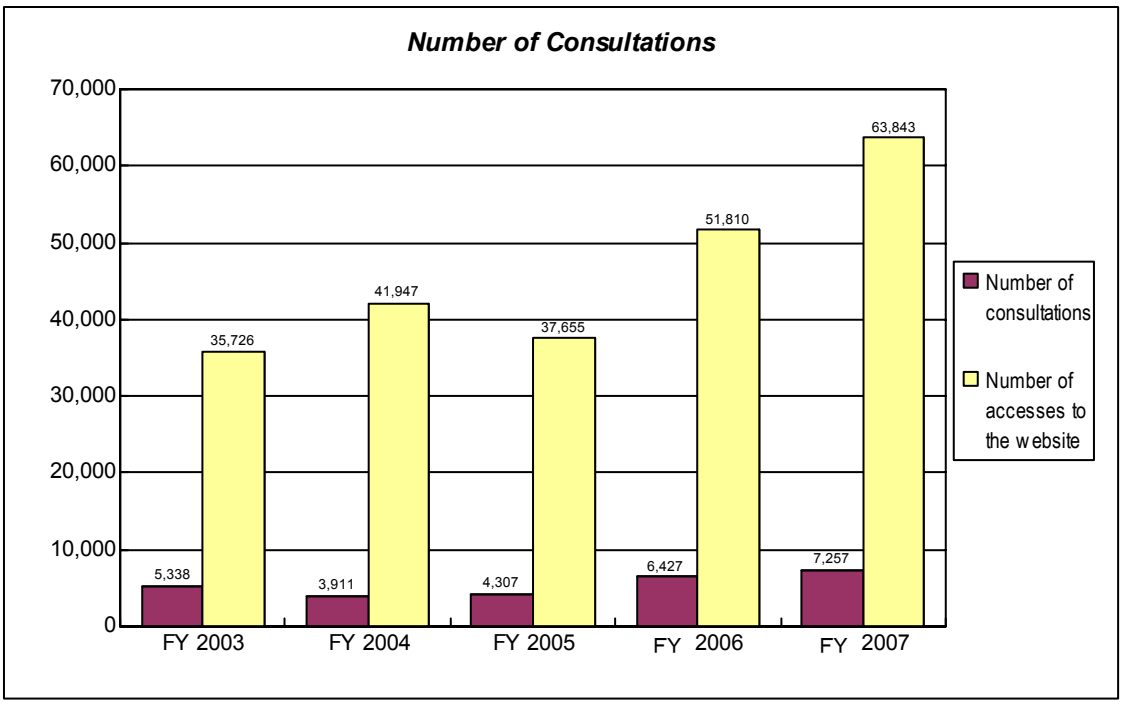
  This was due to the creation of a brochure understandably explaining the relief systems, publicity from enclosing copies of the brochure with magazines published by Japan Medical Association and Japan Pharmaceutical Association, publication of animations summarizing this brochure on PMDA website, and publicity via the Internet.

  Also, the number of accesses to PMDA website in FY 2007 increased by 79% as compared to FY 2003.

  Moreover, after five months of publicity through the Internet and prefectural governments’ websites, there were 101,720 accesses to the web pages used exclusively for publicity and containing overviews of the relief systems.

Fiscal Year	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	Compared with FY 2003
Number of consultations	5,338	3,911	4,307	6,427	7,257	36% increase
Number of web accesses	35,726	41,947	37,655	51,810	63,843	79% increase

Toll-free number: 0120-149-931
Phone: 03-3506-9411
e-mail for relief system consultation: kyufu@pmda.go.jp



4.1.(4) Central management of information through databases

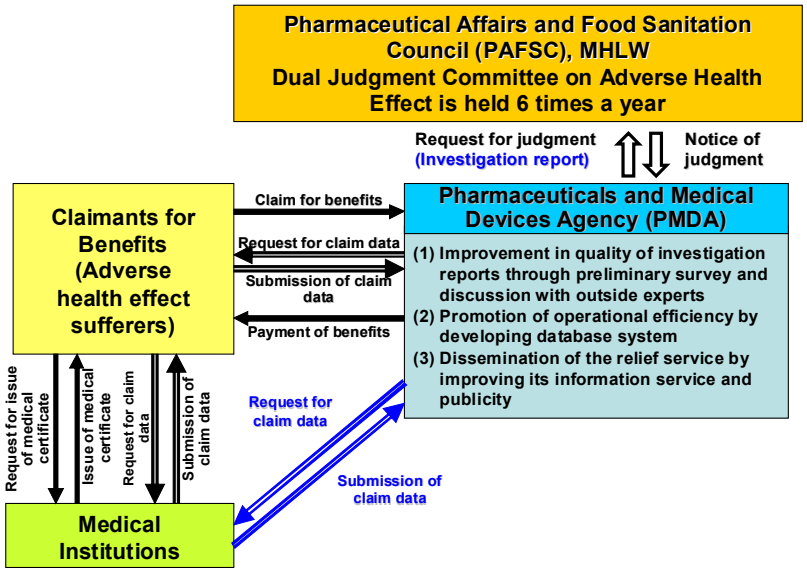
- To make operations more efficient and swift, the Agency checks and properly understands the progress and accumulates data on the relief benefit services for adverse drug reactions and relief benefit services for infections (particularly information related to offending drugs and names of illnesses from adverse drug reactions). Further, in August 2007, it completed the first phase of the development of the Integration and Analysis System for Databases on Relief Benefit Services that can analyze the accumulated data from various angles and utilize them for service standardization.

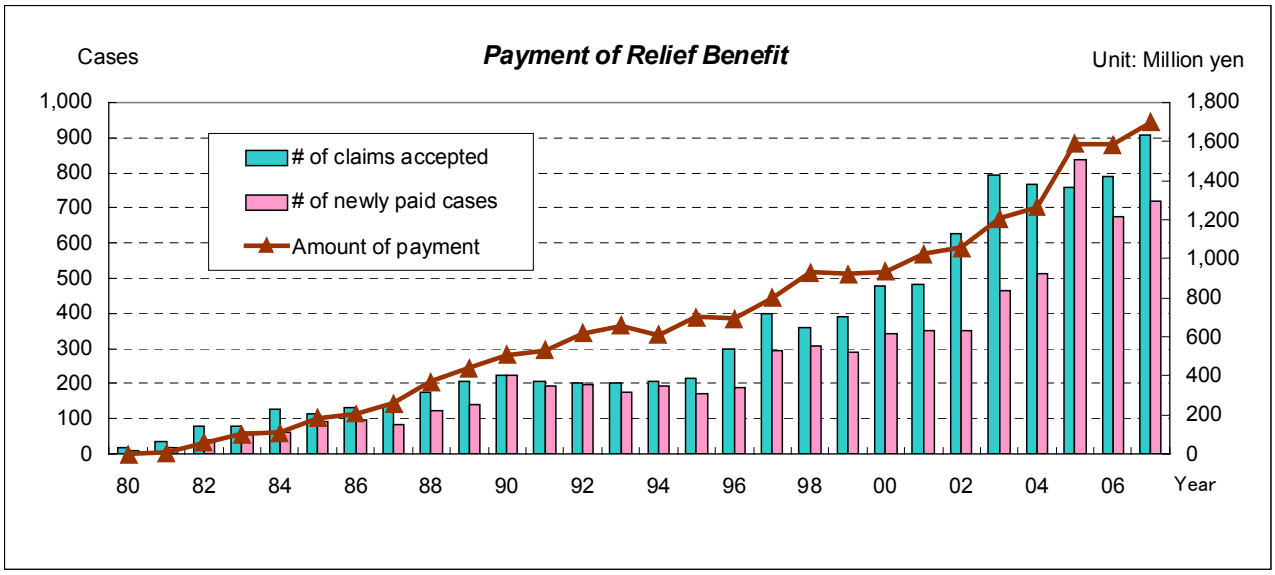
4.1.(5) Prompt processing of relief benfit claims

- In order to conduct prompt administrative processing of relief benefit services, the Agency investigates and organizes the facts given in the contents of claims upon receiving a claim for relief benefit services, and requests the Minister of Health, Labour and Welfare to make a medical and pharmaceutical judgment on the claim. For this purpose, the following operations are conducted:

  i) Fact-finding investigations, etc., of the relevant incident included in the claim
  ii) Creation of a summary chart tracing the case over time
  iii) Creation of investigation reports.

Flow of Adverse Health Effect Relief Services





FY 2007

- Relief services for adverse drug reactions
  → Number of applications: 908
  Number of cases of approval/rejection: 855 (of which 718 were judged approved)
- Relief services for infections
  → Number of applications: 9
  Number of cases of approval/rejection: 5 (of which 3 were judged approved)

- The Agency also sets the time period for standard administrative processing of claims from when they are submitted until approval or rejection judgments are made (including the time required for a medical and pharmaceutical judgment to be made by MHLW) at 8 months. Through collaborations with MHLW, the Agency plans to process 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.

- The Agency and MHLW worked together to develop a system for sharing the paperwork for medical and pharmaceutical judgment and decided to allocate 2 months to MHLW and 6 months to the

Agency (excluding the time periods when administrative processing is not possible because of additional or supplementary documents and investigations are required of claimants or medical institutes) and established a scheme wherein a list of pending matters is periodically prepared to determine the appropriate management of the processing time for paperwork.

- The achievement rate for FY 2007 was 74.2%, 8.9 point increase from 65.3% in FY 2006, as a result of the intensive processing of paperwork.

(vi) Adverse drug reaction relief services

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

a. Actual performance of adverse drug reaction relief

The actual performance for FY 2007 is shown below:

Fiscal Year	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Number of claims	793	769	760	788	908
Number of judged cases	566	633	1,035	845	855
Approved	465	513	836	676	718
Rejected	99	119	195	169	135
Withdrawn	2	1	4	0	2
Cases in progress*	820	956	681	624	677
Achievement rate†	17.6%	14.5%	12.7%	65.3%	74.2%
Median processing time	10.6 months	12.4 months	11.2 months	6.6 months	6.4 months

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

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

b. Number of claims by type of benefits

The numbers of claimants filed in FY 2007 by type of benefits are shown below:

(Cases)

Fiscal Year		FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Number of claims		793	769	760	788	908
Types of Benefits	Medical expenses	640	613	602	643	730
	Medical allowances	683	650	659	694	786
	Disability pensions	68	73	78	60	70
	Pension for raising handicapped children	9	14	5	14	10
	Bereaved family pensions	56	54	41	31	33
	Lump-sum benefits for bereaved families	42	47	48	51	72
	Funeral expenses	98	101	84	88	105

Note: A claim could include more than one kind of benefits.

c. Judgment status according to types of benefits

The status of judgments made in FY 2007 by type of benefits is shown below:

(Thousand yen)

Types	FY 2003		FY 2004		FY 2005		FY 2006		FY 2007	
	Number of cases	Amount of payment	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	603	67,603
Medical allowances	408	35,388	472	42,711	757	70,073	624	60,034	651	62,668
Disability pensions	22	552,869	24	592,028	33	653,143	35	692,446	42	730,007
Pension for raising handicapped children	2	16,991	4	17,810	17	40,639	6	30,131	7	35,760
Bereaved family pensions	32	335,829	31	412,167	44	502,468	22	493,010	20	501,454
Lump-sum benefits for bereaved families	30	217,148	19	137,041	32	228,708	34	229,446	39	286,373
Funeral expenses	61	11,205	48	9,167	74	14,010	53	10,386	63	12,661
Total	922	1,204,243	1,046	1,262,647	1,674	1,587,567	1,346	1,582,956	1,425	1,696,525

Note 1: "Number of cases" means judged cases. "Amount of payment" means benefits paid for both new and continuing cases.
Note 2: The amount of money was rounded off to the nearest thousand yen. Therefore, the total of the values does not necessarily match the sum of individual values.

(vii) Infections derived from biological products relief

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

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

a. Actual performance of relief for infections

The actual performance for FY 2007 is shown below:

Fiscal Year	FY 2004	FY 2005	FY 2006	FY 2007
Number of claims	5	5	6	9
Number of judgments	2	6	7	5
Approved	2	3	7	3
Rejected	0	3	0	2
Withdrawn	0	0	0	0
Cases in progress*	3	2	1	5
Achievement rate†	100.0%	50.0%	100.0%	100.0%
Median processing time	3.0 months	5.6 months	3.8 months	3.8 months

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

b. Number of claims by type of benefits

The numbers of claims filed in FY 2007 by type of benefits are shown below.

(Cases)

Fiscal Year		FY 2004	FY 2005	FY 2006	FY 2007
Number of claims		5	5	6	9
Types of benefits	Medical expenses	5	5	5	7
	Medical allowances	5	5	5	8
	Disability pensions	0	0	0	1
	Pension for raising handicapped children	0	0	0	0
	Bereaved family pensions	0	0	1	0
	Lump-sum benefits for bereaved families	1	0	0	0
	Funeral expenses	1	0	1	0

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

c. Judgment status by type of benefits

The status of judgments made in FY 2007 by type of benefit is shown below:

(Thousand yen)

Type of benefits	FY 2004		FY 2005		FY 2006		FY 2007	
	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	2	161	3	475	6	473	3	102
Medical allowances	2	142	3	249	6	497	3	352
Disability pensions	—	—	—	—	—	—	—	—
Pension for raising handicapped children	—	—	—	—	—	—	—	—
Bereaved family pensions	—	—	—	—	1	1,387	—	2,378
Lump-sum benefits for bereaved families	—	—	—	—	—	—	—	—
Funeral expenses	—	—	—	—	1	199	—	—
Total	4	302	6	724	14	2,556	6	2,833

Note: The amount of money was rounded off to the nearest thousand yen. Therefore, the total of the values does not necessarily match the sum of values.

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

- To plan for collaboration between divisions within the Agency, information on judged cases relating to eligibility for relief benefits for adverse drug reactions and relief benefits for infections in FY 2007 was provided to the Office of Safety after excluding personal information.

4.1.(7) Surveys on actual status of effects from adverse drug reactions (investigative research as 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 drug reactions, the Agency implements health and welfare services for sufferers from adverse health effects (Article 15, Paragraph 1, Item 1-b of the Law for the Pharmaceuticals and Medical Devices Agency).

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

As part of health and welfare services, the Agency established an Investigative Research Team for Improvements in the Quality of Life of Sufferers from Severe and Rare Adverse Health Effects Caused by Pharmaceuticals in April 2006 based on the results of a survey (March, 2007) on the actual condition of adverse health effects stemming from adverse drug reactions conducted in FY 2005, and initiated investigative research to obtain materials for reviewing the ideal way to provide required services and measures for improving the QOL of sufferers from severe and rare adverse health effects for which general measures for disabled people do not necessarily provide sufficient support.

The reports on the Investigative Research were provided by the leaders of the Investigative Research Team on November 14, 2007, and were publicly announced on the website after disclosure to the Relief Committee session held on December 13, 2007.

Contents of the Research

The Agency collects, analyzes, and evaluates reports, such as survey forms, etc., from sufferers from adverse health effects regarding the condition of various efforts in their daily life (60 volunteers in FY 2007).

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

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

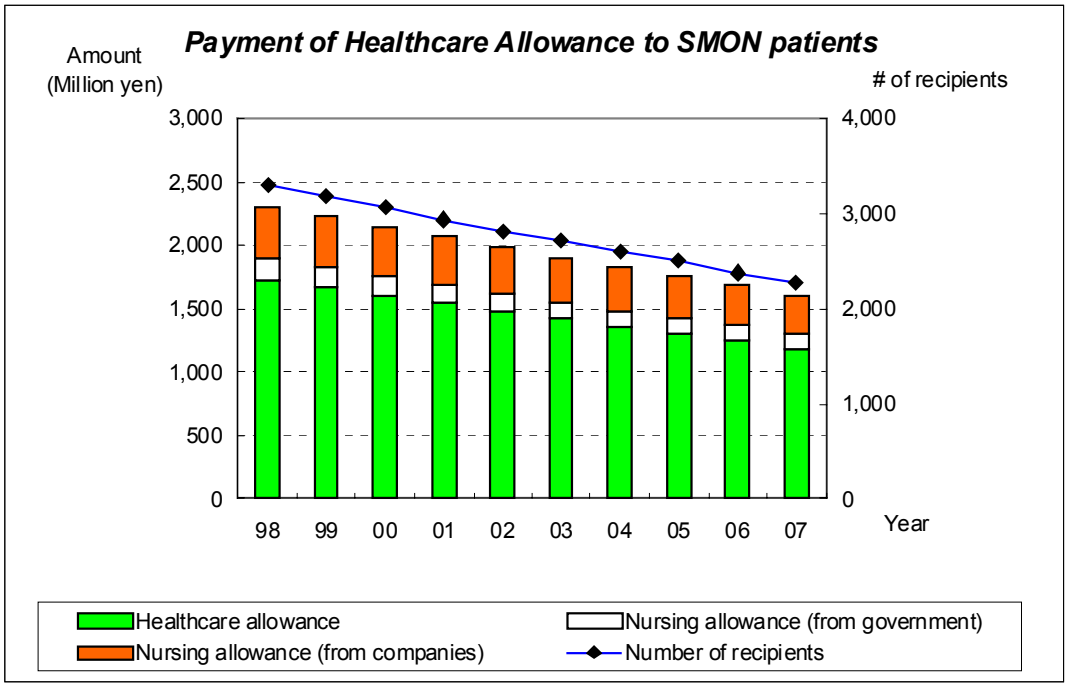
In order to appropriately provide healthcare allowances, etc., for SMON patients and HIV-positive patients affected through blood products, the Agency implemented appropriate operations based on the contents of consignment contracts, giving due consideration to the confidentiality of personal information.

(i) 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 court. In FY 2007, the number of patients receiving such allowances was 2,269, and the total amount of payments was 1.601 billion yen.

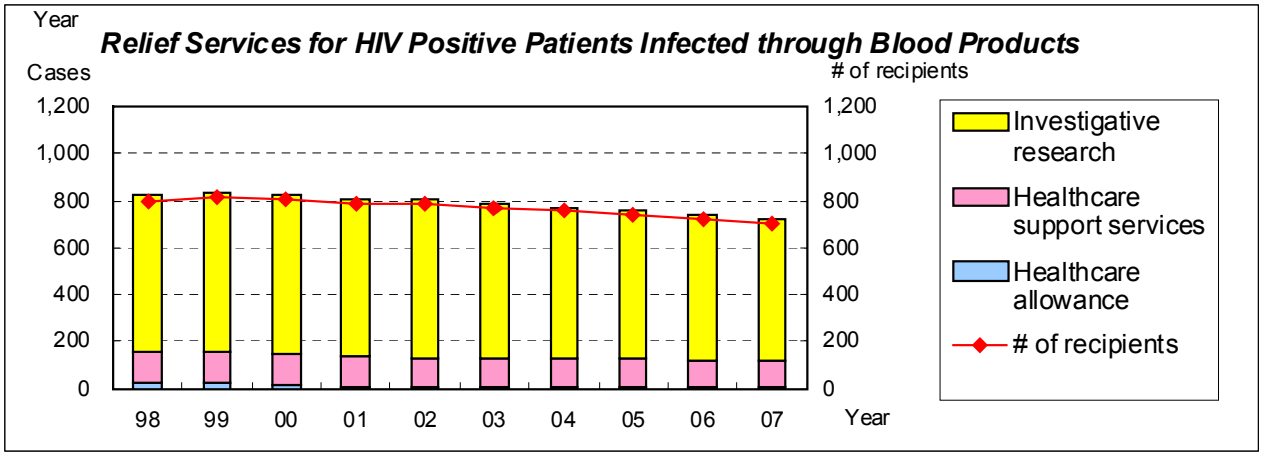
Fiscal Year		FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Number of recipients		2,713	2,598	2,504	2,381	2,269
Amount paid (thousand yen)		1,901,829	1,829,332	1,757,774	1,683,500	1,601,134
Breakdown	Healthcare allowance	1,417,469	1,359,056	1,305,168	1,251,622	1,191,245
	Nursing allowance (from companies)	349,933	342,357	330,086	315,027	299,108
	Nursing allowance (from the government)	134,427	127,920	122,520	116,850	110,781

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



(ii) AIDS-related services (healthcare allowances)

- The Agency provides the three services below for HIV-positive patients afected through blood products. Of the HIV-positive patients who received benefits in FY 2007, 604 patients received allowances relating to investigative research, 117 patients received allowances for healthcare support services and 3 patients received healthcare allowances. The total number of patients receiving allowances was 724 patients, and the total amount of payments was 561 million yen.
  a. Payment of healthcare allowances for HIV-positive patients, as services for investigative research.
  b. Payment of healthcare allowances for AIDS patients for whom a settlement has been reached in court, as healthcare support services.
  c. Payment of special allowances, etc., for AIDS patients for whom a settlement has not been reached in court, as healthcare allowances.



Fiscal Year	FY 2003		FY 2004		FY 2005		FY 2006		FY 2007	
	Number of Recipients	Amount of payment (Thousand yen)	Number of Recipients	Amount of payment (Thousand yen)	Number of Recipients	Amount of payment (Thousand yen)	Number of Recipients	Amount of payment (Thousand yen)	Number of Recipients	Amount of payment (Thousand yen)
Investigative research	662	355,343	647	348,446	638	341,017	618	334,653	604	327,857
Healthcare support services	127	221,400	124	210,600	121	210,300	120	210,000	117	224,796
Healthcare allowance	3	8,733	3	8,706	3	8,706	3	8,678	3	8,084
Total	789	576,477	772	567,752	762	560,023	741	553,331	724	560,737

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

- The Agency also started the service of providing benefits to individuals affected by hepatitis C according to the Law on Special Measures concerning the Payment of Benefits to Assist the Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus on January 16, 2008. The number of benefit recipients was 108, with ¥2,360 million as the total amount paid in FY 2007.

4.2 Reviews and Related Services/Safety Measures

To enable for the public to safely use pharmaceuticals and medical devices that have international standards, through reviews and related services and safety measures, the Agency is required 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 FY 2007 plan.

4.2.(1) Faster access to the latest pharmaceuticals and medical devices

(iii) Ensuring the benefits of pharmaceuticals and medical devices for the public and healthcare professionals

- The Agency is required 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 benefit 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), allowing consolidation of review functions. By taking the following kinds of measures, further improvements in the system were able to be planned.
  1) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency

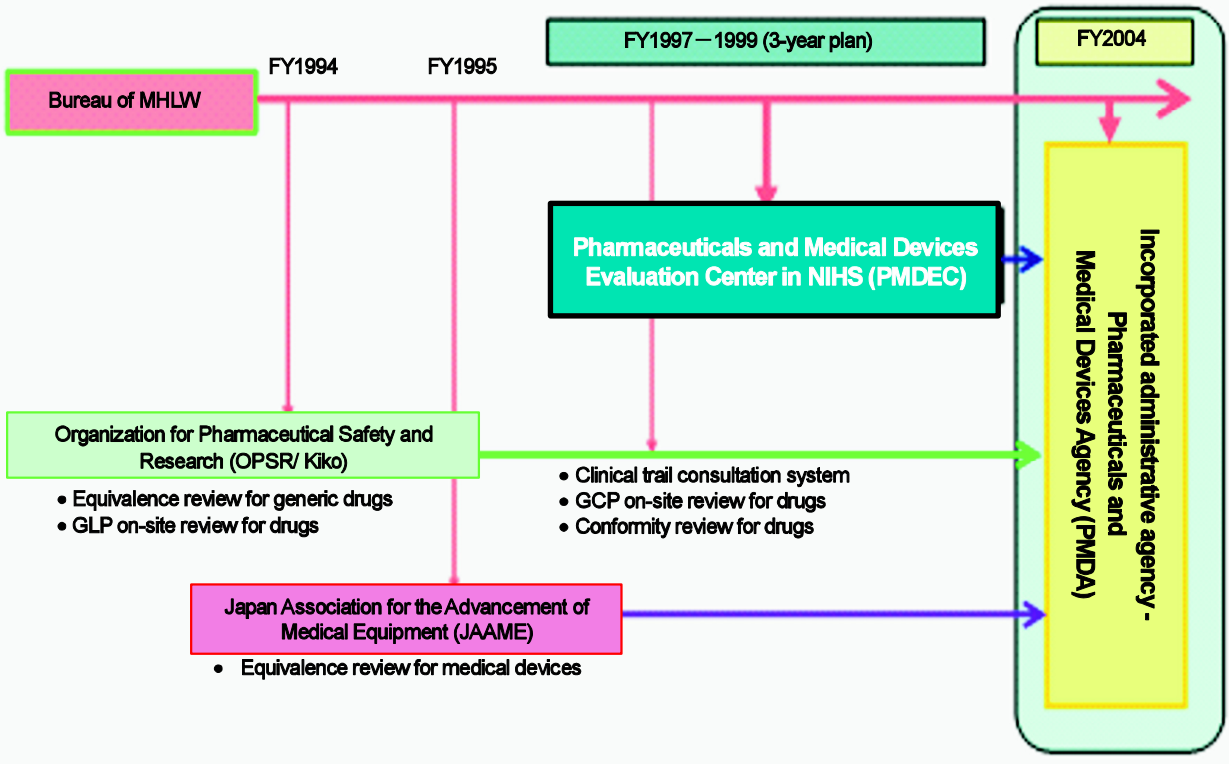
(PMDA), was established through the integration of three separate organizations responsible for reviews and related services.

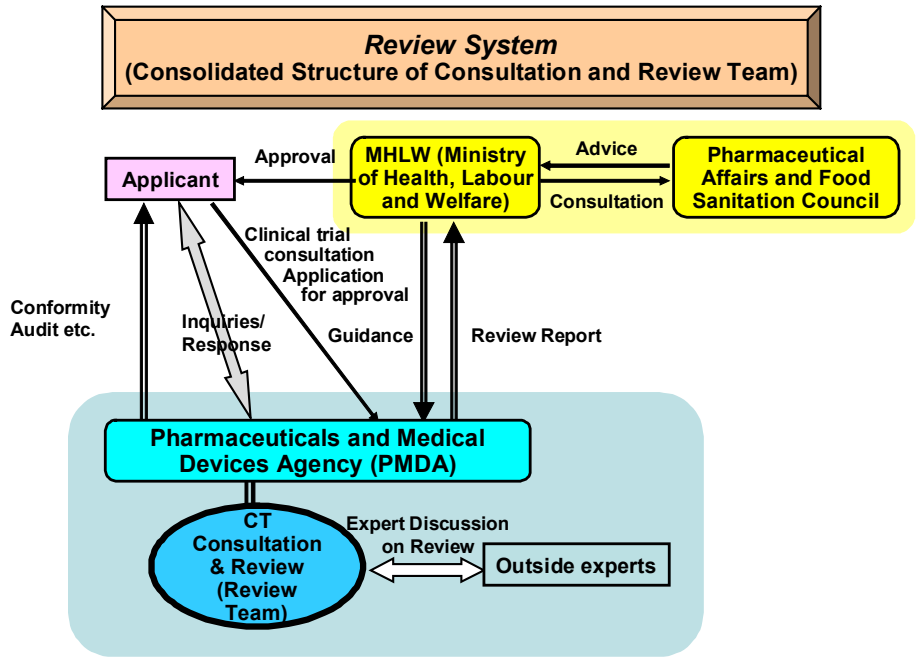
2) The Agency decided to greatly increase the number of its staff by about 100, including reviewers, within the effective period for the Mid-term targets.

3) Under the new system of the Agency, the entire review process from consultations regarding clinical trials until review operations is conducted by the same team with the same staff members for consistency and coordination. (As consultations on clinical trials 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.)

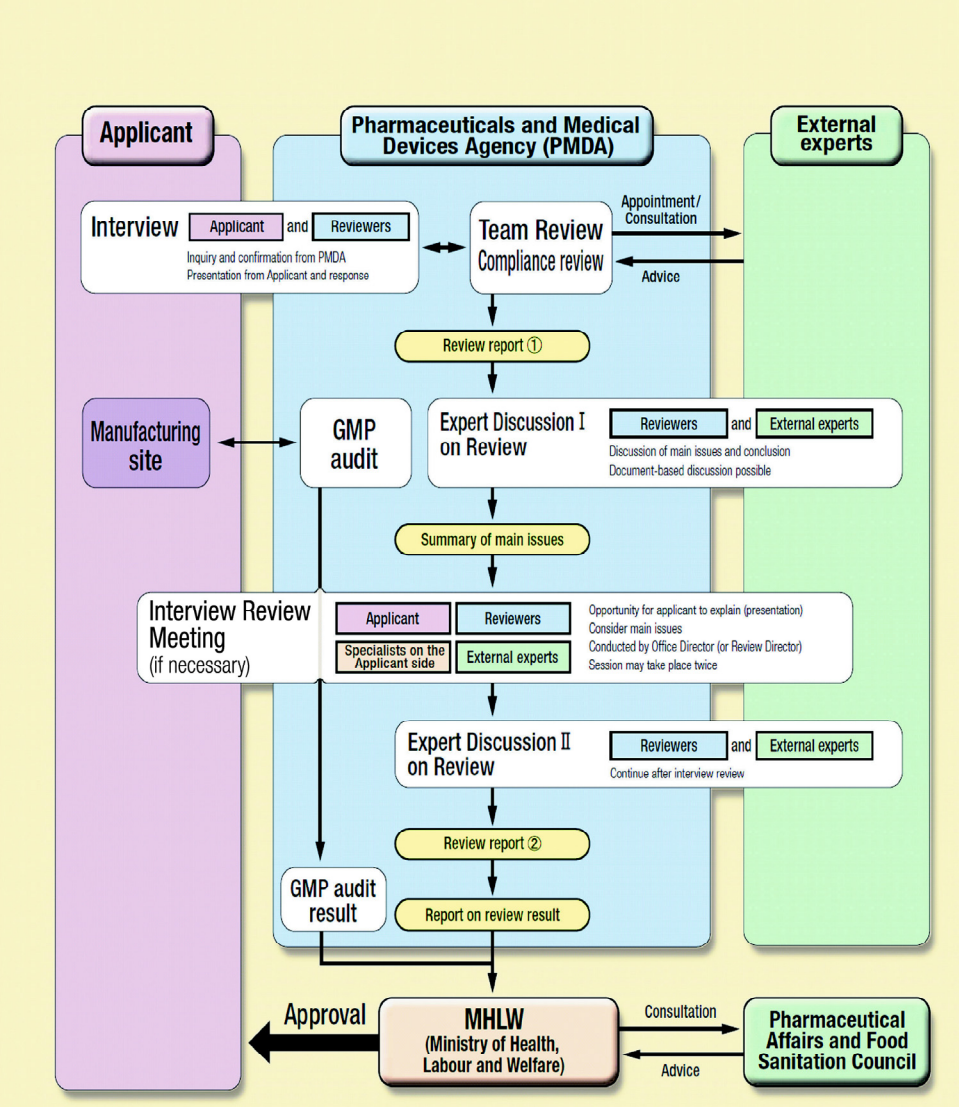
4) To respond to new needs in the future, the Agency is reinforcing its functions for reviewing medical devices, as well as enhancing reviews of biological and biotechnology-derived products.

