THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

ANNUAL REPORT FY 2008

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I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1 History and Objective of PMDA

- As lessons learned from diseases caused by drugs such as thalidomide-induced fetal malformations and subacute myelo-optical neuropathy (SMON), the Fund for Adverse Drug Reactions Suffering Relief was established in October 1979 based on stipulations in the Adverse Drug Reaction Suffering Relief Fund 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 drugs.

- In 1997, the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) was established at the National Institute of Health Sciences (NIHS) in order to develop a full-scale 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 equivalence reviews of medical devices as a designated investigative body under the Pharmaceutical Affairs Law.

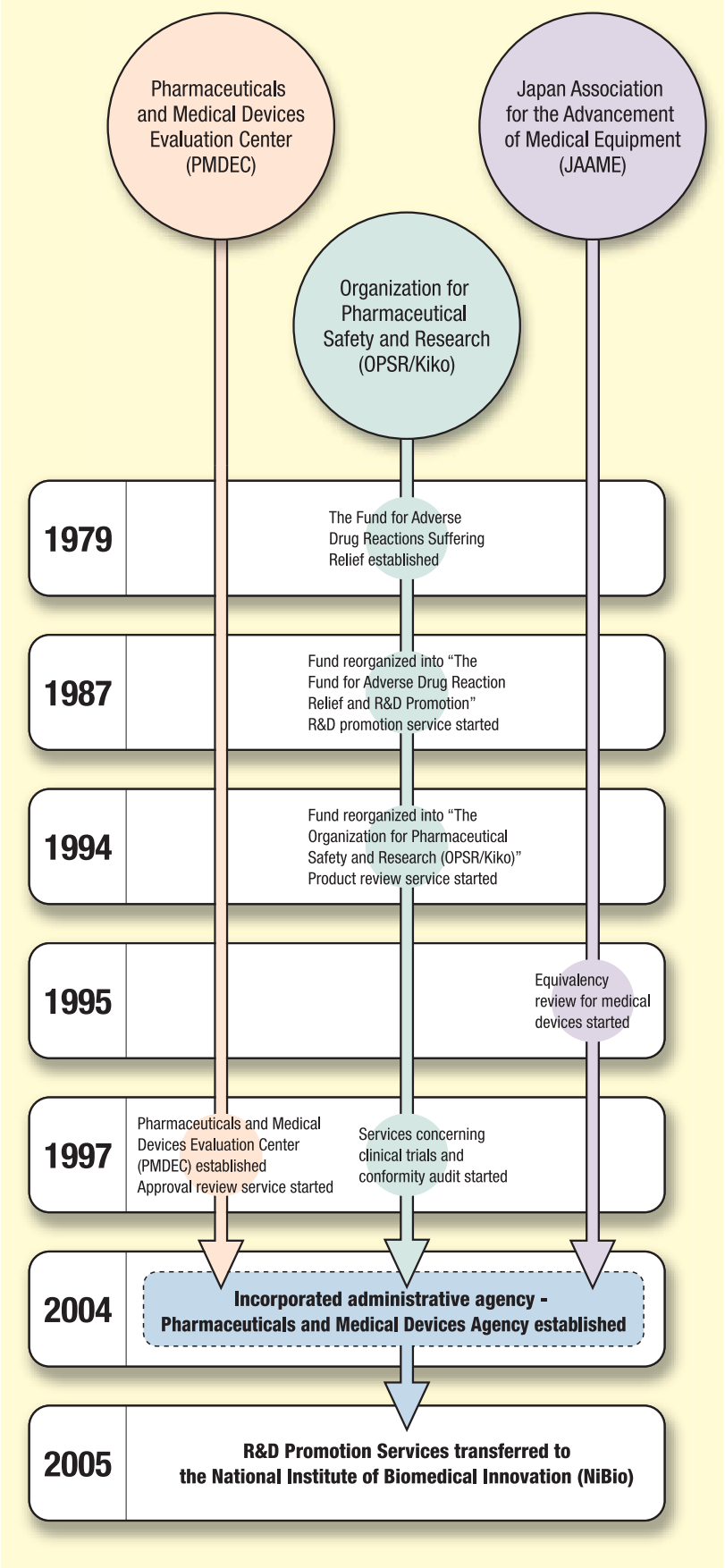
- From 1997 to 1999, there was a systematic and drastic increase in the number of the staff engaging in reviews and post-marketing safety measures at the former Ministry of Health and Welfare and the three organizations above (from 121 staff members in 1996 to 241 in 1999). However, there was a limit 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 Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to PMDEC, OPSR/Kiko, and JAAME in order to further enhance reviews and post-marketing safety measures. In 2002, a legislative bill for the 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 drugs and medical devices through a system that is consistent from pre-clinical research to approval (Reviews); and collecting, analyzing, and providing information on post-marketing safety (Safety Measures).

  Previously, one of the objectives of PMDA was to promote basic research and development of drugs and medical devices that contribute to maintaining and improving the health of the nation (Promotion of R&D). However, the Regulatory Division and the Research Promotion

Division were separated, and services for promotion of R&D were transferred to the National Institute of Biomedical Innovation (NiBio) in April 2005, in order to allow PMDA to focus specifically on reviews, safety measures, and relief services for adverse health effects.


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, PMDA 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, PMDA started to provide benefits to sufferers of adverse health effects caused by infections from drugs and medical devices manufactured by using ingredients and materials derived from biological entities (Relief Service for Infections Derived from Biological Products).

- In January 2008, PMDA 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).

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

2.2 Review Services

- In accordance with the Pharmaceutical Affairs Law, PMDA reviews the efficacy, safety, and quality of drugs and medical devices for which regulatory approval applications have been submitted, based on the current scientific and technological standards. In addition, PMDA conducts re-examinations/re-evaluations of drugs and medical devices and reviews of applications for confirmation of the quality and safety of cell and tissue based products prior to the first-in-man study (hereinafter referred to as “application for pre-clinical quality and safety confirmation”) as well as reviews of applications for confirmation of clinical use of 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, PMDA provides face-to-face guidance and consultations on clinical trials of new drugs and medical devices as well as on clinical trials for re-examinations/re-evaluations of approved products (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 Practices (GLP), Good Clinical Practices (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 the requirements of the Ministerial Ordinance on Good Manufacturing Practices (GMP), and whether there is a system for manufacturing products of appropriate quality (GMP/QMS Inspection Services).

2.3 Post-marketing safety Measures

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

(i) Services for centrally collecting and organizing information on the post-marketing safety of drugs and medical devices from a broad range of sources, such as reports from the private sector, information from medical institutions, information from foreign regulatory agencies, and presentations at academic conferences, relating to adverse drug reactions, malfunctions, and infections (Collection and Organization of Information).

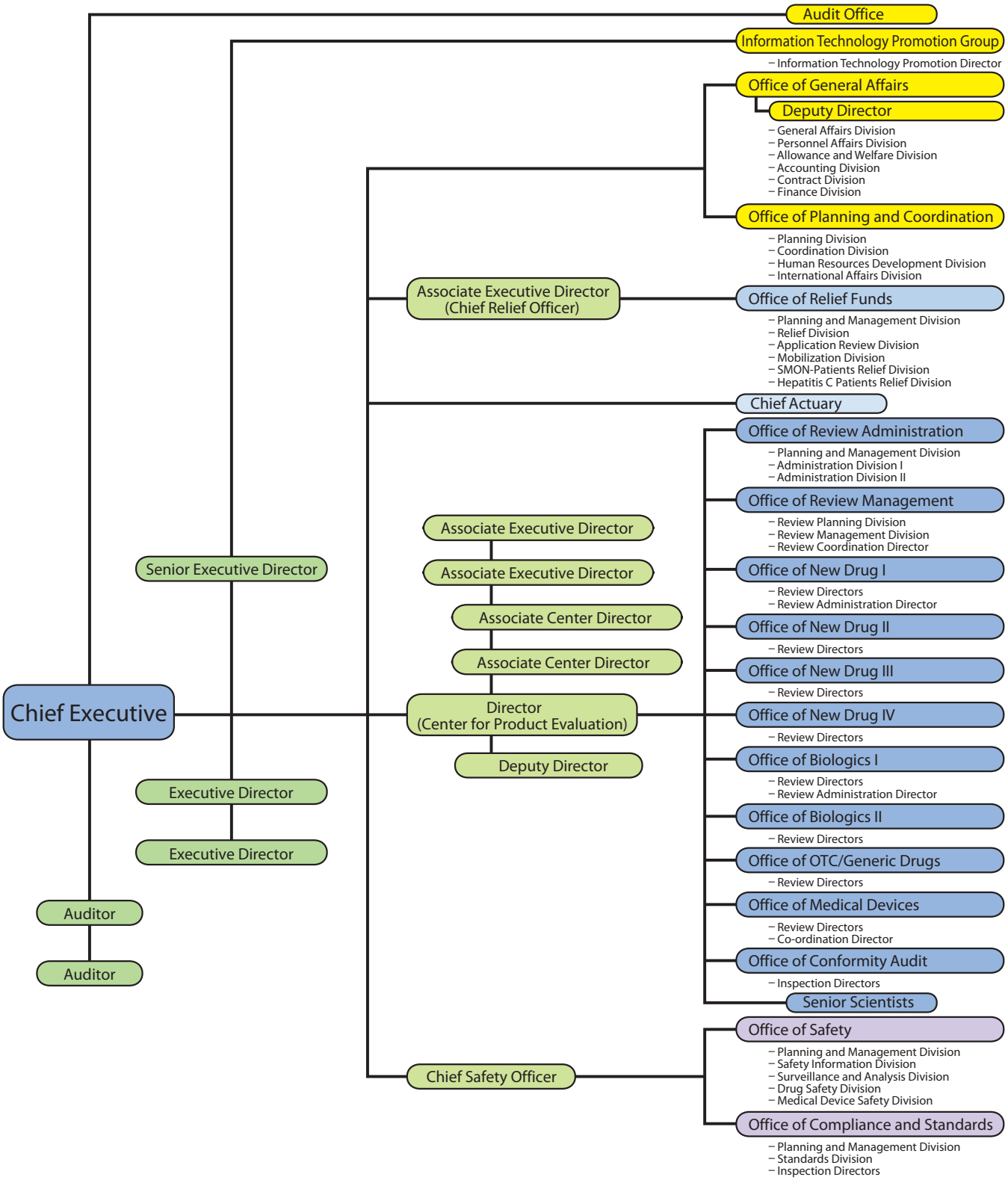
(ii) Services for conducting research and reviews relating to safety measures based on the information collected in (i) above (Research and Review Services).

(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 safety information on drugs 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 PMDA (FY 2008)



II. OPERATING PERFORMANCE FOR FY 2008

PART 1 Development of the "Second Mid-term Targets" and the "Second Mid-term Plan"

1.1 Development of the "Second Mid-term Targets" and the "Second Mid-term Plan"

- As of February 27, 2009, from the Minister of Health, Labour and Welfare, PMDA received the "Second Mid-term Targets," which stipulate targets in relation to the management of operations to be achieved by PMDA during the period from April 2009 to March 2014, after the targets were deliberated at a meeting of the Medical Care and Welfare Group of the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (held on February 18, 2009).

- PMDA also developed a draft of the Second Mid-term Plan under the guidance of the Ministry of Health, Labour and Welfare, by hearing the opinions of relevant parties including the members of the Advisory Council, the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare, the pharmaceutical and medical device industry, and the Japan Confederation of Drug-induced Sufferers Organizations, and by receiving information on the draft of Mid-term Targets from the Ministry of Health, Labour and Welfare in advance. After the draft of the Second Mid-term Plan was deliberated at the third Advisory Council Meeting (held on February 6, 2009) and at a meeting of the Medical Care and Welfare Group of the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (held on February 18, 2009), it was submitted to the Minister of Health, Labour and Welfare as of February 27, 2009, and was approved as of March 31, 2009.

1.2 Points of the Second Mid-term Plan

Target Points of the PMDA Second Mid-term Plan

1. — Proactive Operational Development from a Fresh Perspective —

The Agency shall:

- Complete the PMDA safety triangle by strengthening cooperation among review divisions, safety divisions and relief divisions.
- Promote international cooperation based on the "PMDA International Strategic Plan."
- Promulgate regulatory science by promoting joint graduate school program, research exchange, information provision, etc.
- Make concerted efforts to appropriately evaluate state-of-the-art technologies, such as biotechnology, genomics, and regenerative medicine, to utilize the data mining method, and to respond to Super Special Consortia.

2. — Activities to Improve Services and Conduct Effective Management of Operations —

The Agency shall:

- Seek recommendations and opinions on improvements from third-party review institutions in

order to develop an internal control process and to increase transparency and efficiency (in terms of cost control) in the management of operations, and examine the feasibility of relocating the office with a view to managing operations more effectively and efficiently.

- Promote optimization of operations and systems based on the Optimization Plan for Operations and Systems.

- Improve services to the public by providing information based on the PMDA Public Relations Strategic Plan.

3. — Promotion of Relief Services for Adverse Health Effects —

The Agency shall:

- Inform the public of the relief system for adverse health effects and promote understanding of the system by conducting effective public relations activities directed toward patients and healthcare professionals respectively, and by making use of in-school educational opportunities.

- Further reduce the administrative processing period between application for relief benefits and approval decision-making.

(First-term Plan)		(Second-term Plan)
60% of all applications should be processed within 8 months	→	60% of all applications should be processed within 6 months.

- Initiate consultation services to address mental issues of sufferers of adverse health effects caused by adverse drug reactions, as part of health and welfare services.

4. — Activities to Provide Better Pharmaceuticals and Medical Devices More Promptly and Safely —

The Agency shall:

- Set and achieve targets for solving the drug lag by steadily implementing the project management system, introducing a new evaluation system from the development stage, strengthening the approval review system, and promoting efficiency improvement.

Total review time for new pharmaceuticals (priority review items) (median)

At the end of the First-term Plan (end of FY 2008)		At the end of the Second-term Plan (end of FY 2013)
12 months	→	9 months

- Promote not only international harmonization by strengthening cooperation with the United States, the European Union, Asian countries, and relevant international organizations, but also proactive participation in Global Clinical Trials.

- Provide high-quality clinical trial consultations and develop a system to respond to all consultations.

- Set targets for shortening review times for over-the-counter (OTC) drugs and generic drugs.
- Set and achieve targets for solving the device lag based on action plans, by introducing the three-track system, strengthening other systems for approval review of medical devices, and promoting efficiency improvement.

Total review time for new medical devices (priority review items) (median)		
At the beginning of the Second-term Plan (end of FY 2009)	→	At the end of the Second-term Plan (end of FY 2013)
16 months		10 months

- Efficiently conduct reliability and conformity audits by gradually introducing document-based inspection at sponsor site, and promote the implementation of efficient GMP/QMS audits by proactively conducting on-site inspections at overseas manufacturing sites in Asian countries, etc.

5. — Prevention of Occurrence and Expansion of Adverse Drug Reactions by Enhancing Post-marketing Safety Measures —

The Agency shall:

- Organize assessment teams in individual fields to appropriately respond to the sophisticated and specialized evaluation of information on adverse drug reactions of pharmaceuticals, and improve the system for collecting, analyzing, and evaluating safety information.
- Enhance safety measures by developing infrastructures to access clinical information databases, including Receipt data, by FY 2013.
- Develop a consistent system for managing the safety of pharmaceuticals from the clinical trial stage through the post-marketing stage, thereby making it possible to take more effective and reasonable safety measures.

PART 2 Development of Fiscal Year 2008 Plan

2.1 Development and Implementation of Fiscal Year 2008 Plan

- PMDA is required to develop the Mid-term Plan in accordance with the Mid-term Targets designated by the Minister of Health, Labour and Welfare, and to obtain the Minister's approval for the plan (the first Mid-term Targets is between April 2004 and March 2009). In order to achieve the Mid-term Plan, PMDA is required to develop a plan for each fiscal year, submit these plans to the Minister, and announce these plans to the public.

  PMDA developed a plan for FY 2008, the final year of the first Mid-term Plan, submitted it to the Minister of Health, Labour and Welfare at the end of 2007, and is implementing operations in accordance with this plan.

  On January 27 and March 16, 2009, PMDA notified the Minister of Health, Labour and Welfare of the increase in the outlay budget of specified relief benefits for relief payments 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 fiscal year 2008 plan was developed based on the modified Mid-term Targets and Mid-term Plan as well as operational performance for FY 2007 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.

- PMDA 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 2007, PMDA announced its three priority issues for FY 2008 at the 1st Advisory Council Meeting held on June 20, 2008. The priority issues are as follows:

  (i) Enhancement of review services
  (ii) Enhancement of post-marketing safety measure 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 2008, PMDA organized the issues that should be implemented within FY 2008 and announced these issues as "Priority Issues for Operations in the Second Half" of FY 2008 at the 3rd Advisory Council Meeting held on February 6, 2009.

2.2 Evaluation Results of Operating Performance in FY 2007

- It is stipulated that the each ministry in charge of an incorporated 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).

  On August 18, 2008, PMDA received the results of an evaluation on its performance for FY 2007 from the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare, which is responsible for conducting evaluations on PMDA. The overall evaluation results

consisted of 17 As and 3 Bs out of 20 evaluation items (the Bs were for “collection and management of contributions” and “expeditious operation and improvement of the system (pharmaceuticals and medical devices)”).

PMDA posted these evaluation results on the PMDA website and reported the results at the meeting of the Advisory Council that was held on October 1, 2008.

Note: Five-level grading of S, A, B, C, and D with S being the highest
S: Significantly exceeding the level prescribed in the Mid-term Plan
A: Exceeding the level prescribed in the Mid-term Plan
B: Somewhat exceeding the level prescribed in the Mid-term Plan
C: Slightly below the level prescribed in the Mid-term Plan
D: Below the level prescribed in the Mid-term Plan, therefore requiring drastic improvements

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

Classification in the mid-term and fiscal year plan		Evaluation items		Evaluation result	
				FY2006 performance	FY2007 performance
Part 1 Improvement in overall operations and quality in services of the PMDA eg. services to the publilc					
(1) Efficient and Flexible Operations		1	Operation through target management/top management	A	A
		2	Ensuring of transparency by establishing deliberative bodies	A	A
(2) Cost reduction by increased efficiency of operations		3	Expense savings	A	A
		4	Collection and management of contributions	A	B
(3) Improvement of services to the public		5	Strengthening of the consultation system and disclosure of the work of the Agency	B	A
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 (2) Proactive public relations activity toward familiarity with the System (3) Expansion of the scale of the consultation office		6	Provision of information on the System and strengthening of the consulatation system	A	A
(4) Unified management of information through the database (5) Expeditious processing of relief applications through fact-finding study and other measures		7	Expeditious processing of applications and improvement of the system	S	A
(6) Promotion of appropriate communication of information through cross-functional collaboration (7) Consideration of conducting surveys on adverse health effects, etc.		8	Conduct of cross-functional collaboration and surveys on adverse health effects	A	A
(8) Appropriate conduct of relief services for SMON patients and those patients infected with HIV from blood preparations (9) Appropriate conduct of payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus		9	Conduct of relief services for SMON patients and those patients infected with HIV from blood preparations and payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products	A	A
2 Reviews and related operations/ post-marketing safety measures					
(1) Faster access to the latest pharmaceuticals and medical devices		10	Expeditious operation and improvement of the system (pharmaceuticals)	A	B
		11	Expeditious operation and improvement of the system (medical devices)	A	B
		12	Expeditious operation and improvement of the system (clinical trial consultations)	B	A
(2) Improvement in reliability of reviews and related operations/post-marketing safety measures		13	Improvement in quality of review and related operations/post-marketing safety measures	A	A
		14	Promotion of appropriate clinical trials	A	A
		15	Promotion of transparency of review and related operations/ post-marketing safety measures	A	A
(3) Reinforcement of information management and emergency management		16	Collection of ADR information	A	A
		17	Provision of safety information to companies and healthcare professionals	A	A
		18	Provision of safety information to patients and consumers	A	A
Part 3 Budget, income and expenditure plan, and financial plan		19	Budget, income and expenditure plan, and financial plan	A	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 (2) Ensuring security		20	Personnel issues and establishment of security	A	A

Evaluation scale on performance of Incorporated Administrative Agency of MHLW				
	S	Significantly exceeding the level prescribed in the midterm-plan	1	0
	A	Exceeding the level prescribed in the midterm-plan	17	17
	B	Somewhat exceeding the level prescribed in the midterm-plan	2	3
	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

- As for the results of the evaluations conducted by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW), the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications submitted its conclusions twice as of November 26, 2008, and January 7, 2009, in which it highlighted the following issues concerning the evaluation results for PMDA:

(1) As for the PMDA's endeavors to reform its total personnel expenditure, the standard amount for FY 2007 was 609,545,000 yen while the standard amount for FY 2005 was 545,454,000 yen according to its remuneration standards that had been released to the public (an increase of 11.1%, excluding revisions of remuneration in accordance with recommendations of the National Personnel Authority). This increase was not expected in the PMDA's specific reduction plan. On the other hand, it is explained in PMDA's Operating Performance Report that "personnel expenditure for FY 2007 was reduced by approximately 3.3% (in comparison with personnel expenditure per person for FY 2005) owing to the introduction of a new remuneration system," which is not consistent with the standard amounts and the actual values in the remuneration standards released to the public. The Evaluation Committee of the MHLW evaluated PMDA's performance only based on this explanation in the Report, but no evaluation is presented based on the values released to the public.

Future evaluations should be conducted to promote the PMDA's endeavors, after the performance of its endeavors based on the values released to the public is verified and after prospects for reducing personnel expenditure by 5% or more in 5 years, including future reduction plans, are clarified based on the achievements for the years passed from the beginning of its endeavors.

(2) As for the Pharmaceuticals and Medical Devices Agency (note: names of other agencies are omitted), the index in comparison with national government employees (in consideration of age) in FY 2007 increased year-on-year, but the verification results of the reasons have not been clarified in the evaluation.

As it is considered to be more difficult to win social understanding on the remuneration standards if they are higher year-on-year, the reasons should be clarified in future evaluation results and the PMDA's endeavors to realize appropriate remuneration standards should be promoted.

(3) As for the Pharmaceuticals and Medical Devices Agency (note: names of other agencies are omitted), what is explained in the Operating Performance Report is different from the standard amount and the actual values of personnel expenditure, as part of its remuneration standards released to the public, in the context of its endeavors to reform the total personnel expenditure. The evaluations by the Evaluation Committee of the MHLW were conducted based on this explanation in the Report. However, the verification of the PMDA's endeavors based on the values released to the public has not been clarified in the evaluation results.

Future evaluations should be conducted to promote the PMDA's endeavors, after the performance of its endeavors based on the values released to the public is verified and after prospects for reducing personnel expenditure by 5% or more in 5 years, including future reduction plans, are clarified in the evaluation results based on the achievements for the years passed from the beginning of its endeavors.

(4) As for six agencies (including the Pharmaceuticals and Medical Devices Agency [note: names of other agencies are omitted]), there is no reference in the evaluation results to the appropriateness of the development of regulations in relation to contracts.

The appropriateness of the development of regulations in relation to contracts should be more strictly evaluated and should be clarified in the evaluation results after the existence and details of such regulations are grasped.

(5) As for four agencies, although the actual amounts of noncompetitive optional contracts increased from FY 2006 to FY 2007 as is shown in Table 3-(2), there is no reference to this issue, including the causes, in the evaluation results.

Therefore, in evaluating the implementation and progress of future plans for the review of optional contracts, it should be noted that the verification results of the causes of increase in optional contract amounts need to be clarified in the evaluation results.

2.3 Results of the Provisional Evaluation on Performance during the Effective Period for the Mid-term Targets

- PMDA received results of the "provisional evaluation on its performance during the effective period for the Mid-tern targets" as of August 27, 2008, conducted by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare. The overall evaluation results, calculated by averaging evaluation results for the past four years from 2004 to 2007, consisted of 18 As and 2 Bs out of 20 evaluation items (the 2 Bs were for "expeditious operation and improvement of the system (medical devices) and (clinical consultations)").

  PMDA posted these evaluation results on its website and reported the results at the Advisory Council Meeting held on October 1, 2008.

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

Results of the Provisional Evaluation on Performance during the Effective Period for the Mid-term Targets

Classification in the mid-term and fiscal year plan		Evaluation items		Evaluation result: Provisional evaluation
Part 1 Improvement in overall operations and quality in services of the PMDA eg. services to the publilc				
	(1) Efficient and Flexible Operations	1	Operation through target management/top management	A
		2	Ensuring of transparency by establishing deliberative bodies	A
	(2) Cost reduction by increased efficiency of operations	3	Expense savings	A
		4	Collection and management of contributions	A
	(3) Improvement of services to the public	5	Strengthening of the consultation system and disclosure of the work of the Agency	A
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 (2) Proactive public relations activity toward familiarity with the System (3) Expansion of the scale of the consultation office	6	Provision of information on the System and strengthening of the consulatation system	A
	(4) Unified management of information through the database (5) Expeditious processing of relief applications through fact-finding study and other measures	7	Expeditious processing of applications and improvement of the system	A
	(6) Promotion of appropriate communication of information through cross-functional collaboration (7) Consideration of conducting surveys on adverse health effects, etc.	8	Conduct of cross-functional collaboration and surveys on adverse health effects	A
	(8) Appropriate conduct of relief services for SMON patients and those patients infected with HIV from blood preparations (9) Appropriate conduct of payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus	9	Conduct of relief services for SMON patients and those patients infected with HIV from blood preparations and payment services for individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products	A
2 Reviews and related operations/ post-marketing safety measures				
	(1) Faster access to the latest pharmaceuticals and medical devices	10	Expeditious operation and improvement of the system (pharmaceuticals)	A
		11	Expeditious operation and improvement of the system (medical devices)	B
		12	Expeditious operation and improvement of the system (clinical trial consultations)	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
		14	Promotion of appropriate clinical trials	A
		15	Promotion of transparency of review and related operations/ post-marketing safety measures	A
	(3) Reinforcement of information management and emergency management	16	Collection of ADR information	A
		17	Provision of safety information to companies and healthcare professionals	A
		18	Provision of safety information to patients and consumers	A
Part 3 Budget, income and expenditure plan, and financial plan		19	Budget, income and expenditure plan, and financial plan	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 (2) Ensuring security	20	Personnel issues and establishment of security	A

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

PART 3 Improvement in Overall Management of Operations and Service Quality of PMDA

3.1 Efficient and Flexible Management of Operations

3.1.(1) Operation through management by objectives

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

- In order to do so, PMDA 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 the Agency's annual plan for FY 2008.