Transition of approval review system on drugs and medical devices





Flowchart of review process for approval



Actual Results of Review Services in FY 2007

Reviews:

Pharmaceuticals

(i) Number of Expert Discussions conducted: 231 (182 in written form, 49 through meetings)

(ii) Applications discussed at the Drug Committees (PAFSC): 51
Review reports made to the Drug Committees (PAFSC): 29

Medical devices and *in vitro* diagnostics

(i) Number of Expert Discussions conducted: 115 (98 in written form, 17 through meetings)

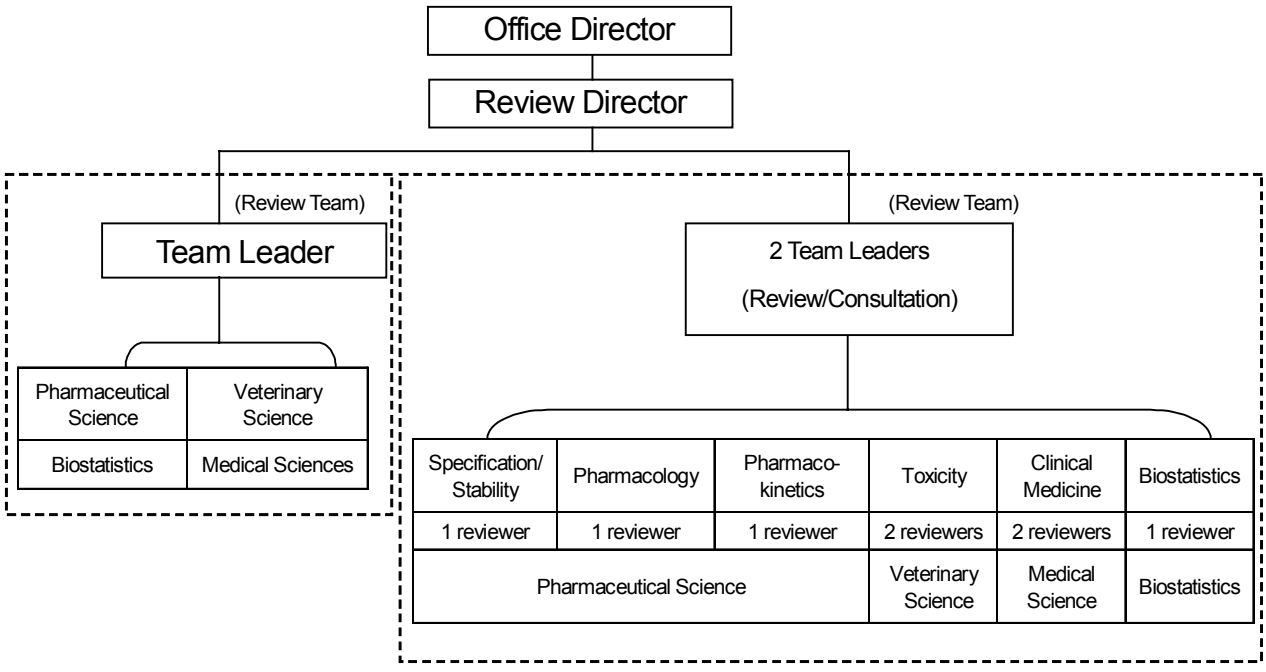
(ii) Applications discussed at the Drug Committees (PAFSC): 10
Review reports made to the Drug Committees (PAFSC): 71
(60 cases for medical devices, 11 cases for *in vitro* diagnostics)

- Reviews of new drugs were conducted by review teams consisting of experts under the guidance of an office director and a review director. In most cases, the team members had academic degrees in pharmaceutical science, medicine, veterinary medicine, biostatistics, or other specialized courses. The review team is fundamentally comprised of team leader(s), deputy team leader(s), and reviewers specialized in quality, toxicity, pharmacology, pharmacokinetics, clinical medicine, and biostatistics.

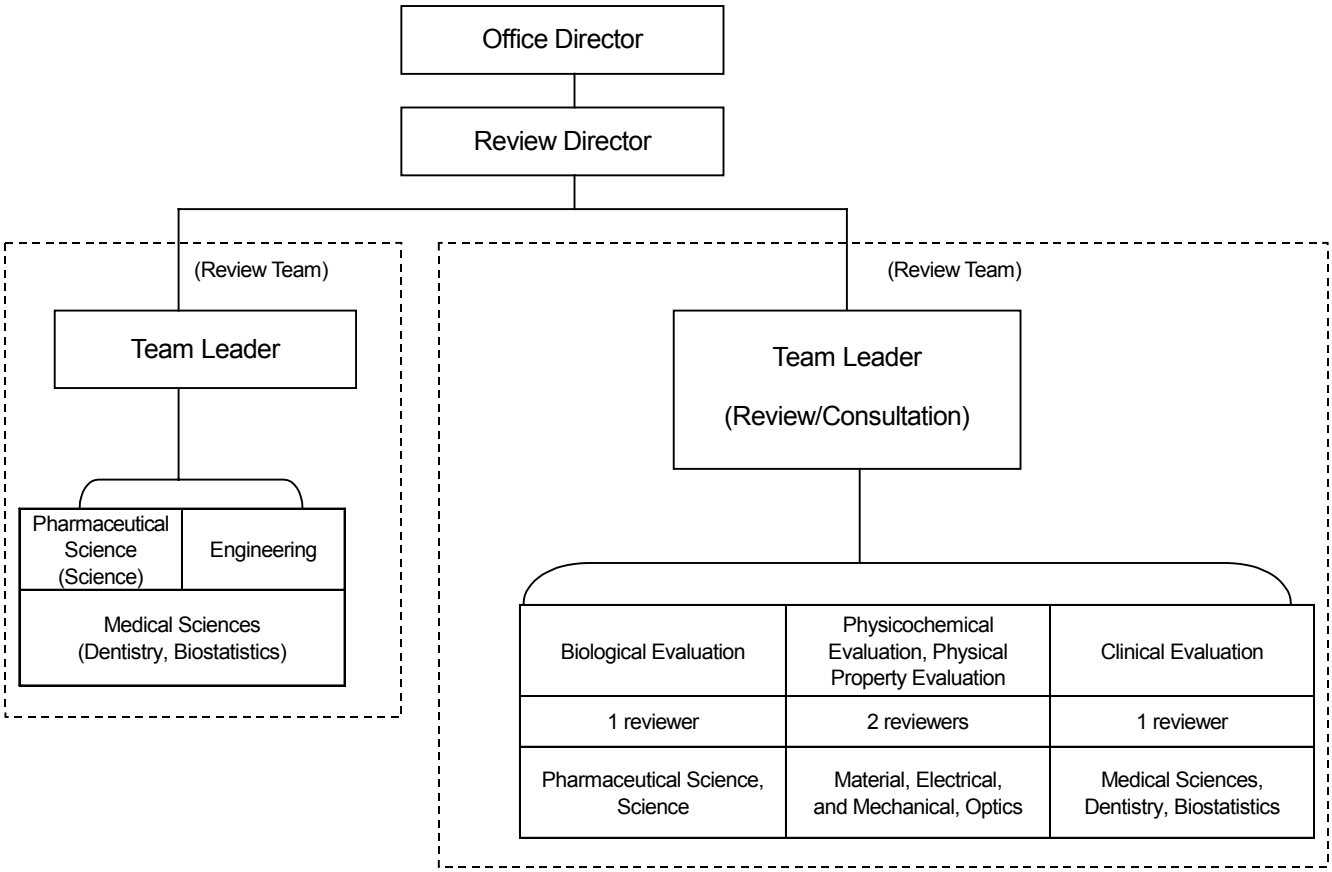
- Similarly, under the guidance of an office director and a review director, reviews of new medical devices were conducted by review teams consisting of experts who usually have academic degrees in engineering, pharmacology, medicine, dentistry, veterinary medicine, statistics, etc. The review team is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

Organization Chart for Reviews

Structure of a Review Team for New Drugs



Structure of a Review Team for New Medical Devices



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

Therapeutic Categories in the Offices of New Drugs

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	Antineoplastic drugs
	Anti-AIDS drugs	Anti-HIV agents
Office of New Drug II	Category 2	Cardiovascular drugs, antiparkinsonian drugs, antithrombotics, anti-Alzheimer's drugs
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs
	Radiopharmaceuticals	Radiopharmaceuticals
	In vivo diagnostics	Contrast media
Office of New Drug III	Category 3	Central/peripheral nervous system drugs, sensory organ drugs (except drugs classified in Category 6-1), narcotics
Office of New Drug IV	Category 6-1	Respiratory tract drugs, anti-allergy drugs for internal use, sensory organ drugs for inflammatory diseases
	Category 6-2	Hormone drugs, drugs for metabolic disorders (including diabetes mellitus, osteoporosis, gout, and inborn errors of metabolism)
Office of Biologics I	Blood products	Blood coagulation factor products, Gene therapy, Cartagena Protocol
	Biotechnological products	Antibody products
Office of Biologics II	Biological products	Vaccines, antitoxic serum
	Cellular and tissue-derived products	Cell therapy products

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

Therapeutic Categories in the Office of Medical Devices

Therapeutic Category	
Category 1	Mainly for ophthalmology and otorhinolaryngology
Category 2	Mainly for dentistry
Category 3-1	Mainly for cerebral, cardiovascular, respiratory, and psychoneurologic (materials) areas (intervention devices)
Category 3-2	Mainly for cerebral, cardiovascular, respiratory, and psychoneurologic (materials) areas (excluding intervention devices)
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 laboratory tests (*in vitro* diagnostics)
Category 8	Mainly for multicategory medical devices, advanced electronic medical devices, other uncategorized medical devices

- The Agency conducted face-to-face consultations on clinical trials for new drugs based on the 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.

- The Agency conducted face-to-face consultations on new medical devices based on the 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 overseas, to comprehend their needs.

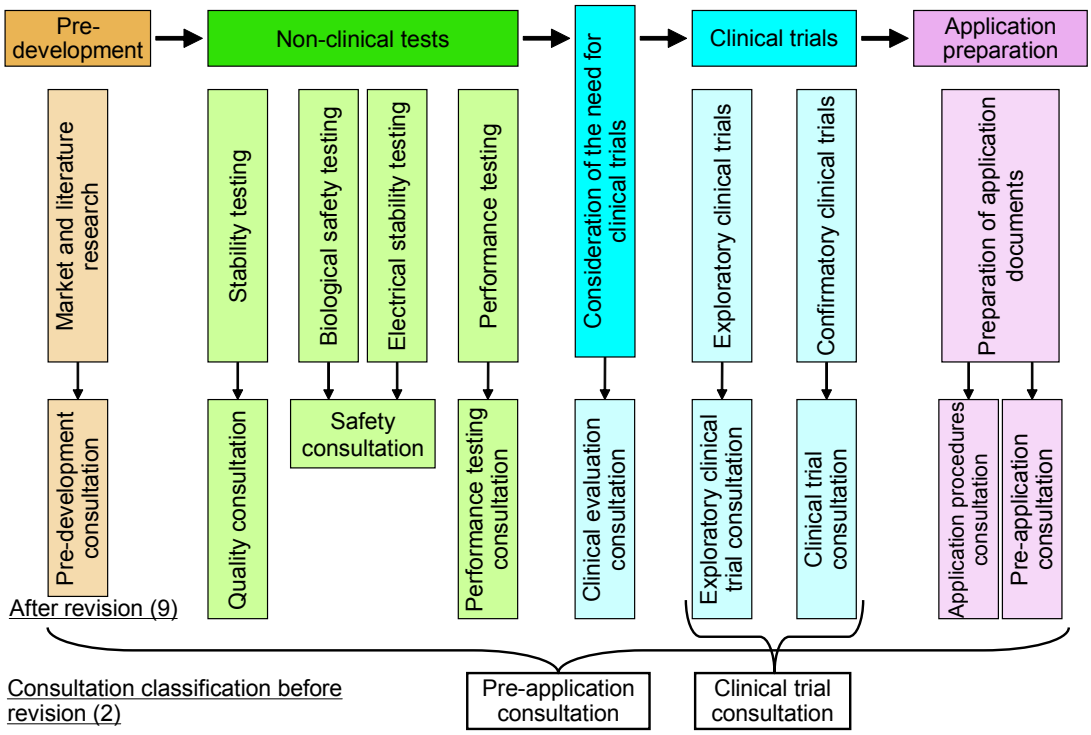
  Note: A total of 664 PMDA staff members participated in 296 domestic and international academic societies and seminars.

- 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 the Problems Concerning Use of Unapproved Drugs (chaired by Dr. Tomomitsu Hotta, Director of National Hospital Organization Nagoya Medical Center) has been conducting investigations ever since its establishment under MHLW in January 2005. The Agency has applied results from investigations conducted by this panel when providing consultations on clinical trials and review applications.

- In FY 2007, in order to promote development and speed up approval reviews by providing detailed advice that meets various needs at each stage, the clinical trial consultations on medical devices and *in vitro* disgnostics were improved to provide specific advice for each development stage of medical devices.

Expansion of the consultation menu by development stage

<Helping to promote development and speed up approval reviews by providing detailed advice that meets various needs at each stage of development>



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

For pharmaceuticals that use cellular tissue and that are developed with state-of-the-art technology such as pharmacogenomics and regenerative medicine, there is an extremely high need for advice on product development and 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 on preparation of documents for pharmaceuticals using cellular tissue in 2007.

(iv) Efforts for efficient and prompt reviews

- With changes made to the Mid-term plan in response to the recommendations of the Council for Science and Technology Policy, the Agency decided to reduce the drug lag by 2.5 years (consisting of 1.5 years for development and 1.0 year for approval review) by FY 2011. To achieve this goal, measures are being taken, including i) increasing the number of personnel involved in the review process, ii) improving training, iii) reducing the development period by significant expansion of and improvement in consultation, iv) reinforcing and improving the transparency of the progress management of reviews, v) responding to international joint clinical trials and state-of-the-art technology, vi) clarifying review standards, vii) developing guidance toward the introduction of a system of preliminary review, and viii) a trial operation of a project management system.

a. Increasing personnel

- A total of 236 employees are to be hired in the three years to FY 2009. In FY 2007,

applications were accepted four times on a routine basis. According to the recruitment results of FY 2007, 151 out of some 1,070 applicants were informally accepted (including 77 who were finally employed) and hired in technical positions.

To increase the number of applicants, the Agency employed various measures including the holding of briefings to explain the services, visits by executives and employees to universities and hospitals, strengthened announcement of recruitment at academic meetings, revision of job posting brochures and webpages, placement of job postings on job information websites, and placement of job postings in academic journals (see 3.4.(4) Securing Human Resources through Open Recruitment).

b. Improvements in training

- In April 2007, the Agency started a new training program on a trial basis that includes case studies, mainly at the Offices of New Drugs. Based on the lessons learned from the trial operation, the Agency launched the new training program on a full scale in October 2007. A mentoring system was also put in place to reinforce duty coaching, and the trial operation of the system began in October 2007.

c. Reducing the development period through large-scale improvements in consultation

- In FY 2008, the Agency plans to develop a guidance system for the implementation of a new consultation and review system. The objectives of this new system are to substantially increase the number of consultations that are accepted, and to reduce the waiting time for consultations. Other efforts that will begin in FY 2009 include improvements to the consultation menu and the introduction of a consultation and review system including a preliminary evaluation of application descriptions. The Agency plans to increase the total number of consultations per year up to 1,200 for FY 2011.

- The number of consultations in FY 2007 was 281 (the target was 280) and 21 consultations were withdrawn. The average number of consultations per ingredient related to submitted items in FY 2007 was 2.0 relative to the target of 2.0.

- A working group (WG) assigned to handle technical matters pertaining to clinical consultation was established jointly with the Japan Pharmaceutical Manufacturers Association (JPMA), the Pharmaceutical Research and Manufacturers of America (PhRMA), and the European Federation of Pharmaceutical Industries and Associations (EFPIA). This WG began reviews of actions to ensure large-scale improvements in consultation services, such as the abolition of the point system and improvements in the consultation menu with the intention of reducing the waiting time. As a result, a notification on improvement in the schedule adjustment method was issued on March 3, 2007.

d. Reinforcement and improvements in the transparency of the progress management of reviews

- It was decided that by FY 2011 the median total review time for standard review items submitted for application in and after FY 2004 was to be 12 months (9 months for administration and 3 months for the applicant). The median total review time for priority items was to be 9 months (6 months for administration and 3 months for the applicant). The FY 2007 target for this goal was a median total review time of 21 months (13 months for

administration and 8 months for the applicant) for standard review items, and a median total review time of 12 months (6 for administration and 6 for the applicant) for priority review items. The median total review times for new drugs approved in FY 2007 are as follows:

Median Total Review Time for New Drugs for which Applications Were Filed for Approval and Approved after FY 2004

		FY 2005	FY 2006	FY 2007
Standard review items	Total review time	18.1 months	20.3 months	20.7 months (29.5 months)
	Administrative review time	10.3 months	12.8 months	12.9 months (17.7 months)
	Applicant review time	7.2 months	6.9 months	7.9 months (11.2 months)
	No. of applications	15	29	53
Priority review items	Total review time	4.9 months	13.7 months	12.3 months (19.4 months)
	Administrative review time	2.8 months	6.4 months	4.9 months (7.7 months)
	Applicant review time	2.2 months	6.0 months	6.5 months (12.0 months)
	No. of applications	9	20	20

Note: Values in parentheses are 80% of the reference values.

Median Administrative TC Metrics for Standard Review

	From application to first consultation	From first consultation to inquiries about important matters	From inquiries about important matters to Expert Discussion	From Expert Discussion to approval
FY 2007	2.1 months (2.6 months) 44	0.7 months (1.4 months) 48	5.9 months (10.7 months) 50	2.3 months (3.2 months) 51

Note: Values in parentheses are 80% of the reference values.

- The review time was slightly increased for standard items compared with that in FY 2006. This is because in FY 2006, the reviewers focused particularly on what are called “stockpiled items,” or applications submitted in and before FY 2003, and almost all of these reviews were completed. In FY 2007, the reviewers focused on items submitted in the fiscal year (FY 2004) when the Agency was established and almost all of these reviews were completed. The number of approvals in FY 2007 totaled 81, representing a small increase from the 77 approvals in FY 2006.

e. Responses to multi-national clinical trials, state-of-the-art technology, etc.

- The Agency formulated a document titled “Basic Concept on Global Clinical Trials,” received public comments, and issued the document as a notification of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated September 28, 2007. Of 508 protocol applications submitted in FY 2007 (which represented the total number of initial protocol applications and protocol applications), 38 were for multi-national clinical trials.

f. Clarification of the review standards

- The proposed basic concept for review was developed at the WG for reviews and other services reform set up under the Headquarters for PMDA Reform. The proposed concept was

verified with respect to its validity by each review team and incorporated the opinions of the people concerned. This information was then explained to personnel responsible for reviews in the form of "Points to Be Considered by the Review Staff Involved in the Evaluation Process of New Drug." The concept was also put on PMDA website on April 17, 2008.

g. Development of the guidance for the introduction of a system by which preliminary evaluation (evaluation of efficacy and safety from the clinical Trial consultation stage) is conducted.

- A working group assigned to handle technical matters of clinical trial consultation and review was established jointly with JPMA, PhRMA, and EFPIA. The working group reviewed the measures with the objective of evaluating efficacy and safety from the stage of clinical trial consultation.

h. Trial of the project management system

- In October 2007, a review team implemented the project management system on a trial basis. Specifically, one member of the review team was assigned as progress coordinator. The coordinator comprehended the progress of reviews by and the review schedule of two sub-teams within that team as needed, and when the review progress began to fall behind schedule, the coordinator provided information to the review director of the review team. The sub-teams efficiently assigned or switched reviewers depending on the progress of reviews. Each sub-team comprehended and analyzed past review processes.

(v) Implementation of approval review

a. Approval reviews for new drugs

- For new drugs, the Agency aims to review 80% of all filed NDAs within a review time of 12 months. In order to reach this target, the Agency:
  1) Reinforced the review system and improved its operational efficiency by increasing the number of reviewers for categories in which reviewing applications was considered to be difficult because of item bias in the approval applications for new drugs.
  2) Regularly discussed its review policy with MHLW and managed the review process through the Progress Management Committee for Review-Related Operations within the Agency so that review operations can be conducted smoothly;
  3) Made efforts to properly manage the review process by observing guidelines for implementing reviews and inspections, keeping reviewers informed about review-related information and developing standard operating procedures.

- With regard to new drugs (pharmaceuticals that are clearly different from 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, medicine, veterinary medicine, biostatistics, etc.

- With regard to review services for new drugs, in order to ensure consistency among the review teams and carry out review work promptly and appropriately, the Agency developed the Implementation Manual for Approval Reviews of New Drugs regarding reviews and related procedures, and the Standard Operating Procedures (SOPs) 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.
  The directors of the review divisions assessed the operational progress on a routine basis. Based on the reports from these directors, the Director, Deputy Director, and Associate Center Director of the Center for Product Evaluation provided necessary guidance at liaison meetings for review-related divisions.

- The status of approval reviews for new drugs in FY 2007 is shown below:

Number of Approved Pharmaceuticals etc.

	FY 2004	FY 2005	FY 2006	FY 2007
Prescription drugs	3,742	2,199	2,390	3,648
OTC drugs	1,781	1,570	1,030	1,329
In vitro diagnostics	502	281	136	199
Quasi-drugs	2,972	2,611	2,287	2,236
Cosmetics	0	0	0	0
Total	8,997	6,661	5,843	7,412
Breakdown				
New drugs (cases)	49	60	77	81
Priority review items out of NDAs above (cases)	22	18	24	20

Note: 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)

Number of Approved New Drugs

	FY 2004	FY 2005		FY 2006		FY 2007	
			Applications filed in and after FY 2004†		Applications filed in and after FY 2004†		Applications filed in and after FY 2004†
All new drugs							
No. of approvals	49	60	24	77	49	81	73
Median review time	(8.6 months) [65%]	(12.0 months) [50%]*	(8.6 months) [83%]	(13.7 months) [39%]*	(10.5 months) [59%]	(11.6 months) [54%]*	(10.5 months) [60%]
Median total review time	13.5 months	22.4 months	16.2 months	21.7 months	19.2 months	20.1 months	19.2 months
Priority review items							
No. of approvals	22	18	9	24	20	20	20
Median review time	(2.8 months) [86%]	(8.9 months) [28%]*	(2.8 months) [56%]	(7.3 months) [42%]*	(6.4 months) [50%]	(4.9 months) [65%]*	(4.9 months) [65%]
Median total review time	4.5 months	20.4 months	4.9 months	15.6 months	13.7 months	12.3 months	12.3 months
Standard items							
No. of approvals	27	42	15	53	29	61	53
Median review time	(12.3 months) [41%]	(14.2 months) [41%]*	(10.3 months) [73%]	(15.5 months) [23%]*	(12.8 months) [41%]	(14.5 months) [41%]*	(12.9 months) [47%]
Median total review time	23.4 months	22.4 months	18.1 months	27.4 months	20.3 months	22.0 months	20.7 months

Note: Percentage in brackets indicates that of the number of applications reviewed within 12 months after application for all new drugs and standard items and within 6 months for priority review items.

**Also include NDAs filed in and before March 2004, which are excluded from the targets in the Mid-term plan.*

† The data indicate the number of applications filed in and after April 2004 among those filed in FY 2005, 2006, and 2007.

Review Status of NDAs

New drug (FY of application)	Cases*	Approved	Withdrawn	Under review
Applications submitted on and before March 31, 2004	139	104 (8)	25 (2)	10 [−10]
FY 2004	87	77 (13)	9 (0)	1 [−13]
FY 2005	57	41 (21)	6 (2)	10 [−23]
FY 2006	101 (−2)†	41 (35)	7 (7)	53 [−44]
FY 2007	91	4 (4)	0	87 [87]
Total	475	267 (81)	47 (11)	161 [−3]

** 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 2006 is two less than that shown in the previous annual report because the Agency integrated two separate applications for a single ingredient into one application and had such two dual applications.

Note 1: Values in parentheses indicate those processed in FY 2007 (included in values on their left)

Note 2: Values in brackets indicate difference from FY 2006

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 of review result to approval
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
FY 2007	Number of processed cases/	63 cases	65 cases	72 cases	72 cases
	Review process time (median)*	85.0 days	381.0 days	20.5 days	57.0 days

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

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

Review status of new drugs overall

- With respect to the approval status in FY 2007, the Agency attained an achievement level of 60% for the performance target within 12 months by reviewing 44 out of 73 applications for new drug approval submitted in and after April 2004. The median review time was 10.5 months. When the applications submitted in and before March 2004 were included, the achievement rate was 54% (44 out of 81), and the median review time was 11.6 months.

- The number of new drugs approved in FY 2007 increased by 4 from the previous fiscal year because of progress in the development of the review system. The median review time for all new drugs filed was improved to 11.6 months from 13.7 months in 2006.

- As for the 139 applications submitted before the establishment of PMDA (in and before March 2004) and the 336 applications submitted after the establishment of PMDA (in and 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 in and before March 2004, the Agency was able to process 129 of those through approvals or withdrawals by FY 2007. In order to achieve the target for the review time earlier, the Agency is progressing with reviews of such applications vigorously so that it can strive 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 time of 6 months by the end of the effective period for the Mid-term targets.

- Reviews of approval applications for orphan drugs and other pharmaceuticals that are regarded as having particularly high medical necessity (i.e., pharmaceuticals for serious diseases with distinctly superior efficacy or safety to existing pharmaceuticals or treatment methods) were conducted on a priority basis as priority review items, and 20 applications were approved in FY 2007. In FY 2007, there were 16 applications for priority reviews of pharmaceuticals regarded as having particularly high medical necessity. Five of these applications were accepted as priority review items, 3 were judged to be non-priority review items, and 8 are currently being reviewed.

b. Approval reviews for new medical devices

- For new medical devices, the Agency aimed for an achievement level of 90% of applications for the target review time of 12 months. As with approval reviews of new drugs, in order to attain these goals, the Agency discussed and took specific measures to improve and accelerate reviews, such as by establishing operating procedures for reviews and inspections.

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

- To ensure consistency among review teams and to carry out reviews on new medical devices promptly and appropriately, the Agency prepared the Implementation Manual for Approval Reviews of New Medical Devices, which describes reviews and review-related procedures, and developed standard operating procedures (SOPs) relating to various operations. The Agency also collected monthly data on the achievement level of the target review time and informed the reviewers of the achievement status.

- With regard to the progress of reviews etc., the Progress Management Committee for Review-Related Operations (whose mission is to enable the Chief Executive and other Agency management to comprehend the progress of approval review services without fail and improve its progress), continued to monitor and examine operational progress in order to achieve the Midterm plan for review time and ensure rapid and accurate review processes.
  In the review divisions, the Director of the Office of Medical Devices monitors operational progress on a routine basis, and at liaison meetings for review-related divisions, the Director,

Deputy Director, and Associate Center Directors of the Center for Product Evaluation provide necessary guidance.

The status of approval reviews for new medical devices in FY 2007 is shown below:

Number of Approved New Medical Devices

		FY 2004	FY 2005	FY 2006	FY 2007
Medical devices (total)		3,309	1,827	1,342	2,222
Priority review items (included in total)		2	0	1	4
Previous data	**New medical devices**	**8**	**11**	**23**	**26**
	With no approval standards; and clinical data required	-	0	5	14
	With no approval standards; and no clinical data required	-	16	189	552
	With approval standards; and no clinical data required	-	3	444	1,141
	Controlled medical devices (with no approval standard or certification standard; and no clinical data required)	-	1	146	335
	Improved medical devices	154	263	136	78
	Generic medical devices	3,147	1,533	399	76

Approval Status of New Medical Devices

	FY 2004	FY 2005		FY 2006		FY 2007	
			Applications filed in and after FY 2004†		Applications filed in and after FY 2004†		Applications filed in and after FY 2004†
All new medical devices							
No. of approvals	8	11	5	23	15	26	23
Median review time	(12.7 months) [50%]*	(7.7 months) [82%]*	(1.8 months) [100%]	(6.0 months) [83%]*	(3.4 months) [100%]	(8.6 months) [73%]*	(8.2 months) [83%]
Median total review time	35.8 months	22.4 months	10.3 months	19.7 months	15.3 months	17.1 months	15.1 months
Priority review items							
No. of approvals	2	0	0	1	1	4	4
Median review time	(9.3 months) [50%]*			(5.7 months) [100%]*	(5.7 months) [100%]	(8.6 months) [75%]*	(8.6 months) [75%]
Median total review time	24.0 months			14.2 months	14.2 months	15.7 months	15.7 months
Standard items							
No. of approvals	6	11	5	22	14	22	19
Median review time	(15.0 months) [33%]*	(7.7 months) [82%]*	(1.8 months) [100%]	(6.3 months) [82%]*	(3.2 months) [100%]	(8.7 months) [73%]*	(7.7 months) [84%]
Median total review time	43.3 months	22.4 months	10.3 months	19.8 months	15.7 months	18.9 months	15.1 months

Note: Percentage in brackets indicates that of the number of applications reviewed within 12 months after application for all medical devices and standard items and within 9 months for priority review items.

** Also includes the applications filed in and before March 2004, which are excluded from the targets in the Midterm plan.*

† The data indicate the number of applications filed in and after April, 2004 among those filed in FY 2005, 2006, and 2007.

Review Status of New Medical Devices

New medical devices (FY of application)	Cases*	Approved†	Withdrawn	Under review
Applications submitted in and before March 31, 2004	132	51 (8)	75 (3)	6 [−11]
FY 2004	56	28 (13)	16 (0)	12 [−13]
FY 2005	7	6 (3)	0	1 [−3]
FY 2006	24	13 (11)	1 (0)	10 [−11]
FY 2007	37	4 (4)	1 (1)	32 [32]
Total	256 (37)	102 (39)	93 (4)	61 [−6]

** Values in the Cases column are the numbers of applications for new medical devices.*

† The number of approved items includes improved medical devices.

Note 1. Values in parentheses indicate those processed in FY 2007 (included in values on their left)

Note 2. Values in brackets indicate difference from FY 2006

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 Dxpert Discussion to notification of review result	4. From notification of review result to approval
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
FY 2007	Number of processed cases/	8 cases	15 cases	15 cases	23 cases
	Review process time (median)*	53.0 days	402.0 days	151.0 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).*

Note 1: Expert Discussions were held several times as needed.

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

Review status of new medical devices overall

- In FY 2007, the Agency approved all applications for new medical devices submitted in and after April 2004 (19 out of 23 cases) within 12 months, reaching an achievement level of 83% for the target review time. The median review time was 8.2 months. However, when applications submitted in and before March 2004 are included, the achievement ratio decreases to 73% (19 out of 26 applications), and the median review time becomes 8.6 months.

- For the 132 applications submitted before the establishment of PMDA (in and before March 2004) and the 124 applications submitted after the establishment of PMDA (in and after April 2004), the Agency processed reviews taking the target review 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 in and before March 2004, the Agency was able to process 126 of these applications through approvals or withdrawals by FY 2007. However, in order to achieve the target for the review time earlier, the Agency is progressing with reviews of such application vigorously so that it can strive 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 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 2007, there was four approvals. There was one new application for priority review, and its validity is currently being investigated.

Status of development of approval standards

- In order to support MHLW in developing approval standards for medical devices, the Committee on Medical Device Approval Standards held three meetings, and the Expert Committee on Medical Device Review Guidelines held one meeting in FY 2007.
  The numbers of established standards for approval and certification reported to MHLW in FY 2007 were as follows:

FY of report	FY 2006	FY 2007	Total
Approval standards	6	7	13
Certification standards	0	14	14
Review guidelines	0	1	1

The number of standards established by MHLW in FY 2007 based on the reports from the Agency is shown below:

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

Established in:	FY 2004	FY 2005	FY 2006	FY 2007	Total
Approval standards	0	17	8	10	35
Certification standards	363	9	24	0	396
Review guidelines	0	0	0	0	0

- The Agency established a database system of medical device approval standards and began to provide outside organizations with information on the certification and approval standards (including the review guidelines) and the Japanese Industrial Standards (JIS) on which those standards are based.

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

- The Agency conducted efficient on-site and document inspections of approval application dossiers for new drugs and medical devices as well as on the tests on which these application documents are based, to determine whether such documents were gathered in accordance with Good Laboratory Practice (GLP; standards indicated in ministerial ordinances relating to standards for implementing non-clinical tests relating to the safety of pharmaceuticals), Good Clinical Practice (GCP; standards indicated in ministerial ordinances relating to standards for implementing clinical trials for pharmaceuticals), Good Post-

Marketing Surveillance Practice (GPMSP; standards indicated in ministerial ordinances relating to standards for post-marketing surveys on pharmaceuticals) and the conformity standards for the application documents.

Numbers of Conducted Conformity Audits

		FY 2004	FY 2005	FY 2006	FY 2007
Document conformity audits		161	136	426	774
	Pharmaceuticals	161	135	251	234
	Medical devices	—	1	175	540
GLP conformity audits		20	39	31	27
	Pharmaceuticals	20	37	23	23
	Medical devices	—	2	8	4
GCP conformity audits*		73	131	149	132
	New drugs	68	120	137	122
	Generic drugs	5	11	12	9
	Medical devices	—	0	0	1
GPSP conformity audits†		27	82	103	107

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

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

Note 1: GLP: Good Laboratory Practice

Note 2: GCP: Good Clinical Practice

Note 3: GPMSP: Good Post-Marketing Surveillance Practice

Note 4: GPSP: Good Post-marketing Study Practice

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

1) Review of the conformity audit system

The Agency began a review of the conformity audit system further to the 2nd Midterm plan by, for example, shifting from the current document conformity audit method, where the relevant data and materials are delivered to the Agency for audit, to the auditor visit method, where the Agency staff directly visit the applicant company for audit.

2) Diffusion of the knowledge of the interpretation of GCP operations

The Agency conducted consultations with medical institutions which were subjected to on-site inspection on matters related to GCP after audit completion. The Agency also made an effort to improve the explanation of case examples by highlighting points to consider in conducting clinical trials through the Conformity Audit page on the Agency's website. To deepen understanding regarding 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.

Number of GCP Workshop Participants

Place	FY 2006	FY 2007
Tokyo	1,303	1,212
Osaka	454	495
Total	1,757	1,707

3) 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.

- The Agency shifted GCP inspection system from the division chief system to the inspection director system as part of the effort to reinforce the linkage between document inspection and GCP on-site inspection in July 2007.

- Although a standard administrative processing time for conformity audit services has not been set, the Agency made efforts so that the review time for approval reviews for relevant items were not affected, resulting in no delays in the approval reviews for these audit services in FY 2007.

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

- In accordance with the 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 time each month and informing the reviewers of these levels, monthly meetings of the Progress Management Committee for Review-Related Operations were continuously held to monitor and examine operational progress.

• The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2007 are as follows:

Number of Approved Generic Drugs and Others

	FY 2004	FY 2005	FY 2006	FY 2007
Generic drugs	3,476	1,919	2,152	3,278
Number of approved applications filed in and after April 2004 (breakdown)	1,468	1,782	2,029	3,228
Median review time (for the applications filed in and after April 2004)	3.3 months	7.3 months	4.0 months	4.5 months
Achievement rates on the target time (for the applications filed in and after April 2004)	100%	98%	93%	95%
OTC drugs	1,781	1,570	1,030	1,329
Number of approved applications filed in and after April 2004 (breakdown)	270	1,163	923	1,309
Median review time (for the applications filed in and after April 2004)	8.7 months	7.8 months	6.3 months	4.0 months
Achievement rates on the target time (for the applications filed in and after April 2004)	83%	84%	85%	90%
Quasi-drugs	2,972	2,611	2,287	2,236
Number of approved applications filed in and after April 2004 (breakdown)	1,431	2,575	2,275	2,230
Median review time (for the applications filed in and after April 2004)	5.6 months	5.3 months	5.5 months	5.2 months
Achievement rates on the target time (for the applications filed in and after April 2004)	89%	86%	67%	83%
Total	8,229	6,100	5,469	6,843
Number of approved applications filed in and after April 2004 (breakdown)	3,169	5,520	5,227	6,767

Note: The median and TC achievement rate for OTC drugs and quasi-drugs in FY 2007 were calculated using data from the period from the completion of the audit to the notification of GMP results by prefectures.

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 2007	2	96	68	97	1,093	0	21	1,377
Approved in FY 2007	0	59	36	142	1,089	0	3	1,329

Quasi-drugs

Category of application	1 and 3	2	Total
Filed in FY 2007	119	2,308	2,427
Approved in FY 2007	76	2,160	2,236

Note 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*

Note 2: Each application belongs to the category for which it was submitted.

Note 3: Each approval belongs to the category in which it was granted.

Note 4: The number of quasi-drugs includes that of insecticides and rodenticides for which an application for approval as quasi-drugs was filed.

Reviews Conducted for Generic Drugs by Fiscal Year

Classification	Fiscal year	No. of applications	No. of approvals	Withdrawal, etc.†	Under review
Generic drugs	FY 2004	2,992 (2,966)*	3,476	12	2,470
	FY 2005	1,829	1,919	221	2,159
	FY 2006	2,631	2,152	173	2,465
	FY 2007	3,729	3,278	160	2,756
OTC drugs	FY 2004	1,955 (2,622)*	1,781	6	2,790
	FY 2005	1,131	1,570	144	2,207
	FY 2006	1,236	1,030	181	2,232
	FY 2007	1,377	1,329	113	2,167
Quasi-drugs	FY 2004	3,068 (1,865)*	2,972	23	1,938
	FY 2005	2,286	2,611	118	1,495
	FY 2006	2,503	2,287	96	1,615
	FY 2007	2,427	2,236	118	1,688

** Values in parentheses show applications not yet reviewed as of March 31, 2004 (taken over from the Center for Product Evaluation)*

† Values in the column Withdrawal, etc. include the number of items switched to other review categories during the review.

- With regard to achievement levels in FY 2007 of the target standard administrative processing time for applications submitted in and after April 1, 2004, the Agency attained an achievement level of 95% by reviewing 3,067 out of 3,228 applications for generic drugs within 12 months, 90% by reviewing 1,177 out of 1,309 applications for OTC drugs within 10 months and 83% by reviewing 1,840 out of 2,230 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 Notification No. 960 issued by Director-General of the Pharmaceutical Affairs Bureau, the Ministry of Health and Welfare, dated October 1, 1985.

Document Conformity Audit Conducted for Generic Drugs by Fiscal Year

	FY 2004	FY 2005	FY 2006	FY 2007
Number of audits	1,090	941	628	1,135

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

- In FY 2007, the Japanese Pharmacopoeia Draft Committee held a total of 67 meetings and finalized 62 new monographs and 85 amendments for the second supplement of the 15th edition of the Japanese Pharmacopoeia (JP) (to be published in September 2009). The draft was posted on the Agency's website for public comment. The Agency also called for comments on 41 reference ultraviolet visible absorption spectra and reference infrared absorption spectra in FY 2007.

  Drafts for the Japanese Pharmacopoeia reported to MHLW thus far are as follows:

Month and year reported	September 2005	March 2007
New monographs	102	90
Amendments	276	171

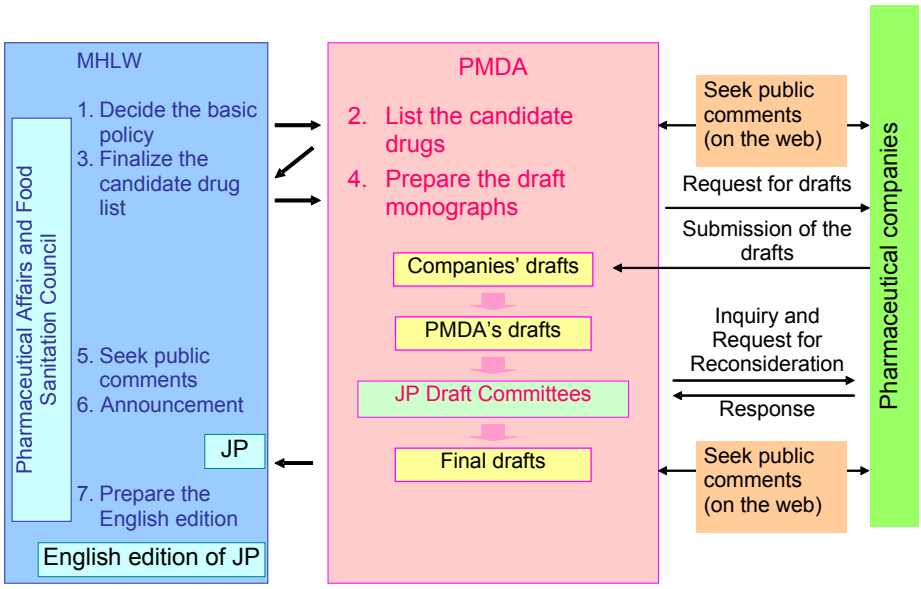
Note: The JP drafts prepared include drafts for the official monographs shown in this table as well as drafts for general notices, general rules for preparations, general rules for crude drugs, general tests, processes, and apparatus, and general information. The Agency provided a report on those drafts to MHLW 6 months before the normal publication timing.

Public Announcement on the Japanese Pharmacopoeia by MHLW

Public announcement of the Pharmacopoeia (month and year announced)	15th edition of the Japanese Pharmacopoeia as amended (March 2006)	1st supplement to the 15th edition of the Japanese Pharmacopoeia as amended (September 2007)
New monographs	102	90
Amendments	272	170
Deletion	8	6
Total	1,483	1,567

- The Agency opened a web page to provide information on the Japanese Pharmacopoeia and started to provide relevant information such as the condition of the JP draft review or international harmonization of pharmacopoeial standards, in addition to calling for comments on drafts.

Flow of Revision of Japanese Pharmacopoeia



(vi) Improvement of clinical trial consultations

- In addition to improving pre-application consultations, the Agency is required to give priority to conducting consultations on clinical trials 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.

- With regard to the priority clinical trial consultation system for pharmaceuticals considered to be of particularly high medical necessity, the Agency received applications for six ingredients in FY 2007 and designated four ingredients (all applications filed in FY 2007) as being applicable to priority clinical trial consultation (a review is under way for the remaining two ingredients). None were rejected as inapplicable. The Agency conducted a total of 22 clinical trial consultations related to the designated ingredients.

For medical devices, there were no applications for priority clinical trial consultations. For both pharmaceuticals and medical devices, there were no applications for consultations on 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 (CTC) for New Drugs

	FY 2004	FY 2005	FY 2006	FY 2007
Applications for CTC	334	339 (243)*	473 (327)*	435 (325)*
Conducted CTC	193	218	288	281
Withdrawn	23	14	7	21
Total	216	232	295	302

** Values in parentheses do not include reapplications caused by rejection.*

- In FY 2007, the Agency conducted 302 clinical trial consultations (including 21 withdrawals) in relation to a goal of 280 clinical trial consultations.

- The Agency established goals for efficient consultation, that is, that the process from a face-to-face consultation to the settlement of records should be completed in 30 business days for 10% of all applications submitted. The established goals also require that the process to the first face-to-face clinical trial consultation should be completed in 30 business days for 50% of all applications submitted. In FY 2007, 186 (62.2%) out of 299 applications were processed within 30 days from the face-to-face consultation to the settlement of records, and 11 (75.0%) out of 16 were processed within 30 business days to the first face-to-face consultation (with respect to priority clinical trial consultation).

- The Agency promoted simple clinical trial consultations and support for Multi-national clinical trials. In FY 2007, it received 62 applications for consultations on Multi-national clinical trials for new active ingredients, of which 56 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 for 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 2007

Category	Apr	May	Jun	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Total
Category 1 (Gastrointestinal drugs etc.)	1	2	3	2	2	2	1	1	3	3	4	3	27
Category 2 (Cardiovascular drugs)	5	4	4	3	2	4	2	5	4	5	4	4	46
In vivo diagnostics	0	0	1	0	1	0	0	0	0	1	0	0	3
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	1	1	0	2
Category 3 (Central / peripheral nervous system drugs etc.)	4	3	4	4	4	4	2	4	2	3	3	2	39
Category 4 (Antibacterial agents etc.)	1	3	3	2	2	0	1	1	1	0	2	0	16
Anti-AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 5 (Drugs for the urogenital system etc.)	1	0	1	2	2	2	1	0	1	1	2	1	14
Category 6-1 (Respiratory tract drugs etc.)	1	2	1	0	2	2	3	4	4	2	2	3	26
Category 6-2 (Hormone drugs)	2	1	3	3	2	2	3	2	4	3	3	3	31
Antineoplastic drugs	4	5	2	4	4	5	4	5	3	3	4	7	50
Biologics	3	1	1	0	0	2	2	1	2	1	0	0	13
Cellular and tissue-derived products*	0	1	1	0	0	1	1	1	1	0	2	1	9
Blood products	0	1	0	1	0	1	1	0	0	0	0	1	5
Compliance to conformity criteria	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	22	23	24	21	21	25	21	24	25	23	27	25	281
Withdrawn	0	2	1	3	0	2	6	2	2	0	0	3	21
Grand Total	22	25	25	24	21	27	27	26	27	23	27	28	302

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

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

Number of Clinical Trial Consultations for New Medical Devices

	FY 2004	FY 2005	FY 2006	FY 2007
Applications for CT consultation*	9	33	46	76
Medical devices	7	32	43	75
In vitro diagnostics	2	1	3	1
Conducted CT consultations	8	30	42	72
Medical devices	6	29	39	71
In vitro diagnostics	2	1	3	1
Withdrawn	0	0	0	0
Medical devices	0	0	0	0
In vitro diagnostics	0	0	0	0
Total (Conducted consultations and withdrawals)	8	30	42	72
Medical devices	6	29	39	71
In vitro diagnostics	2	1	3	1

** Applications submitted after arrangement of schedule.*

Number of Clinical Trial Consultations for New Medical Devices by Category Conducted in FY 2007

Consultation category	Applications for CTC	Conducted CTC	Withdrawals	Total (Conducted consultations and withdrawals)
Consultation for preparation of documents for pharmaceuticals that are cellular and tissue-derived	1	1	0	1
CT/Pre- application consultations for medical devices or *in vitro* diagnostics	38 (1)*	44 (1)*	0	44 (1)*
Reliability standard compliance consultation for medical devices or *in vitro* diagnostics	0	0	0	0
Pre-development consultation for medical devices	5	2	0	2
Application procedure consultation for medical devices or *in vitro* diagnostics	3	2	0	2
Safety consultation for medical devices (excluding biological ones)	1	1	0	1
Quality consultation for medical devices (excluding biological ones)	0	0	0	0
Performance testing consultation for medical devices	1	1	0	1
Clinical evaluation consultation for medical devices	20	15	0	15
Exploratory clinical trial consultation	1	1	0	1
Safety consultation for biological medical devices	0	0	0	0
Quality consultation for biological medical devices	1	0	0	0
Additional consultation for medical devices and *in vitro* diagnostics	5	5	0	5
Total	76	72	0	72

** Numbers in parentheses indicate the number of in vitro diagnostics included.*

(vii) Promotion of international harmonization

The Agency is required 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 time (the sum of the processing time on the reviewer side and the processing time on 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 toward international harmonization such as through ICH

- In FY 2007, the Agency continued to actively participate in ICH Steering Committee Meetings and Expert Working Group Meetings, and promoted further international harmonization by planning for the consistency of Japanese standards with international standards such as for developing review data, which were agreed upon among Japan, the U.S., and EU in ICH Meetings.

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

  Note: 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 Agency participated (relating to reviews and safety measures)

- ICH Expert Working Groups
  - ICH Meeting in Brussels
  - ICH Meeting in Yokohama
  - ICH Tokyo Symposium

  Topics discussed in FY 2007
  - Specifications for Electronic Submission of Pharmaceutical 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)
  - Genotoxicity: A Standard Battery for Genotoxicity Testing of Pharmaceuticals (S2 [R1])
  - Non-clinical Safety Studies of Anti-cancer Agents (S9)
  - Pharmaceutical Development (addendum)(Q8 [R1])
  - 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
- WHO Workshop on Monitoring and Preparation of Pharmaceuticals

- In order to build a specific 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 FDA of the U.S. and EMEA of EU while collaborating with MHLW.

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

IEC/TC/87 (Ultrasonics)
ISO/TC/121 (Anesthetic and respiratory equipment)
ISO/TC/150 (Implants for surgery, artificial heart)
ISO/TC/194 (Biological evaluation of medical devices)
ISO/TC/198 (Sterilization of health care products)
GHTF SG1 (Regulatory systems)
GHTF SG3 (Quality systems)
GFTF SG4 (Regulatory auditing)
GFTF SG5 (Clinical evidence)
Regulatory Affairs Professionals Society (RAPS)
IVD Conference (IVD regulation)

b. Efforts to introduce a total review time

- In working toward 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.

- The number of new drugs that were approved in FY 2007 was 81, and the median review time (PMDA review time) for these applications was 11.6 months, whereas the median total review time was 20.1 months. Applications for 73 of these approved drugs were submitted in and after April 2004, of which the median review time (PMDA review time) was 10.5 months and the median total review time was 19.2 months.
  (Refer to the Number of Approved New Drugs.)

- The number of new medical devices that were approved in FY 2007 was 26, and the median review time (PMDA review time) for these applications was 8.6 months, whereas the median total review time was 17.1 months. Applications for 23 of these approved medical devices were submitted in and after April 2004, of which the median review time (PMDA review time) was 8.2 months and the median total review time was 15.1 months.
  (Refer to the Number of Approved New Medical Devices.)

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

4.2.(2) Improvement in reliability of operations

(i) Planned recruitment of staff with advanced expertise and systematic provision of training opportunities

a. Staff recruitment

- In order to ensure smooth enforcement of the amended 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 3.4.(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 3.4.(2), Systematic Implementation of Staff Training).

(ii) Development of a GMP/QMS audit system

Based on the amended Pharmaceutical Affairs Law that came into effect on April 1, 2005, conformance of methods for manufacturing control and quality control at manufacturing sites for pharmaceuticals, etc., with requirements specified in GMP Ministerial Ordinance on Drugs and Quasi-drugs*, and/or QMS Ministerial Ordinance on Medical Devices and *In Vitro* Diagnostics† is a pre-requisite for approval. Therefore, in addition to the manufacturing sites already licensed by the

Minister of Health, Labour and Welfare, the following manufacturing sites became subject to investigations by the Agency: 1) foreign manufacturing sites related to all products that require regulatory approval; 2) domestic manufacturing sites 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 in 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 in 2004

Note 1: GMP = Good Manufacturing Practice, standards for manufacturing control and quality control

Note 2: QMS = Quality Management System

- Therefore, the Agency continued to recruit GMP/QMS auditors to form a system of 37 inspectors as of April 1, 2008. At the same time, the Agency is also promoting educational training for GMP/QMS auditors as well as training programs, both domestic and overseas, including seminars hosted by the Pharmaceutical Inspection Cooperation Scheme (PIC/S), a European-based international organization for GMP audits.

GMP/QMS Audits Conducted According to the Amended Pharmaceutical Affairs Law

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

	FY 2007				
	Applied	Completed		Withdrawn	In progress
Pharmaceuticals*	1,011	893	(233)	55	444
In vitro diagnostics	85	84	(1)	0	44
Quasi-drugs	3	0	(0)	0	3
Medical devices	1,006	1,021	(12)	15	348
Total	2,105	1,998	(246)	70	839

** Excluding In vitro diagnostics.*

Note: Values in parentheses show the number of on-site inspectionss.

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

On-site Inspections of Overseas Manufacturing Sites of Drugs by Region

	Europe	North, Central and South America	Asia	Africa	Total
FY 2005	2	8	2	0	12
FY 2006	13	20	2	1	36
FY 2007	22	22	8	0	52

Note: FY 2006: France, Netherlands, Ireland, Denmark, Finland, Austria, USA, South Korea, Indonesia, and South Africa

FY 2007: France, UK, Denmark, Spain, Ireland, Belgium, Italy, Netherlands, USA, Puerto Rico, China, Singapore, and India

On-site inspections of Overseas Manufacturing Sites of Medical Devices by Region

	Europe	North, Central and South America	Asia	Africa	Total
FY 2005	1	1	0	0	2
FY 2006	5	10	0	0	15
FY 2007	1	10	0	0	11

Note: FY 2006: Ireland, Switzerland, USA, and Puerto Rico
FY 2007: France, USA, and Puerto Rico

- The administrative processing times of GMP/QMS audits in FY 2007 are shown below:

Processing Time of GMP/QMS Audits According to the Amended Pharmaceutical Affairs Law

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

** Excluding in vitro diagnostics.*

- The processing status of audits of manufacturing facilities conducted in FY 2007 at domestic manufacturing sites under authorization from the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Sites, is shown below:

Number of Audits of Buildings and Facilities for Domestic Manufacturing Sites

	FY 2005		FY 2006		FY 2007	
Drugs*	12	(8)	30	(23)	16	(14)
In vitro diagnostics	1	(1)	6	(6)	2	(2)
Medical devices	2	(1)	1	(0)	0	(0)
Total	15	(10)	37	(29)	18	(16)

** Excluding In vitro diagnostics.*
Note: Values include withdrawn cases. Values in parentheses show the number of on-site inspections.

- The processing status of audits of manufacturing facilities conducted in FY 2007 at overseas manufacturing sites under authorization from the Minister, as based on the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments is shown below:

Number of Audits of Buildings and Facilities for Overseas Manufacturing Sites

	FY 2005	FY 2006	FY 2007
Drugs*	69	614	387
In vitro diagnostics	9	85	69
Quasi-drugs	29	73	57
Medical devices	127	971	1,682
Total	234	1,743	2,195

** Excluding In vitro diagnostics.*
Note: Values include withdrawn cases. All cases were document audits.

- The Agency conducts on-the-spot inspections, questioning, and sampling with regard to manufacturers, etc., under instructions from MHLW. The number of on-the-spot inspections

conducted in FY 2007 is shown below:

Number of On-the-spot Inspections

		FY 2005	FY 2006	FY 2007
Domestic manufacturers	Drugs*	15	11	27
	In vitro diagnostics	0	0	1
	Medical devices	0	0	2
Foreign manufacturers	Drugs*	2	3	5
	In vitro diagnostics	0	0	0
	Medical devices	0	2	0
Total		17	16	35

** Excluding In vitro diagnostics*

- The Agency conducts simple consultations on GMP/QMS audits. The number of simple consultations on GMP/QMS audits conducted in 2007 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2007
Pharmaceuticals*	28
In vitro diagnostics	3
Quasi-drugs	0
Medical devices	10
Total	41

** Excluding In vitro diagnostics.*

(iii) Use of outside 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, 2008, the number of commissioned experts is 896 including outside experts commissioned for matters relating to safety measures.)

(iv) System development for more efficient review services

- In addition to a new application/review system used by the Agency, Pharmaceutical and Food Safety Bureau in 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, audits, 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 audit authorities, recording of review memorandums, preparation of approval certificates and management of the approval registration list.

- In FY 2007, 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) Transition to the integrated database environment of the device system

- Upon expiration of the lease period of the medical device review system, the Agency shifted to the existing database environment (integration with the new application/review system). Database integration resulted in a reduction in operational management workload and achieved smooth monitoring and coordination of the linkages between systems. Associated with database integration, the Agency repaired the new application/review system to successfully achieve a remarkable reduction in the number of errors in the new application/review system. Prior to the repair, over 200 errors were reported each day.

2) Repair of the support system for surveys on pharmaceuticals, etc.

- Resulting from the change to JAN codes, changes were made to ingredient codes and ingredient specifications. The Agency responded to those changes by making appropriate repairs to the support system. System functions were also reinforced for improved efficiency of reviews and audits, including improvement in fax transmission capability for inquiries or replacement instructions, and the enhancement of slip preparation capability for audit-related services.

3) Outsourcing of the service to support requirement definition, etc. related to review function for eCTD

- In order to further improve the efficiency of review services for the diffusion of applications for approval in eCTD format, the Agency outsourced the service to support requirement definition, etc. for the review comment management function to eliminate the need for the provision of paper documents in the review procedure.

(v) Reinforcement of partnerships with foreign regulatory authorities

- In order to reinforce the structure for international operations, the Agency divided the Training and International Division into the Human Resources Development Division and the International Affairs Division to enhance the processes of information gathering and provision. Also, the Agency promoted reinforcement of partnerships with regulatory authorities in the U.S. and Europe relating to operations for reviews and post-marketing 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 ICH, GHTF and PDG, as well as in meetings of for 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 DIA Annual Meeting in the U.S., at DIA EURO Meeting in Spain, at APEC Network Meeting in Taiwan, and at IFPMA Asian Regulatory Conference in Malaysia, etc. to improve the international recognition of the Agency. The Agency also made efforts to expand its cooperative framework with Asian countries by visiting China, South Korea, and other countries (refer to II-Part 4.2.(1)-(v)-a., Approaches Toward International Harmonization such as Through 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 FDA (Food and Drug Administration), EMEA (European Medicines Evaluation Agency), etc. The Agency also exchanged information with FDA and EMEA on methods for conducting operations, etc. The Agency also participated in the 2nd Meeting of Regulatory Officials in Europe, USA, and Asia held in Ireland in December 2007, and exchanged notes with regulators in various countries including FDA.
2) It was decided that the 2008 East Asian Pharmaceutical Regulatory Symposium, which aims to establish a cooperative relationship in East Asian countries centering on Japan, China, and South Korea, would be held in Tokyo in April 2008. The Agency served as a liaison for the countries involved and made preparations for the symposium.
3) Based on the Administrative Rules on Overseas Training on a Long-term Basis, the Agency dispatched one employee each to EMEA and OECD after recruiting personnel who were interested in being dispatched and screening the applicants.
4) The Agency received foreign trainees, including four from Indonesia, one from the U.S. (Mansfield trainee), and four from China.

(vi) Evaluation of the latest technologies, such as biotechnology and genomics and cooperation in developing national guidelines

- As the Agency is required to raise the standards for guidance and review techniques for the latest 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 (notification regarding applications for type 1 use under the Cartagena Law, notification regarding products derived from cellular and tissue, evaluation guidelines regarding biosimilars/follow-on biologics, and guidelines for clinical vaccine research).

- Recombinant human serum albumin (HSA), which is important in preventing infections, requires caution for yeast allergy, but has been approved for the first time worldwide. Autologous cultured epidermis has become the first-approved regenerative medicine product in Japan. In addition, the precipitated H5N1 influenza vaccine has been approved as a measure against the spread of the new influenza virus (H5N1 strain).

- 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 pharmacogenomics 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 MHLW and commencing reviews directed toward developing specific guidelines. In FY 2007, PDG held seven unofficial meetings with the private sector to share information on pharmacogenomics and exchange opinions.

- In January 2008, the 2nd PMDA Biologics Symposium was held by PMDA with reviewers participating from South Korea and Canada, in addition to FDA and EU nations. The purpose of the symposium was to conduct international exchange of up-to-date information relating to review items on biologics, such as cellular and tissue-derived products and genetically-modified proteins, so that such information can be applied to consultations and review services.

- The Agency held five meetings for specialized discussions on pharmaceutical names and reported 29 Japanese accepted names (JAN) to MHLW. Five application consultations for international nonproprietary names (INN) were also conducted. The Agency participated in the WHO-hosted conference on INN in May and November.
  Note: JAN = Japanese Accepted Names
  INN = International Non-proprietary Names

(vii) Promotion of appropriate clinical trials

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

- For the purpose of contributing to the promotion of the development of clinical trial systems at medical institutions (from which trainees are dispatched), the Agency implemented Training for Clinical Research Coordinators (beginner training, lectures in September 2007 and practical training from October 2007 to February 2008; advanced training, lectures from November 2007 to January 2008; data management training, lectures and practical training in February 2008) to pharmacists and nurses from medical institutions.

Trainees in FY 2007

Beginner training	137
Advanced training	94
Data management training	146

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

(viii) 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 relevant companies, and also with the cooperation of MHLW, posted information on the approval of new drugs, etc., on the Post-marketing Safety Information site of the Agency's 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 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 Dossiers that contain overviews of application dossiers, 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 Issued by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW.

- In FY 2007, the Agency finalized 77 review reports and 30 summaries of application dossiers to be officially disclosed.