- To comprehend the progress of operating plans in each office, from October to November 2008, PMDA conducted a hearing with its directors about the actual operating performance up to the end of September 2008 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 in December 2008.

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

- PMDA 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, PMDA also plans to build an organizational system where management decisions by the Chief Executive are speedily reflected in operations.

- To this end, since FY 2007, PMDA has been establishing opportunities for the Chief Executive to directly comprehend the progress of operations and provide necessary instructions, and has also been reinforcing liaison and coordination of its general operations.

  Specifically, PMDA has regularly (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 twice in FY 2008) for the Headquarters for PMDA Reform, which is headed by the Chief Executive, development of the Second Mid-term Plan was reported at each stage.

- In order to appraise the reviews of drugs/medical devices and clinical trial consultations, PMDA regularly (4 times in FY 2008) 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 headed by the Chief Executive was established with the aim of further reinforcing the structure of information systems management of PMDA. With approval for the implementation policy and schedule of the optimization of operations and systems, requirements were defined in cooperation with the deputy CIO, as an operation for FY 2008. In the course of the discussion, consensus was built within PMDA to fundamentally reconstruct a system that would contribute to improvement in operational efficiency in response to the increase in the number of reviewers and other employees. It was decided that servers and databases would be integrated at the first stage of the implementation of optimization and that integration systems for review

operations would be developed at the second stage, and it was approved that the Optimization Plan for Operations and Systems would be revised and publicized in a way to reflect such changes (two meetings were held during FY 2008).

Moreover, at the Committee on Investment in Information Systems, which is under the Headquarters, PMDA appraised the appropriateness of the investment in the development of new systems and the modification of existing systems from the perspectives of cost-effectiveness and technical difficulties and selected systematic and efficient investment options according to the Chief Executive's business judgment (two meetings were held during FY 2008).

- In order to maintain sound financial performance and adequate operations, the Financial Management Committee, headed by the Chief Executive, has been holding regular meetings (12 meetings in FY 2008), during which reports on the monthly application status for user fees for each review division, reports on the monthly cash flow analysis, and reports on the declared amount of contributions were made.

- PMDA 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, PMDA convened task force meetings five times, starting in February 2007, concerning medical devices and *in vitro* diagnostics. PMDA also convened meetings of six working groups, established under the task force, a total of 58 times

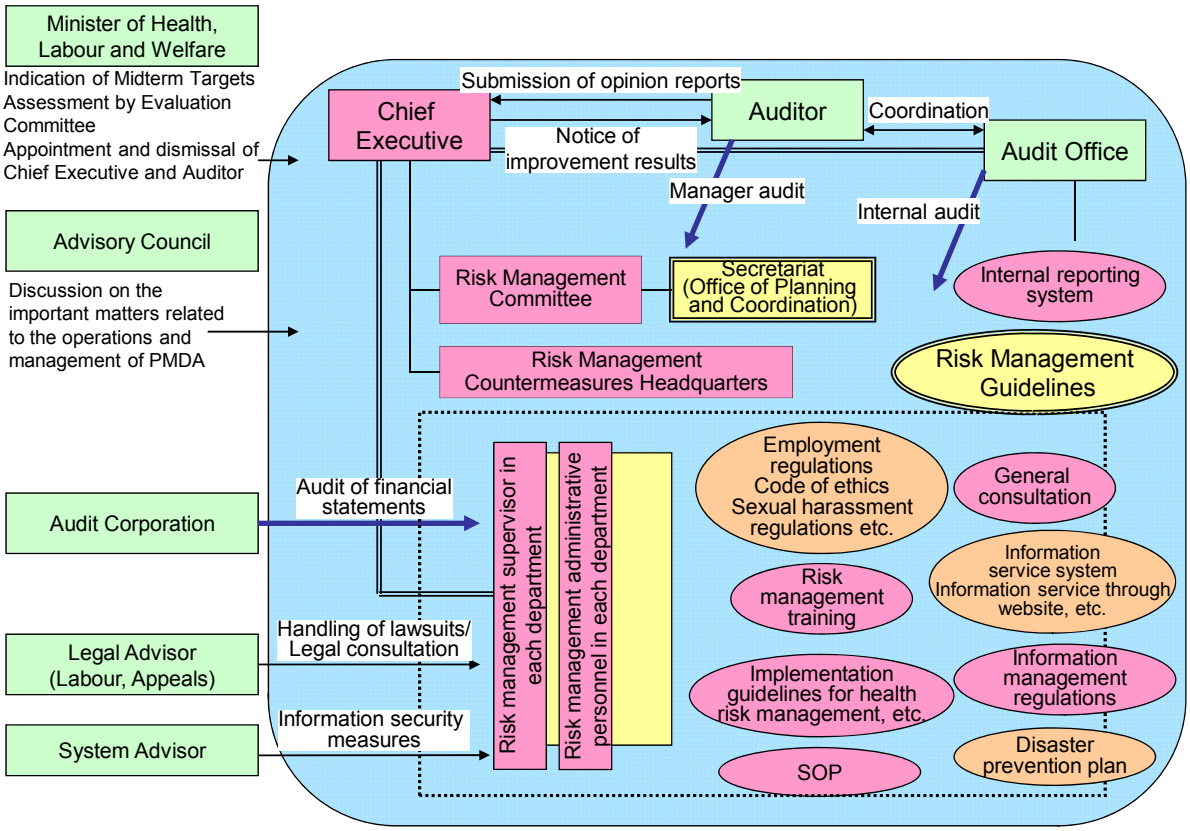
- The Risk Management Committee held 12 meetings in FY 2008 to monitor the risk management of PMDA, and examined the appropriateness of document and information management by reviewing the operational flow.

  PMDA executives and employees have also continued to 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, PMDA informed all executives and employees of the disaster preparedness plan.

PMDA Risk Management System



Note: Risks PMDA may face:

a. Risks to the organization
   - Possibility of an event that damages or may damage the reputation of PMDA in society
   - Possibility of an event that significantly hinders or may hinder PMDA's execution of operations
   - Possibility of an event that financially damages or may damage PMDA

b. Risks that PMDA should address as part of its tasks
   - Risks relating to PMDA's operations and that have the possibility of causing or expanding critical adverse health effects due to drugs, medical devices, etc. (drugs, medical devices, quasi-drugs, and cosmetics, as well as agents and equipment subject to clinical trials).

3.1.(3) Development of PMDA Philosophy and all kinds of strategic plans

- PMDA developed its philosophy in September 2008 and posted it on the front page of its website, with the aim of clearly transmitting its mission to the outside world in order to pave the way to achieve the goal of changing to "global PMDA" from Japan's PMDA, supported by the public and relevant parties engaged in drugs and medical devices, as a commitment of its staff to share a single purpose of daily duties toward this target.

PMDA Philosophy

PMDA continues to improve the public health and safety of our nation by reviewing applications for marketing approval of pharmaceuticals and medical devices, conducting post-marketing safety measures, and providing relief to people who have suffered from adverse drug reactions.

We conduct our mission in accordance with the following principles:

- We pursue the development of medical science while performing our duty with greater transparency based on our mission to protect public health and the lives of our citizens.
- We will be the bridge between the patients and their wishes for faster access to safer and more effective drugs and medical devices.
- We make science-based judgments on quality, safety, and efficacy of medical products by training personnel to have the latest technical knowledge and wisdom in their field of expertise.
- We play an active role within the international community by promoting international harmonization.
- We conduct services in a way that is trusted by the public based on our experiences from the past.

- From the viewpoint of systematically promoting PR activities as a whole during the effective period for the Second Mid-term Targets in consideration of the needs of the public and international perspectives, PMDA developed the PMDA Public Relations Strategic Plan (July 11, 2008) as a basic policy for its overall PR activities during the period and decided to improve services to the public by proactively providing information in line with the strategic plan.

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

3.1.(4) Advisory Council meetings

- To create opportunities for exchanges of opinions between academic experts of diverse fields, PMDA established the Advisory Council (chaired by Masaaki Hirobe, Professor Emeritus 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 drugs, etc. By providing recommendations and improvement measures for operations and the management system, the Council works to secure fairness and transparency of the PMDA's operations, in addition to contributing to the streamlining of operations. Under the Advisory Council, the Committee on Relief Services (chaired by Hideaki Mizoguchi, Director of the Saitama Prefecture Red Cross Blood Center) and the Committee on Reviews and Safety Operations (chaired by Masaaki Hirobe, Professor Emeritus at the University of Tokyo) were also formed to discuss specialized issues relating to operations, and the dates of the meetings and specific agendas for FY 2008 are shown below.

  In FY 2008, new members of the Advisory Council, Committee on Relief Services and Committee on

Review and Safety Operations were elected because the term of their predecessors expired (including commissioned external experts of the Committee on Relief Services, chosen from the public).The Council and the Committees have been made up of new members since the second Advisory Council meeting held on October 1, 2008.

Advisory Council—FY 2008

Agenda for the 1st Meeting (June 20, 2008)

(1) PMDA Annual Report for FY 2007
(2) Financial Report for FY 2007
(3) Priority issues in FY 2008 operations
(4) Implementation of reforms of PR activities
(5) Report on the employment status of personnel from the private sector
(6) Others

Agenda for the 2nd Meeting (October 1, 2008)

(1) Election of the chairman and the acting chairman
(2) Evaluation results of the operational performance for FY 2007 and provisional evaluation results of the operational performance for the effective period for the Mid-term Targets
(3) Issues to be addressed in the next Mid-term Plan
(4) Conflict of interests
(5) Report on the employment status of personnel from the private sector
(6) Others

Request for approval (January 21, 2009)

(1) Amendments to the budget for FY 2008 of the Pharmaceuticals and Medical Devices Agency

Agenda for the 3rd Meeting (February 6, 2008)

(1) Principal achievements up to the end of November 2008 and priority issues in the latter half of FY 2008
(2) Second Mid-term Plan (draft)
(3) Rate of contribution (draft)
(4) Revision of the operation manual (draft)
(5) Restrictions with respect to employing personnel from the private sector
(6) PMDA International Strategic Plan
(7) Others

Agenda for the 4th Meeting (March 16, 2009)

(1) Second Mid-term Plan
(2) Fiscal year 2009 plan (draft)
(3) Budget for FY 2009 (draft)
(4) Report on the employment status of personnel from the private sector
(5) Cash contributions received by commissioned external experts in relation to Expert Discussions
(6) Amendments to the budget for FY 2008
(7) Others

Committee on Relief Services—FY 2008

Agenda for the 1st Meeting (June 16, 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) Annual Report for FY 2007
(3) Fiscal year 2008 plan
(4) Implementation of reforms of PR activities
(5) Others

Agenda for the 2nd Meeting (December 25, 2008)

(1) Election of the chairman and nomination of the acting chairman
(2) Principal achievements up to the end of October 2008 and issues to be addressed hereafter
(3) Issues to be addressed in the next Mid-term Plan
(4) FY 2008 recalculation of the rate of contribution to the adverse drug reaction fund (draft)
(5) Others

Committee on Review and Safety Operations—FY 2008

Agenda for the 1st Meeting (June 10, 2008)

(1) Annual Report for FY 2007
(2) Fiscal year 2008 plan
(3) Implementation of reforms of PR activities
(4) Report on the employment status of personnel from the private sector
(5) Others

Agenda for the 2nd Meeting (December 17, 2008)

(1) Election of the chairman and the acting chairman
(2) Principal achievements up to the end of October 2008 and issues to be addressed hereafter
(3) Issues to be addressed in the next Mid-term Plan
(4) Conflict of interests
(5) Implementation of consultation services to support venture companies
(6) Report on the employment status of personnel from the private sector
(7) Others

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

- Because the amount of the specified relief benefit paid from the specified relief account increased more than estimated, deliberations were made on amendments to the budget for FY 2008 due to change in the budgeted expenditure at the meeting held in rotation on January 21, 2009, and the 4th Advisory Council Meeting held on March 16, 2009, and amendments were made to the FY 2008 plan.

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

3.1.(5) Approaches for an efficient operation system

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

  In review divisions that required flexible approaches in particular, PMDA continued to adopt a structure where, in addition to adopting a group system, Review Directors are placed underneath the Office Directors, and the Review Directors are in charge of each review team.

  PMDA also invites commissioned external experts to ask for their professional opinions relating to scientifically significant matters at Expert Discussions on reviews and post-marketing safety measures.

  (914 commissioned external experts as of March 31, 2009)

  Similarly, PMDA invites commissioned external experts to ask for their opinions on adverse drug reactions and adverse health effects caused by infections derived from biological products.

  (62 commissioned external experts as of March 31, 2009)

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

- Based on the need to secure fairness and transparency of judgment in discussions by commissioned external experts, PMDA developed the Notice of the Implementation of Expert Discussions at the Pharmaceuticals and Medical Devices Agency (December 25, 2008) as a regulation for the conflict of interests that included the establishment of a system that would fully secure transparency and that could be verified by outside parties by releasing review reports and the conflict of interests of commissioned external experts. Reports are made to the Advisory Council on the receipt of cash contributions and contract money by the external experts to whom PMDA has asked to participate in Expert Discussions on approval reviews and safety measures.

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

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

3.1.(6) Standardization of operating procedures

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

3.1.(7) Development of databases

- In FY 2008 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 PMDA, and improvements in the security of the e-mail system were carried out.

  PMDA promoted the development of databases in order to systematically organize and store documents as well as to make it easy to collect and analyze information, by providing indices to drafts that had been approved in the past and recorded in CD-R and developing databases from such information. PMDA also upgraded databases in order to apply such information widely to its operations.

- The notifications issued by the MHLW and PMDA that are relevant to the Agency's operations or that require broad dissemination of information to the public are posted on the following website:

  http://www.pmda.go.jp/operations/notice.html

3.1.(8) Promotion of the optimization of operations and systems

- Based on the Plan for the Development of e-Government (decided at the Liaison Meeting of the Chief Information Officers (CIO) of the Ministries and Agencies held on July 17, 2003) and the Measures for the Realization of Optimal Operations/Systems at Independent Administrative Institutions (decided at the Liaison Meeting of the Chief Information Officers (CIO) of the Ministries and Agencies held on June 29, 2005), PMDA developed the Optimization Plan for Operations and Systems and publicized it on March 28, 2008.

  In FY 2008, PMDA defined requirements for the integration of servers and databases as the first stage of optimization by making use of external professionals, and established a foothold for the construction of a new integrated system for review operations as the second stage of optimization.

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, PMDA 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 curbing personnel expenses by reviewing the remuneration 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. PMDA is to develop an annual budget plan based on the Mid-term Plan and achieve the Mid-term Targets by appropriately operating within the planned budget.

- In FY 2008, in order to more efficiently execute operations with regard to personnel expenses within the annual budget plan, PMDA steadily paid personnel expenses in accordance with the new remuneration policy based on the personnel evaluation system, which has been introduced since April 2007, and the structural reform of the remuneration system of national government employees. Moreover, with regard to non-personnel expenses, PMDA promoted general competitive bidding based on the Plan for the Review of Optional Contracts, which was developed in December 2007, and it continued from last year in an attempt to reduce procurement costs arising from the purchase of expendables, such as copy papers, and the purchase of additional office furniture necessitated by increase in employees, as well as rental contracts of personal computers, through the introduction of competition.

  Consequently, PMDA successfully reduced general administrative expenses, excluding unused personnel expenses for vacant positions, by 4.8% of the size of the budget subject to efficiency improvement.

3.2.(2) Cost control of operating expenses

- By increasing efficiency of operations through promoting computerization, PMDA 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 FY 2004
  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 operating expenses is based on the Mid-term Targets for cost control as directed by the Minister of Health, Labour and Welfare. PMDA is to develop an annual budget plan based on the Mid-term Plan and achieve the Mid-term Targets by appropriately operating within the planned budget.

- In FY 2008, PMDA promoted general competitive bidding as well as control of general administrative expenses. In the meantime, PMDA steadily managed the execution of operations and strived to reduce costs while securing necessary operations, taking account of the trend of user fees and contributions, which are the financial sources of operations.

  Consequently, PMDA 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 initially

expected, by 6.6% compared with the budget amount, which was considered to be the target of efficient execution.

3.2.(3) Competitive bidding

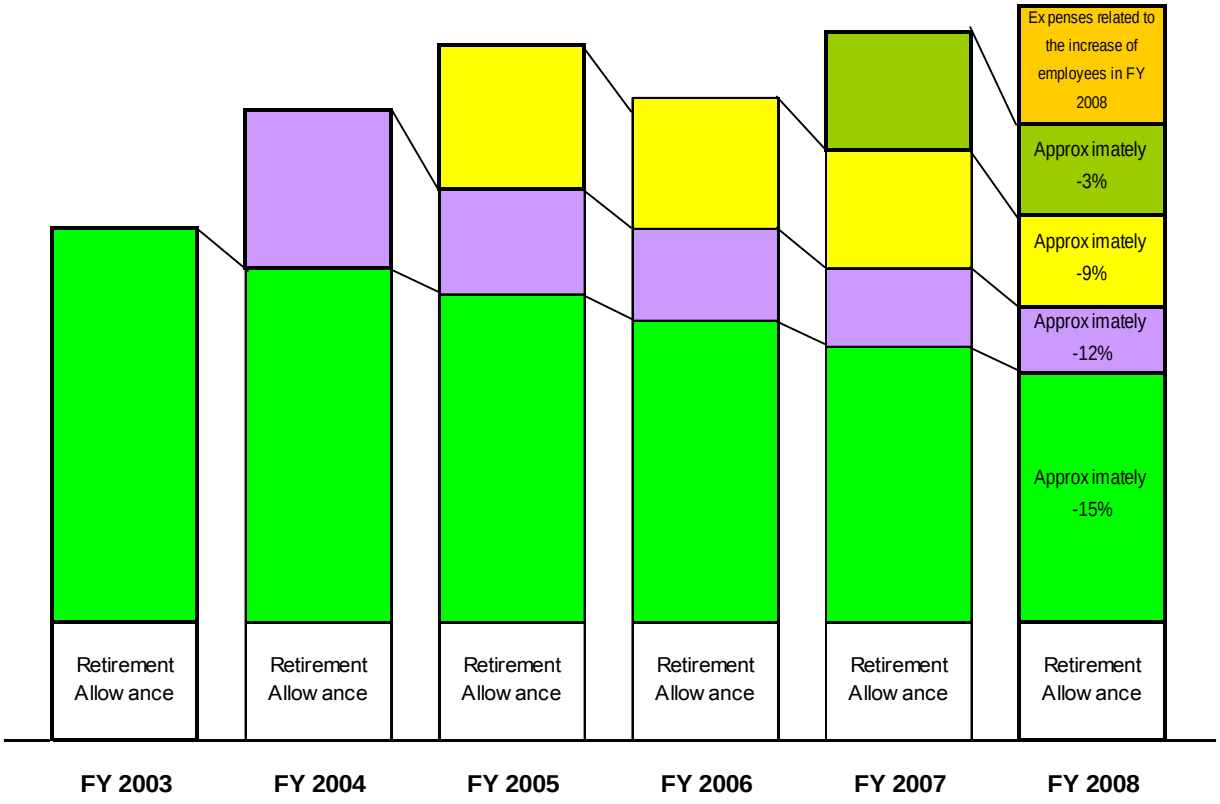
- With regard to matters to be reviewed in FY 2008 based on the Plan for the Review of Optional Contracts, PMDA shifted matters related to both general administrative expenses and operating expenses to general competitive bidding and promoted bidding for all contracts. As a result of that, the ratio of competitive contract methods including planning competition and open recruitment increased by 13.5% year on year.

Competitive Bidding

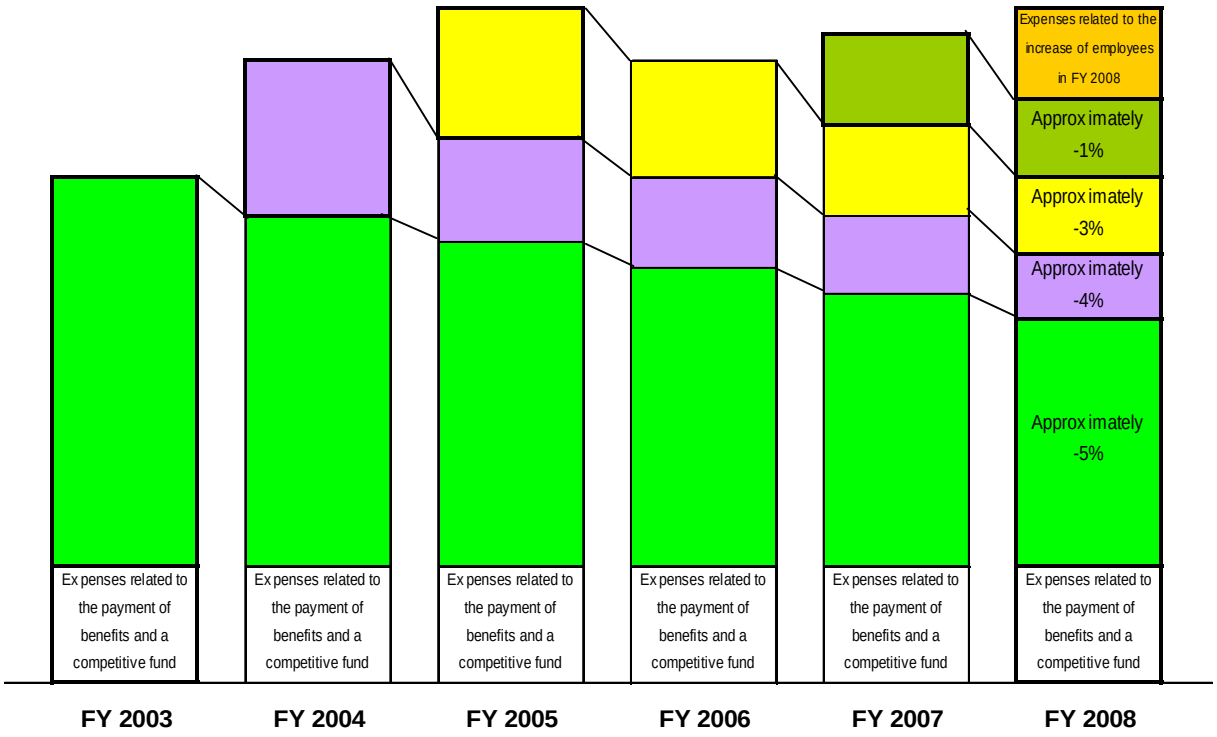
	FY 2007	FY 2008	Change
General competitive bidding (including planning competition and open recruitment)	66 bids (33.5%)	101 bids (47.0%)	35 bids (13.5%)
Noncompetitive optional contracts	131 bids (66.5%)	114 bids (53.0%)	-17 bids (-13.5%)
Excluding contracts in relation to office lease, for which shift to competitive bidding is not appropriate	104 bids (52.8%)	91 bids (42.3%)	-13 bids (-10.5%)
Total	197 bids	215 bids	18 bids

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

a. General Administrative Expenses (See 3.2.(1) for details.)



b. Operating Expenses (See 3.2.(2) for details.)



3.2.(4) Collection and management of contributions

- Contributions from marketing authorization holders of the industry enable PMDA to secure financial resources for relief for adverse health effects such as adverse drug reactions and infections derived from biological products and other operations to improve the quality, efficacy, and safety of drugs 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 drugs and medical devices.

- PMDA automatically processed basic data such as those concerning newly approved products (drugs 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 post-marketing safety measures fund in an integrated fashion. Consequently, PMDA efficiently conducted the operations of contribution collection management, such as the calculation of transaction value which constitutes the basis of the contribution amount and the management of the data concerning unpaid contributions. PMDA was also able to ensure convenience for contributors through continuing consignment contracts with four major banks and the Postal Savings Operation Centers (post offices) for receipt of contributions, resulting in prompt transfer of funds.

- In the Mid-term Plan, PMDA 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 2008, the resulting contribution collection rate for the adverse drug reaction fund was 99.6%, and the rate for infection contributions was 100%.

- Similarly, PMDA sets the contribution collection rate for contributions to post-marketing 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 2008, the resulting contribution collection rate for contributions to safety measures was 99.0%.

FY 2008 Contribution Collection Results

Category		Subjects (cases)	Number of payers who made contributions (cases)	Collection rate (%)	Contribution amount (Million yen)
ADR contributions	MAH	753	752	99.9%	3,722
	Pharmacy	8,047	8,015	99.6%	8
	Total	8,800	8,767	99.6%	3,730
Infection contributions	MAH	96	96	100%	620
Post-marketing safety measures contributions	MAH of drugs	659	657	99.7%	520
	MAH of medical devices	2,273	2,199	96.7%	197
	MAH of drugs & medical devices	197	197	100%	567
	Pharmacy	8,047	8,013	99.6%	8
	Total	11,176	11,066	99.0%	1,292

- To efficiently improve contribution collection rates,

1) PMDA continued to commission the Japan Pharmaceutical Association (JPA) to collect contributions from marketing authorization holders of pharmacy-compounded drugs.
2) PMDA continued to 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. PMDA also created and distributed a handbook on the procedure for declaring and making contributions in order to make the procedure known to all the parties obligated to make contributions. Also, written requests for making contributions were sent to all contributors who have not yet made contributions, with the exception of marketing authorization holders of pharmacy-compounded drugs.

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

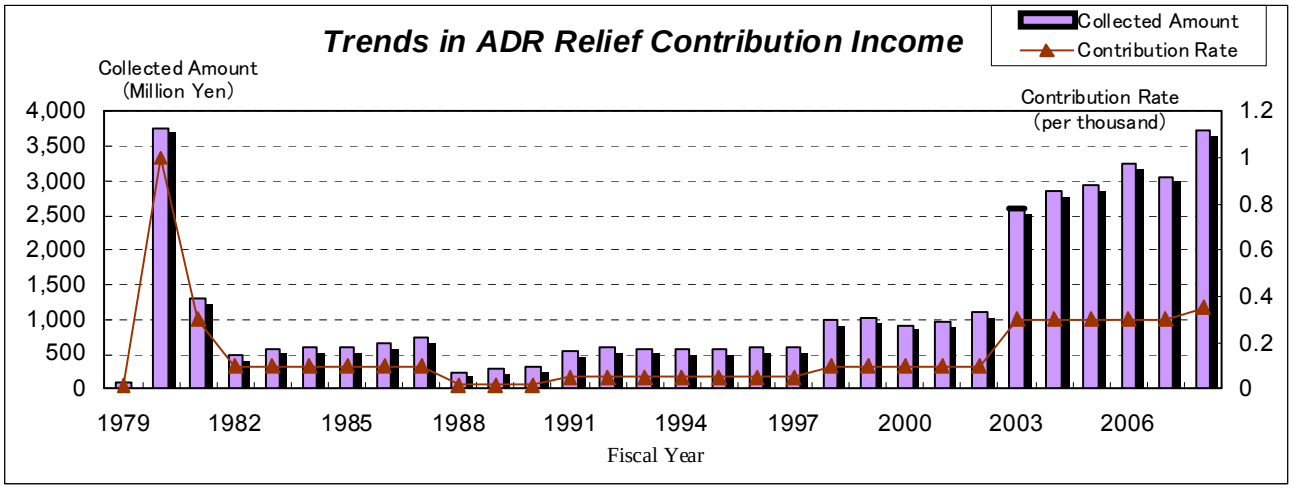
a. Adverse drug reaction fund

- To fund the adverse drug reaction relief service, PMDA has collected contributions to adverse drug reaction funds from marketing authorization holders of approved drugs. In FY 2008, the contribution rate applied to such marketing authorization holders was 0.35/1000 and the collected amount was 3,730 million yen.

(Million yen)

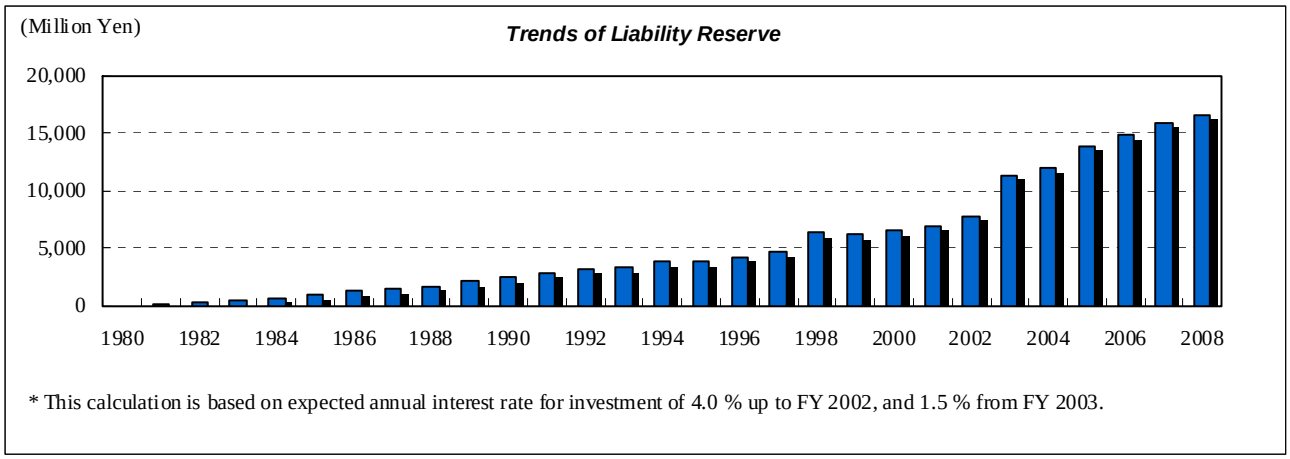
Fiscal year	FY 2003 [Number of MAHs]	FY 2004 [Number of MAHs]	FY 2005 [Number of MAHs]	FY 2006 [Number of MAHs]	FY 2007 [Number of MAHs]	FY 2008 [Number of MAHs]
MAH of approved drugs	2,596 [842]	2,844 [833]	2,923 [787]	3,240 [778]	3,049 [762]	3,722 [752]
MAH of pharmacy-compounded drugs	11 [11,175]	11 [10,550]	10 [9,993]	9 [8,968]	8 [8,309)	8 [8,015]
Total amount	2,607	2,855	2,933	3,249	3,057	3,730
Contribution rate	0.3/1000	0.3/1000	0.3/1000	0.3/1000	0.3/1000	0.35/1000

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



b. Liability reserve

- To cover the estimated relief benefit service costs that eligible persons will receive in the future, PMDA 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 2008 was 16,579 million yen.



(ii) Collected contributions for relief for infections derived from biological products

- To fund the relief service for infections derived from biological products, PMDA has collected infection contributions from marketing authorization holders of approved biological products. In FY 2008, the contribution rate applied to such marketing authorization holders was 1/1000 and the collected amount was 620 million yen.

(Million yen)

Fiscal year	FY 2004 [Number of MAHs]	FY 2005 [Number of MAHs]	FY 2006 [Number of MAHs]	FY 2007 [Number of MAHs]	FY 2008 [Number of MAHs]
MAH of approved biological products	554 [108]	553 [105]	556 [101]	574 [98]	620 [96]
Contribution rate	1/1000	1/1000	1/1000	1/1000	1/1000

(iii) Collected contributions for post-marketing safety measures

- To fund services for improvements in quality, efficacy, and safety of drugs, etc., PMDA has collected contributions to safety measures from marketing authorization holders of drugs and medical devices. In FY 2008, the contribution rate applied to such marketing authorization holders was 0.11/1000 and the collected amount was 1,292 million yen.

(Million yen)

Fiscal year	FY 2004 [Number of MAHs]	FY 2005 [Number of MAHs]	FY 2006 [Number of MAHs]	FY 2007 [Number of MAHs]	FY 2008 [Number of MAHs]
MAH of drugs/medical devices	1,091 [3,076]	1,143 [2,982]	1,211 [3,180]	1,219 [3,094]	1,284 [3,053]
MAH of pharmacy-compounded drugs	10 [10,541]	10 [9,987]	9 [8,960]	8 [8,297]	8 [8,013]
Total amount	1,101	1,153	1,220	1,227	1,292
Contribution rate	0.11/1000	0.11/1000	0.11/1000	0.11/1000	0.11/1000

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

- The introduction of the new remuneration policy based on the personnel evaluation system, which has been introduced since April 2007, and the reform of the remuneration structure of national government employees allowed PMDA to successfully reduce personnel expenses for FY 2008 by approximately 6.6% (compared with personnel expenses per person for FY 2005).

- PMDA compared the remuneration system for its staff for FY 2007 with that for national government employees in order to win the understanding of the public on its remuneration standards, and released the results by posting them on its website.

Fiscal year	FY 2005 (Base year)	FY 2006	FY 2007	FY 2008
Unit personnel expense per person	@ 8,281 thousand yen	@ 8,057 thousand yen	@ 8,052 thousand yen	@ 7,787 thousand yen
Rate of personnel expense reduction (unit personnel expense per person)		-2.7 %	-2.8 %	-6.0 %
Rate of personnel expense reduction (corrected value) (unit personnel expense per person)		-2.7 %	-3.3 %	-6.6 %

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

3.3 Improvement of Services to the Public

3.3.(1) General consultation service

- Based on the General Consultation Guidelines that specify how to handle inquiries directed to PMDA and how to reflect comments and opinions to improve operations, PMDA manages a general consultation service and makes questionnaires available at the reception desk, enabling the collection of comments and opinions of visiting customers regarding its overall operations. Since June 2007, PMDA has been receiving comments and opinions via its website as well as FAX so that citizens can transmit their opinions and requests easily. In FY 2008, PMDA provided the same service.

- Among the 2,622 inquiries that PMDA received in FY 2008, 1,240, or approximately 50% of the total inquiries received, were those relating to applications and consultations for drugs and medical devices.

	Inquiry/consultation	Complaint	Opinion/request	Other	Total
FY 2008	2,522 (1,212)	1 (1)	99 (27)	0 (0)	2,622 (1,240)

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 marketing approval for drugs and medical devices, separately from this general consultation service.

3.3.(2) Responses to consultations, complaints, and claims of dissatisfaction from the private sector regarding reviews and post-marketing safety operations

- In addition to responding to consultations and complaints from general consumers, PMDA 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 PMDA 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 2008, PMDA handled consultations in such a way for 165 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	3
	Category 4		Antibacterial agents, vermifuge, antifungal agents, antiviral agents (excluding AIDS drugs)	0
	Oncology drugs		Antineoplastic agents	25
	AIDS drugs		Anti-HIV agents	0
Office of New Drug II	Category 2		Cardiovascular drugs, antiparkinsonian drugs, antithrombotics, anti-Alzheimer's drugs	5
	Category 5		Reproductive system drugs, genitourinary system drugs, combination drugs	0
	Radio-pharmaceuticals		Radiopharmaceuticals	0
	In vivo diagnostics		Contrast media	1
Office of New Drug III	Category 3		Central/peripheral nervous system drugs, sensory organ drugs (excluding drugs classified in category 6-1), narcotics	39
		Category 3-1	Central/peripheral nervous system drugs (excluding anesthetic drugs)	7
		Category 3-2	Anesthetic drugs, sensory organ drugs (excluding drugs for inflammatory diseases), anesthesia	6
Office of New Drug IV	Category 6-1		Respiratory tract drugs, anti-allergy drugs, sensory organ drugs for inflammatory diseases	28
	Category 6-2		Hormone drugs, drugs for metabolic disorders (excluding combination drugs)	42
Office of Biologics I	Blood products		Blood coagulation factor products, confirmation of gene therapy, confirmation of compliance with Cartagena Protocol	0
	Bio-CMC		Quality of antibody products	1
Office of Biologics II	Biological products		Vaccines, antitoxin	8
	Cellular and tissue-derived products		Cell therapy drugs	0
Total				165

Note: Category 3 was divided into Category 3-1 and Category 3-2 as of December 1, 2008. The number of cases that belong to Category 3 includes those between April 1, 2008, and November 30, 2008, before the division. The numbers of cases that belong to Category 3-1 and Category 3-2, respectively, include those between December 1, 2008, and March 31, 2009, after the division.

- In FY 2004, PMDA 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. PMDA continues to operate the system in FY 2008 as well.

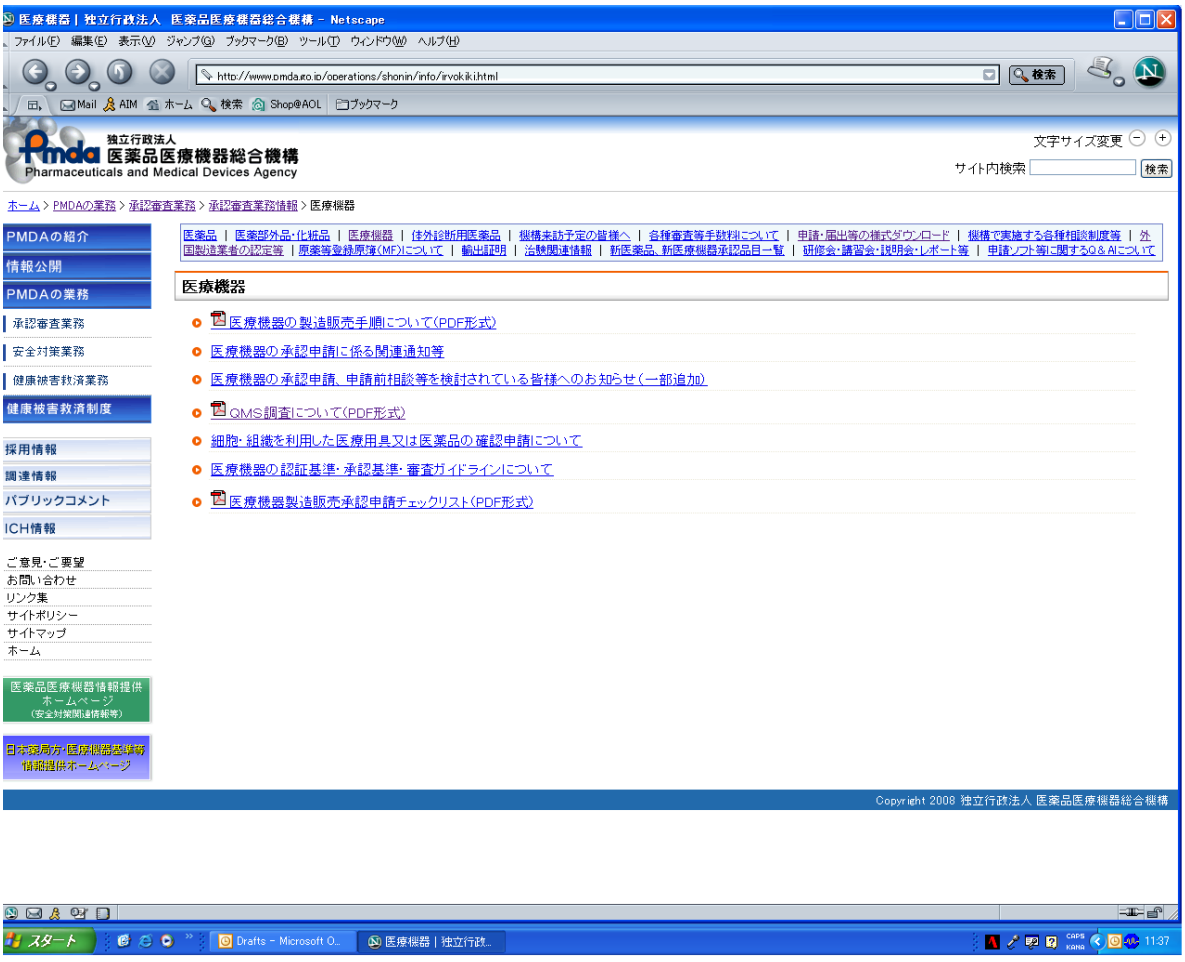
- In addition, PMDA developed a consultation manual to handle complaints, etc., from relevant companies. From among the complaints received from relevant companies, PMDA is reviewing those that would be helpful in improving its operations.

3.3.(3) Improvement in the PMDA website

- PMDA has prepared and posted on its website the Annual Report in FY 2007, which concerns the operating performance of FY 2007, and Principal Achievements up to the End of October 2008 (between April and October) and Future Undertakings, which concerns the operating performance between April and October 2008.

- In addition, materials and minutes of the Advisory Council meetings and other meetings were also posted on its website sequentially to provide relevant information.

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



3.3.(4) Proactive PR activities

- From the viewpoint of systematically promoting PR activities as a whole during the effective period for the Second Mid-term Targets in consideration of the needs of the public and international perspectives, PMDA developed the PMDA Public Relations Strategic Plan (finalized on July 11, 2008) as a basic policy for its overall PR activities during the period and decided to improve services to the public by proactively providing information in line with the strategic plan.

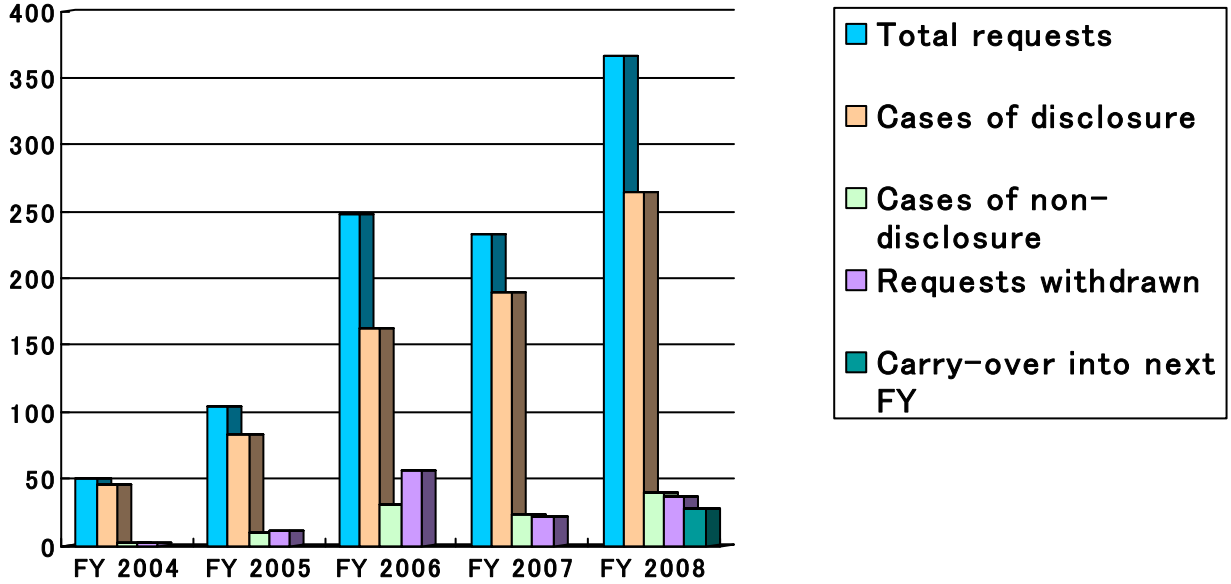
3.3.(5) Disclosure request for corporate documents

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

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	182	1	22	0	2	0
FY 2008	367	36	14	250	6	29	5	1	27
Total	1002	126	58	686	20	80	5	13	27

Note: The petition of objection was filed once in FY 2008. As of March 31, 2009, this petition is being discussed at the Information Disclosure and Personal Information Protection Review Board of the Cabinet Office.



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	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	Aggregate
Individuals	35	74	113	86	99	407
Corporate (e.g., drug manufacturers)	14	25	132	143	250	564
Press	1	5	3	4	18	31
Total	50	104	248	233	367	1,002

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	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	Examples
Approval review	8	22	90	115	263	Marketing notification for products not subject to approval
GLP/GCP/GMP/QMS etc. audits	32	69	117	74	52	Notice of GCP audit results
Post-marketing safety	8	13	40	44	52	ADR report
Others	2	0	1	0	0	Business trip order forms
Total	50	104	248	233	367	

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

3.3.(6) Disclosure request for personal information

- The status of requests for the disclosure of personal information based on the Act on the Protection of Personal Information Held by Incorporated Administrative Agencies is shown below.

Number of Requests for Disclosure of Personal Information

	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 2007	3	0	2	1	0	0	0	0	0
FY 2008	5	0	0	3	2	0	0	0	0
Total	8	0	2	4	2	0	0	0	0

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

Number of Requests for Disclosure of Personal Information by Requester

Requester/FY	FY 2007	FY 2008	Total
Identical person	1	3	4
Legal representative (person with parental authority, etc.)	2	0	2
Others	0	2	2
Total	3	5	8

Number of Requests for Disclosure of Personal Information by Operational Category

Operational category/FY	FY 2007	FY 2008	Total	Examples
Office of Relief Funds	3	5	8	Application for decision, etc.
Total	3	5	8	

3.3.(7) Auditing and related matters

- In addition to implementing audits through an external accounting firm in accordance with the system for incorporated administrative agencies and through the Agency's Auditor, PMDA also conducts internal auditing systematically through the Audit Office for operations and accounts, from the perspective of internal control. The results of these audits are publicly reported to ensure transparency in the Agency's management and operations.

- In FY 2008, PMDA conducted internal audits on the management status of information systems, the status of contracts, the storage status of cash and cash equivalents/articles, and the status of compliance with the rule restricting the employment of personnel from the private sector.

3.3.(8) Report on the financial standing

- From the perspective of ensuring the transparency of expenditures, PMDA disclosed its financial standing for FY 2007, including the use of review fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2008 on its website.

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

- PMDA publicly announced the follow-up of the Plan for the Review of Optional Contracts for FY 2007 on its website in July 2008. PMDA also released information on noncompetitive optional contracts, which were concluded in FY 2008, on its website in March 2009.

3.4 Personnel Issues

3.4.(1) Review of a personnel evaluation system

- According to the Mid-term Targets of PMDA, it is required to conduct proper personnel evaluation taking individual performance of full-time employees into consideration, and the Mid-term Plan of PMDA 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, PMDA fully introduced the personnel evaluation system in April 2007 after conducting trials targeting at all full-time employees from April to September 2006, and appropriately reflected the results in pay raise in July 2008.

  In order to ensure the proper implementation of the personnel evaluation system, PMDA provided briefing sessions for all employees, and took up the personnel evaluation system as a subject of the training course for new recruits.

3.4.(2) Systematic implementation of staff training

- In the operations for reviews, post-marketing safety measures, and relief service conducted by PMDA, an extremely high level of expertise is required. In addition, rapid strides are constantly being made in the advancement of scientific technology for developing drugs and medical devices. Under such circumstances, it is necessary for PMDA to appropriately implement capacity development to enhance the level of expertise of its staff. Therefore, in FY 2007, PMDA reorganized the existing training courses into two training courses: the General Training Course and the Specialized Training Course. Consequently, employees can attend programs systematically. PMDA continued to provide these training courses in FY 2008. Furthermore, in order to provide efficient and effective training tailored to the capabilities and qualifications of individual employees, PMDA actively deployed external institutions and experts, striving to reinforce training. PMDA also facilitated the participation of employees in academic conferences both in Japan and overseas to improve their knowledge and technological expertise.

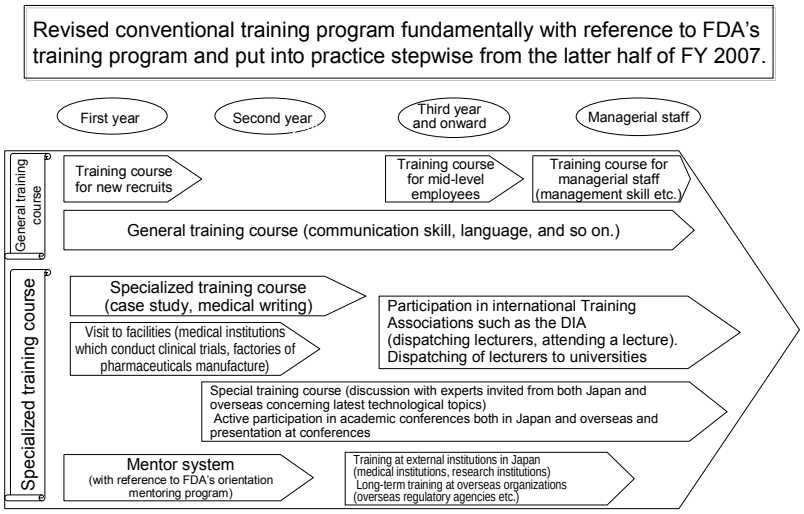
- Specifically, the Training Committee formulated plans for new recruit training, internal training, and external training based on the needs of each division. Various training programs, as introduced below, were implemented.

  (i) PMDA conducted a training course for new recruits in April and October 2008.
  (ii) PMDA dispatched an aggregate of 51 employees to universities both in Japan and overseas as well as foreign drug regulatory authorities for the purpose of training.
  (iii) As special training programs, PMDA also held 16 training sessions on technical issues, inviting experts belonging to domestic or foreign regulatory authorities, corporations, and universities.
  (iv) PMDA conducted training on business writing and business etiquette twice in the first half and once in the second half. PMDA also conducted compliance training and OJT-trainer development training once in the second half as well as bookkeeping training for career-track employees once by making use of external institutions.
  (v) As general training, PMDA conducted English conversation training between August and December 2008. PMDA also conducted TOEIC examinations in May 2008 and January 2009, for the purpose of assessing the effect of English conversation training as well as improving the linguistic ability of employees.
  (vi) PMDA conducted a training program by 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 PMDA from respective standpoints. PMDA also conducted one training program aimed at acquiring basic knowledge on the protection of personal information.
  (vii) PMDA 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)
  (viii) PMDA conducted a total of 13 training sessions on pharmaceutical regulations for mid-level employees from July to December 2008 by inviting lecturers not only internally but also from the Ministry of Health, Labour and Welfare and external relevant institutions.
  (ix) With cooperation of ACCJ member companies, PMDA conducted on-the-job training for two days in November 2008, by making use of orthopedic medical devices.

- PMDA provided new recruits with the opportunity to visit various facilities between June 2008 and February 2009: seven plants where drugs are manufactured, four where medical devices are manufactured, and four medical institutions.

- In addition, the status of participation in academic conferences from each division were tracked and checked every fiscal quarter (1,009 participants in total as of the end of March 2009)

Human resource training and development



3.4.(3) Appropriate personnel allocation

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

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

3.4.(4) Securing human resources through open recruitment

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

- Because the revised Mid-term Plan as of the end of FY 2006 based on the Report of the Council for Science and Technology Policy set the number of permanent employees at the end of the period (at the end of FY 2008) as 484, PMDA was required to recruit capable persons for areas where more manpower is needed, based on the recruitment plan for each job category. PMDA held information sessions on career opportunities, conducted the open recruitment of technical permanent employees four times in FY 2008 by making use of its website as well as job information websites, and decided to recruit new employees, formally or informally, as shown below.