Review reports on new medical devices

- It was decided that the Agency should publish review reports on medical devices in response to the issuance of the Notification by the Director of the Office of Medical Devices Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated September 21, 2005, which specifies the publication procedures, etc. In FY 2007, the Agency disclosed review reports for 7 applications.

Review reports on OTC drugs and quasi-drugs

- It was decided that the Agency should sequentially publish review reports on OTC drugs and quasi-drugs in response to the issuance of the Notification by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated March 31, 2006, which specifies the publication procedures, etc. In FY 2007, the Agency disclosed 9 review reports for OTC drugs and 2 for quasi-drugs.

(ix) Preparation and publication of the english version of review reports

- In order to provide information on the Agency's review services and post-marketing safety measures to overseas countries, the Agency decided to post the English version of the review reports on the Agency's website. In FY 2007, the Agency prepared and published the English version of two review reports.

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

(i) Basic direction of post-marketing safety measures

- In order to improve the safety of marketed 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 such a way 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 126,000 reports on adverse drug reactions submitted to PMDA from within and outside of Japan each year, and approximately 17,000 reports on malfunctions of medical devices from within and outside of Japan are submitted to PMDA yearly. The Agency inputs this information into a database and promotes the sharing of this information with MHLW. In addition, the Agency is making efforts to take effective safety measures for pharmaceuticals and medical devices in the post-marketing stage by enhancing 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 MHLW every week based on daily reviews conducted by the supervising team in 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 healthcare professionals and people 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 Post-marketing Safety Information site of the Agency's 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 Mid-term plan in order to establish measures to prevent adverse drug reactions from occurring.

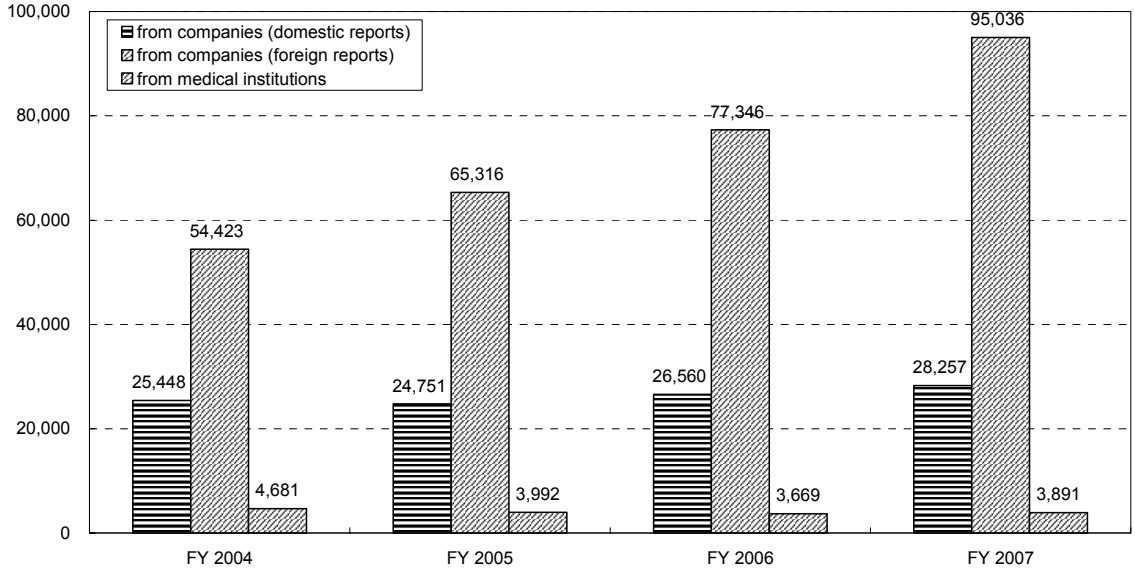
- In addition, the Agency plans to enhance safety measures by working on those that are capable of "predicting and preventing" through active scientific evaluation and analysis, and by building a sentinel medical institution network and applying the data mining technique to detect signals.

Collection of adverse reaction reports, etc.

1) Number of reports relating to pharmaceuticals

	FY 2004	FY 2005	FY 2006	FY 2007
Reports from companies	82,624	92,678	106,285	125,938
(cases of adverse drug reactions, Japanese)	(25,142)	(24,523)	(26,309)	(27,988)
(cases of infections caused by pharmaceuticals, Japanese)	(306)	(228)	(251)	(269)
(cases of adverse drug reactions, foreign)	(54,312)	(64,650)	(77,314)	(95,015)
(cases of infections caused by pharmaceuticals, foreign)	(111)	(666)	(32)	(21)
(research reports)	(1,311)	(971)	(818)	(858)
(foreign corrective action reports)	(420)	(563)	(485)	(695)
(periodic infection reports)	(1,022)	(1,077)	(1,076)	(1,092)
Reports from medical professionals	4,594	3,992	3,669	3,891
Total	87,218	96,670	109,954	129,829

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

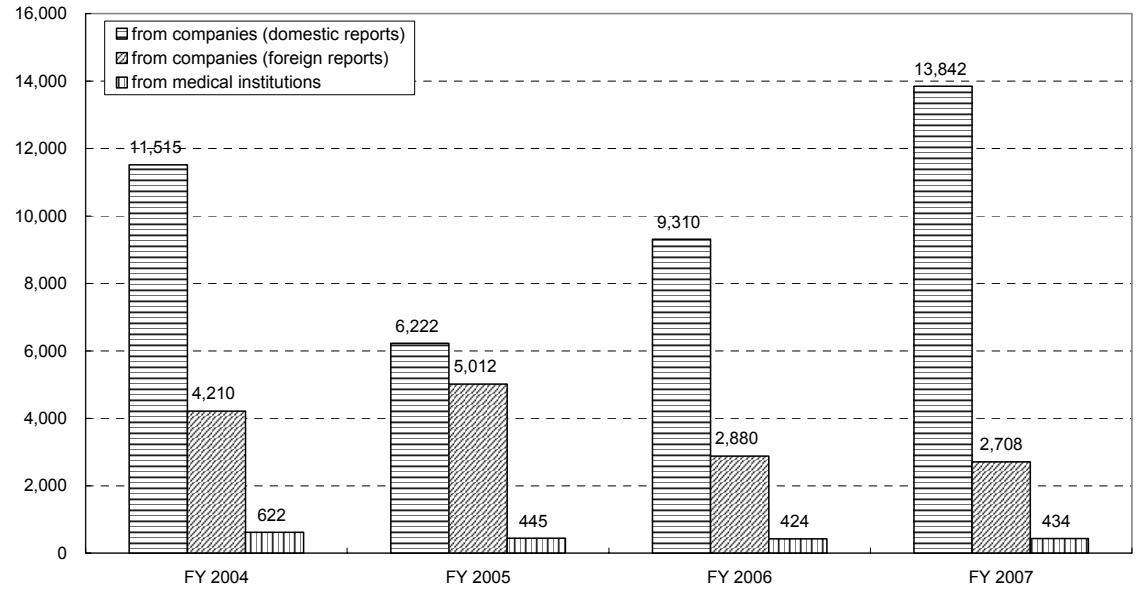


2) Number of reports relating to medical devices

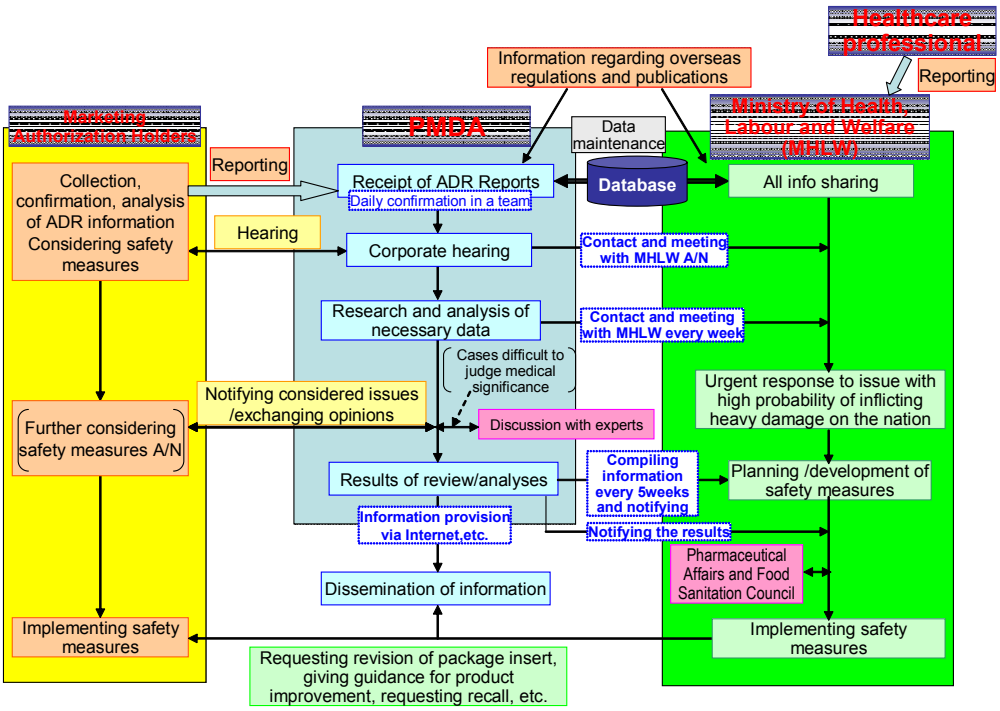
	FY 2004	FY 2005	FY 2006	FY 2007
Reports from companies	16,264	11,802	12,770	17,142
(cases of malfunctions of medical devices, Japanese*)	(11,515)	(6,222)	(9,310)	(13,842)
(cases of malfunctions of medical devices, foreign*)	(4,210)	(5,012)	(2,880)	(2,708)
(research reports)	(157)	(37)	(36)	(15)
(foreign corrective action reports)	(287)	(436)	(482)	(525)
(periodic infection reports)	(95)	(95)	(62)	(52)
Reports from medical professionals	622	445	424	434
Total	16,886	12,247	13,194	17,576

** 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



(ii) 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 the Data Mining Method?**
>
> The data mining method is technology that extracts, from among a large amount of data accumulated in the database, highly correlative events that occur frequently and simultaneously. The term “data mining” refers to the 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.

- Regarding the basic signal extraction techniques (i.e., six techniques including those introduced in foreign countries) that were subjected to detailed review in FY 2005 (in terms of the number of detections, increase or decrease in the number of detections, or quality of detection), the Agency narrowed them to three (ROR, GPS, and BCPNN) as a result of sensitivity and specificity analysis and correlation analysis conducted together with advanced review (stratified analysis, analysis of interaction with coadministred drugs, and adverse-reaction grouping) by the end of FY 2006. In FY 2007, the Agency conducted surveys on how the data mining technique was used by regulators in foreign countries and interviewed personnel in charge of adverse-reaction evaluation on the subject of operations processes. The Agency prepared the specifications of a new database system that could utilize the data mining method as a support tool that matches the operations flow of a new safety measures operation, and also launched the development of an operations support system supporting all aspects of safety measures. The Agency also conducted an

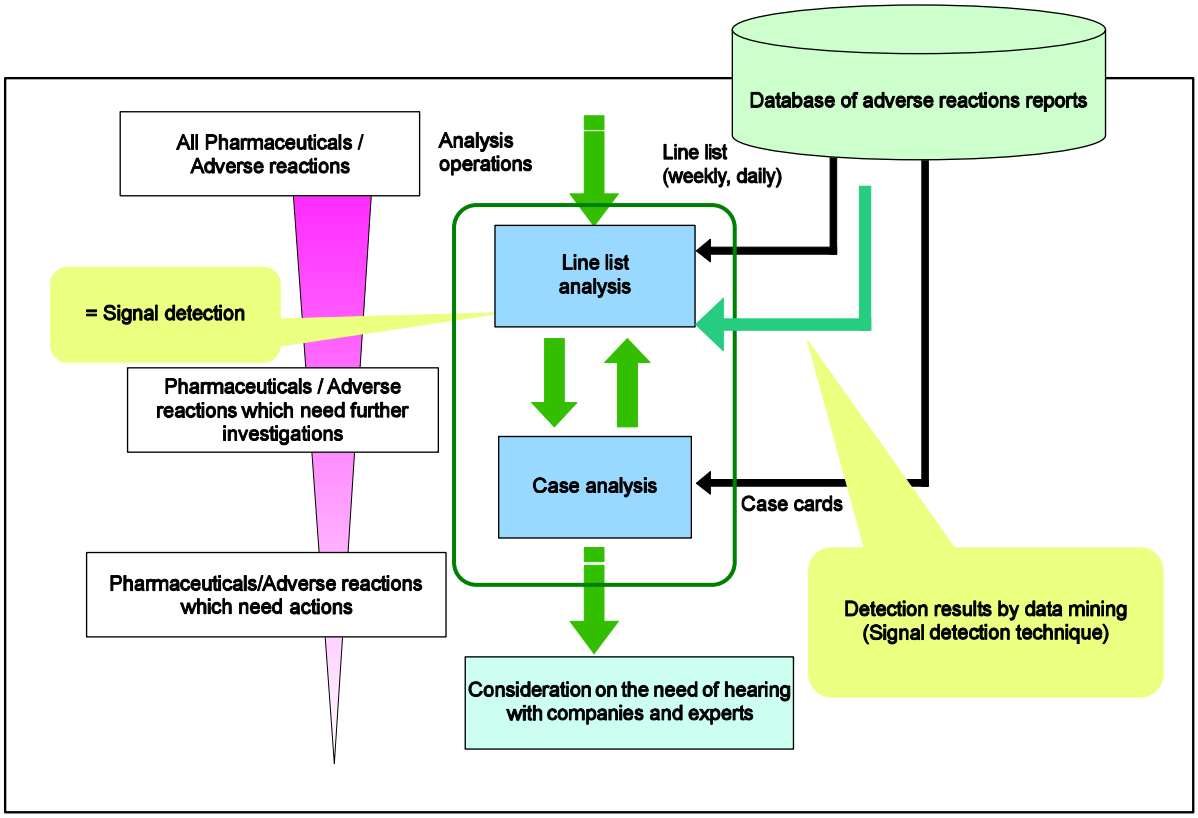
experiment to evaluate the amount and contents of combinations of drugs and adverse drug reactions with respect to the function of primary screening, and to ascertain whether a signal is detected. In addition, the Agency developed a tool based on correlation analysis to support nonroutine analytical operations. This tool will be used as a means to advance data mining, and the Agency has started reviewing its utility.

- In FY 2008, the Agency plans to introduce the system to safety measures operations by the end of the year (upon completion of the Midterm target period) after a trial operation.

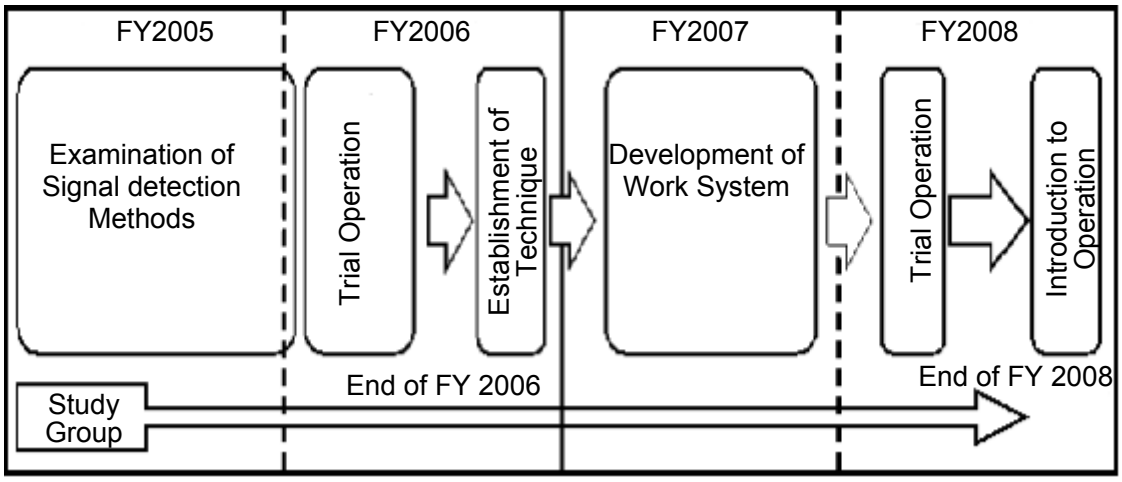
- The status of reviews relating to the implementation of safety measures for the data mining method is posted on the following website:

http://www.info.pmda.go.jp/kyoten/dm.html

Introducing the Data Mining Method into Safety Measures



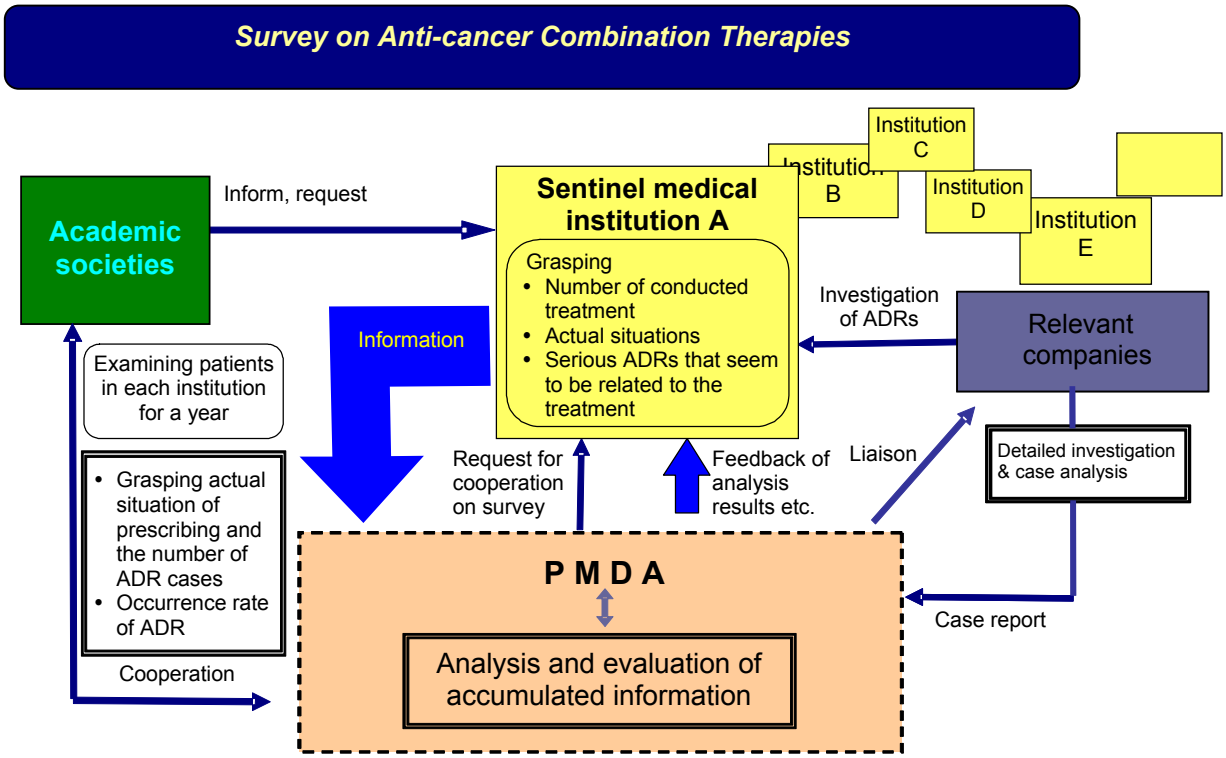
Schedule for Introducing the Data Mining Method (Planned)



(iii) Building a sentinel medical institution network

- As the Agency plans to emphasize 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 the survey on anti-cancer combination therapies (22 therapies). After finishing follow-up of all relevant patients at the end of June 2007, the Agency studied data entry and analysis techniques, and in February 2008 completed final analysis on 3,505 registered patients and a total of 563 reported cases of adverse drug reactions from 75 participating institutions. The final report is to be posted on PMDA website in June 2008 (a target date).



Reference: ***Therapies Subject to Survey on Anti-cancer Combination Therapies (22 Therapies*)***

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

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)*

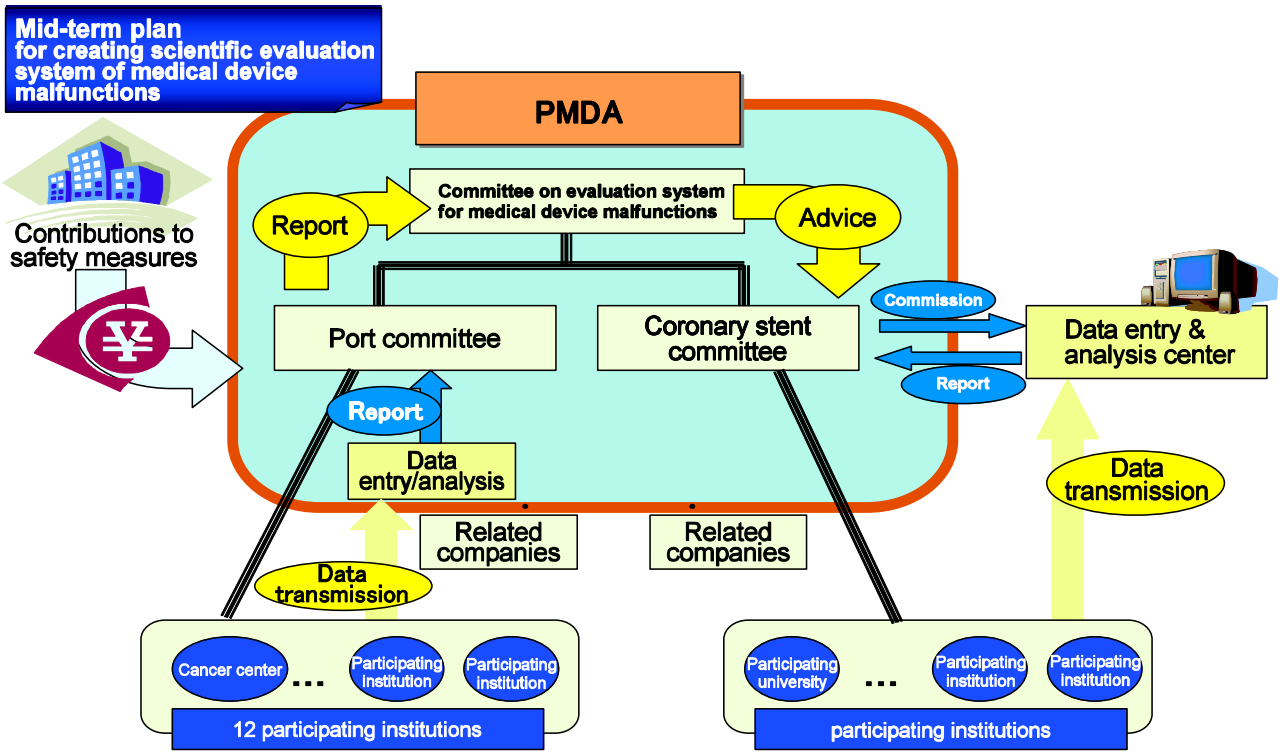
11. (1) ESHAP (Malignant lymphoma)
(2) DHAP (Malignant lymphoma)
12. (1) Cisplatin (Pediatric solid tumor)
(2) Carboplatin (Pediatric solid tumor)
(3) Cisplatin (Medulloblastoma)
13. Actinomycin (Ewing's sarcoma family of tumors)
14. (1) EC therapy (Breast cancer)
(2) CEF therapy (Breast cancer)

- In collaboration with MHLW's evidence collection for pediatric pharmacotherapy, the Agency conducted studies to obtain pediatric safety data for pharmaceuticals whose package inserts note that safety in pediatric patients has not been established, if their revisions are requested by academic societies, or if pediatric safety data from multiple companies is considered necessary, in order to understand problems associated with collecting pediatric safety data.

- In 2007, additional patient data for the retrospective cohort study on hyponatremia caused by the administration of maintenance fluid using electronic medical records (conducted in 2006 as a pediatric trial study using 1,291 case data from three institutions) was obtained from one institution, and the data was analyzed. Subjects, whose serum sodium levels decreased from 136 mEq/L or higher at baseline to below 136 mEq/L after administration, were defined as hyponatremia cases. In the group of 487 cases in which serum sodium values were available before and after administration of the maintenance solution, 91 cases of hyponatremia were found. Three of these cases were classified as grade 2 according to the severity of adverse drug reactions. This study, which was conducted based on the secondary use of electronic medical records of medical institutions, revealed many problems such as those associated with data extraction and processing, and with the use of laboratory and diagnosis (disease name) data. The results of the study were published as a report on the Agency's website in March 2008.

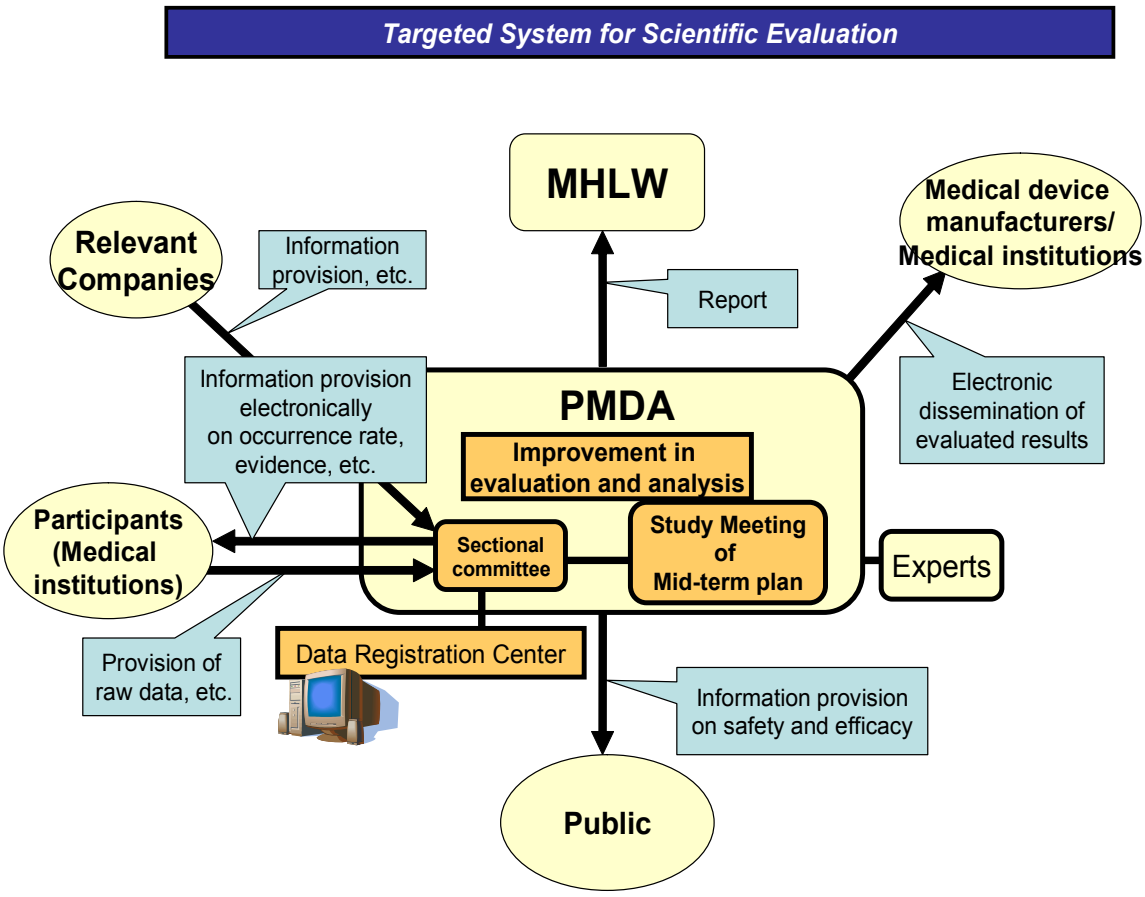
(iv) Review of the system for comprehending and evaluating medical device malfunctions

- The implementation status of surveys and the status of reviews in the sectional committee in charge in FY 2006 regarding coronary stents and implantable central venous access port system (hereinafter referred to as "implantable ports") were reported to the Discussion Group for the System for Evaluating Medical Device Malfunctions in 2007.
  The status of implementation in FY 2007 was as follows:
  a) **Implantable ports**: In 2007, malfunctions were classified by category in order to evaluate malfunctions that were not considered to be due to structural defects. A survey was conducted for the purpose of evaluation, in which registered patients were followed up for one year and preliminary data up to August 2007 was tabulated. In 13 of the 112 patients from 12 institutions who received the implant, 21 problems including subcutaneous leakage of the drug solution, phlebitis, infection of the implant site, changes in catheter position, and resistance during insertion were reported. These reports were examined at the port subcommittee in October 2007. The results of the examination will be published on the Agency's website in April 2008.
  b) **Coronary stents**: In FY 2007, a study protocol was written for the implementation of a survey expected to involve 26 institutions, and have a target patient number of 10,000, and a five-year follow-up period. In June 2007, the Agency selected parties to commission work such as collection of survey slips; and in February 2008, it commenced data collection efforts for 22 institutions that agreed to participate in the study.



Cardiac pacemakers and other tracking medical devices: In FY 2007, a Discussion Group for the Collection and Evaluation of Data for Tracking Medical Devices, comprising specialists, was established. In February 2008, discussions aiming toward the establishment of a tracking system for ventricular assist devices were held.

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



(v) Proper implementation of surveys on reports on adverse drug reactions and medical device malfunctions

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

- In addition, adverse drug reaction reports, reports on infections, etc., that are submitted by healthcare professionals (doctors, pharmacists, etc.) to MHLW are input into PMDA database and managed so that information can be shared with MHLW.

- In conducting surveys on reports on adverse drug reaction and medical device malfunctions, the

Agency has been closely working with the Safety Division of the Pharmaceutical and Food Safety Bureau at 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 MHLW on items for which measures were necessary (such as for revision of package inserts) in FY 2007 is as follows:

	FY 2004	FY 2005	FY 2006	FY 2007
Pharmaceuticals	133	240	131	204
Medical devices	15	18	4	10
Medical safety*	2	2	2	1

** "Medical safety" indicates the number of reports on near- incident cases, which are collected by the Japan Council for Quality Health Care. The Agency 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 MHLW.*

- Safety measures taken by MHLW in FY 2007 based on reports from PMDA are as follows (includes overlapping measures):

		FY 2004	FY 2005	FY 2006	FY 2007
Pharmaceuticals	Instructions for revision to precautions in package insert	149	212	131	202
	Posting articles and cases on the Safety Information on Pharmaceuticals and Medical Devices	33	26	24	86
Medical Devices	Instructions for revision to precautions in package insert or notifications to instruct self-inspection	7	7	0	8
	Posting articles on the Safety Information of Pharmaceuticals and Medical Devices	6	7	0	3

Note: 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 the 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 2007, the Agency took the following approaches to appropriately collect, organize, and examine the adverse drug reaction reports and medical device malfunction reports submitted by the private sector and medical institutions.
  a. Improved the efficiency in receiving adverse drug reaction reports by using data input tools
  b. Increased the staff members specialized in data input
  c. Updated the master files consisting of pharmaceutical and company names
  d. Encouraged staff members to attend academic societies (total of 22 participants) and

gathered information through the academic societies that they participated in

e. Regularly held liaison meetings on both pharmaceuticals and medical devices every week with MHLW

(vi) Digitization of adverse drug reaction reports and medical device malfunction reports

- In FY 2007, as part of effectively and efficiently collecting safety information through utilizing IT, the Agency developed an environment that allows for easy online reporting in order to promote transmission of information on adverse drug reactions, infections, etc. 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 allows for easy data transmission, 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 91.1% on a full-year basis was achieved in FY 2007, exceeding the target of 80%.

Status of Online Reporting for Adverse Drug Reaction Reports, etc.

	FY 2004	FY 2005	FY 2006	FY 2007
Electronic reporting rate (full year)	69.1%	86.4%	90.4%	91.1%

** Online reporting started from October, 2003. As of April 2004, the electronic reporting rate was 50%.*
The target of the Mid-term plan: 80% or more of average annual electronic reporting rate by the end of effective period of the Mid-term target
The target of FY 2007 plan: Ensuring the 80% of electronic reporting rate

Status of Online Reporting for Malfunction Reports

	FY 2004	FY 2005	FY 2006	FY 2007
Electronic reporting rate (full year)	36.8%	86.9%	53.6%	22.1%

Note: In FY 2007, the administrative organ in charge was changed from MHLW to the Ministry of Internal Affairs and Communications (MIC). Online reporting was suspended for approximately one month to facilitate the system switch.
No target was established in the Mid-term plan for electronic reporting of malfunctions.

(vii) Establishment of post-marketing safety system based on seedback of information

a. Feedback to the private sector

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

- In order to contribute to enhancing the risk management system in the private sector, the Agency is building and enhancing a system that enables 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 2008, the agency disclosed 84,094 adverse drug reaction reports and 34,226 medical device malfunction reports that had been submitted up to the end of

March 2007.

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 (on pharmaceuticals, medical devices, and medical safety) from the private sector. Specifically, these medical safety consultations related to revisions to package inserts, post-marketing risk management plans, creation of drug guides for patients, naming and labeling of pharmaceuticals to prevent medical accidents, and improvements in products to prevent medical accidents based on analyses of near-incident cases.

- The number of consultations by category for FY 2007 is shown below:

	FY 2004	FY 2005	FY 2006	FY 2007
Pharmaceuticals	513	557	567	486
Medical devices	722	553	292	260
Medical safety	46	46	44	166

- One reason for the reduction in the number of consultations on medical devices is considered to be the improvements in knowledge and understanding on the part of the consulting party as a result of the consultation services provided from FY 2004. On the other hand, the increase in the number of consultations on medical safety is attributed to the sudden rise in the number of pre-application consultations for name substitution of pharmaceuticals in 2007, as a preventive measure against medical accidents for pharmaceuticals whose names are similar to those of other products, or whose labels do not contain the name or quantity of the active ingredient. The Agency handled all cases in an appropriate and speedy manner.

b. Feedback to healthcare professionals

During FY 2007, 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 agency's website

- The Agency posted information on revisions to package inserts of prescription drugs, etc., on its website within two days after receiving such information. To improve the supply of information on generic drugs, the Agency is asking for revisions to include bioloequivalence test and other results (in accordance with Improving the Supply of Information on Generic Drugs, Notification No. 0324006 of the Safety Division, issued by Director of the Pharmaceutical and Food Safety Bureau [PFSB], dated March 24, 2006) by the end of March 2008. All package insert information on the Agency's website designed to provide information was revised before the end of January 2008.

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

- Following the revision of the Pharmaceutical Affairs Law in June 2006, the Agency commenced posting package inserts of OTC drugs on the Agency's website in March 2007, and there were 7,437 package inserts posted on the site as of the end of March 2008. The pupose of this is to ensure that information supply and consultation systems

are adapted to the degree of risk associated with the pharmaceuticals, and that experts engaged in selling pharmaceuticals have qualifications, and to develop and maintain an environment that can respond appropriately to consultations as well as provide appropriate information.

3) Preparation of information on *in vitro* diagnositics package inserts for posting it on the agency's website

- Information on package inserts of prescription drugs, medical devices, and OTC drugs are provided on the Post-marketing Safety Information site of the Agency's website to ensure their correct usage. Package insert information for *in vitro* diagnostics is targeted to be available within FY 2008. Through cooperation with industry groups, the Agency has conducted pilot tests to view the information on the website under test conditions, and developed tools and systems to convert the package inserts into electronic format.

4) Provision of manuals for management of individual serious adverse drug reactions

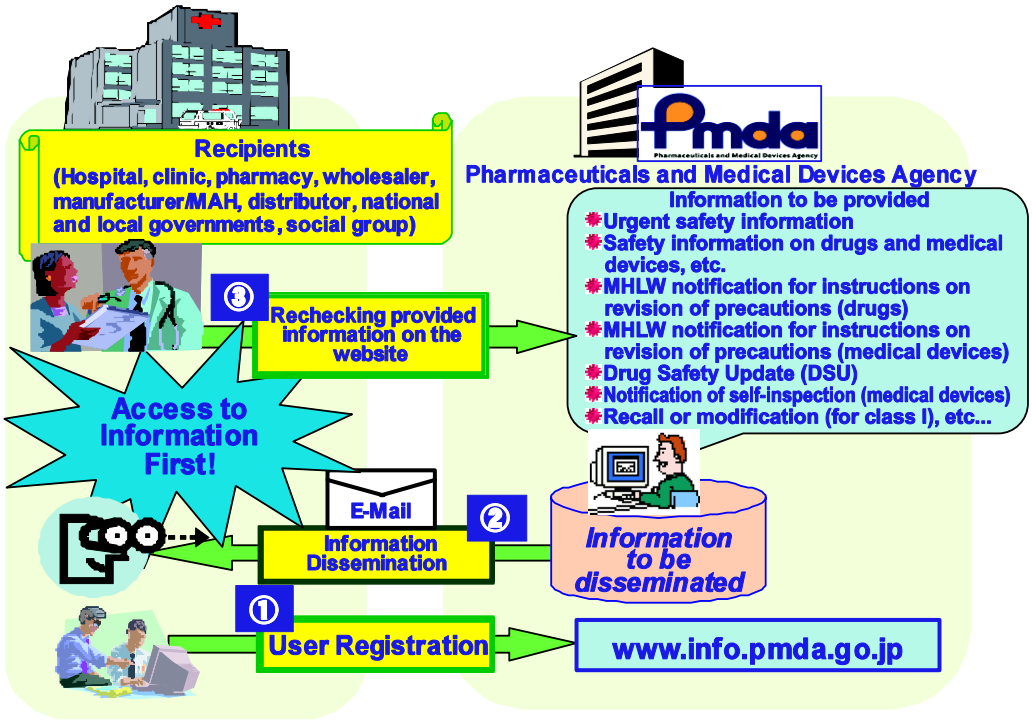
- The manuals for management of individual serious adverse drug reactions made by MHLW have been made available on the Agency's website since November 2006. In FY 2007, manuals for 16 new items were added to the website (total number of items, 25).

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

5) Implementation of the information delivery service for pharmaceuticals and medical devices

- The information delivery service for pharmaceuticals and medical devices, a service providing safety information such as revisions to package inserts and Class I recalls, is provided via e-mail to healthcare professionals who subscribe to the service. A total of 11,965 e-mail addresses were registered as of March 2008. Approximately 30% of these subscribers were hospitals and clinics, approx. 20% were pharmacies, approx. 10% were dentist clinics or other medical facilities, approx. 20% were marketing authorization holders, approx. 10% were distributors, and approx. 10% were classified as other.

E-mail Information Service on Pharmaceuticals and Medical Devices



Number of Push E-mail Service Subscribers by Subscription Content in FY 2007

Subscription content	Number
Recalls (Class I)	43
Pharmaceuticals and Medical Devices Safety information	11
Drug Safety Update (DSU)	10
Revision of PRECAUTIONS of pharmaceuticals	15
Revision of PRECAUTIONS of medical devices	5
Other	3
Total	87

6) Provision of medical safety information

- The Agency has been extracting, evaluating, and examining near-incident cases associated with pharmaceuticals and medical devices from the Project to Collect Information on Medical Incident Reports published by the Japan Council for Quality Health Care. In FY 2007, 412 cases associated with pharmaceuticals and 308 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 292 cases for which deliberations by MHLW were completed, the details of the cases were posted on the Post-marketing Safety Information site of the Agency's website.

Items	Pharmaceuticals	Medical devices
Total subject cases: 292 cases	170	122
1) Cases in which safety measures for the use of pharmaceuticals/medical devices by the marketing authorization holders etc. were considered necessary or possible.	4	7
2) Cases in which measures have already been taken, or are currently being investigated, by the marketing authorization holder etc.	18	25

3) Cases in which a lack of information is considered to hinder the marketing authorization holder's investigations for measures, or cases that were considered to be a result of human error or human factors.	148	90

- In addition, in November 2007, the Agency started to provide medical safety information, which use charts and other tools so that healthcare professionals can easily understand precautions for safe use based on collected near-incident cases and adverse drug reaction and manfunction reports stating much the same events repeatedly or notifying revisions to package inserts repeatedly, while referring to opinions given by healthcare professionals such as physicians, pharmacists, nurses, and clinical engineers and specialists in fields such as ergonomics.

  In FY 2007, the following three pieces of PMDA Medical Safety Information were posted on the Post-marketing Safety Information site of the Agency's website.

	Month and year published	PMDA safety information titles
No.1	Nobember 2007	Points to note in case of obstruction of feeding tube
No.2	November 2007	Recall of Resuscitators
No.3	January 2008	Precautions against improper connection of speech valves etc. to tracheostomy tubes

7) Disclosure of adverse drug reaction cases

- From among the contents of all adverse reaction reports that have been submitted by the private sector since April 2004, the Agency has disclosed information on fiscal year reported, sex, age, primary disease, suspected drug, adverse event, suspected concomitant drug, and outcome on the Post-marketing Safety Information site of the Agency's website, since January 2006. By the end of March 2008, the Agency posted 84,094 reports submitted up to September 2007.

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

A: **Cases for which the causality between the suspected drug and death cannot be ruled out**
Cases for which the possibility that the adverse event alleged to be associated with the suspected drug caused the death cannot be ruled out, 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 no causality between the suspected drug and death can 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 the causality between the suspected drug and death cannot be evaluated because of 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 intended use or usage method of the drug, etc.

8) Disclosure of medical device malfunction cases

- From among the contents of all reports on medical device malfunctions that have been submitted by the private sector since April 2004, the Agency has disclosed information on fiscal year reported, sex, age, outcome, generic name, condition of the medical device, and patient adverse event on the Information Page of the Agency's website designed to provide information on pharmaceuticals and medical devices, since March 2006. By the end of March 2008, the Agency posted 34,226 reports submitted up to September 2007.

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

A: **Cases for which the causality between the medical device used and death cannot be ruled out**
Cases for which the possibility that the adverse event alleged to be associated with the medical device used caused the death cannot be ruled out, 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 and inspections, and the time that had elapsed.

B: **Cases for which no causality between the medical device used and death can 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 and inspections, and the time that had elapsed.

C: **Cases for which the causality between the medical device used and death cannot be evaluated because of 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 intended use or usage method of the device, etc.

9) Support for disclosing relevant information for companies

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

- The Agency translated into English the safety information on pharmaceuticals and medical devices prepared by MHLW and posted the translations on the English website of PMDA.

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 use pharmaceuticals and medical devices safely and securely, the Agency implements a telephone consultation service for drugs and medical devices.

- Drug consultation services have been carried out since July 1994. Starting in February 2005, consultation services have been available even during lunch breaks. Counseling services for consumers and healthcare professionals regarding generic drugs were launched in May 2007, and 122 consultations have been conducted.

Counseling services for consumers regarding medical devices were launched in July 2005.

- In FY 2007, there were 12,477 consultation requests for drugs and 824 requests for medical devices.

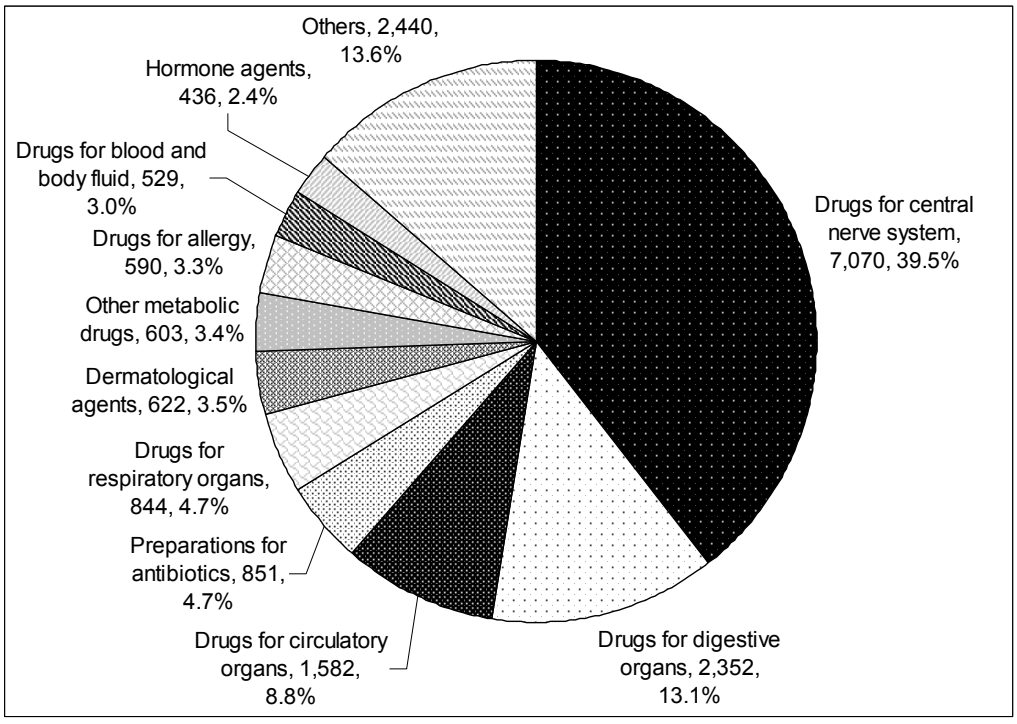
Number of Consultations on Drugs

	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Number of phone calls	6,465 (26.4 cases/day)	7,641 (31.1 cases/day)	7,137 (29.6 cases/day)	7,741 (30.0 cases/day)	8,459 (34.5 cases/day)	8,696 (35.5 cases/day)
Number of consultations	8,770 (35.8 cases/day)	9,906 (40.4 cases/day)	8,790 (36.5 cases/day)	10,505 (43.4 cases/day)	11,696 (47.7 cases/day)	12,477 (50.9 cases/day)

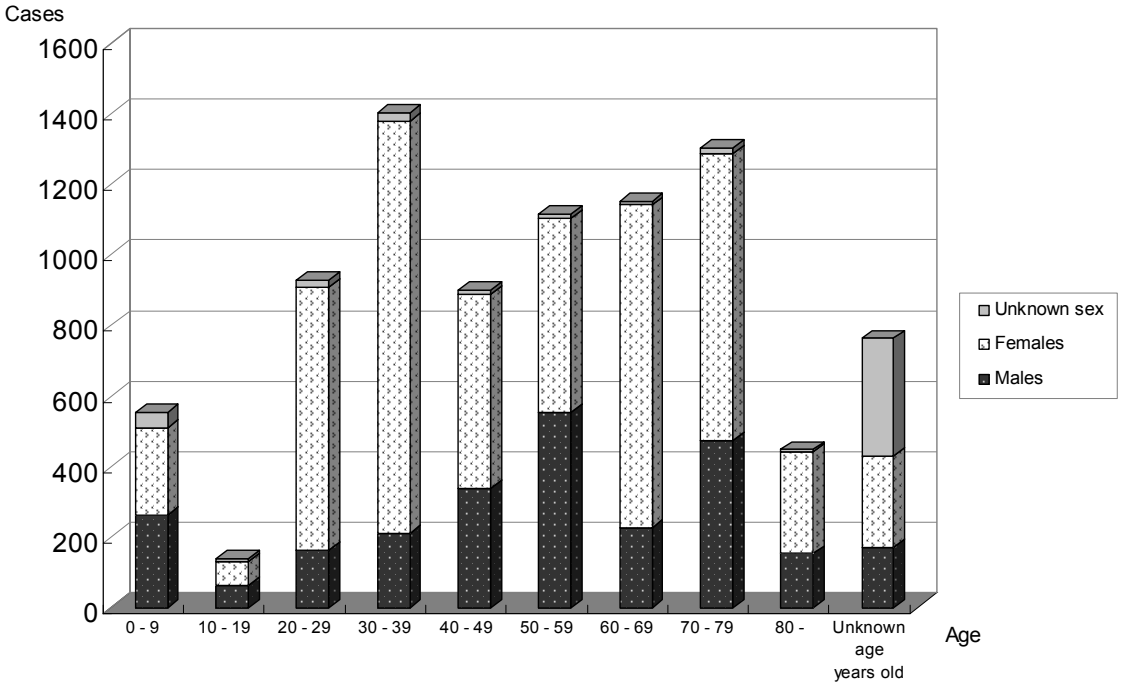
Contents of Consultations on Drugs

Contents of Consultation	FY 2004	FY 2005	FY 2006	FY 2007
(1) Safety	4,211 (47.9%)	5,968 (56.8%)	5,697 (48.7%)	5,731 (45.9%)
(2) Indications	1,194 (13.6%)	1,132 (10.8%)	1,175 (10.0%)	1,175 (9.4%)
(3) Administration and Dosage	669 (7.6%)	771 (7.3%)	828 (7.1%)	1,072 (8.6%)
(4) Interaction	611 (7.0%)	628 (6.0%)	691 (5.9%)	715 (5.7%)
(5) Active ingredients	205 (2.3%)	161 (1.5%)	219 (1.9%)	236 (1.9%)
Other	1,900 (21.6%)	1,845 (17.6%)	3,086 (26.4%)	3,548 (28.4%)
Total	8,790 (100.0%)	10,505 (100.0%)	11,696 (100.0%)	12,477 (100.0%)

Number of Consultations by Major Classification of Therapeutic Category (Total of Top 10 Categories) in FY 2007



Number of Patients (Receiving Counseling) by Age and by Sex in FY 2007



Number of Consultations on Medical Devices with Consumers

	FY 2005*	FY 2006	FY 2007
Number of phone calls	166 (1.0 case/day)	376 (1.5 case/day)	564 (2.3 case/day)
Number of consultations	323 (1.9 case/day)	581 (2.4 case/day)	824 (3.4 case/day)

* The consultation service has been provided since July 2005.

Contents of Consultations on Medical Devices with Consumers

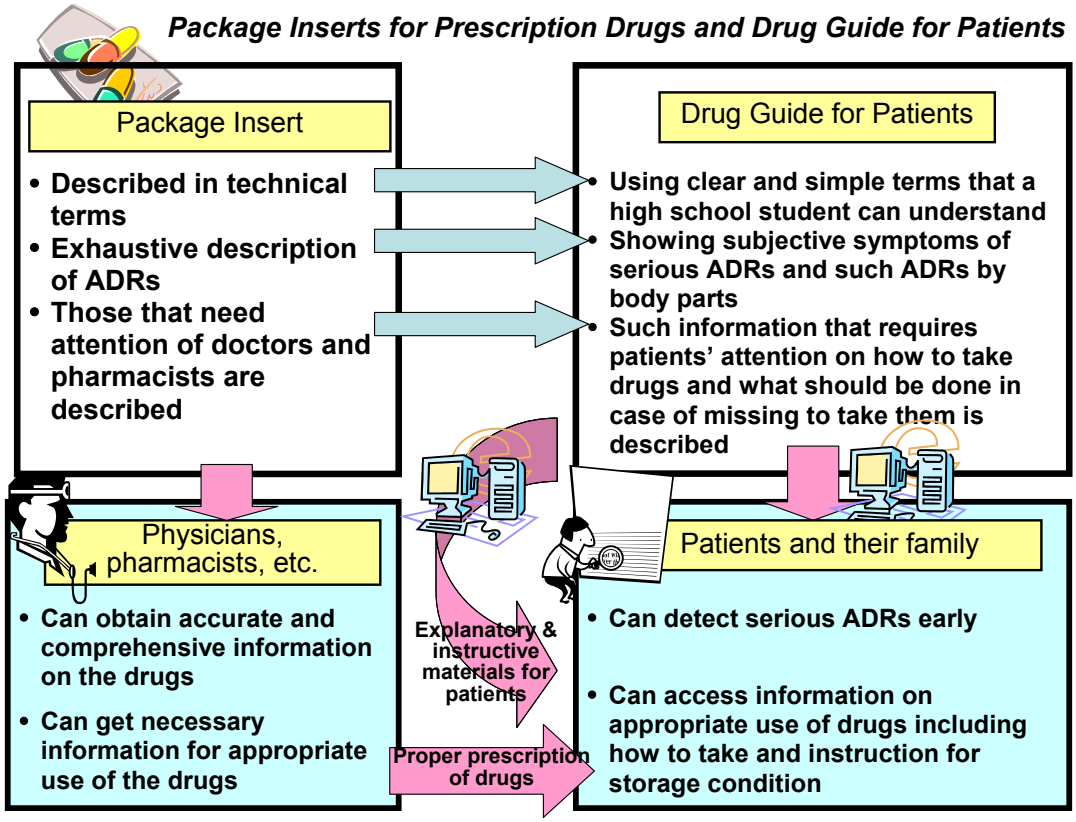
Contents of consultation	FY 2005	FY 2006	FY 2007
(1) Safety	32 (9.9%)	62 (10.7%)	91 (11.0%)
(2) Indications	64 (19.8%)	101 (17.4%)	85 (10.3%)
(3) Performance	25 (7.7%)	45 (7.7%)	37 (4.5%)
(4) Directions for use	12 (3.7%)	16 (2.8%)	12 (1.5%)
Other	190 (58.8%)	357 (61.4%)	599 (72.7%)
Total	323 (100.0%)	581 (100.0%)	824 (100.0%)

2) Publication of the drug guide for patients

- The Drug Guide for Patients, the purpose of which is to make it possible for patients to properly understand prescription drugs and enable them to detect serious adverse reactions at an earlier stage, has been posted on the Agency's website since January 2006. In FY 2007, the Guide contained an additional 33 ingredients in 327 items (which were designated or newly sold thereafter), and 270 ingredients in 1,567 items were posted by the end of March 2008.

- In accordance with the Guidelines for Developing the Drug Guide for Patients (Notification of the Director-General of the Pharmaceutical and Food Safety Bureau, MHLW dated June 30, 2005), the Agency has reviewed and revised the Drug Guide for Patients while continuously obtaining advice from experts (scientific research by MHLW [research on how to provide patients and people with drug safety information]).

Package Inserts for Prescription Drugs and Drug Guide for Patients



Number of Drug Guide for Patients Published

Group of target Pharmaceuticals	was posted by	Number of component	Number of package insert	Number of item
Antidiabetic agents *	Jan. FY 2006	10	44	56
Antirheumatic drug *	Mar. FY 2006	2	9	11
Anticoagulant and antiplatelet agent *		3	44	71
Antiasthmatic drug *		8	13	18
The 100s to 200s of Classification of drugs by efficacy *	Jul. FY 2006	91	348	551
The 300s to 400s of Classification of drugs by efficacy *	Oct. FY 2007	53	292	385
The 500s, 600s, 700s, 800s of Classification of drugs by efficacy *	Jan. FY 2007	76	319	346
Injectable solution	Mar. FY 2007	27	72	129
	Total	270	1141	1567

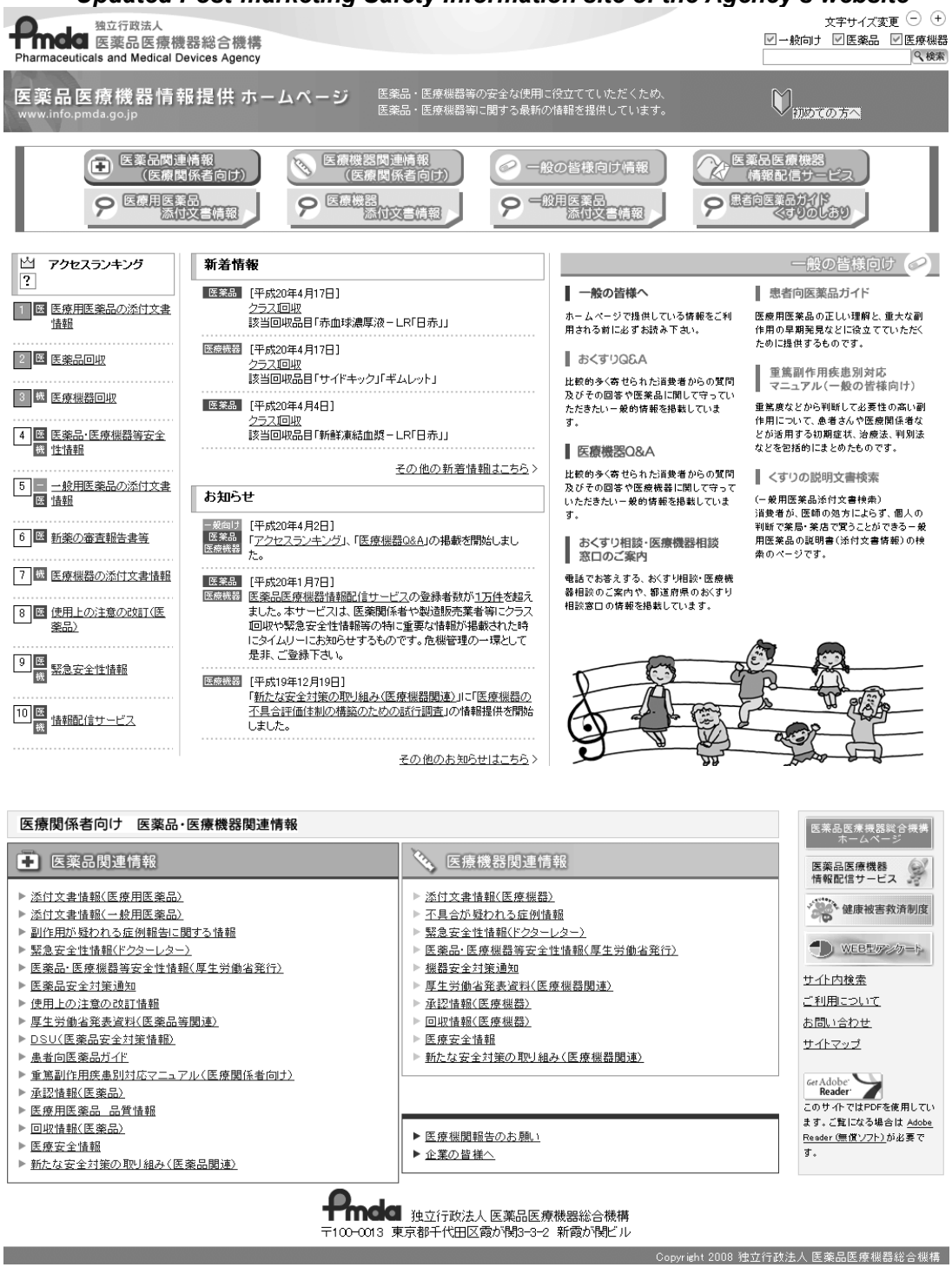
** The numbers of items with asterisk are figures that have been published as of the end of March 2008.*

3) Upgrading Post-marketing Safety Information site of the Agency's website

- In FY 2007, referring to opinions given by the website users, the Agency added icons on the upper part of the top page for linking to content such as Information Related to Pharmaceuticals, Information Related to Medical Devices, and Information for the General Public, and also added icons for links on the information of package inserts, thereby improving the more purpose-oriented user interface.

- With respect to information for the general public, on its revised website, the Agency posted the Drug Guide for Patients, a manual which includes disease-specific countermeasures for serious adverse drug reactions, information on package inserts for OTC drugs, and contact information on the consultation service for pharmaceuticals and medical devices. It also includes Q & As about pharmaceuticals and medical devices, which are questions relatively frequently asked by general consumers in the consultation service for pharmaceuticals and medical devices and answers to them.

Updated Post-marketing Safety Information site of the Agency's website



Q & As about Pharmaceuticals

Q & As about Medical Devices

4) Implementation of post-marketing safety measures workshops

- In November 2007 and January 2008, workshops on the effective use of information on safety measures recommended by the Agency were held for healthcare professionals on the theme of “Information on Pharmaceuticals for Appropriate Use—What Information Is Useful for Clinical Settings?” Over 350 participants attended the workshops. The Agency also gave presentations on the recent revision of precautions in package inserts, the effective use of the Post-marketing Safety Information site of the Agency’s website, and the Agency’s consultation services at workshops held by others and at academic meetings.