  Note: Due to the revision of the Mid-term Plan made at the end of FY 2006, PMDA 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)

Employment through Open Recruitment in FY 2008—as of April 1, 2009

1)	Technical employees (4 times of public recruitment)	
	Number of applicants	About 910
	Number of employment	44
	Number of prospective staff	54
2)	Administrative employees (twice of public recruitment)	
	Number of applicants	About 140
	Number of employment	8

Recruitment Activities (FY 2008)

- Schedule of PMDA information sessions
  - May to June: One session each in Tokyo, Osaka, Sendai and Hiroshima (total participants, 154 persons)
  - September: Two sessions in Tokyo and one session each in Osaka, Nagoya and Fukuoka (total participants, 384 persons)
  - December: Two sessions in Tokyo and one session in Osaka (total participants, 220 persons)
  - March: Two sessions in Tokyo and one session in Osaka (total participants, 258 persons)
- Activities performed in collaboration with directors/employees:
  - Lectures and explanation of the services at universities, etc. by directors/employees
  - OB/OG visits by young employees
  - Advertising via booth displays at academic conferences, etc. (e.g. distribution of brochures and exhibition of posters at the annual meeting of the Japanese Association for Infectious Diseases, the 25th Live Demonstration in Kokura and the Japanese Red Cross Society Symposium (Tokyo/Osaka/Fukuoka/Hokkaido)
- Tools for recruitment activities
  - Brochures for recruitment, posters for recruitment
  - The brochures and posters were sent out to approximately 500 institutions including medical faculties of universities, medical institutions such as university hospitals, pharmacy faculties of universities, pharmacy departments of hospitals, faculties relevant to biostatistics and veterinary science, and research institutions, or distributed at information sessions, etc.
- Information to be posted on job information websites
  - Website presenting job offers for 2010 graduates (NIKKEI NAVI 2010)
  - Website presenting job information for those seeking a career change (NIKKEI CAREER NET. For 1 month from August 29 and for 1 month from November 21)
  - Delivery of direct mails (total 19,196 mails were sent targeting graduate students majoring in pharmacy, science, engineering, agriculture, medicine, etc.)
- Recruitment advertising via academic journals
  - "Japan Medical Journal", "Japanese Journal of Clinical Pharmacology and Therapeutics", "Japanese Journal of Pharmaceutical Health Care and Sciences", the Pharmaceutical Society of Japan (FARUMASHIA), the Japanese Joint Statistical Meeting (collected report of lectures), the 11th Japanese Society of Drug Informatics (program), "Journal of Japan Society of Mechanical Engineers", "Japanese Journal of Medical Electronics and Biological Engineering Academic Journals", the NIKKEI (featuring advertisements of grad hiring)
  - Posting of recruitment contents on the websites in collaboration with the Japan Pharmaceutical Association, the Japanese Society of Hospital Pharmacists, the Japan Pharmacists Education Center, the Japanese Society for Pharmacoepidemiology, the Japan Association of Medical Informatics, the Japanese Society of Drug Informatics, the Japanese Society of Pharmaceutical Health Care and Sciences, the University Hospital Medical Information Network (UMIN)

Numbers of the PMDA Staff

	April 1, 2004	April 1, 2005	April 1, 2006	April 1, 2007	April 1, 2008	April 1, 2009	(At the end of the Second Mid-term Plan) (end of FY 2013)
Total	256	291	319	341	426	521	751
Review divisions	154	178	197	206	277	346	
Safety divisions	29	43	49	57	65	82	

Notes
1. *The expected number of the staff including executives at the beginning of the effective Mid-term period when PMDA was established in April 2004 was 317 (The number includes 11 staff members engaged in the R&D promotion service of PMDA).*
2. *The "Total" includes 6 executives, except for that of 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 (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 (end of FY 2008) was 346*
4. *The review divisions include the Director (Center for Product Evaluation), Associate Executive Directors (excluding Associate Executive Director responsible for Office of Regulatory Science), Associate Center Directors (excluding Associate Center Director responsible for Office of International Programs), Office of Review Administration, Office of Review Management, Offices of New Drug I to V, Offices of Biologics I and II, Office of OTC/Generic Drugs, 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 offices on October 1, 2007. Office of New Drug V was also established on April 1, 2009).*
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

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

- For this purpose, PMDA conducts appropriate personnel management by prescribing, in the work regulations, 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. PMDA also strives to keep its staff members informed of these regulations.

- More specifically, PMDA prepared summaries and a Q & A list concerning relevant regulations, and makes sure to keep the staff informed through the intranet and during new recruit training.

- In addition, from the perspective of further informing the staff about service-related regulations, PMDA has prepared 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) Entrance/exit access control

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

- Specifically, by introducing a security access control system where access to each office is limited only

to staff members through using unique ID cards and by recording the history of when each staff member enters each office, outsiders are not able to enter the rooms unaccompanied.

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

3.5.(2) Security measures for information systems

- Based on the FY 2008 plan, PMDA has strived to ensure the security of the information relating to information systems.

- In order to reinforce the data backup function, PMDA has been storing backup data in the information systems at remote locations since FY 2007.

- In order to increase the use of secure e-mail in the services of the transcription of shorthand notes of face-to-face advice, PMDA revised relevant policies and made further efforts so that the use of secure e-mail might be available in these services from FY 2009.

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

	Number of registered companies	Number of issued certificates
Outside PMDA	43	310
Within PMDA		349

Note: The numbers of registered companies and issued certificates as of the end of March 2009

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, PMDA, 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

(i) Disclosure of cases of payment of benefits on the website

- To enrich the contents of information provided relating to the relief systems and to make the administration of the systems more transparent, PMDA plans to disclose information about actual performance of operations achieved in FY 2008 on the PMDA website. In addition, PMDA has finished posting cases of approval/rejection up to the fourth quarter of FY 2007 on the website with due consideration to protecting personal information. PMDA also plans to provide information on cases in and after FY 2008 successively on the website.

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

(ii) Improvement of brochures, etc.

- To reduce the amount of time required for administrative processing because of incomplete applications, and to make operations more efficient, PMDA carried out the following:

  a) PMDA reviewed the descriptions of a brochure entitled “Do You Know about Relief Systems?” which explains the relief systems clearly, and distributed it. PMDA also posted the brochure (in PDF format) on its website together with animations that summarizes details of the brochure, in order to make it easier to use the brochure.
  b) PMDA reviewed the format for medical certificates necessary for the adverse drug reaction relief system and prepared description samples of medical certificates necessary for the relief system for infections derived from biological products, in order to make it easier for doctors to fill in.
  c) PMDA made it easier to use the relief systems by publicizing the fact that applications and the brochure can be downloaded from its website.

  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, PMDA reviewed methods for effective publicity and carried out the following:

  (i) Publicity through a brochure entitled “Do You Know about Relief Systems?,” which explains the relief systems clearly (this brochure is included in approximately 170,000 magazines published by the Japan Medical Association and in approximately 100,000 magazines published by the Japan Pharmaceutical Association, and it is also distributed on the PMDA website in the form of an

abridged animation version (14 minutes) and a full-text PDF version) and distribution of the brochure and DVDs that summarize the details of the brochure to pharmaceutical universities, faculties of pharmaceutical sciences and nurse training schools

(ii) Introduction of the infection relief system in six specialized magazines and of commissioned payment services for HIV-positive patients in five specialized magazines

(iii) Introduction of the relief systems in programs and abstract journals of four academic conferences including the JHA Congress.

(iv) Participation in medical conventions (the Annual Meeting of the Japanese Dermatological Association, Annual Meeting of the Japan Society of Transfusion Medicine and Cell Therapy, Annual Meeting of the Japanese Society of Neurology (Societas Neurologica Japonica), etc.) and distribution of brochures about and presentations on the relief systems at 8 different conventions

(v) Explanation of the relief systems directly at workshops for vaccination specialists (at eight places in Japan), practical training courses of the Medical Safety Support Center (at four places in Japan), lectures of the School of Pharmacy (Tokyo University of Pharmacy and Life Sciences), workshops on the adverse drug reaction relief systems (Confederation of Tottori Prefectural Democratic Medical Care Associations or *Tottori Miniren*) and the 36th lecture meeting of the Yakugai Ombudsperson "Medwatcher Japan" and the Tie-up Group at Hakodate

(vi) Implementation of publicity at the 22nd 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

(vii) Publicity through newspapers (Yomiuri, Hokkaido, Chunichi/Tokyo, Nishinippon, Kohoku Shimpo, Chugoku Shimbun, and Sports Nippon), transportation (trains) and commercials on the radio, after planning competitions are conducted by making use of external experts

(viii) Expansion of toll-free consultation services (that can be used via cellular phones and public phones)

- The main publicity activities with the help of concerned bodies are as follows:

(i) Publicity in a magazine on drug safety updates (DSU) published by the Federation of Pharmaceutical Manufacturers' Associations 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 medication record book published by the Japan Pharmaceutical Association

(v) Description of the contact information for inquiries on the relief systems on the outer boxes of OTC drugs based on a voluntary agreement in the pharmaceutical industry

Publicity through the Brochure

4.1.(3) Management of the consultation service

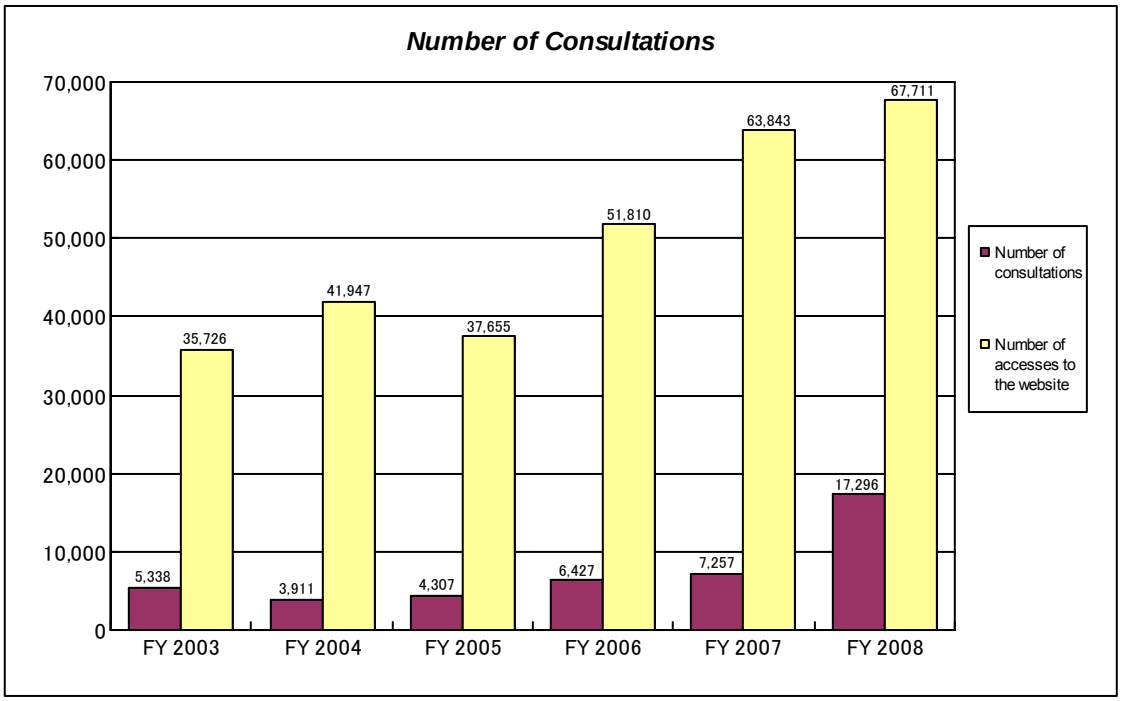
- In the FY 2008 plan, the goal of PMDA was to increase the number of consultations and accesses to its website, both by 20% compared with FY 2003, but the actual number of consultations in FY 2008 increased by 224% compared with FY 2003.

  This was due to the creation of a brochure that explains the relief systems clearly, publicity by enclosing copies of the brochure in magazines published by the Japan Medical Association and the Japan Pharmaceutical Association, publicity by distributing animations that summarize the brochure on the PMDA website, introduction of access to toll-free phone services via cellular phones and public phones, and descriptions of contact information for inquires on the relief systems on the outer boxes of OTC drugs based on a voluntary agreement in the pharmaceutical industry.

  Also, the number of accesses to the PMDA website in FY 2008 increased by 90% compared with FY 2003.

Fiscal Year	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	Compared with FY 2003
Number of consultations	5,338	3,911	4,307	6,427	7,257	17,296	224% increase
Number of web accesses	35,726	41,947	37,655	51,810	63,843	67,711	90% increase

Toll-free number: 0120-149-931
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, PMDA 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 March 2009, it completed the second 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.

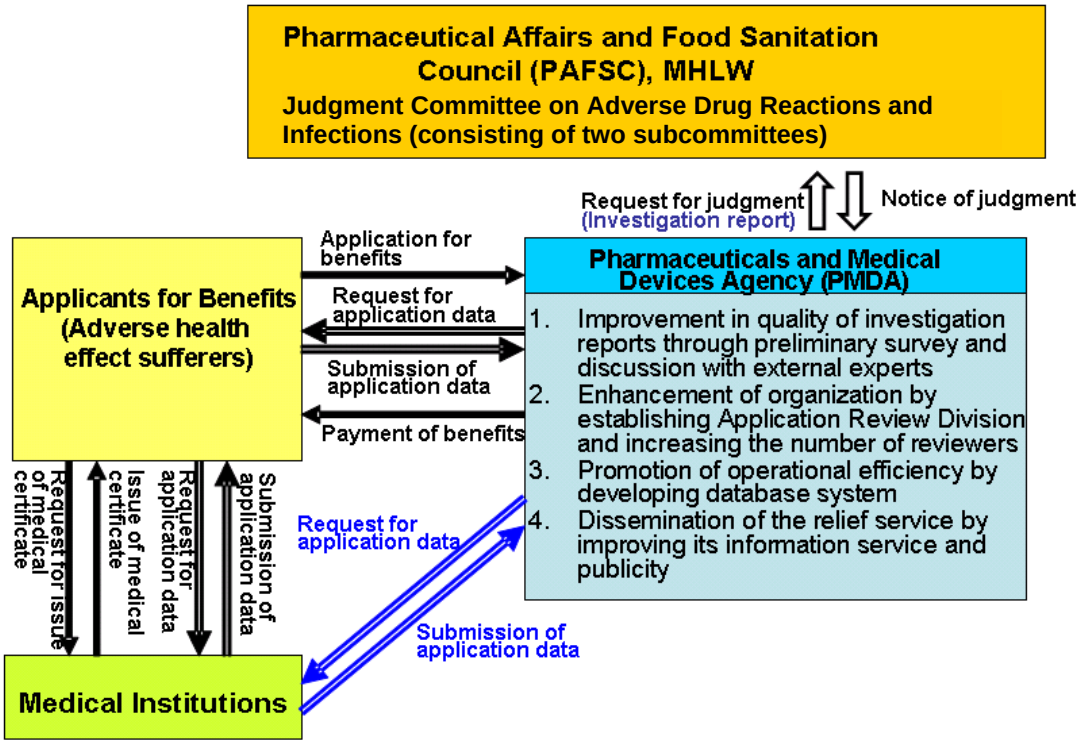
4.1.(5) Prompt processing of relief benefit claims

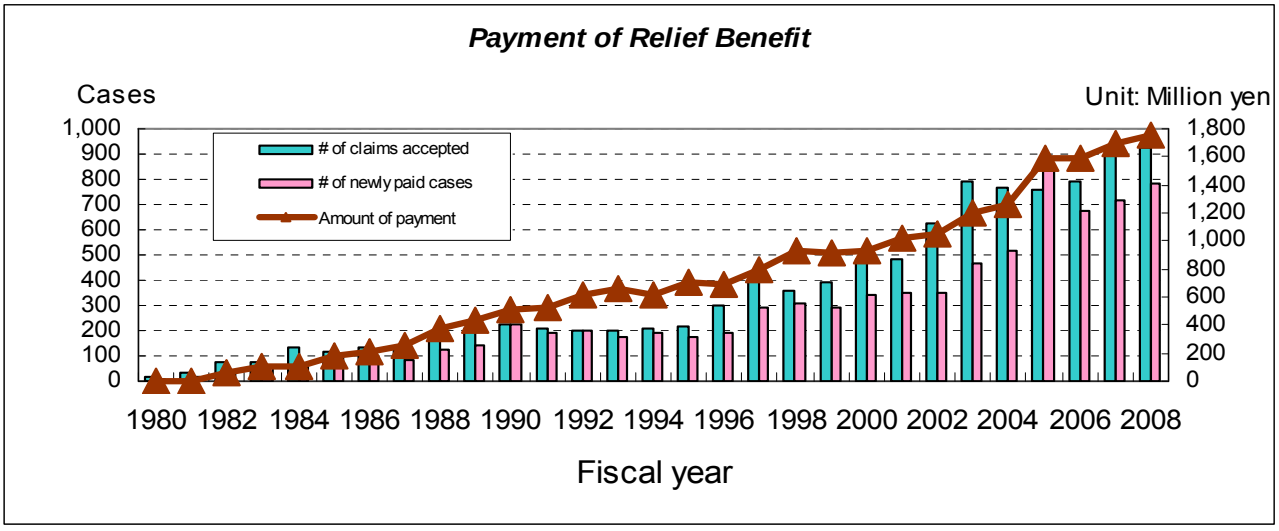
- In order to conduct prompt administrative processing of relief benefit services, PMDA, upon receiving a claim for relief benefit, investigates and organizes the facts given in the contents of such claim, and requests the Minister of Health, Labour and Welfare (MHLW) to make a medical and pharmaceutical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

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

Flow of Adverse Health Effect Relief Services

Improvement of Adverse Health Effect Relief Services





FY 2008

- Relief services for adverse drug reactions
  → Number of claims: 926
  Number of cases of approval/rejection: 919 (of which 782 were judged approved)
- Relief services for infections
  → Number of claims: 13
  Number of cases of approval/rejection: 11 (of which 6 were judged approved)

- PMDA also set 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. In FY 2008, which was the last year of the

effective period for the Mid-term Targets, PMDA planned to process claims for benefits smoothly through collaborations with MHLW, thereby completing 60% or more of the cases judged (regardless of approval/rejection) in the fiscal year within the standard administrative processing time.

- PMDA discussed with MHLW for sharing the administrative processing time and decided to allocate 2 months for MHLW to make medical and pharmaceutical judgments and 6 months to PMDA (excluding the time periods when administrative processing is not possible because of additional or supplementary documents and investigations are required of claimants or medical institutions), and it have periodically prepared a list of pending cases to appropriately manage the processing time for paperwork.

- The achievement rate for FY 2008, which is the final year of the First Mid-term Plan, was 74.3%, a significant increase from the target of 60%, as a result of the continuous intensive processing of paperwork.

(i) Adverse drug reaction relief services

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

a. Actual performance of adverse drug reaction relief

The actual performance for FY 2008 is shown below:

Fiscal Year		FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of claims		793	769	760	788	908	926
Number of judged cases		566	633	1,035	845	855	919
	Approved	465	513	836	676	718	782
	Rejected	99	119	195	169	135	136
	Withdrawn	2	1	4	0	2	1
Cases in progress*		820	956	681	624	677	684
Achievement rate†		17.6%	14.5%	12.7%	65.3%	74.2%	74.3%
Median processing time		10.6 months	12.4 months	11.2 months	6.6 months	6.4 months	6.5 months

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

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

b. Number of claims by type of benefit

The numbers of claimants filed in FY 2008 by type of benefit are shown below:

(Cases)

Fiscal Year		FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of claims		793	769	760	788	908	926
Types of benefits	Medical expenses	640	613	602	643	730	769
	Medical allowances	683	650	659	694	786	824
	Disability pensions	68	73	78	60	70	79
	Pension for raising handicapped children	9	14	5	14	10	7
	Bereaved family pensions	56	54	41	31	33	26
	Lump-sum benefits for bereaved families	42	47	48	51	72	49
	Funeral expenses	98	101	84	88	105	78

Note: A claim could include more than one type of benefit

c. Judgment status by type of benefit

The status of judgments made in FY 2008 by type of benefits is shown below:

(Thousand yen)

Types	FY 2003		FY 2004		FY 2005	
	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
Medical allowances	408	35,388	472	42,711	757	70,073
Disability pensions	22	552,869	24	592,028	33	653,143
Pension for raising handicapped children	2	16,991	4	17,810	17	40,639
Bereaved family pensions	32	335,829	31	412,167	44	502,468
Lump-sum benefits for bereaved families	30	217,148	19	137,041	32	228,708
Funeral expenses	61	11,205	48	9,167	74	14,010
Total	922	1,204,243	1,046	1,262,647	1,674	1,587,567

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

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

Note 2: 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) Infections derived from biological products relief

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

* Biological products refer to drugs, quasi-drugs, cosmetics, or medical devices that are manufactured using materials or ingredients derived from human beings or other living matter (excluding plants), which are designated as special products requiring extreme caution from the perspective of health care by the Minister of Health, Labour and Welfare upon hearing opinions from the Pharmaceutical Affairs and Food Sanitation Council.

a. Actual performance of relief for infections

The actual performance for FY 2008 is shown below:

Fiscal Year		FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of claims		5	5	6	9	13
Number of judgments		2	6	7	5	11
	Approved	2	3	7	3	6
	Rejected	0	3	0	2	5
	Withdrawn	0	0	0	0	0
Cases in progress*		3	2	1	5	7
Achievement rate†		100.0%	50.0%	100.0%	100.0%	100.0%
Median processing time		3.0 months	5.6 months	3.8 months	3.8 months	5.2 months

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

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

b. Number of claims by type of benefit

The numbers of claims filed in FY 2008 by type of benefit are shown below.

(Cases)

Fiscal Year		FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of claims		5	5	6	9	13
Types of benefits	Medical expenses	5	5	5	7	11
	Medical allowances	5	5	5	8	13
	Disability pensions	0	0	0	1	0
	Pension for raising handicapped children	0	0	0	0	0
	Bereaved family pensions	0	0	1	0	0
	Lump-sum benefits for bereaved families	1	0	0	0	1
	Funeral expenses	1	0	1	0	1

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 2008 by type of benefit is shown below:

(Thousand yen)

Types of benefits	FY 2004		FY 2005		FY 2006		FY 2007		FY 2008	
	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	2	161	3	475	6	473	3	102	5	204
Medical allowances	2	142	3	249	6	497	3	352	6	386
Disability pensions	—	—	—	—	—	—	—	—	—	—
Pension for raising handicapped children	—	—	—	—	—	—	—	—	—	—
Bereaved family pensions	—	—	—	—	1	1,387	—	2,378	—	2,378
Lump-sum benefits for bereaved families	—	—	—	—	—	—	—	—	1	7,135
Funeral expenses	—	—	—	—	1	199	—	—	1	199
Total	4	302	6	724	14	2,556	6	2,833	13	10,302

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.

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

- To plan for collaboration between divisions within PMDA, information on judged cases relating to eligibility for relief benefits for adverse drug reactions and relief benefits for infections in FY 2008 was provided to the Office of Safety after excluding personal information.

4.1.(7) Surveys on actual state 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, PMDA 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, PMDA 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 state of adverse health effects stemming from adverse drug reactions conducted in FY 2005, and initiated investigative research to obtain reference materials for examining the ideal way to provide services and measures for improving the QOL of sufferers from severe and rare adverse health effects, for which general measures for disabled people do not necessarily provide sufficient support.

The reports on the Investigative Research in FY 2006 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.

The reports for FY 2007 were also provided by the leaders on November 17, 2008, and were publicly announced on the website after disclosure to the Relief Committee session held on December 25, 2008.

Contents of the Research

PMDA collects, analyzes, and evaluates reports, such as survey forms, etc., from sufferers from adverse health effects regarding the condition of various efforts in their daily life (61 volunteers in FY 2008).

Investigative Research Team

Leader	Kazuaki Miyata	President of Nihon Fukushi University
	Takao Takahashi	Professor, School of Medicine, Keio University (Department of Pediatrics)
	Kazuo Tsubota	Professor, School of Medicine, Keio University (Department of Ophthalmology)
	Chieko Matsunaga	Section Director, Research Section, Planning and Research Division, the National Center for Persons with Severe Intellectual Disabilities, Nozominosono

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

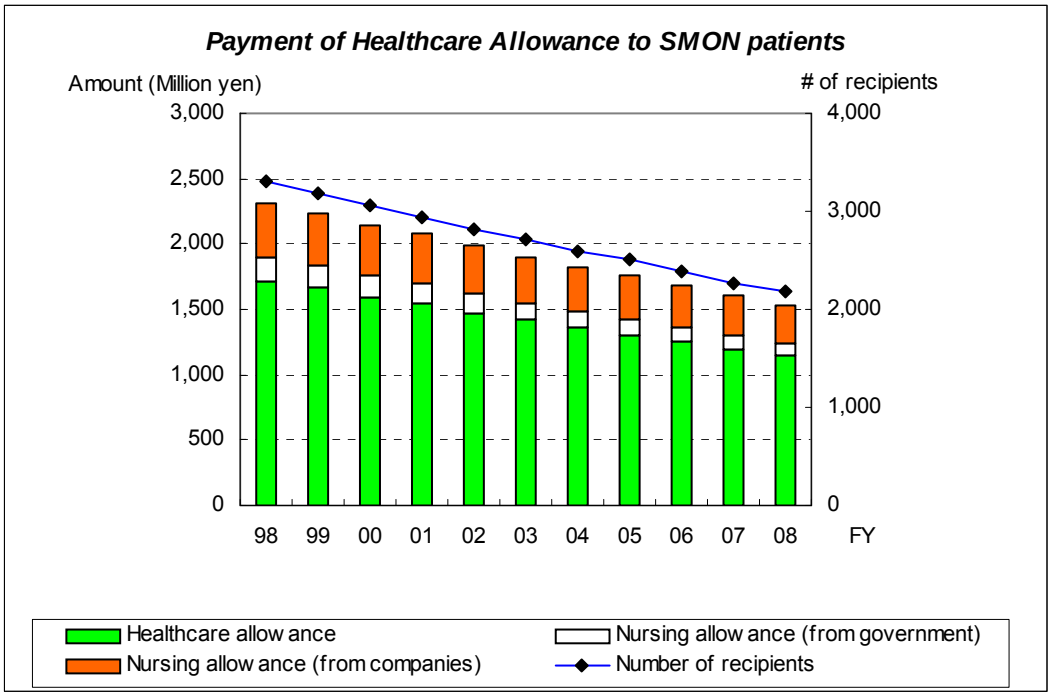
In order to appropriately provide healthcare allowances, etc., for SMON patients and HIV-positive patients affected through blood products, PMDA implemented appropriate operations based on the contents of consignment contracts, giving due consideration to the confidentiality of personal information.

(i) Services for SMON patients (healthcare allowances)

- PMDA provides healthcare allowances and nursing care allowances for SMON patients for whom a settlement has been reached in court. In FY 2008, the number of patients receiving such allowances was 2,180, and the total amount of payments was 1,532 million yen.

Fiscal year		FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of recipients		2,713	2,598	2,504	2,381	2,269	2,180
Amount paid (thousand yen)		1,901,829	1,829,332	1,757,774	1,683,500	1,601,134	1,531,745
Break down	Healthcare allowance	1,417,469	1,359,056	1,305,168	1,251,622	1,191,245	1,140,517
	Nursing allowance (from companies)	349,933	342,357	330,086	315,027	299,108	284,981
	Nursing allowance (from the government)	134,427	127,920	122,520	116,850	110,781	106,247

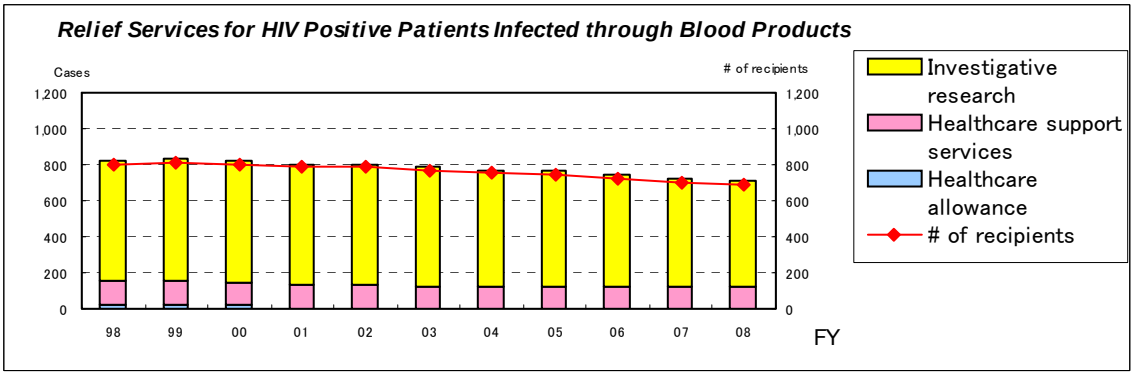
Note: Since the numbers are rounded off to the nearest thousand yen, the amount paid does not always match the sum of the amounts for the breakdown categories.