Number of Posted Items on the Post-marketing Safety Information Site of the Agency's Website as of March 2008

Types of provided information		Number of posted information						
		FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Package insert information *1								
	Prescription drugs	11,045 sheets	11,380 sheets	11,516 sheets	11,706 sheets	11,819 sheets	12,341 sheets	13,090 sheets
	Medical devices	-	-	-	-	1,524 sheets	3,995 sheets	5,462 sheets
	OTC drugs	-	-	-	-	-	3,306 sheets	7,437 sheets
Drug guide for patients *1		-	-	-	-	23 ingredients (150 items)	237 ingredients (1,240 items)	270 ingredients (1,567 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	323 cases
Urgent safety information (by pharmaceutical companies)		13 cases	20 cases	23 cases	23 cases	23 cases	24 cases	24 cases
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ))		-	-	1 cases	11 cases	21 cases	31 cases	41 cases
Notification of safety measures for medical devices								
	Notification of self-assessment	-	-	-	42 cases	45 cases	45 cases	45 cases
	Notification of revisions of labeling	-	-	-	10 cases	20 cases	21 cases	28 cases
	Notification related to medical devices	-	-	-	2 cases	33 cases	35 cases	54 cases
Information about case reports on suspected ADR (provided in new form)		-	-	-	-	3,884 cases	48,584 cases	84,094 cases
Information about case reports on suspected malfunction		-	-	-	-	1,750 cases	17,345 cases	34,226 cases
Notification related to preventive measures for medical accidents		1 cases	1 cases	11 cases	14 cases	18 cases	21 cases	26 cases
PMDA Medical Safety Information								3 cases
Manuals for management of individual serious adverse drug reactions							9 cases	25 cases
Information about approved new drugs - Review reports, summary of application materials		119 ingredients (291 items)	127 ingredients (311 items)	114 ingredients (268 items)	137 ingredients (308 items)	203 ingredients (435 items)	261 ingredients (559 items)	308 ingredients (642 items)
A list of prescription 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	811 ingredients/ formulation
		(1,780 items)	(1,971 items)	(3,083 items)	(3,513 items)	(3,737 items)	(3,737 items)	(3,900 items)
Information about withdrawals of pharmaceuticals or medical devices *2		1,378 cases	2,150 cases	1,329 cases	1,295 cases	1,453 cases	2,128 cases	2,777 cases
E-mail service of pharmaceuticals and medical devices information								
	E-mails issued *3	-	-	-	-	92 e-mails	93 e-mails	87 e-mails
	Subscribers	-	-	-	-	2,892 addresses	6,762 addresses	11,965 addresses
Number of visitors to the website *4		76 million	87 million	107 million	233 million	289 million	391 million	497 million

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

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

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

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

III. SUPPLEMENTARY INFORMATION

Table 1. FY2007 List of Approved Products: New Drugs

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
1	Apr. 18, 2007	1	Visiclear Tablets (Zeria Pharmaceutical Co., Ltd.)	Approval	Monobasic sodium phosphate monohydrate/dibasic sodium phosphate anhydrous	A new combination drug indicated for bowel cleansing as a preparation for colonoscopy.
1	Apr. 18, 2007	2	Nesp Injection Syringe 10 μg Nesp Injection Syringe 15 μg Nesp Injection Syringe 20 μg Nesp Injection Syringe 30 μg Nesp Injection Syringe 40 μg Nesp Injection Syringe 60 μg Nesp Injection Syringe 120 μg (Kirin Brewery Co., Ltd.)	Approval Approval Approval Approval Approval Approval Approval	Darbepoetin alfa (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of renal anemia in dialysis patients.
1	May 24, 2007	3	Omepral Tablets 10 (AstraZeneca K.K.) Omeprazon Tablets 10 mg (Mitsubishi Pharma Corporation)	Change Change	Omeprazole	Drugs with a new indication and dosage for the treatment of non-erosive reflux disease.
1	Sep. 28, 2007	4	Cyanokit Injection Set (Merck Ltd., Japan)	Approval	Hydroxocobalamin	Drugs with a new indication and dosage for the treatment of cyanogen and cyanide poisoning.
1	Oct. 19, 2007	5	Regpara Tablets 25 mg Regpara Tablets 75 mg (Kirin Pharma Co., Ltd.)	Approval Approval	Cinacalcet hydrochloride	A drug containing a new active ingredient indicated for the treatment of secondary hyperparathyroidism in patients on maintenance dialysis.
1	Nov. 13, 2007	6	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new indication and dosage for use as maintenance therapy in Crohn's disease. [Orphan drug]
1	Feb. 29, 2008	7	Pentasa Tablets 250 (Nisshin Kyorin Pharmaceutical Co., Ltd.)	Change	Mesalazine	A drug with a new dosage for use in pediatric patients for the treatment of ulcerative colitis (excluding severe patients) and Crohn's disease.
1	Feb. 29, 2008	8	Hebsbulin-IH for Intravenous (Benesis Corporation)	Change	Polyethylene glycol-treated human anti-HBs immunoglobulin	A drug with a new indication and dosage for the prevention of hepatitis B recurrence in HBs antigen-positive recipients after liver transplantation and of hepatitis B occurrence in recipients after liver transplantation from HBc antigen-positive donors.
2	Apr. 18, 2007	9	Arixtra Injection for Subcutaneous 1.5 mg Arixtra Injection for Subcutaneous 2.5 mg (GlaxoSmithKline K.K.)	Approval Approval	Fondaparinux sodium	Drugs containing a new active ingredient indicated for the prevention of venous thromboembolism in high-risk patients who have undergone lower-extremity orthopedic surgery. [Priority review]
2	Apr. 18, 2007	10	Zetia Tablets 10 mg (Schering-plough K.K.)	Approval	Ezetimibe	A drug containing a new active ingredient indicated for the inhibition of cholesterol absorption.
2	Jul. 31, 2007	11	Selara Tablets 25 mg Selara Tablets 50 mg Selara Tablets 100 mg (Pfizer Japan Inc.)	Approval Approval Approval	Eplerenone	Drugs containing a new active ingredient indicated for the treatment of hypertension.
2	Jun. 21, 2007	12	Tambocor Tablets 50 mg Tambocor Tablets 100 mg (Eisai Co., Ltd.)	Change Change	Flecainide acetate	Drugs with a new indication for the treatment of tachyarrhythmia (paroxysmal atrial fibrillation and flutter).
2	Jun. 21, 2007	13	Ephedrine Hydrochloride Injection Fuso (Fuso Pharmaceutical Industries, Ltd.) Ephedrine Nagai Injection 40 mg (Dainippon Sumitomo Pharma Co., Ltd.) Ephedrine Hydrochloride Injection Sanken (Sanwa Kagaku Kenkyusho Co., Ltd.)	Change Change Change	Ephedrine hydrochloride	Drugs with a new indication and route of administration, or the intravenous route for the treatment of hypotension occurring during anesthesia,G20 and without intramuscular injection administered for their approved indications.

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
2	Aug. 23, 2007	14	Aricept Tablets 3 mg Aricept Tablets 5 mg Aricept Tablets 10 mg Aricept D Tablets 3 mg Aricept D Tablets 5 mg Aricept D Tablets 10 mg Aricept Fine Granules 0.5% (Eisai Co., Ltd.)	Change Change Approval Change Change Approval Change	Donepezil hydrochloride	Drugs with a new indication and dosage for patients with severe dementia of the Alzheimer' s type.
2	Oct. 19, 2007	15	Careload LA Tablets 60 μg (Toray Industries, Inc.) Berasus LA Tablets 60 μg (Kaken Pharmaceutical Co., Ltd.)	Approval Approval	Beraprost sodium	Drugs with a new indication and dosage and in a new dosage form for the treatment of pulmonary arterial hypertension. [Priority review]
2	Oct. 19, 2007	16	Sigmart Injection 2 mg Sigmart Injection 12 mg Sigmart Injection 48 mg (Chugai Pharmaceutical Co., Ltd.)	Change Change Change	Nicorandil	Drugs with a new indication and dosage for the treatment of acute cardiac failure including the acute exacerbation period of chronic cardiac failure.
2	Oct. 19, 2007	17	Plavix Tablets 25 mg Plavix Tablets 75 mg (Sanofi-Aventis K.K.)	Change Change	Clopidogrel sulfate	Drugs with a new indication and dosage for acute coronary syndrome (unstable angina and non-ST-elevation myocardial infarction) in patients in whom percutaneous coronary intervention (PCI) is considered. [Priority review]
2	Jan. 25, 2008	18	Clexane Subcutaneous Injection Kit 2000 IU (Sanofi-Aventis K.K.)	Approval	Enoxaparin sodium	A drug containing a new active ingredient indicated for the prevention of venous thromboembolism in patients who have undergone total hip replacement, total knee replacement and hip fracture surgery. [Priority review]
2	Jan. 25, 2008	19	Amerge Tablets 2.5 mg (GlaxoSmithKline K.K.)	Approval	Naratriptan hydrochloride	A drug containing a new active ingredient indicated for the treatment of migraine.
2	Jan. 25, 2008	20	Recomodulin Injection 12800 (Asahi Kasei Pharma Corporation)	Approval	Thrombomodulin alfa (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of disseminated intravascular coagulation (DIC).
2	Jan. 25, 2008	21	Revatio Tablets 20 mg (Pfizer Japan Inc.)	Approval	Sildenafil citrate	A drug with a new indication and dosage for the treatment of pulmonary arterial hypertension. [Orphan drug]
2	Feb. 29, 2008	22	Vasolan Tablets 40 mg (Eizai Co., Ltd.)	Change	Verapamil hydrochloride	A drug with a new indication for the treatment of tachyarrhythmia (atrial fibrillation and flutter, and paroxysmal supraventricular tachycardia).
2	Mar. 19, 2008	23	Brevibloc Injection 100 mg (Maruishi Pharmaceutical Co., Ltd.)	Change	Esmolol hydrochloride	A drug with a new dosage indicated for the emergency treatment of supraventricular tachyarrhythmia occurring during surgery.
3	Apr. 18, 2007	24	Mikelan LA Ophthalmic Solution 1% Mikelan LA Ophthalmic Solution 2% (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval	Carteolol hydrochloride	Drugs in a new dosage form indicated for the treatment of glaucoma and ocular hypertension.
3	Jul. 31, 2007	25	Topina Topina Tablets 50 mg TopinaTablets 100 mg (Kyowa Hakko Kogyo Co., Ltd.)	Approval Approval Approval	Topiramate	Drugs containing a new active ingredient indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy not fully responding to other antiepileptic therapies.
3	Jul. 31, 2007	26	Eslax Intravenous 1% (Organon Japan)	Approval	Rocuronium bromide	A drug containing a new active ingredient indicated for inducing muscular relaxation during anesthesia and tracheal intubation.
3	Jul. 31, 2007	27	Travatanz Ophthalmic Solution 0.004% (Alcon Japan Ltd.)	Approval	Travoprost	A drug containing a new active ingredient indicated for the treatment of glaucoma and ocular hypertension.
3	Aug. 23, 2007	28	Fentanyl Injection 0.1 mg Sankyo Fentanyl Injection 0.25 mg Sankyo (Daiichi Sankyo Propharma Co., Ltd.)	Change	Fentanyl citrate	Drugs with a new dosage for use in pediatric patients for inducing general anesthesia and for inducing analgesia during general anesthesia. Expedited review.
3	Oct. 19, 2007	29	Salagen Tablets 5 mg (Kissei Pharmaceutical Co., Ltd.)	Change	Pilocarpine hydrochloride	A drug with a new indication for the treatment of oral dryness in patients with Sjögren's syndrome.

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
3	Oct. 26, 2007	30	Concerta Tablets 18 mg Concerta Tablets 27 mg (Janssen Pharmaceutical K.K.)	Approval Approval	Methylphenidate hydrochloride	Drugs with a new indication for the treatment of attention-deficit/hyperactivity disorder (AD/HD) in children. Expedited review.
3	Jan. 25, 2008	31	Lonasen Tablets 2 mg Lonasen Tablets 4 mg Lonasen Powder 2% (Dainippon Sumitomo Pharma Co., Ltd.)	Approval Approval Approval	Blonanserin	Drugs containing a new active ingredient indicated for the treatment of schizophrenia.
3	Jan. 25, 2008	32	Champix Tablets 0.5 mg Champix Tablets 1 mg (Pfizer Japan Inc.)	Approval Approval	Varenicline tartrate	Drugs containing a new active ingredient indicated as a smoking-cessation aid for nicotine-dependent smokers. Expedited review.
3	Mar. 19, 2008	33	Durotep MT Patch 2.1 mg Durotep MT Patch 4.2 mg Durotep MT Patch 8.4 mg Durotep MT Patch 12.6 mg Durotep MT Patch 16.8 mg (Janssen Pharmaceutical K.K.)	Approval Approval Approval Approval Approval	Fentanyl	Drugs with a new dosage form indicated for pain relief in cancer patients with moderate to severe pain.
4	Apr. 18, 2007	34	Valtrex Granules 50% (GlaxoSmithKline K.K.)	Change	Valaciclovir hydrochloride	A drug with a new indication and dosage for the treatment of varicella in children.
4	Jul. 31, 2007	35	Geninax Tablets 200 mg (Toyama Chemical Co., Ltd.)	Approval	Garenoxacin mesilate	A drug containing a new active ingredient indicated for the treatment of laryngopharyngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, infections secondary to chronic respiratory disease, otitis media, and sinusitis.
4	Jul. 31, 2007	36	Beselna Cream 5% (Mochida Pharmaceutical Co., Ltd.)	Approval	Imiquimod	A drug containing a new active ingredient indicated for the treatment of condyloma acuminatum (limited to the external genitals or perianal region).
4	Aug. 23, 2007	37	Takepron Capsules 15 Takepron Capsules 30 Takepron OD Tablets 15 Takepron OD Tablets 30 (Takeda Pharmaceutical Co., Ltd.) Omepral Tablets 10 mg Omepral Tablets 20 mg (AstraZeneca K.K.) Omeprazon Tablets 10 mg Omeprazon Tablets 20 mg (Mitsubishi Pharma Corporation) Pariet Tablets 10 mg (Eisai Co., Ltd.) Pasetocin Capsules Pasetocin Tablets 250 (Kyowa Hakko Kogyo Co., Ltd.) Sawacillin Capsules Sawacillin Tablets 250 (Takeda Pharmaceutical Co., Ltd.) Amolin Capsules 125 Amolin Capsules 250 10% Amolin Fine Granules (Astellas Pharma Inc.) Amopenixin Capsules 250 (Nipro Pharma Corporation) Flagyl (Shionogi & Co., Ltd.) Asuzol tablets (Fuji Pharma Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change	Lansoprazole Omeprazole Rabeprazole sodium Amoxicillin Metronidazole	Drugs with a new indication and dosage for use as a secondary eradication therapy for infection with *Helicobacter pylori* (3-drug combination therapy consisting of one-week dosing of a proton pump inhibitor (PPI), amoxicillin (AMPC), and metronidazole to patients in whom primary eradication therapy with PPI, AMPC, and clarithromycin was unsuccessful).
4	Sep. 28, 2007	38	Clavamox Dry Syrup for Pediatric Use (GlaxoSmithKline K.K)	Change	Clavulanate potassium/Amoxicillin hydrate	A drug with a new indication for the treatment of superficial skin infections, deep skin infections, lymphangitis and lymphadenitis, chronic pyoderma, laryngopharyngitis, tonsillitis, acute bronchitis, cystitis, and pyelonephritis.
4	Sep. 28, 2007	39	Valtrex Tablets 500 Valtrex Granules 50% (GlaxoSmithKline K.K)	Change Change	Valaciclovir hydrochloride	Valtrex Tablets 500: A drug with a new indication and dosage for the treatment of varicella in adults and children.

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
4	Jan. 25, 2008	40	Gracevit Tablets 50 mg Gracevit Fine Granules 10% (Daiichi Sankyo Co., Ltd.)	Approval Approval	Sitafloxacin hydrate	A drug containing a new active ingredient indicated for the treatment of laryngopharyngitis, tonsillitis (including peritonsillitis and peritonsillar abscess), acute bronchitis, pneumonia, infections secondary to chronic respiratory disease, cystitis, pyelonephritis, urethritis, cervicitis, otitis media, sinusitis, periodontal inflammation, pericoronitis and jaw inflammation.
4	Nov. 13, 2007	41	Rocephin Intravenous 0.5 g Rocephin Intravenous 1 g Rocephin Intravenous Drip 1 g Bag (Chugai Pharmaceutical Co., Ltd.)	Change Change Change	Ceftriaxone sodium	Drugs with a new dosage for use in children, premature infants, and neonates.
4	Feb. 29, 2008	42	Habekacin Injection 25 mg Habekacin Injection 75 mg Habekacin Injection 100 mg Habekacin Injection 200 mg (Meiji Seika Kaisha, Ltd.)	Change Change Change Approval	Arbekacin sulfate	Drugs with a new dosage and in a new dosage form indicated for the treatment of septicemia and pneumonia caused by arbekacin-sensitive methicillin-resistant *staphylococcus aureus* (MRSA).
5	Apr. 18, 2007	43	Imidafenacin Uritos Tablets 0.1 mg (Kyorin Pharmaceutical Co., Ltd.) Staybla Tablets 0.1 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval Approval	Imidafenacin	Drugs containing a new active ingredient indicated for the treatment of micturition urgency, pollakiuria, and urge incontinence associated with overactive bladder.
5	Jul. 31, 2007	44	Divigel 1 mg (Pola Pharma Inc.)	Approval	Estradiol	A drug in a new dosage form, or gel, indicated for the treatment of vasomotor symptoms (hot flushes and sweating) associated with menopausal disorders and ovarian deficiency symptoms.
5	Jul. 31, 2007	45	Cialis Tablets 5 mg Cialis Tablets 10 mg Cialis Tablets 20 mg (Eli Lilly Japan K.K.)	Approval Approval Approval	Tadalafil	Drugs containing a new active ingredient indicated for the treatment of erectile dysfunction (patients unable to obtain or maintain erections sufficient for satisfactory sexual activity).
5	May 24, 2007	46	Levitra Tablets 5 mg Levitra Tablets 10 mg Levitra Tablets 20 mg (Bayer Yakuhin Ltd.)	Change Change Approval	Vardenafil hydrochloride hydrate	Drugs with a new dosage indicated for the treatment of erectile dysfunction (patients unable to obtain or maintain erections sufficient for satisfactory sexual activity).
5	Oct. 19, 2007	47	Dinagest Tablets 1 mg (Mochida Pharmaceutical Co., Ltd.)	Approval	Dienogest	A drug containing a new active ingredient indicated for the treatment of endometriosis.
5	Oct. 19, 2007	48	Artcereb Irrigation and Perfusion Solution for Cerebrospinal Surgery (Ostuka Pharmaceutical Factory, Inc.)	Approval	N/A because of a new combination drug	A new combination drug indicated for irrigation during craniotomy/trepanation and spinal surgery, and perfusion during endoscopic neurosurgery.
5	Mar. 19, 2008	49	Bicanate Infusion (Ostuka Pharmaceutical Factory, Inc.)	Approval	N/A because of a combination drug	A combination drug similar to other products indicated for the supply/correction of extracellular fluid in the cases where circulating blood and interstitial fluid decrease, and for the correction of metabolic acidosis.
6-1	Apr. 18, 2007	50	Alvesco 50 μg Inhaler 112 puffs Alvesco 100 μg Inhaler 112 puffs Alvesco 200 μg Inhaler 112 puffs Alvesco 200 μg Inhaler 56 puffs (Teijin Pharma Ltd.)	Approval Approval Approval Approval	Ciclesonide	Drugs containing a new active ingredient indicated for the treatment of asthma.
6-1	Apr. 18, 2007	51	Adoair 100 Diskus Adoair 250 Diskus Adoair 500 Diskus (GlaxoSmithKline K.K)	Approval Approval Approval	Salmeterol xinafoate/Fluticasone propionate	A new combination drug indicated for the treatment of asthma (in the case where a combination of inhaled corticosteroids and inhaled long-acting β_2 agonists is necessary).
6-1	Jul. 31, 2007	52	Singulair Fine Granules 4 mg (Banyu Pharmaceutical Co., Ltd.) Kipres Fine Granules 4 mg (Kyorin Pharmaceutical Co., Ltd.)	Approval Approval	Montelukast sodium	Drugs with a new dosage and in a new dosage form, or fine granules, indicated for the treatment of asthma in children aged 1 or more and less than 6 years.

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
6-1	Sep. 28, 2007	53	Calonal Fine Granules 20%	Change	Acetaminophen	Drugs with a new indication and dosage for use as an antipyretic/analgesic in pediatric patients. Expedited review.
			Calonal Fine Granules 50%	Change		
			Calonal Tablets 200	Change		
			Calonal Tablets 300	Change		
			Calonal Syrup 2%	Change		
			Calonal Suppositories 100	Change		
			Calonal Suppositories 200	Change		
			(Showa Yakuhin Kako Co., Ltd.)			
			Pyrinazin Powder	Change		
			(Astellas Pharma Inc.)			
			Anhiba Suppositories 50 mg for Pediatric Use	Change		
			Anhiba Suppositories 100 mg for Pediatric Use	Change		
			Anhiba Suppositories 200 mg for Pediatric Use	Change		
			(Abbott Japan Co., Ltd.)			
			Pyretinol	Change		
			(Iwaki Seiyaku Co.,Ltd.)			
			Acetaminophen Tablets 200 mg "Isei"	Change		
			(Isei Co., Inc.)			
			Cocarl Dry Syrup 20% for Pediatric	Change		
			Cocarl Dry Syrup 40%	Change		
			Cocarl Tablets 200 mg	Change		
			(Sanwa Kagaku Kenkyusho Co., Ltd.)			
			Paraceta Suppositories 100	Change		
			Paraceta Suppositories 200	Change		
			(Sioe Pharmaceutical Co., Ltd.)			
			Acetaminophen Tablets 200 mg (TYK)	Change		
			Acetaminophen Suppositories 100	Change		
			Acetaminophen Suppositories 200	Change		
			Acetaminophen Fine Granules 20% (TYK)	Change		
			(Taisho Pharmaceutical Co., Ltd.)			
			Calsil Fine Granules 20%	Change		
			Calsil Tablets 200	Change		
			Calsil Syrup 2% for Pediatric Use	Change		
			Calsil Suppositories 200 for Pediatric Use	Change		
			Calsil Suppositories 100 for Pediatric Use	Change		
			(Taiyo Yakuhin Co., Ltd.)			
			Atmiphen Tablets 200	Change		
			Atmiphen Dry Syrup 20%	Change		
			(Takata Seiyaku Co., Ltd.)			
			Acetaminophen Tablets 200 "Tatsumi"	Change		
			Acetaminophen Fine Granules 20% "Tatsumi"	Change		
			(Tatsumi Kagaku Co., Ltd.)			
			Anyrume Tablets 200 mg	Change		
			Anyrume Tablets 300 mg	Change		
			Anyrume S	Change		
			Anyrume S Suppositories 200	Change		
			Anyrume Fine Granules	Change		
			(Choseido Pharmaceutical Co., Ltd.)			
			Atenemen 20% Fine Granules	Change		
			Atenemen Tablets 200 mg	Change		
			Atenemen Suppositories 100 mg	Change		
			Atenemen Suppositories 200 mg	Change		
			(Tsuruhara Pharmaceutical Co., Ltd.)			
			Acetaminophen "Hachi"	Change		
			(Oriental Pharmaceutical and Synthetic Chemical Co., Ltd.)			
			Sarutu Fine Granules 20%	Change		
			Sarutu Tablets 200 mg	Change		
			Sarutu Syrup for Pediatric 2%	Change		
			Sarutu Dry Syrup for Pediatric 20%	Change		
			(Towa Pharmaceutical Co., Ltd.)			
			Aphlogis Suppositories 100	Change		
			Aphlogis Suppositories 200	Change		

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
			(Nissin Pharmaceutical Co., Ltd.)			
			Acetaminophen Tablets 200 mg "NP"	Change		
			Acetaminophen Fine Granules 20%	Change		
			(Nipro Pharma Corporation)			
			Alpiny Suppositories 50	Change		
			Alpiny Suppositories 100	Change		
			Alpiny Suppositories 200	Change		
			(Hisamitsu Pharmaceutical Co., Inc.)			
			Aspain	Change		
			(Maruishi Pharmaceutical Co., Ltd.)			
			Napa	Change		
			Napa Dry Syrup 20%	Change		
			(Merck Seiyaku Ltd.)			
			Acetaminophen "Yoshida"	Change		
			(Yoshida Pharmaceutical Co., Ltd.)			
6-1	Oct. 19, 2007	54	Claritin Tablets 10 mg Claritin RediTabs 10 mg Claritin Dry Syrup 1% (Schering-plough K.K.)	Change Change Approval	Loratadine	Drugs with a new dosage and in a new dosage form, or dry syrup, for use in pediatric patients.
6-1	Jan. 25, 2008	55	Singulair Tablets 5 mg Singulair Tablets 10 (Banyu Pharmaceutical Co., Ltd.) Kipres Tablets 5 mg Kipres Tablets 10 (Kyorin Pharmaceutical Co., Ltd.)	Approval Change Approval Change	Montelukast sodium	Drugs with a new indication and dosage and in a new dosge form for the treatment of allergic rhinitis.
6-1	Jan. 25, 2008	56	Talymus Ophthalmic Suspension 0.1% (Senju Pharmaceutical Co., Ltd.)	Approval	Tacrolimus hydrate	A drug with a new route of administration indicated for the treatment of vernal conjunctivitis (in the case where anti-allergic drugs are not sufficiently effective). [Orphan drug]
6-2	Apr. 18, 2007	57	Myozyme 50 mg for Intravenous Infusion (Genzyme Japan K.K.)	Approval	Alglucosidase alfa (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of type 2 glycogenosis. [Orphan drug]
6-2	Apr. 18, 2007	58	Actonel Tablets 17.5 mg (Takeda Pharmacdeutical Co., Ltd.) Benet Tablets 17.5 mg (Ajinomoto Co., Inc.)	Change Change	Risedronate sodium hydrate	Drugs with a new dosage and in a new dosage form indicated for the treatment of osteoporosis (once-weekly dosing).
6-2	May 24, 2007	59	Glufast Tablets 5 mg Glufast Tablets 10 mg (Kissei Pharmaceutical Co., Ltd.)	Change	Mitiglinide calcium hydrate	Drugs with a new indication for use in combination with α-glucosidase inhibitors to reduce glycemic excursions in patients with type 2 diabetes mellitus in whom diet and exercise therapy is not sufficiently effective.
6-2	Aug. 23, 2007	60	NovoRapid 300 NovoRapid 300 FlexPen NovoRapid 100 U/mL Vial NovoRapid 30 Mix NovoRapid 30 Mix FlexPen (Novo Nordisk Pharma Ltd.)	Approval Approval Approval Approval Approval	Insulin aspart (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of diabetes mellitus where insulin therapy is indicated. A change has been made to the manufacturing process of the drug substance. Pharmaceutical formulations, manufacturing processes, indications, and dosage are the same as those in the approved formulations.
6-2	Oct. 04, 2007	61	Elaprase 6 mg for Intravenous Infusion (Genzyme Japan K.K.)	Approval	Idursulfase (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of mucopolysaccharidosis II. [Orphan drug]
6-2	Oct. 19, 2007	62	Levemir 300 Levemir 300 FlexPen (Novo Nordisk Pharma Ltd.)	Approval Approval	Insulin detemir (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of diabetes mellitus where insulin therapy is indicated.
6-2	Nov. 13, 2007	63	Fastic Tablets 30 Fastic Tablets 90 (Ajinomoto Co., Inc.) Starsis Tablets 30 mg Starsis Tablets 90 mg (Astellas Pharma Inc.)	Change Change Change Change	Nateglinide	Drugs with a new indication for reducing glycemic excursions in patients with type 2 diabetes mellitus (in the case where therapy with biguanides in addition to diet and exercise therapy is not sufficiently effective).