(ii) AIDS-related services (healthcare allowances)

- PMDA provides the three services below for HIV-positive patients affected through blood products. Of the HIV-positive patients who received benefits in FY 2008, 587 patients received allowances relating to investigative research, 121 patients received allowances for healthcare support services and 2 patients received healthcare allowances. The total number of patients receiving allowances was 710 patients, and the total amount of payments was 538 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	
	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
Healthcare support services	127	221,400	124	210,600	121	210,300
Healthcare allowance	3	8,733	3	8,706	3	8,706
Total	789	576,477	772	567,752	762	560,023

Fiscal year	FY 2006		FY 2007		FY 2008	
	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	618	334,653	604	327,857	587	320,122
Healthcare support services	120	210,000	117	224,796	121	211,800
Healthcare allowance	3	8,678	3	8,084	2	6,300
Total	741	553,331	724	560,737	710	538,222

4.1.(9) Appropriate implementation 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

- PMDA 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 660, with 13,632 million yen as the total amount paid in FY 2008.

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

4.2 Reviews and Related Services/Post-marketing Safety Measures

To enable for the public to safely use drugs and medical devices of international standards, through reviews and related services and post-marketing safety measures, PMDA is required to provide better drugs and medical devices to clinical practice settings faster and with greater safety, ensure that drugs and medical devices are used properly, prevent health hazards, and respond appropriately and promptly if hazards should occur, so that drugs and medical devices can fulfill their purpose over a longer period of time. Therefore, PMDA has taken the following operations to reinforce the systems for consultation/review and post-marketing safety measures, and to organically link the operations to achieve the Mid-term Targets and FY 2008 plan.

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

(i) Ensuring the benefits of drugs and medical devices for the public and healthcare professionals

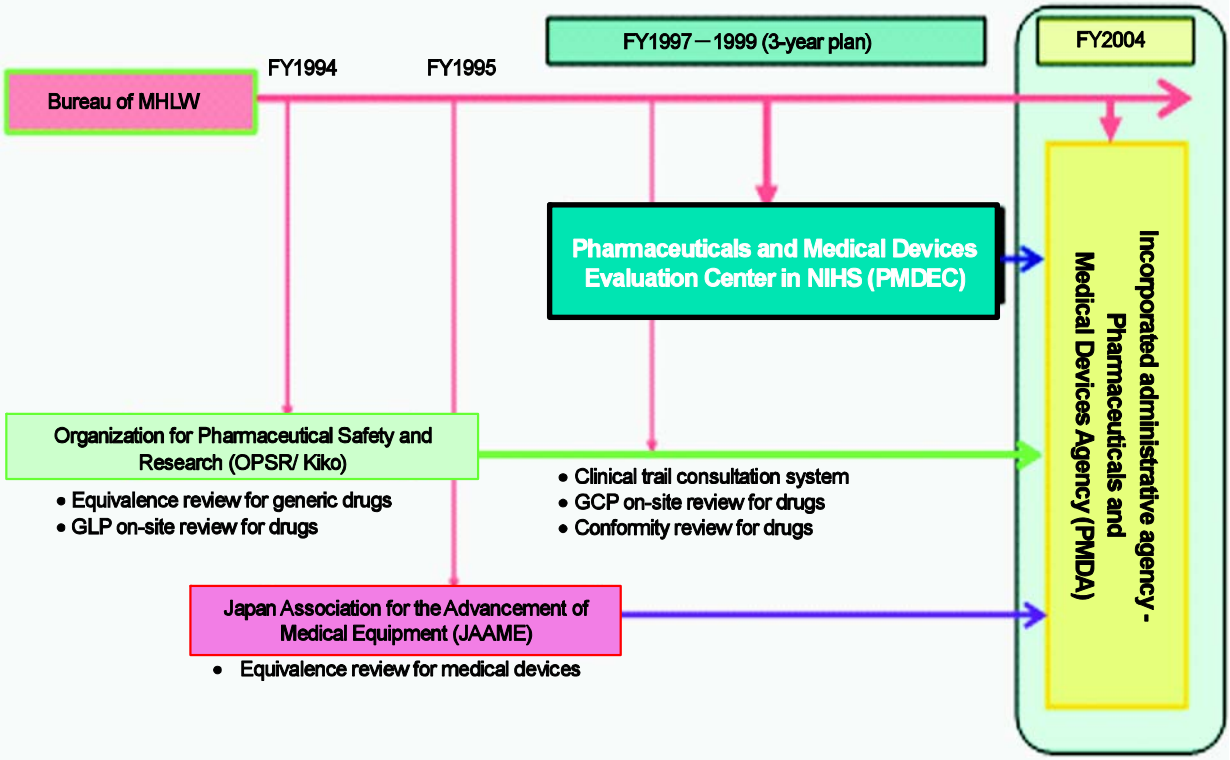
- PMDA is required to ensure that the public and healthcare professionals enjoy the benefits of the latest and safe drugs and medical devices promptly and to the fullest extent, and to ensure that pharmaceutical companies benefit from this prompter access.

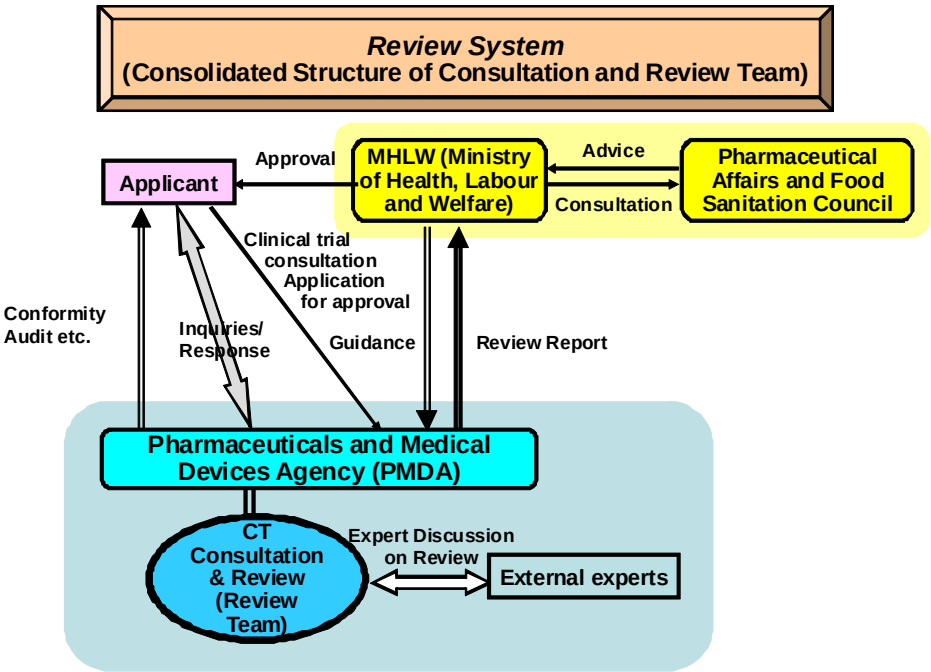
a. Implementation structure for clinical trial consultations and reviews

- The review system for drugs 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 drugs and medical devices to the Ministry of Health, Labour and Welfare (MHLW), allowing consolidation of review functions. By taking the following kinds of measures, further improvements in the system were made.

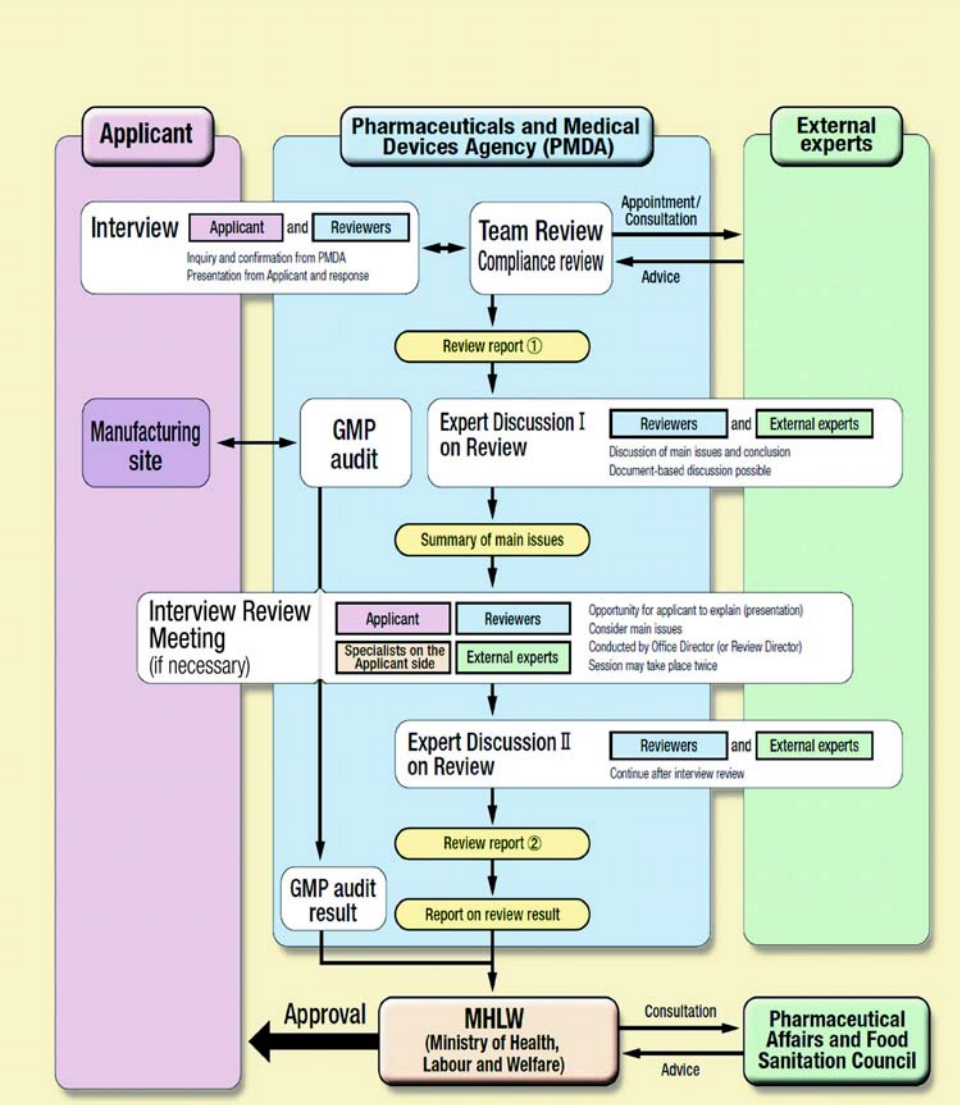
  1) In order to provide consistency across the operations and improve their efficiency, a new incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency (PMDA), was established through the integration of three separate organizations responsible for reviews and related services.
  2) PMDA 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 PMDA, the entire review process from clinical trial consultations until review operations is conducted by the same team with the same staff members for consistency and coordination. (As clinical trial consultations 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, PMDA 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 2008

Reviews:

Drugs

(i) Number of Expert Discussions conducted: 231 (181 in written form, 50 through meetings)

(ii) Applications discussed at the Drug Committees (PAFSC): 54
Review reports submitted to the Drug Committees (PAFSC): 27

Medical devices and *in vitro* diagnostics

(i) Number of Expert Discussions conducted: 82 (75 in written form, 7 through meetings)

(ii) Applications discussed at the Drug Committees (PAFSC): 8
Review reports submitted to the Drug Committees (PAFSC): 76
(60 for medical devices, 16 for *in vitro* diagnostics)

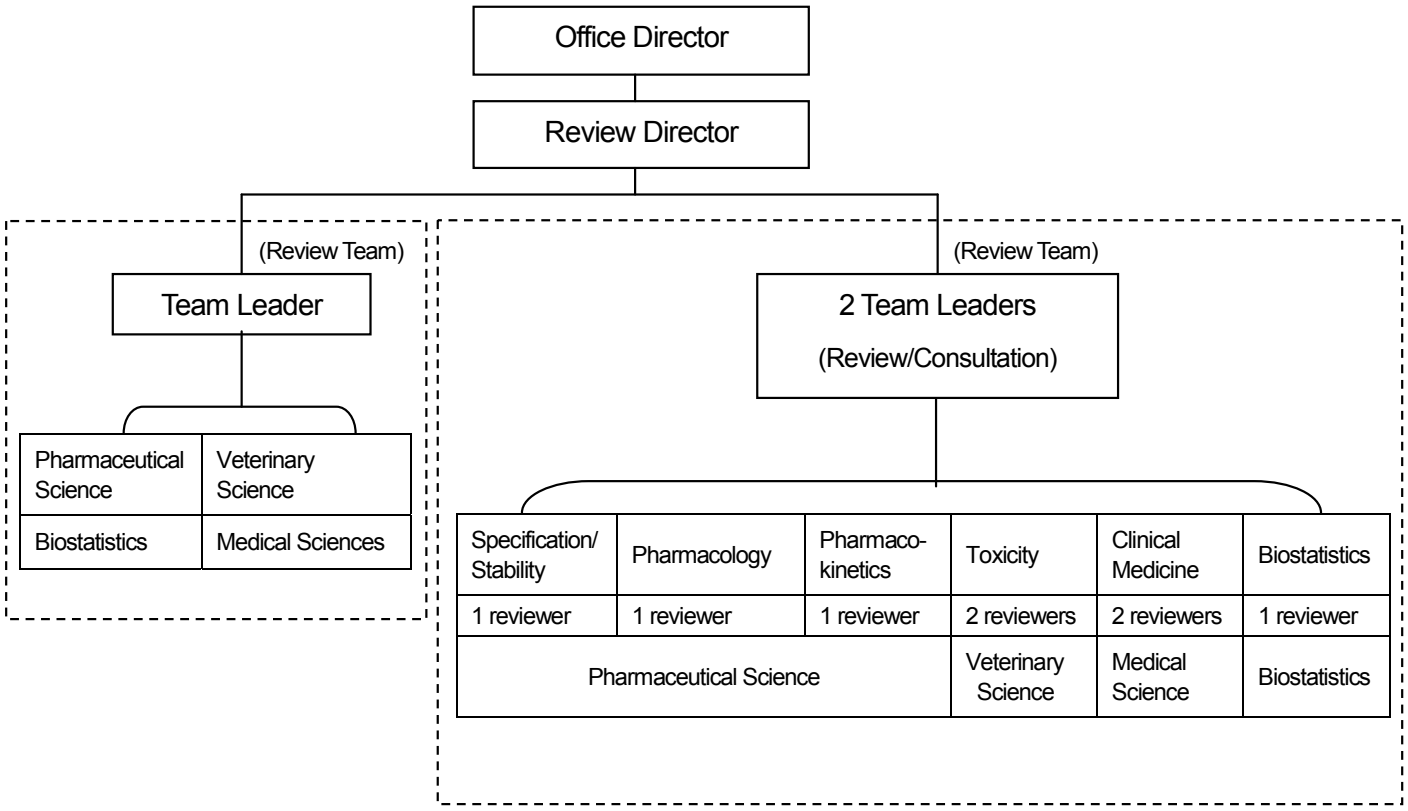
- Reviews of new drugs were conducted by review teams consisting of experts under the guidance of an office director and a review director. In most cases, the team members had

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.

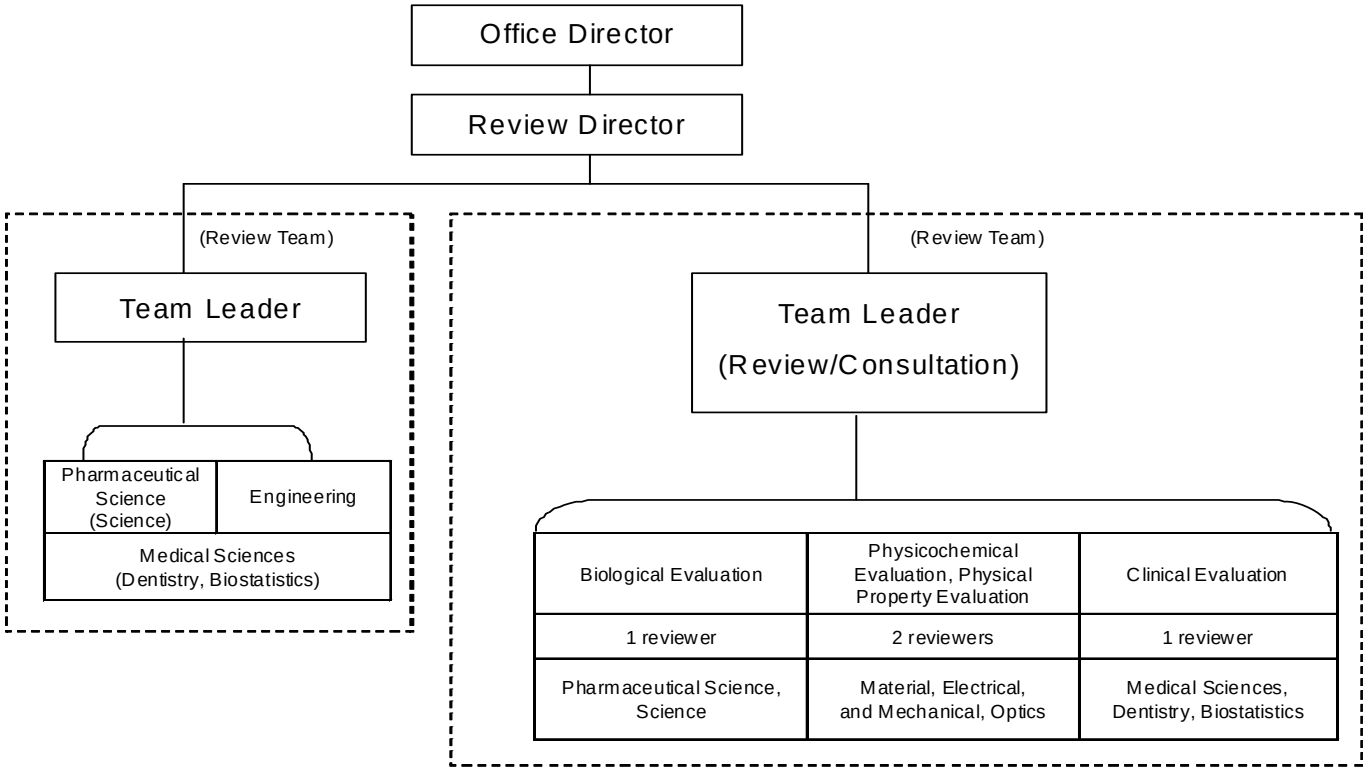
- Similarly, under the guidance of an office director and a review director, reviews of new medical devices were conducted by review teams consisting of experts who usually have academic degrees in engineering, pharmacology, medicine, dentistry, veterinary medicine, statistics, etc. The review team is 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 (excluding AIDS drugs)
	Oncology drugs	Antineoplastic drugs
	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 3-1	Central/peripheral nervous system drugs (excluding anesthetic drugs)
	Category 3-2	Anestheteic drugs, sensory organ drugs (excluding drugs for inflammatory diseases), 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
	Bio-CMC	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

- PMDA 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.

- PMDA 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

- PMDA has actively exchanged opinions with healthcare professionals by participating in academic conferences, etc., both in Japan and overseas, to comprehend their needs.
  Note: A total of 1009 PMDA staff members participated in 350 domestic and international academic conferences and seminars

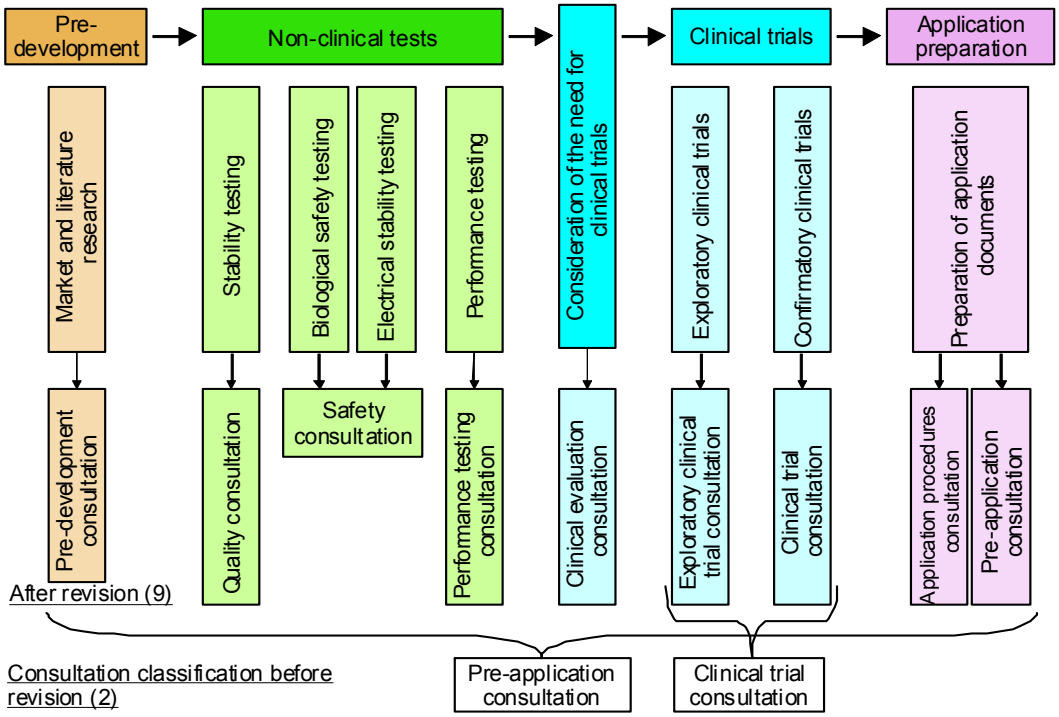
- In order to periodically grasp the needs of academic societies and patients regarding drugs approved in Europe and the U.S. but not yet in Japan, the Investigational Committee for Usage of Unapproved Drugs (chaired by Dr. Tomomitsu Hotta, Director of National Hospital Organization Nagoya Medical Center) has been conducting investigations ever since its establishment under the MHLW in January 2005. PMDA has applied results from investigations conducted by this committee when providing clinical trial consultations and reviews of applications for approval.

  In addition, the same efforts were made for medical devices based on the examination results at the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Needs) (chaired by Dr. Soichiro Kitamura, Honorary Director-general of National Cardiovascular Center) established in October 2006.

- Since 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* diagnostics have been 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.

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For products 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, PMDA have established new categories for consultations on preparation of documents for products using cellular tissue since FY 2007.

(ii) Efforts for prompt reviews of new drugs and improvement of their quality

- With changes made to the Mid-term Plan in response to the recommendations of the Council for Science and Technology Policy, PMDA 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 have been 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 global clinical trials, vi) clarifying review standards, vii) developing guidance toward the introduction of a system of prior assessment consultation, and viii) implementation 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 2008, applications were accepted four times on a routine basis. According to the recruitment results

of FY 2008, 98 out of some 910 applicants were informally accepted (including 44 who were finally employed) and hired in technical positions.

To increase the number of applicants, PMDA employed various measures including the holding of information sessions on career opportunities, visits by executives and employees to universities and hospitals, strengthened announcement of recruitment at academic meetings, revision of job posting brochures and web pages, 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

- PMDA conducted case study trainings, mainly for reviewers at the Offices of New Drugs using the FDA's training program as a reference. In April 2008, PMDA also introduced a mentoring system on a full scale that had been put in place on a trial basis in October 2007, to reinforce coaching at work.

- PMDA continues conducting dispatching of its staff to Japanese and overseas universities for training, visit training at outside facilities/institutions (e.g. drug manufacturing plants, medical device manufacturing plants and medical institutions) for new personnel, and special workshops to learn about technical issues by inviting Japanese and overseas regulators and experts.

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

- In FY 2008, PMDA increased the number of clinical trial consultation personnel and established a system so that it could flexibly manage consultations. As a result, PMDA ensured the capacity to process approximately 420 consultations and meet the demands of all clinical trial consultations.

- From consultations held in August 2008, the schedule adjustment method was improved. Specifically, an application should be made 2 months before the consultation, although it was previously submitted 3 months before the consultation. Also, in order to meet all of the demands for clinical trial consultations, the scheduling method was modified from the previous one which decided a date in the descending order of applicants in terms of the points calculated based on the specified rules. In the current method, the date is decided according to the contents of applications while taking the calculated points into consideration. When the consultation schedule can not be fixed in the desired month, it is arranged within 1 month before or after that month.

- The number of consultations in FY 2008 was 315 (the target was 420) and 23 consultations were withdrawn while basically all consultations applied for were processed. The average number of consultations per active ingredient related to submitted items in FY 2008 was 1.8 relative to the target of 2.0.

- For the introduction of a system of prior assessment consultation, PMDA conducted a questionnaire survey with companies and developed an implementation outline. With the introduction of the system of prior assessment consultation in FY 2009 and improvement of the consultation menu, PMDA plans to increase the capacity of consultations per year up to 1,200 for FY 2011.

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 regulatory review and 3 months for the applicant). The median total review time for priority items is to be 9 months (6 months for regulatory review and 3 months for the applicant). The FY 2008 target for this goal was a median total review time of 20 months (13 months for regulatory review and 8 months for the applicant) for standard review items, and a median total review time of 12 months (6 months for regulatory review and 6 months for the applicant) for priority review items.

  The median total review times for new drugs approved in FY 2008 are as follows:

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

		FY 2005	FY 2006	FY 2007	FY 2008
Standard review items	Total review time	18.1 months	20.3 months	20.7 months (29.5 months)	22.0 months (27.6 months)
	Regulatory review time	10.3 months	12.8 months	12.9 months (17.7 months)	11.3 months (18.5 months)
	Applicant-elapsed time	7.2 months	6.9 months	7.9 months (11.2 months)	7.4 months (14.1 months)
	No. of applications	15	29	53	53
Priority review items	Total review time	4.9 months	13.7 months	12.3 months (19.4 months)	15.4 months (19.1 months)
	Regulatory review time	2.8 months	6.4 months	4.9 months (7.7 months)	7.3 months (8.3 months)
	Applicant-elapsed time	2.2 months	6.0 months	6.5 months (12.0 months)	6.8 months (11.4 months)
	No. of applications	9	20	20	24

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

Median Regulatory TC Metrics for Standard Review

	From application to first consultation	From first consultation to inquiries about important matters	From inquiries about important matters to Expert Discussion	From Expert Discussion to approval
FY 2008	2.0 months (2.5 months) 45 applications	0.6 months (1.1 months) 48 applications	6.3 months (12.1 months) 59 applications	2.2 months (3.4 months) 50† applications

*Note * Values in parentheses are the reference values (80% values).*
† The number of applications does not include those approved without undergoing Expert Discussion.

- The total review time (median) increased for standard items compared with that in FY 2007. This is because the reviewers focused particularly on applications submitted in FY 2006, when many applications were filed.

  In detail, the regulatory review time (median) was shortened by 1.6 months compared with that in FY 2007, and the applicant review time (median) was also reduced by 0.5 months. Despite this, the total review time increased.

  This may be attributed to that there are some items with a total review time of more than 1,000 days because of the conduct of an additional clinical trial and the longer time required for

re-submission of documents due to inadequacies in application dossiers.

- The total review time (median) of priority review items increased compared with that in FY 2007 mainly because of an increase in the regulatory review time.

  This is because the reviewers took time to complete the reviews due to an increase in the number of priority review items. Among approved applications in FY 2008, priority review items accounted for 31% and the percentage was higher than that in FY 2007 (27%).

e. Approach to global clinical trials

- In order to reduce the drug lag, it was necessary to promote global clinical trials and clarify basic concepts on their implementation. Therefore, a document titled Basic Principles on Global Clinical Trials (Notification from the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated September 28, 2007) was formulated. PMDA uses this document at face-to-face consultations and reviews.

  Of 524 protocol applications submitted in FY 2008, 82 were for global clinical trials.

f. Clarification of the review standards

- As the basic concept of review, the Points to be Considered by the Review Staff Involved in the Evaluation Process of New Drug were formulated on April 17, 2008 from the perspective of clarification of review standards. This information was then explained to reviewers and was also put on the PMDA website and used at reviews, etc.

- The progress of the PMDA review had been informed to the applicants at meetings, etc. by the directors of review divisions in each review stage. In order to more properly notify the progress of review, the review progress that should be provided from the reviewers to applicants was organized as a document titled, the Way of Information Sharing between an Applicant and Pharmaceuticals and Medical Devices Agency during the Review Process for New Drugs on March 19, 2009. This information was then explained to the personnel responsible for reviews and put on the PMDA website.

g. Preparation for the introduction of a system of prior assessment (efficacy and safety evaluation before formal new drug application submission)

- A system to preliminarily evaluate the quality, efficacy and safety from the clinical trial consultation stage was internally examined and also reviewed by the “Working Group on Technical Issues of Clinical Trial Consultation and Review” established jointly with the JPMA, PhRMA, and EFPIA. The system was decided to be introduced on a trial basis in FY 2009, and a notification on the outline of its implementation was issued on March 30, 2009.

- In order to introduce the prior assessment consultation system in FY 2009, the Service Description Document for Review and Safety Measure Services were revised (authorized by the Minister of Health, Labour and Welfare on March 31, 2009).

h. Implementation of the project management system

- As an effort to further accelerate reviews and related services, the project management system was introduced in April 2008 for progress control and coordination of reviews of new

drugs.

In the implementation of the project management system, the personnel in charge of controlling and coordinating the progress of reviews was appointed in the Offices of New Drugs, and the Office of Review Management was newly established in the review division to organize information of the progress.

- Furthermore, the Council in the Review Segment for Verification of Progress with the Director of the Center for Product Evaluation as its head was established in the review division to control the progress of reviews, and meetings were held from April 2008. (Eight meetings were held in 2008)

  In the Council in the Review Segment for Verification of Progress, opinions for the advancement of the system are exchanged, information on the actuality and issues related to the entire review status for new drugs is shared, countermeasures and future policies are examined as necessary, and the review status of items other than new drugs under review is grasped.

(iii) Efforts for prompt reviews of medical devices and improvement of their quality

- In response to the 2008 Basic Policy for Economic and Financial Reforms (Cabinet decision on June 27, 2008), the MHLW formulated the Action Program to Accelerate Reviews of Medical Devices (dated December 11, 2008). The document specifies that the period until approval for medical devices should be reduced such as by prompt reviews of medical devices. The main contents are the increase in the number of personnel involved in the review process, improvement of training, the introduction of the 3-track review system and prior assessment consultation system, the clarification of review standards and thorough progress control.

  As a result, PMDA reflected the policies presented in the said program in the Second Mid-term Plan, and carried out preparatory operations to start these efforts for prompt reviews of medical devices and improvement of their quality in FY 2009.

(iv) Implementation of approval review

a. Approval reviews for new drugs

- For new drugs, PMDA aims to review 80% of all filed applications within a review time of 12 months. In order to reach this target, PMDA:

  1) Reinforced the review system by increasing the number of reviewers for categories in which reviewing work was considered to be difficult because of unbalance of the numbers of submitted applications between teams. The review team of “Category 3” was divided into “Category 3-1” and “Category 3-2” on December 1, 2008, and as a result of this, the number of teams was increased;
  2) Regularly discussed its review policy with MHLW and managed the review process through the Progress Management Committee for Review-Related Operations within PMDA 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 (SOPs).

- With regard to new drugs (drugs that are clearly different from approved drugs 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, PMDA developed the Implementation Manual for Approval Reviews of New Drugs regarding reviews and related procedures, and the 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 reviews and related services promptly and appropriately, PMDA had the Progress Management Committee for Reviews and Related Services hold meetings once every 3 months so that the Chief Executive and other executives of PMDA could accurately grasp the progress of approval reviews and related services for improvements in the progress. The Committee thus monitored operational progress, while making efforts to comprehensively consider relevant information on new drugs and examine policies for solving issues.

  The directors of the review division 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 the Council in the Review Segment for Verification of Progress.

- The status of approval reviews for new drugs in FY 2008 is shown below:

Number of Approved Drugs, etc.

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Prescription drugs	3,742	2,199	2,390	3,648	2,332
OTC drugs	1,781	1,570	1,030	1,329	1,821
In vitro diagnostics	502	281	136	199	112
Quasi-drugs	2,972	2,611	2,287	2,236	2,340
Cosmetics	0	0	0	0	0
Total	8,997	6,661	5,843	7,412	6,605
Breakdown					
New drugs (applications)	49	60	77	81	79
Priority review items out of NDAs above (applications)	22	18	24	20	25

Number of Approved New Drugs

	FY 2004	FY 2005	FY 2005 Applications filed in and after FY 2004†	FY 2006	FY 2006 Applications filed in and after FY 2004†	FY 2007	FY 2007 Applications filed in and after FY 2004†	FY 2008	FY 2008 Applications filed in and after FY 2004†
All new drugs									
No. of approvals	49	60	24	77	49	81	73	79	77
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%]	(9.0 months) [70%]*	(9.0 months) [70%]
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	18.9 months	18.8 months
Priority review items									
No. of approvals	22	18	9	24	20	20	20	25	24
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%]	(7.4 months) [32%]*	(7.3 months) [33%]
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	15.6 months	15.4 months
Standard items									
No. of approvals	27	42	15	53	29	61	53	54	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%]	(11.2 months) [57%]*	(11.3 months) [57%]
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	22.1 months	22.0 months

Note: Percentages in brackets indicates the proportions 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 values indicate the data for applications filed in and after April 2004 among those approved in FY 2005, 2006, 2007 and 2008*

Review Status of NDAs

New drug (FY of application)	Applications*	Approved	Withdrawn	Under review
Applications submitted on and before March 31, 2004	139	106 (2)	26 (1)	7 [-3]
FY 2004	87	78 (1)	9 (0)	0 [-1]
FY 2005	57	49 (8)	6 (0)	2 [-8]
FY 2006	101	78 (37)	8 (1)	15 [-38]
FY 2007	87 (-4) †	28 (24)	7 (7)	52 [-31]
FY 2008	82	7 (7)	1 (1)	74 [74]
Total	553	346 (79)	57 (10)	150 [-7]

* *The number of "applications" is 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 2007 is three less than that shown in the previous annual report, because PMDA integrated two separate applications for a single active ingredient into one application, and there were three such dual applications.*
Two applications were deleted because they were changed to be not included in "Applications." One application was added because it was changed to be included in "Applications."
Note 1: Values in parentheses indicate those processed in FY 2008 (included in values on their left)
Note 2: Values in brackets indicate difference from FY 2007

Number of Applications Processed and Time Spent in Each Review Process

	Review process	1. From receipt of applications to first consultation	2. From first consultation to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2006	Number of processed applications	79	54	56	49
	Total review time (median)*	83.0 days	397.5 days	44.5 days	25.0 days
FY 2007	Number of processed applications	63	65	72	72
	Total review time (median)*	85.0 days	381.0 days	20.5 days	57.0 days
FY 2008	Number of processed applications	51	63	79	77
	Total review time (median)*	82.0 days	421.0 days	24.0 days	63.0 days

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

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

Review status of overall new drugs

- With respect to the approval status in FY 2008, PMDA attained an achievement level of 70% for the performance target within 12 months by reviewing 54 out of 77 applications for new drugs submitted in and after April 2004. The median review time was 9.0 months. While the achievement level increased by 10% compared with that in FY 2007, it was slightly lower than the final target achievement level of 80% in the First Mid-term Plan. When the applications submitted in and before March 2004 were included, the achievement rate was 70% (55 out of 79), and the median review time was 9.0 months.

- The number of new drugs approved in FY 2008 decreased by 2 from the previous fiscal year. However, the median review time for all new drugs filed was improved to 9 months from 11.6 months in FY 2007.

- As for the 139 applications submitted before the establishment of PMDA (in and before March 2004) and the 413 applications submitted after the establishment of PMDA (in and after April 2004), PMDA processed reviews in the order of their submission, giving full consideration to the target time for processing reviews. However, PMDA 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 PMDA.

- As for the applications submitted in and before March 2004, PMDA was able to process 132 of those through approvals or withdrawals by FY 2008.

Status of priority reviews

- With regard to priority reviews for drugs specified by the Minister of Health, Labour and Welfare, PMDA 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 drugs that are regarded as having particularly high medical necessity (i.e., drugs for serious diseases with distinctly superior efficacy or safety to existing drugs or therapies) were conducted on a priority basis as

priority review items, and 25 applications were approved in FY 2008. In FY 2008, there were 9 applications requesting priority reviews of drugs regarded as having particularly high medical necessity.

With regard to the results of acceptance of priority reviews requested, 4 applications were "applicable" as priority review items and 11 were judged to be "not applicable" as priority review items including those being under consideration from the previous fiscal year. In the results of acceptance for 9 applications submitted in FY 2008, 3 were "applicable" as priority review items, 5 were judged to be "not applicable" as priority review items, and 1 is currently being under consideration.

- With respect to the approval status in FY 2008, PMDA attained an achievement level of 33% for the performance target within 6 months by reviewing 8 out of 24 applications submitted in and after April 2004. The median review time was 7.3 months. The achievement level decreased and was lower than the final target achievement level of 50% in the First Mid-term Plan that had been attained in the previous fiscal year. This was because it required time for processing due to an increase in the number of priority review items, but the number of approved items increased only by 4 applications. When the applications submitted in and before March 2004 were included, the achievement rate was 32% (8 out of 25), and the median review time was 7.4 months.

Main new approved items

- The main new items approved in FY 2008 (items deliberated by the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council, all of which are new drugs.) are as follows:

Main New Approved Items (New Drugs)

Category	Approval Date	Brand Name (Applicant Company)	Active Ingredient	Notes
AIDS drugs	Jun. 24, 2008	Isentress Tablets 400 mg (Banyu Pharmaceutical Co., Ltd.)	Raltegravir potassium	A drug containing a new active ingredient indicated for the treatment of HIV infection. [Orphan drug]
1	Jul. 16, 2008	Differin Gel 0.1% (Galderma S.A.)	Adapalene	A drug containing a new active ingredient indicated for the treatment of acne vulgaris.
2	Jul. 16, 2008	INOflow for Inhalation 800 ppm (INO Therapeutics LLC)	Nitric oxide	A drug containing a new active ingredient indicated for the treatment of hypoxic respiratory failure (HRF) with concurrent pulmonary hypertension in neonates. [Orphan drug]
3	Jul. 16, 2008	Macugen Ivt Inj. Kit 0.3 mg (Pfizer Japan Inc.)	Pegaptanib sodium	A drug containing a new active ingredient indicated for the treatment of age-related macular degeneration with concurrent choroidal neovascularization. [Orphan drug]

Category	Approval Date	Brand Name (Applicant Company)	Active Ingredient	Notes
6-1	Oct. 16, 2008	Pirespa Tablets 200 mg (Shionogi & Co., Ltd.)	Pirfenidone	A drug containing a new active ingredient indicated for the treatment of idiopathic pulmonary fibrosis. [Orphan drug]
In vivo diagnostics	Oct. 16, 2008	Thyrogen IM Injection 0.9 mg (Sato Pharmaceutical Co., Ltd.)	Thyrotropin human alfa (genetical recombination)	A drug containing a new active ingredient indicated for use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine scintigraphy in patients with differentiated thyroid cancer who have undergone near total or total thyroidectomy. [Orphan drug]
Oncology drugs	Oct. 16, 2008	Thaled Capsule 100 (Fujimoto Pharmaceutical Corporation)	Thalidomide	A drug containing a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
AIDS drugs	Dec. 25, 2008	Celsentri Tablets 150 mg (Pfizer Japan Inc.)	Maraviroc	A drug containing a new active ingredient indicated for CCR5-tropic HIV-1 infection. [Orphan drug]
3	Jan. 21, 2009	Remitch Capsules 2.5 μg (Toray Industries, Inc.)	Nalfurafine hydrochloride	A drug containing a new active ingredient indicated for the treatment of pruritus in hemodialysis patients (for use only when conventional therapies are not sufficiently effective).
6-1	Jan. 21, 2009	Xolair for S.C. Injection (Novartis Pharma K.K.)	Omalizumab (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of bronchial asthma (for use only in patients with intractable bronchial asthma whose asthmatic responses are uncontrollable with conventional therapies).

b. Approval reviews for new medical devices

- For new medical devices, PMDA 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, PMDA 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, PMDA prepared the Implementation Manual for Approval Reviews of New Medical Devices, which describes reviews and review-related procedures, and developed SOPs relating to various operations. PMDA 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), held meetings once every 3 months to monitor and examine operational progress in order to achieve the Mid-term Plan for review time and ensure a prompt 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 the Council in the Review Segment for Verification of Progress, 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 2008 is shown below:

Number of Approved New Medical Devices

		FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Medical devices (total)		3,309	1,827	1,342	2,222	2,459
Of which: priority review items		2	0	1	4	7*
Breakdown	**New medical devices**	**8**	**11**	**23**	**26**	**16**
	Without approval standards, with clinical data	—	0	5	14	31
	Without approval standards, without clinical data	—	16	189	552	563
	With approval standards, without clinical data	—	3	444	1,141	1,512
	Controlled medical devices (without approval standard or certification standard, without clinical data)	—	1	146	335	286
	Improved medical devices	154	263	136	78	31
	Generic medical devices	3,147	1,533	399	76	20

**: Of these, 4 items are new medical devices.*

Approval Status of New Medical Devices

	FY 2004	FY 2005		FY 2006		FY 2007		FY 2008	
			Applications filed in and after FY 2004†		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	16	16
Median review time	(12.7 months)	(7.7 months)	(1.8 months)	(6.0 months)	(3.4 months)	(8.6 months)	(8.2 months)	(8.9 months)	(8.9 months)
	[50%]*	[82%]*	[100%]	[83%]*	[100%]	[73%]*	[83%]	[75%]	[75%]
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	16.0 months	16.0 months
Priority review items									
No. of approvals	2	0	0	1	1	4	4	4	4
Median review time	(9.3 months)			(5.7 months)	(5.7 months)	(8.6 months)	(8.6 months)	(5.8 months)	(5.8 months)
	[50%]*			[100%]*	[100%]	[75%]*	[75%]	[75%]	[75%]
Median total review time	24.0 months			14.2 months	14.2 months	15.7 months	15.7 months	28.8 months	28.8 months
Standard items									
No. of approvals	6	11	5	22	14	22	19	12	12
Median review time	(15.0 months)	(7.7 months)	(1.8 months)	(6.3 months)	(3.2 months)	(8.7 months)	(7.7 months)	(9.8 months)	(9.8 months)
	[33%]*	[82%]*	[100%]	[82%]*	[100%]	[73%]*	[84%]	[75%]	[75%]
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	14.4 months	14.4 months

Note: Percentages in brackets indicates the proportions 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 Mid-term Plan.*

† *The values indicate the data for applications filed in and after April, 2004 among those approved in FY 2005, 2006, 2007, and 2008.*

Review Status of New Medical Devices

New medical devices (FY of application)	Applications*	Approved†	Withdrawn	Under review
Applications submitted in and before March 31, 2004	132	53 (2)	75 (0)	4 [-2]
FY 2004	56	31 (3)	17 (1)	8 [-4]
FY 2005	7	7 (1)	0	0 [-1]
FY 2006	24	16 (3)	3 (2)	5 [-5]
FY 2007	37	20 (16)	1 (0)	16 [-16]
FY 2008	32	1 (1)	0 (0)	31 [31]
Total	288 (32)	128 (26)	96 (3)	64 [3]

* *Values in the Applications 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 2008 (included in values on their left)

Note 2. Values in brackets indicate difference from FY 2007

Number of Applications Processed and Time Spent in Each Review Process

	Review process	1. From receipt of applications to first consultation	2. From first consultation to Expert Discussion	3. From Expert Discussion to notification of review result	4. From notification of review result to approval
FY 2006	Number of processed applications	14	17	10	15
	Total review time (median)*	46.5 days	484.0 days	101.0 days	9.0 days
FY 2007	Number of processed applications	8	15	15	23
	Total review time (median)*	53.0 days	402.0 days	151.0 days	9.0 days
FY 2008	Number of processed applications	19	8	11	16
	Total review time (median)*	46.0 days	479.0 days	132.0 days	24.0 days

* *The days shown in each review process are the median of total review 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 overall new medical devices

- With respect to the approval status in FY 2008, PMDA attained an achievement level of 75% for the performance target within 12 months by reviewing 12 out of 16 applications submitted in and after April 2004. The median review time was 8.9 months. The achievement level decreased by 8% compared with that in FY 2007. It was lower than the final target achievement level of 90% in the First Mid-term Plan. This might have been due to the increase in the number of new personnel involving in the review process and focus on their training and guidance affecting the processing rate. Concerning priority review items, the final target achievement level of 70% was achieved.

  Even when applications submitted in and before March 2004 were counted, the achievement level was the same as those of applications filed in and after April 2004, because in FY 2008, there was no approval of new medical device applications submitted in and before March 2004.

- For the 132 applications submitted before the establishment of PMDA (in and before March 2004) and the 156 applications submitted after the establishment of PMDA (in and after April 2004), PMDA processed reviews taking the target review time sufficiently into consideration. However, PMDA has called for withdrawal of applications that were considered to be difficult to approve due to a lack of response from applicants to inquiries made by PMDA.

- As to the applications submitted in and before March 2004, PMDA was able to process 128 of these applications through approvals or withdrawals by FY 2008. In order to achieve the target for the review time earlier, PMDA is progressing with reviews of such application vigorously so that it can concentrate all resources on the applications submitted after its establishment.

Status of priority reviews

- With regard to priority reviews for medical devices specified by the Minister of Health, Labour and Welfare, PMDA was 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. The achievement level was

75% in FY 2008, thus the target level was attained.

- 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 therapies) were conducted on a priority basis as priority items. In FY 2008, 7 items (4 of these were new medical devices) were approved. There were 2 applications requesting priority reviews of medical devices regarded as having particularly high medical necessity. Of these, 1 application was judged to be "not applicable" as priority review items, and the remaining 1 application is currently under consideration.

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 three meetings in FY 2008.

  The numbers of established standards for approval and certification reported to MHLW in FY 2008 were as follows:

FY of report	FY 2006	FY 2007	FY 2008	Total
Approval standards	6	7	5	18
Certification standards	0	14	86	100
Review guidelines	0	1	2	3

The number of standards established by MHLW in FY 2008 based on the reports from PMDA is shown below:

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

Established in:	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	Total
Approval standards	0	17	8	10	-2*	33
Certification standards	363	9	24	0	17	413
Review guidelines	0	0	0	0	3	3

* *In FY 2008, 2 of the established approval standards were transferred to the certification standards so that the value is a negative number.*

- PMDA 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. In order to promote the transparency and efficiency of the development of the standards, fundamental concepts on basic requirement standards were newly formulated, in addition to a basic development process (outline for development of drafts such as medical device standards), and put on the website of information provision for medical device standards, etc.

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

- PMDA conducted efficient on-site and document inspections concerning 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 compliance with the requirements of the ministerial ordinance on Good Laboratory Practices (GLP), the ministerial ordinance on Good Clinical Practices (GCP), the ministerial ordinance on Good Post-Marketing Surveillance Practices (GPMSP) and the conformity standards for the application documents.

Numbers of Conducted Conformity Audits

		FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Document conformity audits		161	136	426	774	942
	Drugs	161	135	251	234	293
	Medical devices	-	1	175	540	649
GLP audits		20	39	31	27	43
	Drugs	20	37	23	23	32
	Medical devices	-	2	8	4	11
GCP audits *		73	131	149	132	198
	New drugs	68	120	137	122	182
	Generic drugs	5	11	12	9	15
	Medical devices	-	0	0	1	1
GPSP audits †		27	82	103	107	79

* *Values for GCP and GPMSP audits in and after FY 2004 are the number of notifications after evaluation was conducted.*

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

Note 1: GLP: Good Laboratory Practices

Note 2: GCP: Good Clinical Practices

Note 3: GPMSP: Good Post-Marketing Surveillance Practices

Note 4 GPSP: Good Post-marketing Study Practices

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

1) Efforts toward review of the conformity audit system

PMDA included in the Second Mid-term Plan the introduction of the inspector visit method, where the PMDA staff directly visit the applicant company for inspection, in addition to the current document conformity audit method, where the relevant data and materials are delivered to PMDA for review. PMDA carried out preparatory operations for formal implementation in FY 2009 such as partially introducing the said method.

2) Diffusion of the interpretation of GCP operations

PMDA conducted consultations with medical institutions which were subjected to on-site inspection on matters related to GCP after completion of the inspection. PMDA also made an effort to improve the explanation of case examples by highlighting points to consider in conducting clinical trials through the Conformity Audit page of the PMDA website. To promote understanding regarding GCP, PMDA held GCP Workshops in Tokyo and Osaka for people in charge of drug development and pharmaceutical affairs and auditors of pharmaceutical companies, site management organizations (SMOs) and healthcare professionals. In addition, PMDA staff made lectures at academic conferences and other opportunities for healthcare professionals.

Number of GCP Workshop Participants

Place	FY 2006	FY 2007	FY 2008
Tokyo	1,303	1,212	1,338
Osaka	454	495	543
Total	1,757	1,707	1,881

3) Enhancement and reinforcement of GCP on-site inspections

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

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

- Although a standard administrative processing time for conformity audit services has not been set, PMDA 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 2008.

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

- In accordance with the Standard Administrative Processing 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), PMDA 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, PMDA 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 SOPs for various operations. In addition to periodically collecting data on the achievement level of the target review time and informing the reviewers of these levels, meetings of the Progress Management Committee for Review-Related Operations were continuously held to monitor and examine operational progress (4 meetings were held in FY 2008).

- The approval status of generic drugs, OTC drugs and quasi-drugs in FY 2008 are as follows:

Number of Approved Generic Drugs and Others

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Generic drugs	3,476	1,919	2,152	3,278	1,980
Number of approved applications filed in and after April 2004 (breakdown)	1,468	1,782	2,029	3,228	1,960
Median review time (for the applications filed in and after April 2004)	3.3 months	7.3 months	4.0 months	4.5 months	5.3 months
Achievement rates on the target time (for the applications filed in and after April 2004)	100%	98%	93%	95%	83%
OTC drugs	1,781	1,570	1,030	1,329	1,821
Number of approved applications filed in and after April 2004 (breakdown)	270	1,163	923	1,309	1,807
Median review time (for the applications filed in and after April 2004)	8.7 months	7.8 months	6.3 months	4.0 months	3.5 months
Achievement rates on the target time (for the applications filed in and after April 2004)	83%	84%	85%	90%	94%
Quasi-drugs	2,972	2,611	2,287	2,236	2,340
Number of approved applications filed in and after April 2004 (breakdown)	1,431	2,575	2,275	2,230	2,339
Median review time (for the applications filed in and after April 2004)	5.6 months	5.3 months	5.5 months	5.2 months	5.0 months
Achievement rates on the target time (for the applications filed in and after April 2004)	89%	86%	67%	83%	93%
Total	8,229	6,100	5,469	6,843	6,141
Number of approved applications filed in and after April 2004 (breakdown)	3,169	5,520	5,227	6,767	6,106

Note 1: The median and TC achievement rate for OTC drugs and quasi-drugs in FY 2007 and FY 2008 were calculated excluding data from the period from the completion of the audit to the notification of GMP results by prefecture.

Note 2: The number of approved applications includes priority review items of which the standard administrative processing time is 6 months or less.

Reviews Conducted for Generic Drugs and Others 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
	FY 2008	3,893	1,980	199	4,488
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
	FY 2008	2,387	1,821	302	2,439
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
	FY 2008	2,414	2,340	189	1,575

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

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

Application and Approval of OTC Drugs and Quasi-Drugs by Category of Application

OTC drugs

From April 1, 2008 to December 31, 2008

Former category of application	1	2	3	4-1	4-2	OTC test agents	Insecticide, rodenticide	Total
Filed in FY 2008	0	11	21	74	1,558	0	6	1,670
Approved in FY 2008	0	91	48	56	1,611	0	15	1,821

From January 1, 2009 to March 31, 2009

New category of application	1	2	3-1	3-2	3-3	4	5-1	5-2	5-3	5-4	6	7-1	7-2	8	Total
Filed in FY 2008	0	0	0	0	0	5	5	0	0	5	0	10	1	691	717
Approved in FY 2008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Quasi-drugs

Category of application	1, 3	2	Total
Filed in FY 2008	92	2,322	2,417
Approved in FY 2008	114	2,226	2,340

Note1: The categories of application for OTC drugs were amended on January 1, 2009. Categories 1, 2. 3, 4-1 and 4-2 in the column of "Former category of application" in the table correspond to the former categories of application prior to the amendment.