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
6-2	Jan. 25, 2008	64	Nobelzin Capsules 25 mg Nobelzin Capsules 50 mg (Nobelpharma Co., Ltd.)	Approval Approval	Zinc acetate dihydrate	Drugs containing a new active ingredient indicated for the treatment of Wilson's disease (hepatolenticular degeneration). [Orphan drug]
6-2	Mar. 28, 2008	65	Naglazyme 5 mg for Intravenous Infusion (AnGes MG, Inc.)	Approval	Galsulfase (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of mucopolysaccharidosis VI. [Orphan drug]
In vivo Diagnostics	May 24, 2007	66	Magnevist Magnevist Syringe (Nihon Schering K.K.)	Change	Meglumine gadopentetate	A drug with a new dosage for use in magnetic resonance computerized tomography imaging of the brain/spinal cord and body/extremities.
In vivo Diagnostics	Oct. 19, 2007	67	EOB・Primovist Injection Syringe (Bayer Yakuhin Ltd.)	Approval	Gadoxetate sodium	A drug containing a new active ingredient indicated for use in magnetic resonance computerized tomography imaging of liver tumors.
Oncology drugs	Apr. 18, 2007	68	Avastin 100 mg/4 mL for Intravenous Infusion Avastin 400 mg/16 mL for Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Approval Approval	Bevacizumab (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of unresectable advanced/relapsed colorectal cancer. [Priority review]
Oncology drugs	Jul. 31, 2007	69	Metastron Injectable (GE Healthcare Ltd.)	Approval	Strontium (^{89}Sr) chloride	A drug containing a new active ingredient indicated for pain relief in bone scintigraphy-positive metastatic lesions in patients with solid cancers.
Oncology drugs	Aug. 23, 2007	70	TS-1 Capsule 20 TS-1 Capsule 25 (Taiho Pharmaceutical Co., Ltd.)	Change Change	A combination drug of Tegafur, Gimeracil, and Oteracil potassium	Drugs with a new indication for the treatment of biliary cancer in addition to gastric cancer, colorectal cancer, head and neck cancer, non-small cell lung cancer, inoperable or relapsed breast cancer, and pancreatic cancer.
Oncology drugs	Oct. 19, 2007	71	Tarceva Tablets 25 mg Tarceva Tablets 100 mg Tarceva Tablets 150 mg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval Approval	Erlotinib	Drugs containing a new active ingredient indicated for the treatment of unresectable, relapsed/advanced non-small cell lung cancer exacerbated after cancer chemotherapy. [Priority review]
Oncology drugs	Oct. 19, 2007	72	Arranon G Injection 250 mg (GlaxoSmithKline K.K.)	Approval	Nelarabine	A drug containing a new active ingredient indicated for the treatment of relapsed or refractory T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma. [Orphan drug]
Oncology drugs	Dec. 12, 2007	73	Xeloda Tablets 300 (Chugai Pharmaceutical Co., Ltd.)	Change	Capecitabine	A drug with a new indication and dosage for use as a postoperative adjuvant chemotherapy of colon cancer. A drug with a new dosage for the treatment of inoperable or relapsed breast cancer.
Oncology drugs	Dec. 12, 2007	74	Taxol Injection 30 mg Taxol Injection 100 mg (Bristol-Myers K.K.)	Change Change	Paclitaxel	Drugs with a new dosage indicated for the treatment of breast cancer, with once-weekly dosing continuously for 6 weeks followed by a 2-week withdrawal period.
Oncology drugs	Jan. 25, 2008	75	Nexavar Tablets 200 mg (Bayer Yakuhin Ltd.)	Approval	Sorafenib tosilate	A drug containing a new active ingredient indicated for the treatment of unresectable or metastatic renal cell carcinoma. [Priority review]

Category	Approval Date		Trade Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined, new active ingredient)	Notes
Oncology drugs	Jan. 25, 2008	76	1. Zevalin Yttrium (^{90}Y) Injection Set 2. Zevalin Indium (^{111}In) Injection Set (Bayer Yakuhin Ltd.)	Approval Approval	1: Ibritumomab tiuxetan (genetical recombination) Yttrium chloride (90Y) 2: Ibritumomab tiuxetan (genetical recombination) Indium chloride (111In)	1: A drug containing a new active ingredient indicated for the treatment of relapsed or refractory, CD20-positive lyphomas of the following: low-grade B-cell non-Hodgkin's lymphoma and mantle cell lymphoma. 2: A drug containing a new active ingredient indicated for determining the site of ibritumomab tiuxetan (genetical recombination) accumulation. [Orphan drug]
			Rituxan Injection 10 mg/mL (Zenyaku Kogyo K.K.)	Change	Rituximab (genetical recombination)	Pretreatment for indium (111In) ibritumomab tiuxetan (genetical recombination) injection and yttrium (90Y) ibritumomab tiuxetan (genetical recombination) injection. Expedited review.
Oncology drugs	Feb. 29, 2008	77	Herceptin Injection 60 Herceptin Injection 150 (Chugai Pharmaceutical Co., Ltd.)	Change	Trastuzumab (genetical recombination)	Drugs with a new indication and dosage for use as a postoperative adjuvant chemotherapy in patients with HER2-overexpressing breast cancer. [Priority review]
Blood products	Oct. 19, 2007	78	rHSA Bulk Solution Medway Injection 25% Medway Injection 5% (Mitsubishi Tanabe Pharma Corporation) rHSA Bulk Solution—Bipha Stem Injection 25% Stem Injection 5% (Bipha Corporation)	Approval Approval Approval Approval Approval Approval	Human serum albumin (genetical recombination)	Drugs containing a new active ingredient indicated for the treatment of hypoalbuminemia caused by loss of albumin (due to thermal burn, nephrotic syndrome, etc.) and reduced albumin synthesis (cirrhosis, etc.), and hemorrhagic shock.
Biologicals	Oct. 19, 2007	79	Adsorbed Pandemic Influenza Vaccine (H5N1) "Hokken" (The Kitasato Institute)	Approval	Inactivated influenza virus, H5N1 (whole virion)	A drug containing a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
Biologicals	Oct. 19, 2007	80	Adsorbed Pandemic Influenza Vaccine (H5N1) "Biken" (The Research Foundation for Microbial Diseases of Osaka University)	Approval	Inactivated influenza virus, H5N1 (whole virion)	A drug containing a new active ingredient indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
AIDS drugs	Nov. 22, 2007	81	Prezista Tablets 300 mg (Janssen Pharmaceutical K.K.)	Approval	Darunavir ethanolate	A drug containing a new active ingredient indicated for the treatment of HIV infection. [Orphan drug]

Table 2. FY2007 List of Approved Products: New Medical Devices

Category	Approval Date Review time		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Oct. 1, 2007 Total review time: 458 days Regulatory review time: 231 days	1	Excimer Laser Corneal Surgery System EC-5000CXIII (Nidek Co., Ltd.)	Approval	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism, remove corneal surface opacities, and smooth corneal irregularities by laser ablation of corneal tissue. (The original product is in a reexamination period)
1	Jan. 21, 2008 Total review time: 1060 days Regulatory review time: 717 days	2	O_2OPTIX and 8 other trade names (CIBA Vision K.K.)	Change	Instrument & apparatus 72 Soft contact lenses	Oxygen-permeable soft contact lenses using silicone hydrogel, which are indicated for the correction of visual acuity (myopia and hyperopia). Partial change application to add a new intended use of up to 30-day extended wear, which is the first in Japan, to the approved use of daily wear with a 1 month replacement schedule.
1	Feb. 28, 2008 Total review time: 76 days Regulatory review time: 52 days	3	Menicon Lifely (Menicon Co., Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correction of visual acuity	Oxygen-permeable hard contact lenses, which are indicated for daily or up to 30-day extended wear (trade name divisional application of Menicon Tinu, the original product). (The original product is in a reexamination period)
1	Mar. 6, 2008 Total review time: 1742 days Regulatory review time: 650 days	4	Technolas Excimer Laser System (Bausch & Lomb Japan Co., Ltd.)	Approval	Instrument & apparatus 31 Other laser surgical instrument and laser coagulator (ophthalmic excimer laser surgical instrument)	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism by laser ablation of corneal tissue. (The original product is in a reexamination period)
1	Mar. 6, 2008 Total review time: 541 days Regulatory review time: 219 days	5	VISX Excimer Laser System (AMO Manufacturing USA, LLC)	Change	Instrument & apparatus 31 Ophthalmic laser corneal surgery instrument	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism and remove corneal opacities by laser ablation of corneal tissue. Laser-assisted in situ keratomileusis (LASIK) indication was added to previously approved indications, photorefractive keratectomy (PRK) and phototherapeutic keratectomy (PTK). (The original product is in a reexamination period)
3-1	Sep. 28, 2007 Total review time: 457 days Regulatory review time: 245 days	6	ANGIOGUARD XP (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	The first device in Japan to prevent distal emboli with a polyurethane filter to capture and remove embolic substances including thrombi released while a stent is placed in the carotid artery. The effect on the prevention of distal embolization with the use of the stent and the operability were evaluated in clinical studies. [Priority review]
3-1	Sep. 28, 2007 Total review time: 457 days Regulatory review time: 268 days	7	PRECISE for the Carotid Artery (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 7 Stent for the carotid artery	The first stent for the carotid artery in Japan to dilate carotid stenosis and prevent restenosis.The incidence of complications after treatment was evaluated in a clinical study comparing with surgical therapy. [Priority review]
3-2	Oct. 31, 2007 Total review time: 2638 days Regulatory review time: 1045 days	8	SEAMDURA, NEOSEAM (GUNZE Limited)	Approval	Medical products 4 Bioabsorbable artificial dural substitutes	The first bioabsorbable artificial dural substitutes in Japan to compensate for the dural defect. Their clinical performance as dural substitutes was evaluated in clinical studies.
3-2	Feb. 5, 2008 Total review time: 736 days Regulatory review time: 525 days	9	Powerlink Stent Graft System (Cosmotec Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	A stent graft for abdominal aortic aneurysm to prevent blood flow into the aneurysm and its rupture. The incidence of adverse events after treatment was mainly evaluated in clinical studies. (The original product is in a reexamination period)

Category	Approval Date Review time		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
3-2	Mar. 12, 2008 Total review time: 492 days Regulatory review time: 248 days	10	GORE TAG Thoracic Endoprosthesis System (Japan Gore-Tex Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	The first stent graft for thoracic aortic aneurysm in Japan to prevent the blood flow into the aneurysm and its rupture. The incidence of adverse events after treatment was evaluated in a clinical study comparing with surgical therapy. [Priority review]
4	Apr. 13, 2007 Total review time: 71 days Regulatory review time: 55 days	11	SynchroMed EL Pump (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 74 Programmable implantable drug infusion pump	Addition of N'Vision as an applicable programmer to the drug infusion pump indicated for intrathecal baclofen therapy. (Partial change during the reexamination period)
4	May 29, 2007 Total review time: 279 days Regulatory review time: 167 days	12	Concerto C154DWK (Medtronic Japan Co., Ltd)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	Implantable pulse generator that delivers CRT, with function of defibrillator. (The original product is in a reexamination period)
4	Jun. 1, 2007 Total review time: 914 days Regulatory review time: 285 days	13	QuickSite (St. Jude Medical CRMD)	Approval	Instrument & apparatus 7 Implantable pacemaker lead	OTW(Over-The-Wire) type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT(Cardiac Resynchronization Therapy). (The original product is in a reexamination period)
4	Jun. 1, 2007 Total review time: 914 days Regulatory review time: 290 days	14	Epic HF (St. Jude Medical CRMD)	Approval	Instrument & apparatus 12 Other defibrillator and related devices (implantable biventricular pacing pulse generator with defibrillator function)	Implantable pulse generator that delivers CRT, with function of defibrillator. (The original product is in a reexamination period)
4	Jun. 1, 2007 Total review time: 914 days Regulatory review time: 290 days	15	Atlas + HF (St. Jude Medical CRMD)	Approval	Instrument & apparatus 12 Other defibrillator and related devices (implantable biventricular pacing pulse generator with defibrillator function)	Implantable pulse generator that delivers CRT, with function of defibrillator. (The original product is in a reexamination period)
4	Sep. 7, 2007 Total review time: 309 days Regulatory review time: 136 days	16	SynchroMed II Pump (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 74 Programmable implantable drug infusion pump	Drug infusion pump indicated for intrathecal baclofen therapy. (The original product is in a reexamination period)
4	Sep. 28, 2007 Total period: 605 days Regulatory review time: 326 days	17	Intravascular OCT ImageWire (Goodman Co., Ltd.)	Approval	Instrument & apparatus 51 Intravascular optical tomographic catheter	An intravascular optical tomographic catheter that irradiates the vascular wall with near infrared light through internal optical fibers and images for testing the lumens and superficial walls of the coronary arteries by optical coherence tomography (OCT). This is the first medical device in Japan to use OCT for intravascular observation.
4	Sep. 28, 2007 Total review time: 605 days Regulatory review time: 326 days	18	Intravascular OCT Imaging System (Goodman Co., Ltd.)	Approval	Instrument & apparatus 12 OCT diagnostic imaging instrument	A diagnostic imaging system using near infrared light as a light source that images for testing the lumens and superficial walls of the coronary arteries by OCT. This is the first medical device in Japan to use OCT for intravascular observation.

Category	Approval Date Review time		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Dec. 7, 2007 Total review time: 308 days Regulatory review time: 163 days	19	Concerto C174AWK (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	Implantable pulse generator that delivers CRT, with function of defibrillator. (The original product is in a reexamination period)
4	Dec. 27, 2007 Total review time: 202 days Regulatory review time: 83 days	20	Novacor Left Ventricular Assist System (Edwards Lifesciences LLC)	Change	Instrument & apparatus 7 Implantable ventricular assist device	Partial change application to add a new battery because of discontinued battery production and change the controller accordingly. (A partial change during a reexamination period)
4	Feb. 26, 2008 Total review time: 333 days Regulatory review time: 173 days	21	ACUITY Steerable (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable defibrillator/pacemaker lead	OTW(Over-The-Wire) type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT(Cardiac Resynchronization Therapy). (The original product is in a reexamination period)
4	Feb. 28, 2008 Total review time: 183 days Regulatory review time: 180 days	22	QuickSite (St. Jude Medical CRMD)	Change	Instrument & apparatus 7 Implantable defibrillator/pacemaker lead	OTW(Over-The-Wire) type of left ventricular lead used with implantable pulse generators such as CRT-D in CRT(Cardiac Resynchronization Therapy). (Partial change application for extension for shelf life) (The original product is in a reexamination period)
5	Apr. 13, 2007 total review time: 437 days Regulatory review time: 236 days	23	Cool-tip RF System (Tyco Healthcare Japan, Inc.)	Change	Instrument & apparatus 29 Therapeutic electrosurgical unit	A device to coagulate/ablate nonresectable liver tumors using a radiofrequency current (480 kHz). Partial change application mainly to make the generator conform to IEC60601-1-2 (2001). (A partial change during the reexamination period)
5	Apr. 23, 2007 Total review time: 1103 days Regulatory review time: 384 days	24	Given Diagnostic Imaging System (Given Imaging Ltd.)	Approval	Instrument & apparatus 25 Other medical endoscope (capsule electronic endoscope system)	A small intestinal image recording system that consists mainly of a capsule-shaped image transmitter, a sensor array for receiving image data, an image data recorder, and a RAPID workstation for reviewing recorded image data. This is the first medical device in Japan to provide diagnostic images of the small intestinal mucosa through a capsule swallowed by the patient.
6	Mar. 25, 2008 Total review time: 2281 days Regulatory review time: 437 days	25	Dornier Epos Ultra (Dornier MedTech Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Other therapeutic or surgical instruments (electromagnetic induction-type extracorporeal shock wave therapy system)	A low-energy extracorporeal shock wave therapy system for orthopedic use. This is the first device in Japan to relieve the pain of chronic plantar fasciitis with reduced output of the conventional electromagnetic induction-type extracorporeal shock wave lithotripter.
Office of Biologics II	Oct. 29, 2007 Total review time: 1118 days Regulatory review time: 540 days	26	JACE (Japan Tissue Engineering Co., Ltd.)	Approval	Medical products 4 Other surgical/orthopedic materials (autologous cultured epidermis)	Autologous cultured keratinocytes using Green's technique in which keratinocytes derived from the patient's own skin tissue are co-cultured with irradiated 3T3-J2 cells derived from mouse fetuses as a feeder to form a sheet in approximately three to seven layers thick. This is indicated for the treatment of serious large burns that cannot be provided with a sufficient area of donor skin for autologous skin grafting, and of burns in which the total area of deep second-degree (deep dermal) and third-degree (full-thickness) burn is 30% or more of the total body surface area. It is the first medical device of processed human cellullar/tissue product in Japan. [Priority review]

Table 3. FY2007 List of Approved Products: Medical Devices Approved with Clinical Data (Other Than New Medical Devices)

Category	Approval Date Review Time		Trade Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	May 22, 2007 Total review time: 475 days Regulatory review time: 347 days	1	SEED UV-1 (SEED Co., Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correction of visual acuity	Hard contact lenses that are made mainly of methacrylate monomers and that are indicated for daily or up to 1-week extended wear. These lenses have been specially designed to ensure sufficient oxygen permeability and strength. They use a new raw material constituted of a new combination of four already-approved monomers in a new ratio. Clinical studies were mainly conducted to evaluate the safety of these lenses in the eyes.
1	Jun. 19, 2007 Total review time: 627 days Regulatory review time: 335 days	2	Alcon AcrySof ReSTOR Single-Piece (Alcon Japan Ltd.)	Approval	Instrument and apparatus 72 Multifocal posterior chamber lens	Foldable multifocal posterior chamber lens with 12 toric diffraction regions in the anterior center. A new lens design with a diffraction structure that diffracts the incident light into near and far fields is used, and the lens has two focal points. Clinical studies were conducted to evaluate whether the structure provides the expected performance, efficacy, and safety of this product.
1	Jun. 28, 2007 Total review time: 1651 days Regulatory review time: 711 days	3	Moistear and 5 other trade names (Koken Co., Ltd)	Approval	Medical products 4 Other ophthalmic products and related products (punctal plug)	A punctal plug made of atelocollagen to retain tear volume by lacrimal duct occlusion as a symptomatic treatment for aqueous tear deficiency (dry eye). Unlike the conventional silicone plug, the atelocollagen solution is the first medical device intended to achieve embolization by gelatinizing the solution injected into the lacrimal duct at body temperature. Clinical studies were conducted to evaluate the efficacy of this product and the safety of atelocollagen in the eyes.
1	Feb. 5, 2008 Total review time: 427 days Regulatory review time: 302 days	4	O_2OPTIX 2-Week (CIBA VISION K.K.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correction of visual acuity	Soft contact lenses indicated for daily or up to 2-week extended wear, made of a new raw material, silicone hydrogel, with a new combination of the raw materials used in the approved product O_2OPTIX (approval no., 21600BZY00383000) for higher water content. Both spherical and toric lens designs were used. Because a new raw material is used, comparative clinical studies were conducted to evaluate the safety of this product.
1	Feb. 25, 2008 Total review time: 1083 days Regulatory review time: 503 days	5	HiResolution Bionic Ear System (Nihon Bionics Co., Ltd.)	Approval	Instrument & apparatus 7 Other sensory assisting instrument (cochlear implant system)	A cochlear implant system with a new sound processing strategy (HiRes) with higher stimulation rates. Clinical studies were mainly conducted to evaluate the efficacy of HiRes and the safety of this implant whose material and shape differ from those of the conventional product.
1	Mar. 3, 2008 Total review time: 987 days Regulatory review time: 539 days	6	Cataract Surgery INFINITI Vision System (Alcon Japan Ltd.)	Approval	Instrument & apparatus 12 Cataract and vitreous surgery instrument	A surgical system used for extracapsular cataract extraction and anterior vitrectomy that performs various functions such as irrigation, aspiration, phacoemulsification, vitrectomy, and cauterization or coagulation. This product is a system that adds the AquaLase function which delivers balanced saline solution (BSS) to fragment cataracts with fluidic pulses to the approved Ultrasonic Cataract Surgery INFINITI Vision System (approval No. 21500BZY00342000). Because the AquaLase function was introduced for the first time in Japan, clinical studies were conducted to evaluate its clinical use.
1	Mar. 25, 2008 Total review time: 795 days Regulatory review time: 578 days	7	HOYA Airy One month (HOYA Corporation)	Approval	Instrument & apparatus 72 Reusable colored contact lens for correction of visual acuity	Silicone hydrogel soft contact lenses made of a new silicone-containing monomer that are indicated for daily or up to 30-day extended wear. Lenticular lens designs were used. Clinical studies were mainly conducted to evaluate the safety of the lenses made of a new raw material.
3-1	Jun. 7, 2007 Total review time: 1224 days Regulatory review time: 329 days	8	Angio-Seal STS PLUS (Getz Bros. Co., Ltd. [Japan])	Approval	Medical products 4 Bioresorbable local hemostatic device	A device to achieve hemostasis at the femoral artery puncture site after percutaneous catheterization by sandwiching the vascular wall between the anchor from the inside of the punctured vascular wall and the collagen sponge and bioresorbable suture from the outside. This product improves ease of use and suture knotting than the conventional product. Clinical studies were mainly conducted to evaluate whether the device has a hemostatic effect comparable to that of the conventional product.
3-1	Jul. 11, 2007 Total review time: 378 days Regulatory review time: 228 days	9	Express LD Vascular Stent (Boston Scientific Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Stent for iliac arteries	A balloon-expandable stent for iliac arteries. Delivery of this stent is easier because the delivery catheter of this stent has a smaller diameter than those of the conventional products of other companies. The clinical performance (including restenosis rate) of the stent was evaluated in clinical studies.

Category	Approval Date Review Time		Trade Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
3-1	Oct. 23, 2007 Total review time: 337 days Regulatory review time: 256 days	10	NSE PTCA Balloon Catheter (Goodman Co., Ltd.)	Approval	Instrument & apparatus 51 Balloon-expandable catheter for coronary angioplasty	A device in which slipping on balloon expansion is reduced by placing elements along the balloon of the PTCA balloon catheter. Clinical studies were conducted to evaluate the slipping-reducing effect of this product and the safety of the elements.
3-1	Jan. 18, 2008 Total review time: 505 days Regulatory review time: 336 days	11	AngioSculpt PTCA Balloon Catheter (USCI Japan Ltd.)	Approval	Instrument & apparatus 51 Balloon-expandable catheter for coronary angioplasty	A PTCA balloon catheter with a wire outside the balloon to reduce the slipping on expansion. The slipping-reducing effect and safety of the improved product were evaluated in clinical studies.
4	Jun. 1, 2007 Total review time: 914 days Regulatory review time: 285 days	12	Aescula (St. Jude Medical CRMD)	Approval	Instrument & apparatus 7 Implantable pacemaker lead	Left ventricular lead with stylet used with implantable pulse generators such as CRT-D in CRT(Cardiac Resynchronization Therapy).
4	Jun. 4, 2007 Total review time: 349 days Regulatory review time: 290 days	13	Sleep Recorder SD-101 (Kenzmedico Co., Ltd.)	Approval	Instrument & apparatus 21 Instrument for sleep evaluation	A simple testing instrument for sleep apnea syndrome that records and analyzes respiratory waveforms during sleep. It can be used at home as well as in hospitals. It is placed on a mattress, detects subtle pressure changes in parts of the body surface associated with respiration, and expresses them as waveforms. It can measure pressure changes for up to 10 hours under unrestrained conditions. Because this product uses a novel method of detecting respiratory waveforms, it was compared in clinical studies with polysomnography (PSG), the standard test method for sleep apnea syndrome.
4	Jul. 9, 2007 Total review time: 830 days Regulatory review time: 279 days	14	IBI Cardiac Ablation System II (Getz Bros Co., Ltd.)	Approval	Instrument & apparatus 31 Medical cautery instrument	An instrument that electrophysiologically detects the abnormal conduction pathways in the heart with arrhythmia and that ablates these pathways. Major improvements in this product as compared to the conventional product include two temperature sensors for the ablation site to ensure safety and the ability increase the output up to 100 W. Clinical studies were conducted to evaluate the safety of the increased output.
4	Jul. 26, 2007 Total review time: 437 days Regulatory review time: 122 days	15	Revolution (Goodman Co., Ltd.)	Approval	Instrument & apparatus 51 Intravascular ultrasonic catheter for the central circulatory system	A catheter for intravascular ultrasonic diagnostic imaging that incorporates an ultrasonic transducer for ultrasound imaging of the vascular lumen and wall. The ultrasonic frequency was improved to 45 MHz. Clinical results were submitted mainly to evaluate the adverse events associated with the use of this system.
4	Jul. 26, 2007 Total review time: 437 days Regulatory review time: 118 days	16	Volcano In-Vision Gold Imaging System (Goodman Co., Ltd.)	Approval	Instrument & apparatus 12 Cardiovascular ultrasonic diagnostic imaging instrument	A diagnostic imaging instrument intended to image and test the vascular lumen and wall using ultrasound. The ultrasonic frequency has been improved to 45 MHz. Clinical studies were mainly conducted to evaluate the adverse events associated with the use of this system.
4	Oct. 1, 2007 Total review time: 579 days Regulatory review time: 247 days	17	Navistar DS (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter used in myocardial with radiofrequency current and for the electrophysiological examination of the heart to treat type I atrial flutter. It has one 8-mm tip electrode, two temperature sensors, and a maximum power output of 70 W. Clinical studies were conducted because both the electrode length and output in this product is different from that in the conventional product.
4	Nov. 21, 2007 Total review time: 307 days Regulatory review time: 148 days	18	Medtronic Virtuoso DR (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Dual-chamber automatic implantable defibrillator	Implantable defibrillator used to automatically detect and treat atrial fibrillation/tachycardia and ventricular fibrillation/tachycardia. Clinical study results were submitted to evaluate the MVP function (to give priority to self atrioventricular conduction and inhibit unnecessary ventricular pacing), atrial cardioversion function, and atrial antitachycardia pacing function.

Category	Approval Date Review Time		Trade Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
5	Nov. 7, 2007 Total review time: 854 days Regulatory review time: 522 days	19	Toraysulfone HDF (Toray Industries, Inc.)	Approval	Instrument & apparatus 7 Hemodialysis filter	A hemodiafilter using hollow fibers made of polysulfone resin to remove metabolites (including urea, creatinine, water, etc.) in blood during hemodiafiltration for patients with acute and chronic renal failure. Clinical investigation was conducted to evaluate its efficacy and safety because it was the first time that polysulfone resin was used as a raw material of hollow fibers of hemodiafilter.
6	May 8, 2007 Total review time: 768 days Regulatory review time: 253 days	20	CentPillar TMZF Stem (Striker Japan K.K.)	Approval	Medical products 4 Hip prosthesis	A cementless stem made of a titanium alloy for use as a femoral component in hip replacement. The proximal portion of the stem is subjected to surface roughening by plasma spraying of pure titanium followed by plasma coating with hydroxyapatite. Because of the novelty of the raw material and special surface treatment method employed, clinical studies were conducted to evaluate the efficacy and safety of this product in clinical use.
6	Jun. 4, 2007 Total review time: 809 days Regulatory review time: 186 days	21	Trident HA Acetabular Cup System (Striker Japan K.K.)	Approval	Medical products 4 Hip prosthesis	A component system consisting of a shell, dome-hole plug, and ceramic liner used as a acetabular component in hip replacement. Beacuse of the novelty of the ceramic liner into which ceramic and metal layers are integrated and the special shell surface treatment employed, clinical studies were conducted to evaluate the efficacy and safety of this product in clinical use.
6	Jun. 11, 2007 Total review time: 1200 days Regulatory review time: 250 days	22	LactoSorb (Biomet Microfixation, Inc.)	Approval	Medical products 4 Bone setting assembly	An absorbable bone setting assembly made of the copolymer of L-lactate and glycolate. This product was given overseas manufacturing approval as screws, plates, and mesh used for bone setting and reconstruction to treat cranial and facial bone trauma. The improvement in this device is that an absorbable coplymer which has not yet been approved for use as a raw material is used as the raw material. Clinical studies were conducted to evaluate whether the absorption rate of this product is safe for clinical use.
6	Aug. 3, 2007 Total review time: 855 days Regulatory review time: 251 days	23	K-MAX AHT HIP System (Japan Medical Materials Corporation)	Approval	Medical products 4 Hip prosthesis	A system consisting of a titanium alloy stem, an outer cup (both cementless), and screws used for the total hip replacement, partial hip replacement, etc. The proximal portion of the stem and the surface of the outer cup are subjected to surface roughening by spraying pure titanium followed by alkaline heat treatment, and the screw heads are subjected to alkaline heat treatment. Because of the novelty of the surface treatment employed, clinical studies were conducted to evaluate whether this product is effective and safe for clinical use.
6	Oct. 1, 2007 Total review time: 1084 days Regulatory review time: 561 days	24	Aquacel Ag (Bristol-Myers Squibb K.K.)	Approval	Medical products 4 Antimicrobial material	An antimicrobial dressing consisting of 100% fibrous sodium carboxymethylcellulose and silver used to protect wounds deep into the subcutaneous fat tissue, while maintaining a moist environment, promoting healing, and relieving pain. Expected secondary effects include antimicrobial effect of the silver ion on the bacteria existing inside the dressing and at the wound contact area. Clinical studies were conducted to evaluate the antimicrobial activity, wound-healing effect, and safety of this product.
6	Nov. 21, 2007 Total review time: 1274 days Regulatory review time: 299 days	25	Sterile CFRP Cage (Medtronic Sofamor Danek, Co., Ltd.)	Approval	Medical products 4 Bone setting assembly	A spinal cage made of a carbon fiber-reinforced polymer (CFRP). Because the material used in this product is different from that in the approved product, which is made of a titanium alloy, clinical studies were conducted to evaluate whether the product is effective and safe for clinical use.
8	May 30, 2007 Total review time: 1098 days Regulatory review time: 406 days	26	Proton Beam Therapy System PROBEAT (PT-W01) (Hitachi, Ltd.)	Approval	Instrument & apparatus 83 Other medical charged-particle radication therapy system (Proton beam therapy system)	A radiotherapy system using high-energy proton beam. It can shape the dose distribution of proton beam emitted from a synchrotron accelerator (beam energy, 80–200 MeV) to conform three-dimensionally to the size and shape of the affected site, and irradiate the site horizontally and vertically. (On application, the original product is in a reexamination period)
8	Jan. 23, 2008 Total review time: 1784 days Regulatory review time: 944 days	27	Noninvasive Hemoglobin Analyzer R02M (Sysmex Corporation)	Approval	Instrument & apparatus 21 Other single-person bioinformation monitor and related instruments (noninvasive hemoglobin analyzer)	This device irradiates a finger with infrared to near-infrared light and noninvasively measures the amount of light absorption by hemoglobin in the peripheral blood. The pulse oxymeter uses a similar principle to show the oxygen saturation in the arterial blood, whereas the new device is intended for use in screening for severe and moderate anemia and uses a new indicator correlating with blood hemoglobin concentration to show hemoglobin levels in five levels. Clinical studies were conducted to evaluate whether it can be used in screening for anemia as an indicator of hemoglobin levels.

Table 4. Safety Measures Implemented by MHLW and Revision of PRECAUTIONS for Pharmaceuticals, etc. in FY 2007

Safety measures implemented by MHLW in FY 2007

	Pharmaceuticals	Medical devices
Instructions for Revision of PRECAUTIONS	132	6
Publishing information on the Phamaceuticals and Medical Devices Safety Information	24	5

Note: In FY 2007, no instructions for self-inspection of medical devices were issued.