Note 2: Categories of application

OTC drugs

<Former category>

1: Drugs containing new active ingredients (Direct OTC drugs)
2: Drugs containing new active ingredients for OTC (Switch OTC drugs)
3: Relatively innovative drugs excluding above 1 and 2
4-1: Other drugs (Relatively less innovative drugs)
4-2: Other drugs (Drugs that are not innovative)

<New category>

1: Drugs containing new active ingredients (Direct OTC drugs)
2: Drugs with new routes of administration
3-1: Drugs with new indications
3-2: Drugs in new dosage forms
3-3: Drugs with new dosage
4: Drugs containing new active ingredients for OTC (Switch OTC drugs)
5-1: OTC drugs with new routes of administration
5-2: OTC drugs with new indications
5-3: OTC drugs in new dosage forms
5-4: OTC drugs with new dosage
6: New OTC combination drugs
7-1: OTC combination drugs with similar prescription
7-2: OTC drugs with similar dosage forms
8: Other drugs (Relatively less innovative drugs and Drugs that are not innovative)

Quasi-drugs

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

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

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

Note 5: The number of quasi-drugs includes that of insecticides and rodenticides for which an application for approval as quasi-drugs was filed

- With regard to achievement levels in FY 2008 of the target standard administrative processing time for applications submitted in and after April 1, 2004, PMDA attained an achievement level of 83% by reviewing 1,627 out of 1,960 applications for generic drugs within 12 months, 94% by reviewing 1,699 out of 1,807 applications for OTC drugs within 10 months and 93% by reviewing 2,175 out of 2,339 applications for quasi-drugs within 6 months. As a result, PMDA 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	FY 2008
Number of audits	1,090	941	628	1,135	601

- For generic drugs, PMDA implemented surveys to confirm the compliance with the conformity standards (GLP, GCP, and other regulations) for approval application dossiers, by collating them with raw data such as test records, experiment notes, case report forms, etc.

- In FY 2008, the Japanese Pharmacopoeia Draft Committee held a total of 73 meetings and finalized 106 new monographs and 122 amendments for the second supplement of the 15th edition of the Japanese Pharmacopoeia (JP) (to be published in September 2009). PMDA also put general rules for preparations, general tests, monographs, reference ultraviolet visible absorption spectra and reference infrared absorption on the PMDA website and called for comments on them.

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

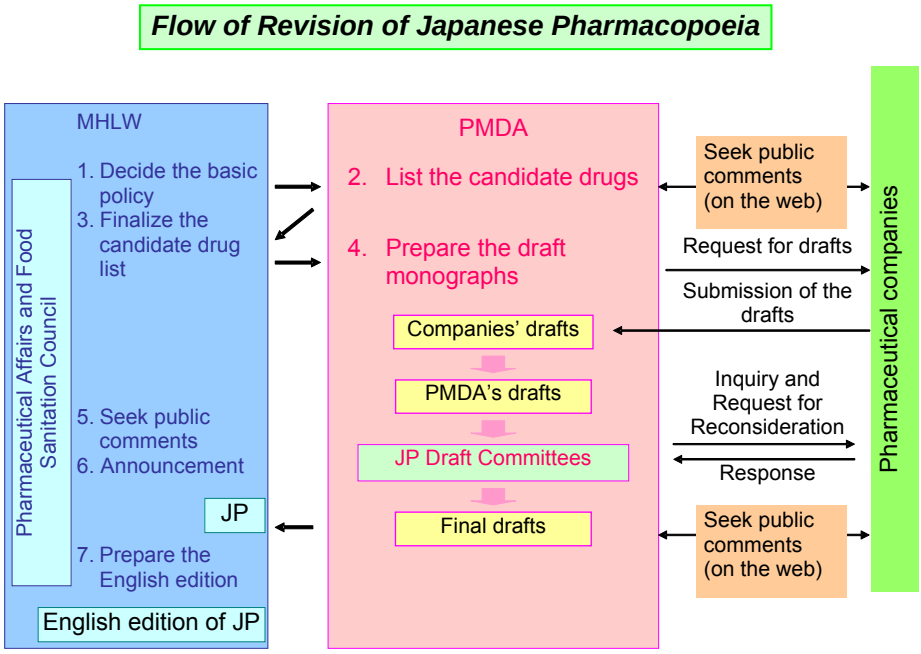
Month and year reported	September 2005	March 2007	November 2008	March 2009
New monographs	102	90	1	106
Amendments	276	171	1	122

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

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)	Amendment to the 15th Japanese Pharmacopoeia as amended (March 2009)
New monographs	102	90	1
Amendments	272	170	1
Deletion	8	6	0
Total	1,483	1,567	1,568

PMDA provided information such as the condition of the JP draft review or international harmonization of pharmacopoeial standards, in addition to calling for comments on drafts on the website of JP-related information. PMDA also opened a website to provide information on the JP in English and started to give information on international harmonization of pharmacopoeial standards to overseas users.
(http://www.std.pmda.go.jp/jpPUB/index_e.html)



(v) Improvement of clinical trial consultations

- In addition to improving pre-application consultations, PMDA is required to give priority to conducting consultations on clinical trials for drugs 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, PMDA succeeded in conducting clinical trial consultations in a prioritized manner as well as consultations on compliance with conformity criteria (GLP, GCP, and other regulations), 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 drugs considered to be of particularly high medical necessity, PMDA received applications for four ingredients in FY 2008 and designated four ingredients (2 applications each filed in FY 2007 and FY 2008) as being applicable to "priority clinical trial consultation" (a review is underway for the remaining two ingredients). None were rejected as inapplicable. PMDA conducted a total of 27 clinical trial consultations related to the designated ingredients.

  For medical devices, there were no applications for priority clinical trial consultations. For drugs, there was one application for consultation on compliance for items designated as priority consultation items, and for medical devices, there was no application of this kind.

b. Acceleration of clinical trial consultations for drugs

- PMDA worked to expedite clinical trial consultations for drugs 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.

Applied Clinical Trial Consultation (CTC) for New Drugs

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Applications for CTC	334	339 (243)*	473 (327)*	435 (325)*	342 (326)*

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

Conducted Clinical Trial Consultation (CTC) for New Drugs

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Conducted CTC	193	218	288	281	315
Withdrawn	23	14	7	21	23
Total	216	232	295	302	338

- In FY 2008, PMDA conducted 338 clinical trial consultations (including 23 withdrawals) in relation to a goal of 420 clinical trial consultations.

- PMDA established the following goals for efficient consultation: (1) The process from a face-to-face consultation to the settlement of records should be completed in 30 business days for 50% of all applications submitted; and (2) The process to the first face-to-face clinical trial consultation should be completed in 30 business days for 50% of all applications submitted (with respect to priority clinical trial consultation). In FY 2008, 286 (87.7%) out of 326 applications were processed within 30 days from the face-to-face consultation to the settlement of records, and 9 (56.3%) out of 16 were processed within 30 business days to the first face-to-face consultation (with respect to priority clinical trial consultation).

- PMDA promoted simple clinical trial consultations and support for global clinical trials. In FY 2008, it received 62 applications for consultations on global clinical trials for new active ingredients, of which 51 were carried out.

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

- PMDA started to accept clinical trial consultations in FY 2008 for "Bio-CMC," which were newly established as a result of the structure of the original Office of Biologics being changed to have two offices in October 2007.

Number of Face-to-face Clinical Trial Consultations Conducted for Drugs by Category in FY 2008

Category	Apr	May	Jun	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Total
Category 1 (Gastrointestinal drugs etc.)	2	3	3	2	4	2	1	3	3	2	1	2	28
Category 2 (Cardiovascular drugs)	3	5	4	4	4	10	5	5	10	2	4	4	60
In vivo diagnostics	1	0	0	0	0	0	1	0	0	0	0	0	2
Radiopharmaceuticals	0	0	0	0	0	0	0	1	0	1	0	0	2
Category 3 (Central / peripheral nervous system drugs etc.)	5	4	4	4	3	6	4	1	4	2	2	1	40
Category 4 (Antibacterial agents etc.)	1	2	3	4	2	2	3	2	1	1	0	1	22
AIDS drugs	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 5 (Drugs for the urogenital system etc.)	1	2	0	2	1	0	1	2	1	2	0	3	15
Category 6-1 (Respiratory tract drugs etc.)	0	2	2	2	3	3	4	4	2	3	1	5	31
Category 6-2 (Hormone drugs)	1	2	2	3	3	7	0	1	1	1	1	1	23
Oncology drugs	4	4	5	5	12	10	1	5	11	3	4	2	66
Bio-CMC	0	0	0	1	1	2	1	1	0	0	0	2	8
Biological products	1	1	1	2	1	0	1	0	3	0	0	1	11
Cellular and tissue-derived products	0	0	0	0	0	0	0	0	1	0	0	0	1
Blood products	0	0	0	0	0	1	1	1	1	0	0	1	5
Compliance with conformity criteria (GLP, GCP and other regulations)	0	0	0	0	0	0	1	0	0	0	0	0	1
Total	19	25	24	29	34	43	24	26	38	17	13	23	315
Withdrawn	1	1	1	0	4	2	3	3	2	1	4	1	23
Grand Total	20	26	25	29	38	45	27	29	40	18	17	24	338

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

Note 2: Consultations on compliance with conformity criteria (GLP, GCP and other regulations) 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	FY 2008
Applications for CT consultation*		9	33	46	76	87
	Medical devices	7	32	43	75	84
	In vitro diagnostics	2	1	3	1	3
Conducted CT consultations		8	30	42	72	76
	Medical devices	6	29	39	71	74
	In vitro diagnostics	2	1	3	1	2
Withdrawn		0	0	0	0	2
	Medical devices	0	0	0	0	2
	In vitro diagnostics	0	0	0	0	0
Total (Conducted consultations and withdrawals)		8	30	42	72	78
	Medical devices	6	29	39	71	76
	In vitro diagnostics	2	1	3	1	2

* *Applications submitted after arrangement of schedule*

Number of Clinical Trial Consultations for New Medical Devices by Category Conducted in FY 2008

Consultation category	Applications for CTC	Conducted CTC	Withdrawals	Total (Conducted consultations and withdrawals)
Consultation for preparation of documents for cell- and tissue-derived products	0	0	0	0
Clinical trial/Pre-application consultation for medical devices or *in vitro* diagnostics	50 (3) *	43 (2) *	1	44 (2) *
Consultation on compliance with conformity criteria for medical devices or *in vitro* diagnostics	0	0	0	0
Pre-development consultation for medical devices	14	11	0	11
Application procedure consultation for medical devices or *in vitro* diagnostics	5	6	0	6
Safety consultation for medical devices (excluding biological devices)	0	0	0	0
Quality consultation for medical devices (excluding biological devices)	1	1	0	1
Performance testing consultation for medical devices	3	2	1	3
Clinical evaluation consultation for medical devices	13	12	0	12
Exploratory clinical trial consultation for medical devices	0	0	0	0
Safety consultation for biological medical devices	0	0	0	0
Quality consultation for biological medical devices	0	1	0	1
Additional consultation for medical devices or *in vitro* diagnostics	1	0	0	0
Total	87	76	2	78

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

(vi) Promotion of international harmonization

- PMDA 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 2008, PMDA continued to actively participate in ICH Steering Committee Meetings and Expert Working Group Meetings, and promoted further international harmonization by improving the consistency of Japanese standards with international standards such as those for developing data for approval review, which were agreed upon among Japan, the U.S., and EU in ICH Meetings.

- Specifically, PMDA 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 drugs in which PMDA participated (relating to reviews and post-marketing safety measures)

  - ICH Expert Working Groups
    ICH Meeting in Brussels
    ICH Meeting in Poland
    ICH Brussels Symposium
    Topics discussed in FY 2008
    - Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use (S2 [R1])
    - Nonclinical Evaluation for Anticancer Pharmaceuticals (S9)
    - Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions (Q4B)
    - Pharmaceutical Development (addendum) (Q8 [R1])
    - Pharmaceutical Quality System (Q10)
    - Development and Manufacturing of Drug Substances (Q11)
    - Q&A on Quality (Q-IWG)
    - Electronic Standards for Transmission of Regulatory Information (M2)
    - Non-Clinical Safety Studies for the Conduct of Human Clinical Trials (M3 [R2])
    - Data Elements and Standards for Drug Dictionaries (M5)
    - Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals (S6 [R1])
    - Data Elements for Transmission of Individual Case Safety Reports (E2B [R3])
    - Development Safety Update Report (E2F)
    - Studies in Support of Special Populations: Geriatrics (E7 [R2])
    - Q&A on the Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs (E14-IWG)
    - Genomic Biomarkers Related Drug Response (E16)
    - Gene Therapy Discussion Group (GTDG)
  - Pharmacopoeial Discussion Group (PDG)
  - MedDRA (Medical Dictionary for Regulatory Activities) Steering Committee Meeting
  - WHO INN meeting

- In order to build a specific system for exchanging information, etc., relating to consultations, reviews, and post-marketing safety measures in cooperation with the U.S. and EU, PMDA holds discussions with the FDA of the U.S. and the EMEA of the EU in collaboration with the MHLW. However, no individual discussion with the EU was made in FY 2008.

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

ISO/TC/106 (dentistry)
ISO/TC/150 (Implants for surgery, artificial organ)
ISO/TC/198 (Sterilization of health care products)
GHTF SG1 IVD-subgroup (IVD regulation)
GHTF SG1 (Premarketing regulations for medical devices)
GHTF SG2 (Post-marketing monitoring systems)
GHTF SG3 (Quality systems)
GFTF SG4 (Regulatory auditing)
GHTF SG5 (Modality of medical examination/ evaluation with medical devices)
Regulatory Affairs Professionals Society (RAPS)
Harmonization by Doing (HBD)

b. Efforts to introduce a total review time

- In working toward introducing the concept of a total review time, PMDA 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 2008 was 79, and the median review time (PMDA review time) for these applications was 9.0 months, whereas the median total review time was 18.9 months. Applications for 77 of these approved drugs were submitted in and after April 2004, of which the median review time (PMDA review time) was 9.0 months and the median total review time was 18.8 months.
(See the table, *Number of Approved New Drugs*.)

- The number of new medical devices that were approved in FY 2008 was 16, and the median review time (PMDA review time) for these applications was 8.9 months, whereas the median total review time was 16.0 months. Applications for 16 of these approved medical devices were submitted in and after April 2004, of which the median review time (PMDA review time) was 8.9 months and the median total review time was 16.0 months.
(See the table, *Number of Approved New Medical Devices*.)

- As approaches directed toward implementing the total review time, PMDA 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, PMDA 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, PMDA recruited competent human resources with high expertise, mainly through open

recruitment, while ensuring its neutrality and impartiality as an incorporated administrative agency (see II-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, PMDA worked to improve the skills and knowledge of its staff by providing them with training opportunities using external training organizations and external experts (see II-3.4.(2), Systematic implementation of staff training).

(ii) Development of a GMP/QMS inspection system

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

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

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

- Therefore, PMDA continued to recruit GMP/QMS specialists to form a system of 40 inspectors as of April 1, 2009. At the same time, PMDA is also promoting educational training for GMP/QMS inspectors 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 inspections.

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

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

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

* *Excluding In vitro diagnostics.*

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

- 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
FY 2008	31	19	32	0	82

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

FY 2008: France, Denmark, Sweden, Spain, Ireland, UK, Netherlands, Belgium, Italy, Austria, Germany, Romania, Slovenia, USA, Canada, Mexico, Puerto Rico, Argentina, China, South Korea, Taiwan, 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
FY 2008	13	17	0	0	30

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

FY 2007: France, USA, and Puerto Rico

FY 2008: Ireland, Italy, UK, Netherlands, Switzerland, Spain, France, USA and Mexico

- The administrative processing times of GMP/QMS inspections in FY 2008 are shown below:

Processing Time of GMP/QMS Inspections 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

	FY 2008	
	Total processing time (median)	PMDA processing time (median)
Drugs *	155 days	100 days
In vitro diagnostics	117 days	46 days
Quasi-drugs	156 days	29 days
Medical devices	131 days	59 days

* *Excluding in vitro diagnostics.*

- The processing status of audits of manufacturing facilities conducted in FY 2008 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	FY 2008
Drugs*	12 (8)	30 (23)	16 (14)	8 (6)
In vitro diagnostics	1 (1)	6 (6)	2 (2)	2 (2)
Medical devices	2 (1)	1 (0)	0 (0)	1 (1)
Total	15 (10)	37 (29)	18 (16)	11 (9)

* *Excluding In vitro diagnostics.*

Note: Values include withdrawn cases. Values in parentheses show the number of on-site inspections out of the total audit cases.

- The processing status of audits of manufacturing facilities conducted in FY 2008 at overseas manufacturing sites, 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	FY 2008
Drugs*	69	614	387	294
In vitro diagnostics	9	85	69	69
Quasi-drugs	29	73	57	39
Medical devices	127	971	1,682	1,191
Total	234	1,743	2,195	1,593

* *Excluding In vitro diagnostics.*

Note: Values include withdrawn applications. All cases were document-based investigations.

- PMDA 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 2008 is shown below:

Number of On-the-spot Inspections

		FY 2005	FY 2006	FY 2007	FY 2008
Domestic manufacturers	Drugs*	15	11	27	13
	In vitro diagnostics	0	0	1	1
	Medical devices	0	0	2	0
Foreign manufacturers	Drugs*	2	3	5	2
	In vitro diagnostics	0	0	0	0
	Medical devices	0	2	0	1
Total		17	16	35	17

* *Excluding In vitro diagnostics*

- PMDA conducts simple consultations on GMP/QMS inspections. The number of simple consultations on GMP/QMS inspections conducted in FY 2008 is shown below:

Number of Simple Consultations Conducted for GMP/QMS Inspections

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

* *Excluding In vitro diagnostics*

(iii) Use of external experts

- PMDA continued with procedures to commission external professionals as external experts for PMDA in order to obtain specialized opinions relating to scientifically important issues at Expert Discussions, etc., for reviews and post-marketing safety measures.
  (As of March 31, 2009, the number of commissioned experts is 914 including external experts commissioned for issues relating to safety measures.)

(iv) System development for more efficient review services

- In addition to a new application/review system used by PMDA, Pharmaceutical and Food Safety Bureau in MHLW, Regional Bureau of Health and Welfare, prefectural governments, pharmaceutical companies, etc, the system for review operations used by PMDA is comprised of the following individual systems necessary for executing reviews, audits, and management of commission: (i) review support system for drugs, etc., (ii) new drug database system, (iii) device system, (iv) conformity audit support system, (v) medical device review support system for medical devices, (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, PMDA is able to manage the progress for the entire process from acceptance of applications and notifications for marketing approval, manufacturer's license, etc. on drugs, quasi-drugs, cosmetics and medical devices, until their enforcement. In

addition, PMDA 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 authorities, recording of review memorandums, preparation of approval certificates and management of the approval registration list.

- In FY 2008, PMDA reviewed the structure and procurement method of the new application/review system in order to achieve the Mid-term Targets and the Mid-term Plan. At the same time, PMDA conducted the following system developments to promptly and efficiently perform review and audit services.

1) Improvement of the new eCTD viewer system (review comment function)

- Based on the requirement definition for review function for eCTD implemented in FY 2007, the eCTD viewer system was improved through the general competitive bidding process to newly add the review comment control function. The review operations using the eCTD viewer system were greatly enhanced. As a result of this improvement, submission of paper documents became unnecessary when an eCTD is filed as the original.

2) Improvement of the function to extract progress control information in the medical device review system

- The improvement of the device system used for management of review information and progress control of review operations for medical devices was performed through the general competitive bidding process. Improvements such as input of inquiries, modification of the entry screen for memo on replacement instruction, addition of screens for verification of conformity audit and QMS inspection, and progress control information extracting function were made. As a result of operational improvement, the review operations for new medical devices were accelerated.

3) Improvement of clinical trial database system functions for changes in matters notified in the protocol application

- For protocol applications, the format of the electronic application will be changed from the SGML format to the XML format on April 1, 2009. In order to handle this change, a system was improved to accept protocol applications in the XML format as with those submitted in the SGML format through general competitive bidding process. In addition to this, improvement such as the enhancement of the search function was carried out; operability greatly improved.

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

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

5) Computerization of documents related to past face-to-face consultations

- PMDA computerized documents related to past face-to-face consultations, which had

been archived in paper media, in the PDF format through the general competitive bidding process, and thus reduced the costs for storage of paper documents.

6) Modification of the management system for adverse drug reaction information responding to the partial revision of safety reporting during clinical studies

- PMDA modified functions such as data receipt and search in the management system for adverse drug reaction information through the general competitive bidding process, and used post-marketing information on adverse drug reactions to assure safety during clinical studies, to facilitate the acceleration and efficiency of approval review operation for drugs.

7) Improvement of the new application system for re-issue of the certificate for drugs master file registration and the consolidation of the history of changes in registered information

- Of the application processing operations such as applications for registration of the drug master file (DMF) and changes in registered items in the new application/review system, PMDA changed reference information for renewal/re-issue of the registration certificate, added print forms enabling certificates to be printed out retrospectively, and modified a program to consolidate the history of changes in registered information. PMDA improved the system through general competitive bidding process to promote the acceleration and efficiency of the review operation.

8) Transfer of image data of attached documents for new drug applications to the exiting search system, improvement of the new drug database system function, and modification of the review support system for drugs, etc. responding to addition of new consultation categories for drugs, etc.

- All the system improvements in the above 1) to 7) were carried out by companies selected through general competitive bidding. As a result, three additional modifications were made within the initial budget for this fiscal year.

(v) Reinforcement of partnerships with foreign regulatory agencies

- From the perspective of implementing PMDA's overall international activities in a organized and systematic manner in collaboration with the MHLW in the targeted time in the Second Mid-term Target period, the PMDA International Strategic Plan (February 6, 2009) were formulated as a basic policy for overall international activities during this period. PMDA determined to play its expected international role with the promotion of proactive international activities according to the said strategic plans and by meeting the needs of Japanese people and people around the world for drugs and medical devices. Also, PMDA promoted reinforcement of partnerships with regulatory agencies in the U.S. and the EU 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 agencies of the U.S. and the EU as well as with those of Asian countries, PMDA participated in international conferences such as for ICH, GHTF, HBD, and PDG, as well as in meetings of the OECD and the WHO, and promoted cooperation with relevant countries with regard to developing international guidelines.

PMDA also provided lectures on its review services and safety measures at the DIA Annual Meeting and RAPS Annual Conference in the U.S., at DIA EURO Meeting in Germany, at the Symposium of APEC Network on Pharmaceutical Regulatory Science in Taiwan, and at FAPA Congress in Singapore, etc. to improve the international recognition of the PMDA. PMDA also made efforts to expand its collaborative relations with Asian countries by visiting China, South Korea, Thailand, Taiwan and other countries. (See II-4.2.(1)-(vi)-a., Approaches toward international harmonization such as through ICH). PMDA also implemented the following measures to further strengthen its partnerships with foreign regulatory agencies.

1) PMDA collected information on the review system and post-marketing safety measures at the FDA (Food and Drug Administration), the EMEA (European Medicines Evaluation Agency), etc. In addition, PMDA exchanged information with FDA and EMEA on methods for conducting operations and other issues. PMDA also participated in the 3rd Meeting of Regulatory Officials in Europe, the US, and Asia held in Singapore in December 2008, and exchanged notes with regulators in various countries including the FDA.
2) Based on the Administrative Rules on Overseas Training on a Long-term Basis, PMDA dispatched one employee each to the FDA and the OECD after recruiting personnel who were interested in being dispatched and screening the applicants.
3) PMDA received foreign trainees, including four from Indonesia, one from the U.S. (Mansfield trainee), and four from China.

- As a result of recent increases in simultaneous clinical trials/development of drugs among 3 East Asian countries (Japan, China and South Korea), the 1st Japan,-China-South Korea Director-General Level Meeting on Pharmaceutical Affairs was held on April 14, 2008 in Tokyo to promote partnership among the regulatory agencies of the 3 countries (Japan, China and South Korea) and re-confirm the importance of drug development in East Asia. In response to this, the below-mentioned public 2008 East Asian Regulatory Symposium was held for the purposes of (i) promotion of the implementation of joint clinical trials in the East Asian region, (ii) prompt development and realization of approval reviews using joint clinical trial data in the East Asian region, and (iii) opinion exchange to allow the specific and effective collaboration in the future toward the achievement of these.

Time and date: April 14, 2008 from 13:30 to 18:00
April 15, 2008 from 9:30 to 18:30
Place: Tokyo International Forum
Theme: “Global drug development and collaboration among the East Asian countries”
Sponsored by: PMDA; Co-sponsored by: MHLW
Supported by: Federation of Pharmaceutical Manufacturers’ Associations of Japan (FPMAJ), Japan Pharmaceutical Manufacturers Association (JPMA), Pharmaceutical Research and Manufacturers of America (PhRMA), European Federation of Pharmaceutical Industries and Associations (EFPIA), Pharmaceutical Society of Japan (PSJ), and Japanese Society of Clinical Pharmacology and Therapeutics (JSCPT)
Program:
Plenary meeting: Opening remarks by the Chief Executive, report from the Director-General Level Meeting, and keynote speeches by Director-Generals in the 3 countries (Japan, China and South Korea)
Session 1: Current status and future direction of drug quality/GMP (Lectures

and panel discussions by experts in Japan, China and South Korea)

Session 2: Post-marketing safety measures (Lectures and panel discussions by experts in Japan, China and South Korea)

Plenary meeting: Global clinical trials and drug development (Lectures and panel discussion by industry group representatives and regulatory agencies in Japan, China, South Korea, Thailand and Singapore; Debate on the current status and issues of drug development in the East Asian region and possibility of mutual collaboration for future advancement)

Attendees: A total of 690 people from 10 countries participated in the symposium, and the symposium was very successful.

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

- As PMDA is required to raise the standards for guidance and review techniques for the latest technologies such as biotechnology and genomics, PMDA utilized external 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 human (auto) and human (allogenic) cellular and tissue and its administrative notice on Q&A, and evaluation guidelines regarding biosimilars/follow-on biologics).