Revision to PRECAUTIONS in the Package Inserts of Pharmaceuticals, instructed by MHLW in FY 2007

Date	Drug name
Apr. 13, 2007	1. Oseltamivir Phosphate
Apr. 19, 2007	1. Pergolide Mesilate 2. Cabergoline
Apr. 27, 2007	1. Risperidone 2. Gadodiamide Hydrate 3. Ampiroxicam 4. Piroxicam (oral dosage form, suppository dosage form) 5. Nisoldipine 6. Theophylline (extended-release oral dosage form) (including pediatric dosage and administration) 7. Oxaliplatin 8. Arsenic Trioxide 9. Miconazole 10. Ivermectin
Jun. 1, 2007	1. Zopiclone 2. Zolpidem Tartrate 3. Triazolam 4. Mycophenolate Mofetil 5. Carboplatin
Jul.6, 2007	1. Alteplase (genetical recombination) 2. Meropenem Trihydrate 3. Oxycodone Hydrochloride Hydrate 4. Amobarbital Barbital Phenobarbital (oral dosage form) Bromovalerylurea Pentobarbital Calcium Chloral Hydrate (oral dosage form) 5. Estazolam Nitrazepam Nimetazepam Haloxazolam Flurazepam Hydrochloride Lormetazepam 6. Quazepam Flunitrazepam (oral dosage form) Brotizolam Rilmazafone Hydrochloride 7. Ambroxol Hydrochloride 8. Fluticasone Propionate (inhalant dosage form) 9. Infliximab (genetical recombination) 10. Etanercept (genetical recombination) 11. Ribavirin (tablet dosage form) Peginterferon Alfa-2a (genetical recombination)
Aug. 8, 2007	1. Telithromycin

Date	Drug name
Aug. 10, 2007	1. Dried Thyroid Levothyroxine Sodium Hydrate 2. Cyclofenil 3. Silodosin 4. Disulfiram 5. Entecavir Hydrate 6. Recombinant Adsorbed Hepatitis B Vaccine (yeast origin) 7. Freeze-dried Live Attenuated Measles and Rubella Combined Vaccine
Sep. 7, 2007	1. Pralidoxime Iodide 2. Accu-Chek Aviva Test Strips 3. Cyclic GB Sensor LFS Quick Sensor Ascensia Easyfill Sensor Ascensia Autodisc Sensor Glutest Sensor Dia Sensor G Sensor Glutest Neo Sensor 4. Blood Glucose Test Kit Blood Glucose Self-monitoring Kit (Excluding Accu-Chek Aviva Test Strips, Cyclic GB Sensor, LFS Quick Sensor, Ascensia Easyfill Sensor, Ascensia Autodisc Sensor, Glutest Sensor, Dia Sensor, G Sensor, Glutest Neo Sensor)
Sep. 21, 2007	1. Amiodarone Hydrochloride (oral dosage form) 2. Amiodarone Hydrochloride (injectable dosage form) 3. Methylphenidate Hydrochloride 4. Tiapride Hydrochloride 5. Verteporfin 6. Liothyronine Sodium 7. Finasteride 8. Pyridoxal Phosphate Pyridoxal Calcium Phosphate Pyridoxine Hydrochloride 9. Miglitol 10. Etidronate Disodium 11. Anastrozole 12. Ceftriaxone Sodium

Date	Drug name
Oct. 31, 2007	1. Tizanidine Hydrochloride 2. Atorvastatin Calcium Hydrate 3. Thiamazole 4. Amitriptyline Hydrochloride Imipramine Hydrochloride Clomipramine Hydrochloride (oral dosage form) Dosulepin Hydrochloride Trazodone Hydrochloride Mianserin Hydrochloride 5. Amoxapine 6. Clomipramine Hydrochloride (injectable dosage form) 7. Setiptiline Maleate Trimipramine Maleate Nortriptyline Hydrochloride Maprotiline Hydrochloride Lofepramine Hydrochloride 8. Sertraline Hydrochloride 9. Paroxetine Hydrochloride Hydrate 10. Fluvoxamine Maleate 11. Milnacipran Hydrochloride 12. Gemeprost 13. Idarubicin Hydrochloride 14. Gadopentetate Dimeglumine 15. Advantage Test Strips S
Nov. 30, 2007	1. Flurbiprofen (oral dosage form) 2. Flurbiprofen Axetil 3. Botulinum Toxin Type A 4. Everolimus 5. Garenoxacin Mesilate Hydrate
Dec. 26, 2007	1. Amantadine Hydrochloride
Dec. 26, 2007	1. Zanamivir Hydrate
Jan. 10, 2008	1. GEM-Premier 3000 PAK 2. Ezetimibe 3. L-Carbocisteine 4. Goserelin Acetate (3.6 mg) 5. Goserelin Acetate (10.8 mg) 6. Doripenem Hydrate 7. Oseltamivir Phosphate 8. Terbinafine Hydrochloride (oral dosage form) 9. Yellow Fever Vaccine 10. Over-the-counter Drugs Containing L-Carbocisteine 11. Over-the-counter Drugs Polygoni Multiflori Radix

Date	Drug name
Feb. 12, 2008	1. Pramipexole Hydrochloride Hydrate 2. Ropinirole Hydrochloride 3. Cyclophosphamide (oral dosage form) 4. Cyclophosphamide (injectable dosage form) 5. Talipexole Hydrochloride 6. Nicorandil (oral dosage form) 7. Moxifloxacin Hydrochloride (oral dosage form)
Mar. 21, 2008	1. Desmopressin Acetate (drug products with the indication for nocturnal enuresis) 2. Desmopressin Acetate (drug products with the indication for central diabetes insipidus) 3. Clopidogrel Sulfate 4. Biapenem 5. Garenoxacin Mesilate Hydrate

Note: Detailed information is available on the Agency's Post-marketing Safety Information website on pharmaceuticals and medical devices.

Table 5. Revision of PRECAUTIONS for and Instructions for Self-inspection of Medical Devices in FY 2007

Revision of PRECAUTIONS for Medical Devices

Date	Title
Apr. 27, 2007	Provision of Guidelines on Standard Connection Procedures and Appropriate Safety Education for the Use of Artificial Heart-Lung Machines, and MHLW-ordered Revision of PRECAUTIONS regarding artificial heart-lung machines
Jun. 15, 2007	MHLW-ordered revisions to package insert regarding feeding tubes for enteral alimentation
Aug. 3, 2007	MHLW-ordered Revision of PRECAUTIONS regarding needleless devices
Sep. 7, 2007	MHLW-ordered Revision of PRECAUTIONS regarding blood glucose meters for self-monitoring
Sep. 21, 2007	MHLW-ordered Revision of PRECAUTIONS regarding the interaction between implantable cardioverter defibrillators and antiarrhythmic drugs
Feb. 27, 2008	MHLW-ordered revisions to package insert regarding drug-eluting coronary stents

Note: Detailed information is available on the Agency's Post-marketing Safety Information website on pharmaceuticals and medical devices.

Instructions for Self-inspection of Medical Devices

In FY 2007, no instructions for self-inspection of medical devices were made.

Table 6. FY 2007 Pharmaceuticals and Medical Devices Safety Information (No. 235-245)

Date	No.	Contents
Apr. 26, 2007	235	1. Uniformity in drop rate of infusion and transfusion sets 2. Project for Japan Drug Information Institute in Pregnancy 3. Safety information available on PMDA website designed to provide information on pharmaceuticals and medical devices 4. List of products subject to Early Post-marketing Phase Vigilance (Reference material) 1. Information on Oseltamivir Phosphate 2. The outlook for pharmacogenomics (Genetic polymorphisms and Warfarin therapy)
May 31, 2007	236	1. Information on post-marketing safety measures for Ticlopidine Hydrochloride and Taxus Express2 coronary stent systems 2. Important Safety Information 1. Edaravone 2. Amiodarone (oral dosage form) 3. Cibenzoline Succinate (oral dosage form) 3. Revision of PRECAUTIONS (No. 186) Oseltamivir Phosphate and 11 others 4. List of products subject to Early Post-marketing Phase Vigilance
Jun. 27, 2007	237	1. The effect of UHF-band RFID devices and advanced-system mobile phones on cardiac pacemakers and other implantable devices 2. Important Safety Information 1. Gadodiamide Hydrate 2. Cabergoline 3. Pergolide Mesilate 4. Risperidone 3. Revision of PRECAUTIONS (No. 187) 1. Ampiroxicam and 7 others 2. Medical devices that are components of artificial heart-lung machines including oxygenators, blood pumps, blood circuits 4. List of products subject to Early Post-marketing Phase Vigilance (Reference material) 1. Manuals for management of individual serious adverse drug reactions 2. Guidelines on standard connection procedures and appropriate safety education for the use of artificial heart-lung machines
Jul. 31, 2007	238	1. Important Safety Information 1. Zolpidem Tartrate 2. Zopiclone 2. Revision of PRECAUTIONS (No. 188) 1. Triazolam and 2 others 2. Enteral tubes and gastric feeding tubes for enteral alimentation (only components with a stylet or guidewire) and 2 others 3. List of products subject to Early Post-marketing Phase Vigilance
Aug. 30, 2007	239	1. Important Safety Information 1. Alteplase (genetical recombination) 2. Oxycodone Hydrochloride Hydrate 3. Meropenem Trihydrate 2. Revision of PRECAUTIONS (No. 189) 1. Amobarbital and 7 others 3. List of products subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
Sep. 27, 2007	240	1. Reports of the adverse effects of influenza vaccines in FY 2006 2. Revision of PRECAUTIONS (No. 190) 1. Telithromycin and 7 others 2. Needleless devices that connect to internal fluid flow channels and 1 other 3. List of products subject to Early Post-marketing Phase Vigilance
Nov. 29, 2007	241	1. "PMDA medical safety information" is new posted on the Pharmaceuticals and Medical Devices Information Website 2. Important Safety Information 1. Amiodarone Hydrochloride (oral dosage form), Amiodarone Hydrochloride (injectable dosage form) 3. Revision of PRECAUTIONS (No. 191) (1) Drugs: Pralidoxime Iodide and 13 others (2) Medical Devices: Glucose meters for self-monitoring and 5 others 4. List of products subject to Early Post-marketing Phase Vigilance
Dec. 26, 2007	242	1. Important Safety Information 1. Atorvastatin Calcium Hydrate 2. Tizanidine Hydrochloride 3. Thiamazole 2. Revision of PRECAUTIONS (No. 192) 1. Amitriptyline Hydrochloride and 11 others 3. List of products subject to Early Post-marketing Phase Vigilance
Jan. 29, 2008	243	1. Revision of PRECAUTIONS (No. 193) Flurbiprofen (oral dosage form) and 6 others 2. List of products subject to Early Post-marketing Phase Vigilance (Reference Material) 1. About Oseltamivir Phosphate (Tamiflu) <The brief summary of the review results by the Subcommittee on Drug Safety (held on December 25, 2007)>
Feb. 28, 2008	244	1. Revision of PRECAUTIONS (No. 194) GEM-Premier 3000 PAK and 10 others 2. List of products subject to Early Post-marketing Phase Vigilance
Mar. 27, 2008	245	1. Treatment of hepatitis viral with interferon products 2. Sudden onset of sleep, etc. associated with non-ergoline dopamine agonists (patients must be advised to refrain from driving, etc.) 3. Important Safety Information 1. Cyclophosphamide (oral dosage form), Cyclophosphamide (injectable dosage form) 4. Revision of PRECAUTIONS (No. 195) Nicorandil (oral dosage form) and 1 other 5. List of products subject to Early Post-marketing Phase Vigilance

Note: Detailed information is available at the Agency's Post-marketing Safety Information website on pharmaceuticals and medical devices.

Table 7. PMDA Medical Safety Information

No.	Date published	Title
1	Nov. 2007	Points to note in case of obstruction of feeding tube
2	Nov. 2007	Recall of Resuscitators
3	Jan. 2008	Precautions against improper connection of speech valves etc. to tracheostomy tubes

** Detailed information is available at the Agency's Post-marketing Safety Information website on pharmaceuticals and medical devices.*

Table 8. Lists of User Fees (partially revised on April 1, 2007; refer to the Attachment revised on April 1, 2008 for a comparison of former and revised fees.)

List of user fees for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Pharmaceutical Affairs Law (Law No. 145, 1960)

Note: The lower rows in the User fees column indicate the articles on user fees to MHLW in the Cabinet Ordinance on Fees related to the Pharmaceutical Affairs Law.

(Yen)

Classification			User fees		
			Review	Conformity	Total
Investigation for manufacturing license of drugs					
New license		On-site		148,100	148,100
				Article 16 (1) 1-a	
		Document		111,500	111,500
				Article 16 (1) 1-b	
Change/Addition of classification		On-site		97,400	97,400
				Article 16 (1) 2-a	
		Document		55,300	55,300
				Article 16 (1) 2-b	
Renewal of existing license		On-site		97,400	97,400
				Article 16 (1) 3-a	
		Document		55,300	55,300
				Article 16 (1) 3-b	
Investigation for foreign manufacturers accreditation of drugs					
New accreditation		On-site		133,300 + travel expences	133,300 + travel expences
				Article 16 (2) 1-a	
		Document		58,100	58,100
				Article 16 (2) 1-b	
Change/Addition of classification		On-site		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 2-a	
		Document		39,700	39,700
				Article 16 (2) 2-b	
Renewal of existing accreditation		On-site		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 3-a	
		Document		39,700	39,700
				Article 16 (2) 3-b	
Drug review (new approval)					
New drug 1 (non-orphan drugs)		First application items	23,788,100	6,559,600	30,347,700
			Article 17 (1) 1-a (1)	Article 17 (2) 1-a	
		Applications with different dosage etc.	2,464,000	1,639,800	4,103,800
			Article 17 (1) 1-a (3)	Article 17 (2) 1-c	
New drug 1 (orphan drugs)		First application items	19,934,100	3,286,000	23,220,100
			Article 17 (1) 1-a (2)	Article 17 (2) 1-b	
		Applications with different dosage etc.	2,061,500	818,100	2,879,600
			Article 17 (1) 1-a (4)	Article 17 (2) 1-d	
New drug 2 (non-orphan drugs)		First application items	11,353,100	2,463,200	13,816,300
			Article 17 (1) 1-a (5)	Article 17 (2) 1-e	
		Applications with different dosage etc.	1,174,300	615,900	1,790,200
			Article 17 (1) 1-a (6)	Article 17 (2) 1-f	
New drug 2 (orphan drugs)		First application items	9,345,700	1,232,500	10,578,200
			Article 17 (1) 1-a (7)	Article 17 (2) 1-g	
		Applications with different dosage etc.	1,004,100	310,100	1,314,200
			Article 17 (1) 1-a (8)	Article 17 (2) 1-h	
Generic prescription drugs (with conformity audits)			412,100	214,000	626,100
			Article 17 (1) 1-a (9)	Article 17 (2) 1-i	
OTC drugs			110,300		110,300
			Article 17 (1) 1-a (10)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17 (1) 1-a (13)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17 (1) 1-a (12)		
		Addition of series	60,300		60,300
			Article 17 (1) 1-a (11)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17 (1) 1-b, c		
New application of change or replacement of brand name			35,600		35,600
			Article 17 (1) 1-e		

Classification				User fees		
				Review	Conformity	Total
(Approval for partial changes to approved matters)						
	New drug 1 (other than orphan)	Changes in indications	First application items	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
		Other		205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
	New drug 1 (orphan)	Changes in indications	First application items	8,434,300	1,232,500	9,666,800
				Article 17 (1) 2-a (4)	Article 17 (2) 2-d	
			Applications with different dosage etc.	875,600	310,100	1,185,700
				Article 17 (1) 2-a (5)	Article 17 (2) 2-e	
		Other		132,700	109,800	242,500
				Article 17 (1) 2-a (6)	Article 17 (2) 2-f	
	New drug 2 (other than orphan)	Changes in indications	First application items	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
		Other		205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
	New drug 2 (orphan)	Changes in indications	First application items	8,434,300	1,232,500	9,666,800
				Article 17 (1) 2-a (4)	Article 17 (2) 2-d	
			Applications with different dosage etc.	875,600	310,100	1,185,700
				Article 17 (1) 2-a (5)	Article 17 (2) 2-e	
		Other		132,700	109,800	242,500
				Article 17 (1) 2-a (6)	Article 17 (2) 2-f	
	Generic drugs (with compliance audit)	Changes in indications	First application items	10,190,500	2,463,200	12,653,700
				Article 17 (1) 2-a (1)	Article 17 (2) 2-a	
			Applications with different dosage etc.	1,057,400	615,900	1,673,300
				Article 17 (1) 2-a (2)	Article 17 (2) 2-b	
		Other		205,100	120,700	325,800
				Article 17 (1) 2-a (3)	Article 17 (2) 2-c	
	OTC drugs			56,400		56,400
				Article 17 (1) 2-a (7)		
	In vitro diagnostics (without approval standards)			295,800		295,800
				Article 17 (1) 2-a (10)		
	In vitro diagnostics (with approval standards)		Basic	143,500		143,500
				Article 17 (1) 2-a (9)		
			Addition of series	31,900		31,900
				Article 17 (1) 2-a (8)		
	Quasi-drugs and cosmetics			35,600		35,600
				Article 17 (1) 2-b, c		
GMP audit of drugs						
	Approval, partial change and manufacture for export	New drugs	Domestic		739,800	739,800
					Article 17 (4) 1-b (1)	
			Overseas		933,500 + travel expences	933,500 + travel expences
					Article 17 (4) 1-b (2)	
		Biological drugs/ Radiopharmaceuticals	Domestic		666,100	666,100
					Article 17 (4) 1-a (1)	
			Overseas		844,400 + travel expences	844,400 + travel expences
					Article 17 (4) 1-a (2)	
		Sterilized drugs/ sterilized quasi-drugs	Domestic		201,300	201,300
					Article 17 (4) 1-c (1)	
			Overseas		229,800 + travel expences	229,800 + travel expences
					Article 17 (4) 1-c (2)	
		Drugs and quasi-drugs other than the above	Domestic		141,200	141,200
					Article 17 (4) 1-d (1)	
			Overseas		155,400 + travel expences	155,400 + travel expences
					Article 17 (4) 1-d (2)	
		Package, labeling, storage, external testing etc.	Domestic		63,800	63,800
					Article 17 (4) 2-a, Article 17 (5) 1-a	
			Overseas		84,800 + travel expences	84,800 + travel expences
					Article 17 (4) 2-b, Article 17 (5) 1-b	

Classification					User fees		
					Review	Conformity	Total
	Renewal of the above	Biological drugs/Radio-pharma-ceuticals	Basic	Domestic		436,000	436,000
						Article 17 (4) 3-a(1)	
				Overseas		554,200 + travel expences	554,200 + travel expences
						Article 17 (4) 3-a (2)	
			Addition of items	Domestic		30,500	30,500
						Article 17 (4) 3-a (1)	
				Overseas		30,500	30,500
						Article 17 (4) 3-a (2)	
		Sterilized drugs/ sterilized quasi-drugs	Basic	Domestic		380,000	380,000
						Article 17 (4) 3-b (1)	
				Overseas		480,000 + travel expences	480,000 + travel expences
						Article 17 (4) 3-b (2)	
			Addition of items	Domestic		12,400	12,400
						Article 17 (4) 3-b (1)	
				Overseas		12,400	12,400
						Article 17 (4) 3-b (2)	
		Drugs and quasi-drugs other than the above	Basic	Domestic		336,500	336,500
						Article 17 (4) 3-c (1)	
				Overseas		409,400 + travel expences	409,400 + travel expences
						Article 17 (4) 3-c (2)	
			Addition of items	Domestic		9,600	9,600
						Article 17 (4) 3-c (1)	
				Overseas		9,600	9,600
						Article 17 (4) 3-c (2)	
		Package, labeling, storage, external testing etc.	Basic	Domestic		258,500	258,500
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		338,100 + travel expences	338,100 + travel expences
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
			Addition of items	Domestic		6,700	6,700
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		6,700	6,700
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
GLP audit of drugs							
	GLP		Domestic			2,062,400	2,062,400
						Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
			Overseas			2,282,600 + travel expences	2,282,600 + travel expences
						Article 17 (3) 1-b, Article 17 (9) 2-a (2)	
GCP audit of drugs							
	New GCP		First application items	Domestic		2,723,200	2,723,200
						Article 17 (3) 2-a	
				Overseas		3,011,900 + travel expences	3,011,900 + travel expences
						Article 17 (3) 2-b	
			Applications with different dosage etc.	Domestic		720,800	720,800
						Article 17 (3) 2-c	
				Overseas		751,800 + travel expences	751,800 + travel expences
						Article 17 (3) 2-d	
	GCP audit of generic drugs			Domestic		645,200	645,200
						Article 17 (3) 2-e	
				Overseas		950,200 + travel expences	950,200 + travel expences
						Article 17 (3) 2-f	

Classification				User fees		
				Review	Conformity	Total
Re-examination of drugs						
	Confirmation/ examination	First application items		806,600	2,673,700	3,480,300
				Article 17 (8) 1-a	Article 17 (9) 1-a	
		Application with different dosage etc.		271,500	892,100	1,163,600
				Article 17 (8) 1-b	Article 17 (9) 1-b	
	GPSP	First application items	Domestic		2,193,300	2,193,300
					Article 17 (9) 2-b (1)	
			Overseas		2,409,600 + travel expences	2,409,600 + travel expences
					Article 17 (9) 2-b (2)	
		Application with different dosage etc.	Domestic		752,600	752,600
					Article 17 (9) 2-b (3)	
			Overseas		772,300 + travel expences	772,300 + travel expences
					Article 17 (9) 2-b (4)	

List of User Fees for Reviews etc. of Medical Devices under the Pharmaceutical Affairs Law (Law No. 145 of 1960)

Note: The lower rows in the User fees column indicate the articles on user fees to MHLW in the Cabinet Ordinance on Fees related to the Pharmaceutical Affairs Law. (Yen)

Classification			User fees		
			Review	Conformity	Total
Investigation for manufacturing license of medical devices					
	New license	On-site		148,100	148,100
				Article 16 (1) 1-a	
		Document		111,500	111,500
				Article 16 (1) 1-b	
	Change/Addition of classification	On-site		97,400	97,400
				Article 16 (1) 2-a	
		Document		55,300	55,300
				Article 16 (1) 2-b	
	Renewal of existing license	On-site		97,400	97,400
				Article 16 (1) 3-a	
		Document		55,300	55,300
				Article 16 (1) 3-b	
Investigation for foreign manufacturing accreditation of medical devices					
	New accreditation	On-site		133,300 + travel expences	133,300 + travel expences
				Article 16 (2) 1-a	
		Document		58,100	58,100
				Article 16 (2) 1-b	
	Change/Addition of classification	On-site		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 2-a	
		Document		39,700	39,700
				Article 16 (2) 2-b	
	Renewal of existing accreditation	On-site		64,600 + travel expences	64,600 + travel expences
				Article 16 (2) 3-a	
		Document		39,700	39,700
				Article 16 (2) 3-b	
Approval review of medical devices (new approval)					
	Medical devices (without approval standards/with clinical data)		3,077,000	664,500	3,741,500
			Article 17 (1) 1-d (1)	Article 17 (2) 1-j	
	Medical devices (without approval standards/without clinical data)		1,164,300	68,500	1,232,800
			Article 17 (1) 1-d (3)	Article 17 (2) 1-l	
	Specially controlled medical devices (with approval standards/without clinical data)		282,900	68,500	351,400
			Article 17 (1) 1-d (2)	Article 17 (2) 1-k	
	Controlled medical devices (with certification standards/without clinical data)		282,900		282,900
			Article 17 (1) 1-d (2)		
	Change of brand name		35,600		35,600
			Article 17 (1) 1-e		
Approval review of medical devices (approval for partial changes to approved matters)					
	Medical devices (without approval standards/with clinical data)		1,538,000	664,500	2,202,500
			Article 17 (1) 2-d (1)	Article 17 (2) 2-g	
	Medical devices (without approval standards/without clinical data)		584,100	37,100	621,200
			Article 17 (1) 2-d (3)	Article 17 (2) 2-i	
	Specially controlled medical devices (with approval standards/without clinical data)		143,500	37,100	180,600
			Article 17 (1) 2-d (2)	Article 17 (2) 2-h	
	Controlled medical devices (with certification standards/without clinical data)		143,500		143,500
			Article 17 (1) 2-d (2)		

Classification					User fees		
					Review	Conformity	Total
QMS review (audit) of medical devices							
	Approval, partial change and manufacture for export	New medical devices		Domestic		739,800	739,800
						Article 17 (4) 1-b (1)	
				Overseas		933,500 + travel expences	933,500 + travel expences
						Article 17 (4) 1-b (2)	
		Biological medical devices, specially controlled medical devices (class IV), etc		Domestic		666,100	666,100
						Article 17 (4) 1-a (1)	
				Overseas		844,400 + travel expences	844,400 + travel expences
						Article 17 (4) 1-a (2)	
		Sterilized medical devices		Domestic		201,300	201,300
						Article 17 (4) 1-c (1)	
				Overseas		229,800 + travel expences	229,800 + travel expences
						Article 17 (4) 1-c (2)	
		Medical devices other than the above		Domestic		141,200	141,200
						Article 17 (4) 1-d (1)	
				Overseas		155,400 + travel expences	155,400 + travel expences
						Article 17 (4) 1-d (2)	
		Package, labeling, storage, external testing, etc.		Domestic		63,800	63,800
						Article 17 (4) 2-a, Article 17 (5) 1-a	
				Overseas		84,800 + travel expences	84,800 + travel expences
						Article 17 (4) 2-b, Article 17 (5) 1-b	
	Renewal of the above	Biological medical devices, specially controlled medical devices (class IV), etc	Basic	Domestic		436,000	436,000
						Article 17 (4) 3-a (1)	
				Overseas		554,200 + travel expences	554,200 + travel expences
						Article 17 (4) 3-a (2)	
			Addition of items	Domestic		30,500	30,500
						Article 17 (4) 3-a (1)	
				Overseas		30,500	30,500
						Article 17 (4) 3-a (2)	
		Sterilized medical devices	Basic	Domestic		380,000	380,000
						Article 17 (4) 3-b (1)	
				Overseas		480,000 + travel expences	480,000 + travel expences
						Article 17 (4) 3-b (2)	
			Addition of items	Domestic		12,400	12,400
						Article 17 (4) 3-b (1)	
				Overseas		12,400	12,400
						Article 17 (4) 3-b (2)	
		Medical devices other than the above	Basic	Domestic		336,500	336,500
						Article 17 (4) 3-c (1)	
				Overseas		409,400 + travel expences	409,400 + travel expences
						Article 17 (4) 3-c (2)	
			Addition of items	Domestic		9,600	9,600
						Article 17 (4) 3-c (1)	
				Overseas		9,600	9,600
						Article 17 (4) 3-c (2)	
		Package, labeling, storage, external testing etc.	Basic	Domestic		258,500	258,500
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		338,100 + travel expences	338,100 + travel expences
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
			Addition of items	Domestic		6,700	6,700
						Article 17 (4) 3-d (1), Article 17 (5) 2-a	
				Overseas		6,700	6,700
						Article 17 (4) 3-d (2), Article 17 (5) 2-b	
GLP audit of medical devices							
	GLP		Domestic			2,062,400	2,062,400
						Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
			Overseas			2,282,600 + travel expences	2,282,600 + travel expences
						Article 17 (3) 1-b, Article 17 (9) 2-a (2)	

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

List of User Fees under the Article 3 of the Administrative Instructions for Review and Other Services of the Independent Administrative Agency Pharmaceuticals and Medical Devices Agency

(Yen)

Classification				User fees	Timing of Payment
Face-to-face consultations					
Clinical trial consultations	Drugs	Consultation on compliance with conformity criteria for drugs		2,875,500 yen per consultation	Payment by the date of application after arrangement of the date of the face-to-face consultation
		Procedural consultation for drugs		139,800 yen per consultation	
		Consultation on biological equivalence testing etc. for drugs		556,000 yen per consultation	
		Quality consultation for drugs		1,478,300 yen per consultation	
		Safety consultation for drugs		1,782,800 yen per consultation	
		Consultation before initiation of phase I study for drugs		4,239,400 yen per consultation	
		Consultation before initiation of the first stage of phase II study for drugs		1,623,000 yen per consultation	
		Consultation before initiation of the second stage of phase II study for drugs		3,028,400 yen per consultation	
		Consultation after completion of phase II study for drugs		6,011,500 yen per consultation	
		Pre-application consultation for drugs		6,011,400 yen per consultation	
		Additional consultation for drugs		2,675,600 yen per consultation	
		Consultation on the protocols of clinical trials for reevaluation and re-examination of drugs		3,320,600 yen per consultation	
		Consultation at completion of clinical trials for reevaluation and re-examination of drugs		3,319,400 yen per consultation	
		Pre-application consultation for new OTC drugs		445,100 yen per consultation	
	Devices and *in vitro* diagnostics	Clinical trial/Pre-application consultation for medical devices or *in vitro* diagnostics		1,594,700 ye per consultation	
		Consultation on compliance with conformity criteria for medical devices		650,300 yen per consultation	
		Pre-development consultation for medical devices		135,200 yen per consultation	
		Safety consultation for medical devices (excluding biological devices)		675,100 yen per consultation	
		Safety consultation for biological medical devices		754,400 yen per consultation	
		Quality consultation for medical devices (excluding biological devices)		650,500 yen per consultation	
		Quality consultation for biological medical devices		753,500 yen per consultation	
		Performance testing consultation for medical devices		690,900 yen per consultation	
		Clinical evaluation consultation for medical devices		854,100 yen per consultation	
		Exploratory clinical trial consultation for medical devices		903,700 yen per consultation	
		Application procedure consultation for medical devices or *in vitro* diagnostics		135,200 yen per consultation	
		Additional consultation for medical devices and *in vitro* diagnostics		927,500 yen per consultation	
		Consultation on preparation of documents for cell- and tissue-based products		223,500 yen per consultation	
Simple consultations		Generic drugs		21,000 yen per consultation	
		OTC drugs		21,000 yen per consultation	
		Quasi-drugs (Including pesticides and rodenticides)		21,000 yen per consultation	
		Medical devices or *in vitro* diagnostics		34,300 yen per consultation	
		Writing applications for new drugs		21,000 yen per consultation	
		GMP/QMS audit		24,700 yen per consultation	
Review for designation of priority face-to-face consultation					
Review for designation of priority face-to-face consultation on drugs				818,800 yen per application	Request to the Agency after advance payment
Review for designation of priority face-to-face consultation on medical devices or *in vitro* diagnostics				818,800 yen per application	
GLP inspection of test facilities					
All test items (for drugs and medical devices)				3,023,800 yen per facility	Request to the Agency after advance payment
All test items (for drugs or medical devices)			Domestic	2,062,400 yen per facility	
			Overseas	2,282,600 yen + travel expenses per facility	
Limited test items				995,200 yen per facility	
Additional compliance accreditation				932,600 yen per facility	
Confirmation of certification on drugs etc.					
Certification of drug products				15,100 yen per item	Request to the Agency after advance payment
Other certifications				8,400 yen per matter of one item	
Use of document storage rooms					
				3,000 yen per day per room	Pay invoice sent from the Agency after the end of use period

Attachment

Comparison of Former and Revised User Fees (revision implemented on April 1, 2008)

(Yen)

Classification			Former user fees	Revised user fees
Drug review (new approval)				
OTC drugs	Switch to OTC status, etc.			1,291,600
				Article 17 (1)1-a (10)
	Others		110,300	110,300
			Article 17 (1) 1-a (10)	Article 17 (1) 1-a (11)
Drug review (approval for partial changes in approved matters)				
Generic drugs	Changes in indications (different from those for approved drugs)	First application items	10,190,500	10,190,500
			Article 17 (1) 2-a (1)	Article 17 (1) 2-a (1)
		Applications with different dosage, etc.	1,057,400	1,057,400
			Article 17 (1) 2-a (2)	Article 17 (1) 2-a (2)
	Changes based on guidelines			35,600
				Article 17 (1) 2-a (7)
	Others		205,100	205,100
			Article 17 (1) 2-a (3)	Article 17 (1) 2-a (3)
OTC drugs	Changes in indications (e.g., direct OTC use)	First application items	10,190,500	10,190,500
			Article 17 (1) 2-a (1)	Article 17 (1) 2-a (1)
		Product with different specifications	1,057,400	1,057,400
			Article 17 (1) 2-a (2)	Article 17 (1) 2-a (2)
	Changes based on guidelines			35,600
				Article 17 (1) 2-a (7)
	Others		56,400	56,400
			Article 17 (1) 2-a (7)	Article 17 (1) 2-a (7)