  PMDA also assisted operations such as the development of guidelines by study groups for evaluation of regenerative medicine and vaccines.

- Through consultations for supporting venture companies and for adapting a special zone for development of state-of-the-art medicine (Super Special Consortia), PMDA collaborated in the development of products to which new technology has been applied. PMDA also started to promptly deal with clinical trial consultations on the topic for adaptation of the Super Special Consortia in March 2009.

- In order to study effects on the safety and efficacy of drugs by genetic factors of individual patients, and to administer drugs to each patient in more appropriate conditions, there are expectations for applications towards drug 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 PMDA to collect information from a scientific standpoint while cooperating with MHLW and commencing reviews directed toward developing specific guidelines. In FY 2008, PMDA periodically held internal meetings and 3 unofficial meetings with companies, etc. to exchange opinions based on the latest information on pharmacogenomics.

- PMDA has held biologics symposiums each year for forming an international common basis for evaluation of the quality, efficacy and safety of biologics. This time, the “3rd PMDA International Symposium on Biologics” was held in February 2009 with the theme of follow-on biologics (biosimilars) by inviting speakers from the EU and US regulatory agencies, industry groups and the WHO, and efforts and trends in each country were discussed.

- PMDA held five meetings for Expert Discussions on drug names and reported 37 Japanese

accepted names (JAN) to MHLW. Eight application consultations for international nonproprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conference on INN in April.

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, PMDA 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), PMDA implemented Training for Clinical Research Coordinators (beginner training, lectures in September 2008 and practical training from September 2008 to February 2009; advanced training, lectures from November 2008 to January 2009; data management training, lectures and practical training in September 2008) to pharmacists and nurses from medical institutions.

Trainees in FY 2008

Beginner training	96
Advanced training	109
Data management training	65

- On the PMDA website, PMDA 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 drugs and ensuring transparency of approval reviews, PMDA has, with the understanding and cooperation of relevant companies, and also with the cooperation of MHLW, provided information on the approval of new drugs, etc., on the Medical Product Information site of the PMDA website, as follows:

Review reports on new drugs

- Based on the contents of the submitted applications, new drugs are classified into two categories: those that are to be deliberated in the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (hereinafter referred to as “deliberation 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 disclosure for deliberation items, whereas Review Reports are subject to disclosure for reported items.

- The information is provided 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 2008, PMDA finalized 91 review reports and 80 summaries of application dossiers to be

officially disclosed.

Review reports on new medical devices

- It was decided that PMDA 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 2008, PMDA disclosed review reports for 8 applications.

Review reports on OTC drugs and quasi-drugs

- It was decided that PMDA 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. Furthermore, this notification was amended on October 31, 2008, and the summaries of application dossiers were sequentially published. In FY 2008, PMDA disclosed review reports for 6 applications and summaries of application dossiers for 25 applications for OTC drugs, and review reports for 1 application and summaries of application dossiers for 8 applications for quasi-drugs.

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

- In order to provide information on PMDA's review services and post-marketing safety measures to foreign countries, PMDA decided to post the English version of the review reports on its website. In FY 2008, PMDA prepared and published the English version of five 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 drugs and medical devices, and to enable patients and healthcare professionals to use them properly, PMDA has been progressing with operations so that reviews and safety measures function in such a way that they are inseparable, by collecting and examining post-marketing safety information efficiently, processing the information speedily and providing appropriate and accurate plans for safety measures and easily understandable safety information promptly.

- There are approximately 152,000 reports on adverse drug reactions submitted to PMDA from within and outside of Japan each year, and approximately 7,000 reports on malfunctions of medical devices from within and outside of Japan are submitted to PMDA yearly. PMDA inputs this information into a database and promotes the sharing of this information with MHLW. In addition, PMDA is making efforts to take effective safety measures for drugs and medical devices in the post-marketing stage by enhancing cooperation between the review divisions and safety divisions, as well as between the relief divisions and safety divisions.

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

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

- PMDA distributes important post-marketing 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 Medical Product Information site of the PMDA website: http://www.info.pmda.go.jp/.

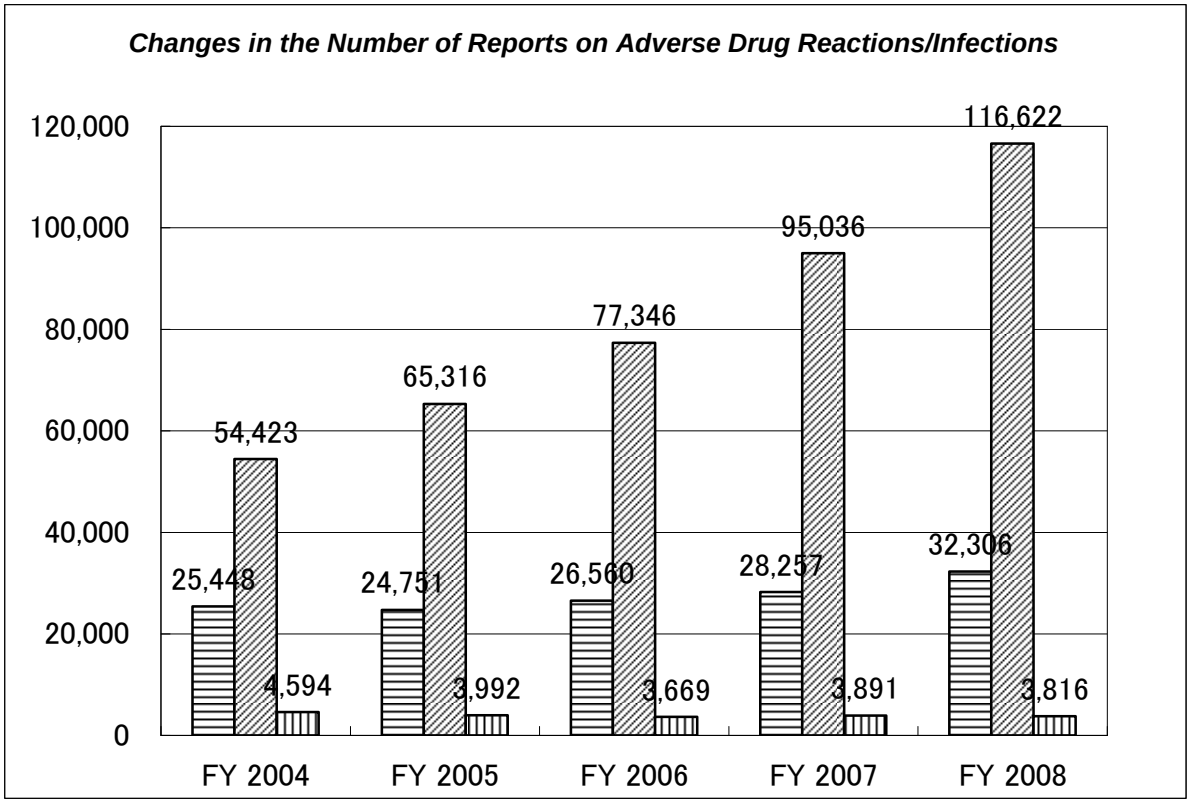
- PMDA completed the system development and introduction of the system into the operational process, so that new safety information can be detected and analyzed by finding relevance with different kinds of information on adverse drug reactions (data mining method), in order to establish measures to prevent adverse drug reactions from occurring.

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

Collection of adverse reaction reports, etc.

1) Number of reports relating to drugs

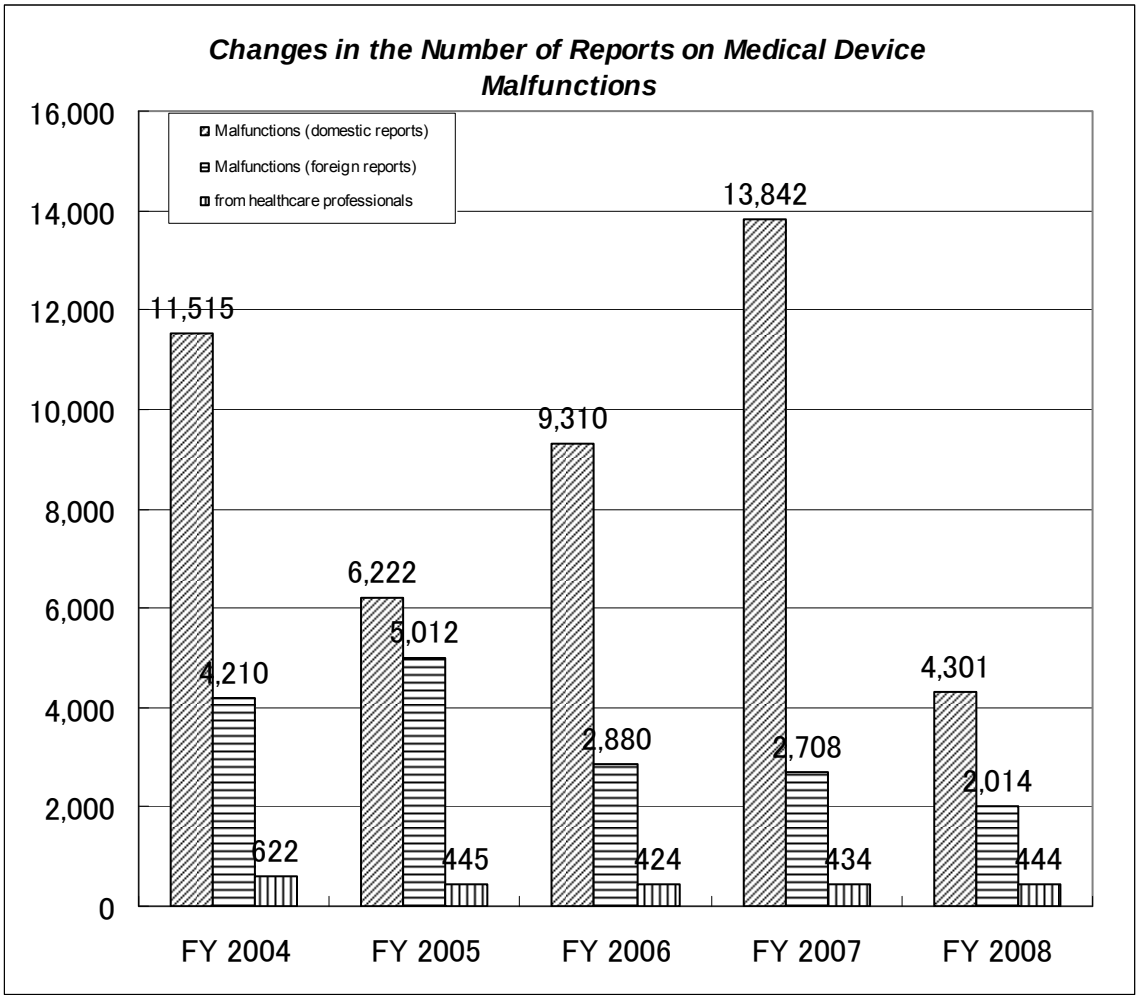
	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Reports from companies	82,624	92,678	106,285	125,938	151,726
(cases of adverse drug reactions, Japanese)	(25,142)	(24,523)	(26,309)	(27,988)	(31,455)
(cases of infections caused by drugs, Japanese)	(306)	(228)	(251)	(269)	(851)
(cases of adverse drug reactions, foreign)	(54,312)	(64,650)	(77,314)	(95,015)	(116,592)
(cases of infections caused by drugs, foreign)	(111)	(666)	(32)	(21)	(30)
(research reports)	(1,311)	(971)	(818)	(858)	(855)
(foreign corrective action reports)	(420)	(563)	(485)	(695)	(869)
(periodic infection reports)	(1,022)	(1,077)	(1,076)	(1,092)	(1,074)
Reports from healthcare professionals	4,594	3,992	3,669	3,891	3,816
Total	87,218	96,670	109,954	129,829	155,542



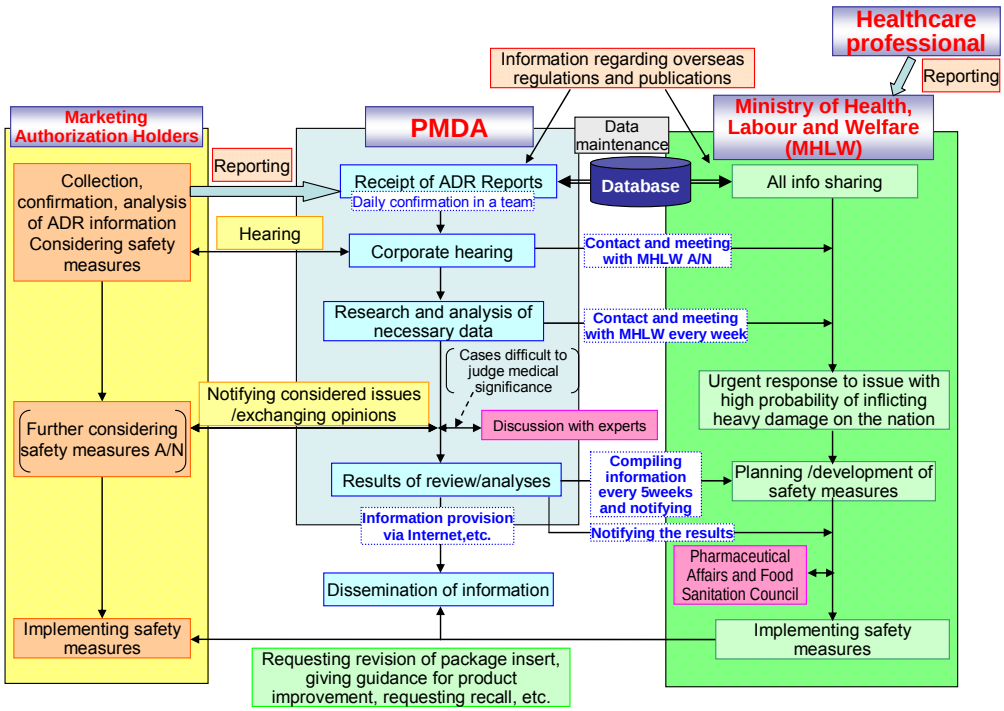
2) Number of reports relating to medical devices

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Reports from companies	16,264	11,802	12,770	17,142	7,137
(cases of malfunctions of medical devices, Japanese*)	(11,515)	(6,222)	(9,310)	(13,842)	(4,301)
(cases of malfunctions of medical devices, foreign*)	(4,210)	(5,012)	(2,880)	(2,708)	(2,014)
(research reports)	(157)	(37)	(36)	(15)	(10)
(foreign corrective action reports)	(287)	(436)	(482)	(525)	(748)
(periodic infection reports)	(95)	(95)	(62)	(52)	(64)
Reports from medical professionals	622	445	424	434	444
Total	16,886	12,247	13,194	17,576	7,581

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



Flowchart for Processing Adverse Reaction Reports



(ii) Introduction of a new method (review of the data mining method)

- PMDA is aiming to implement a method for detecting and analyzing new safety information during the period of the Mid-term Plan by finding correlation in different kinds of data 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 drugs and adverse drug reactions that are likely to have a causal relationship from the database of individual cases of adverse drug reactions.

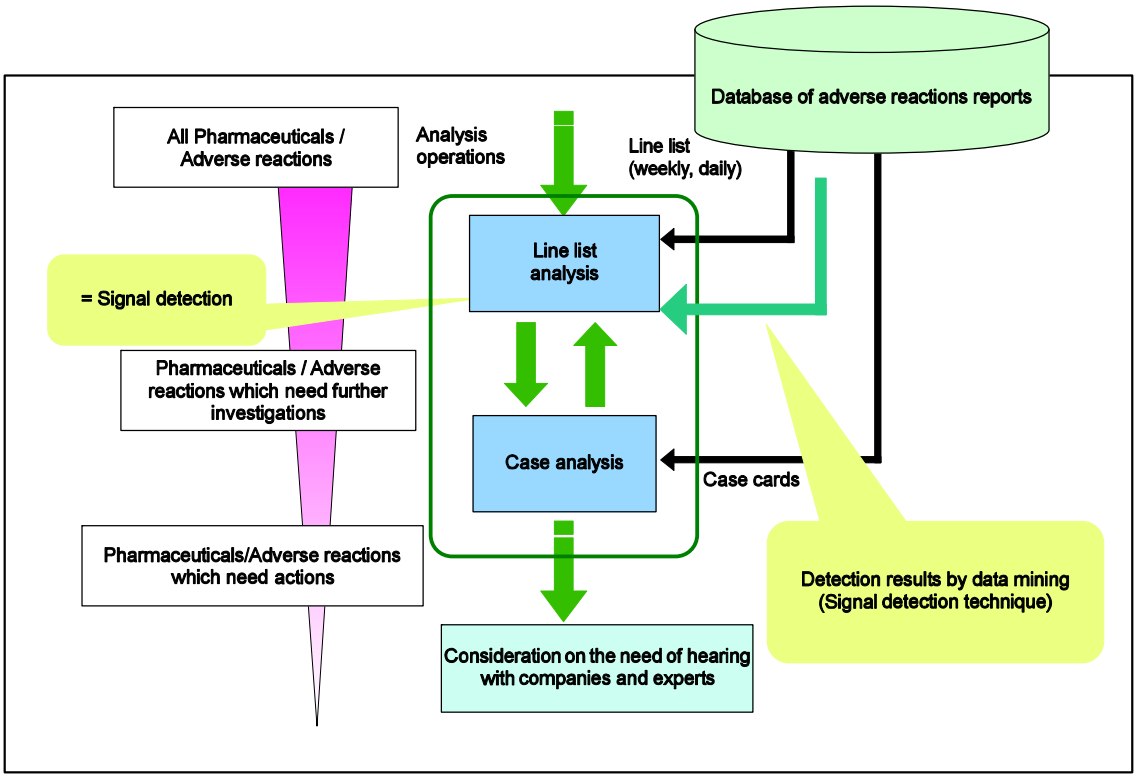
- Regarding the basic signal extraction techniques (i.e., six techniques including those introduced in foreign countries) that were subjected to detailed review in FY 2005 (in terms of the number of detections, increase or decrease in the number of detections, or quality of detection), PMDA narrowed them to three (ROR, GPS, and BCPNN) as a result of sensitivity and specificity analysis and correlation analysis conducted together with advancement review (stratified analysis, analysis of interaction with coadministered drugs, and adverse-reaction grouping) by the end of FY 2006. In FY 2007, PMDA conducted surveys on how the data mining method was used by regulators in foreign countries and interviewed personnel in charge of adverse-reaction evaluation on the subject of operations processes. PMDA prepared the specifications of a new database system that could utilize the data mining method as a support tool that matches the operational flow of new safety measures, and also launched the development of an operations support system supporting all aspects of safety measures. PMDA 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, PMDA developed a tool based on correlation analysis to support non-routine analytical operations. This tool will be used as a means to advance data mining, and PMDA has started reviewing its utility. In FY 2008, PMDA continued to examine the advancement of the data mining method (e.g. procedure to detect duplicated reports), introduced trial application of the data mining method to safety measures operations, organized results during the period of the Mid-term Plan and reviewed future policies. The report was posted on the PMDA website in May 2009.

- In FY 2008, a new support system allowing the utilization of the results of the data mining system was developed after a trial operation. The system can detect adverse drug reactions meeting uniquely specified conditions as signals for adverse drug reactions reported every day. In addition, a new operation flow to check detected signals was established so that data mining results could be easily used in operations. With this system, safety concerns (signals) were more quickly and exhaustively grasped from the adverse drug reaction report database on the same level as the EU and US; thus, a basis for enhancing safety measures operations, such as implementation of prompt and appropriate safety actions and quick provision of safety information, was developed.

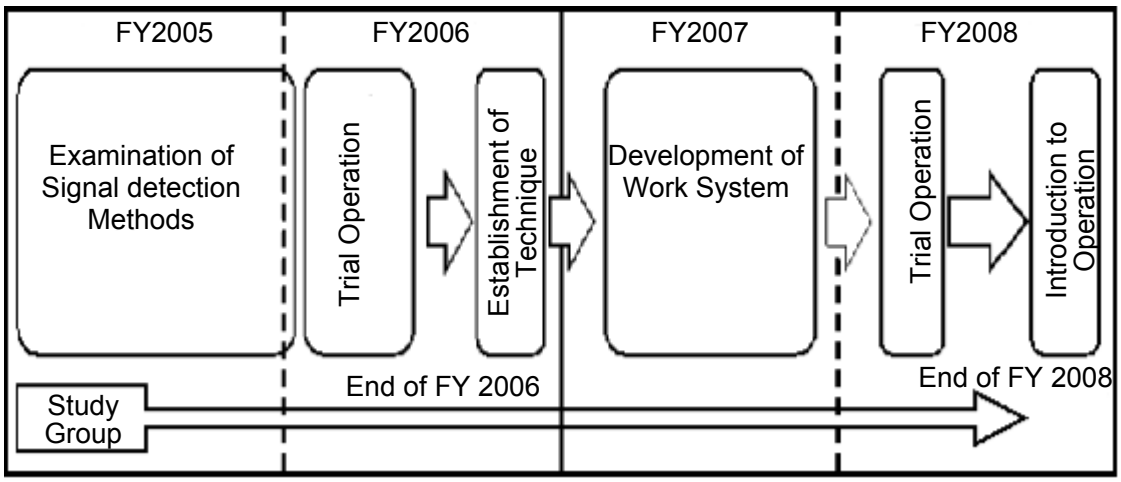
- The status of reviews relating to the implementation of safety measures for the data mining method is posted on the following website:

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

Introducing the Data Mining Method into Post-marketing Safety Measures



Schedule for Introducing the Data Mining Method (Planned)

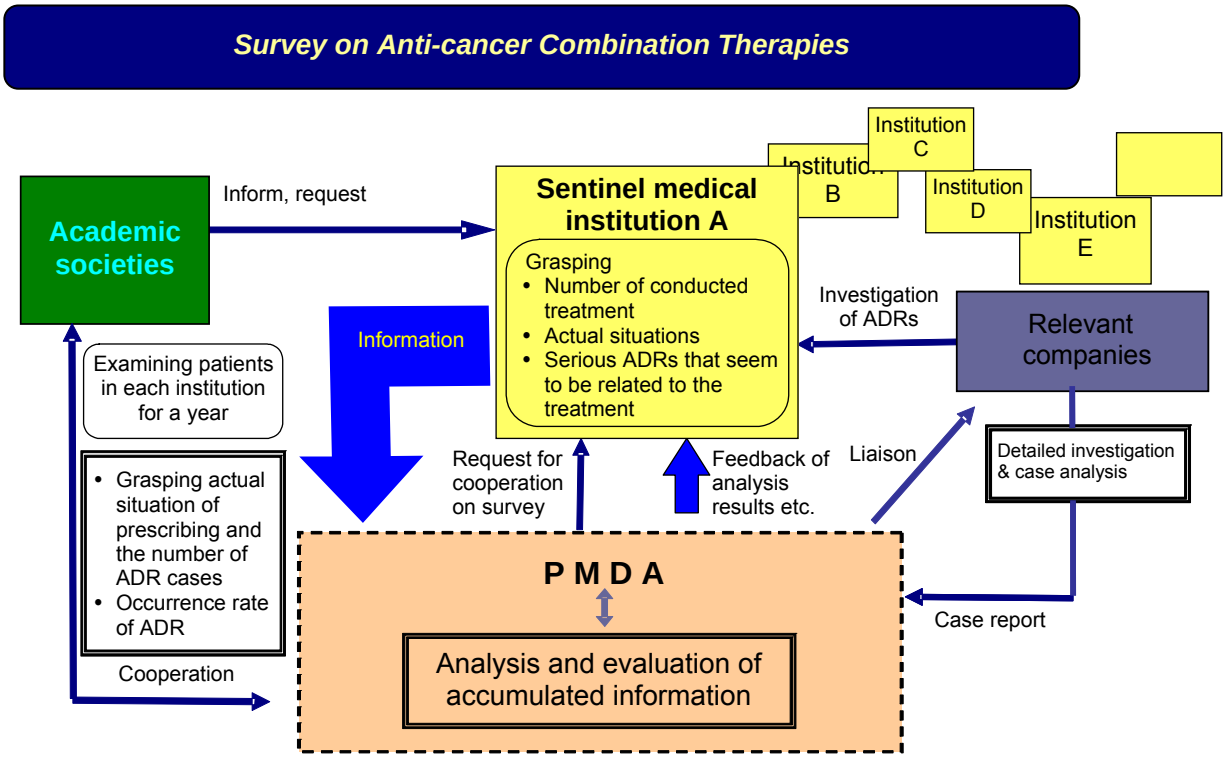


(iii) Building a sentinel medical institution network

- As PMDA works to focus on safety measures in the post-marketing stage in accordance with the Mid-term 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, with the purpose of collecting 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).

- PMDA 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, PMDA 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. Subsequently, an additional analysis was performed, and the final report was posted on the PMDA website in May 2009.



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 order to examine points to consider in extracting information on adverse drug reactions from electronic medical data and to obtain ideas for the next Mid-term Plan, PMDA performed a trial study in July 2008 using a medical institution, which applied for public offering, as the study center. For 3 themes on the combination of drugs and adverse drug reactions, studies using electronic medical records and DPC as information sources were planned. The procedures associated with a total of 4 safety studies (development of the study protocol and consultation with the ethics committee, data extraction, tabulation/ analysis, and the preparation of reports) were completed in March 2009. For one of the themes, "antibiotic (injection) treatment and the onset of pseudomembranous colitis," pseudomembranous colitis was detected in 55 of 7,259 (0.76%) patients investigated in the study using electronic medical records, and pseudomembranous colitis was identified in 10 of 3,335 (0.30%) patients examined in the study using DPC; therefore, there was a difference in the number of patients with adverse drug reactions detected according to the source of information. After taking account of the results of the other themes, future examination topics such as the need to select an information source suitable for study objectives and methods were revealed. The report was put on the PMDA website in May 2009.

- With regard to the establishment of the sentinel medical institution network, a scheme was created to increase the precision of analysis of adverse drug reactions by collecting and analyzing the frequency of specific adverse drug reactions associated with specific drugs and other detailed information in collaboration with medical institutions. In order to apply this to post-marketing safety measures on a full scale, it is necessary to diversify the functions and medical areas of participating medical institutions and increase the number of medical institutions. However, it was found that a considerable amount of costs and personnel would be required to realize this.

  In the course of the study to build the sentinel medical institution network, a trial analysis of electronic data such as electronic medical records and DPC data suggested that the use of existing electronic medical examination data might enable the collection and analysis of detailed

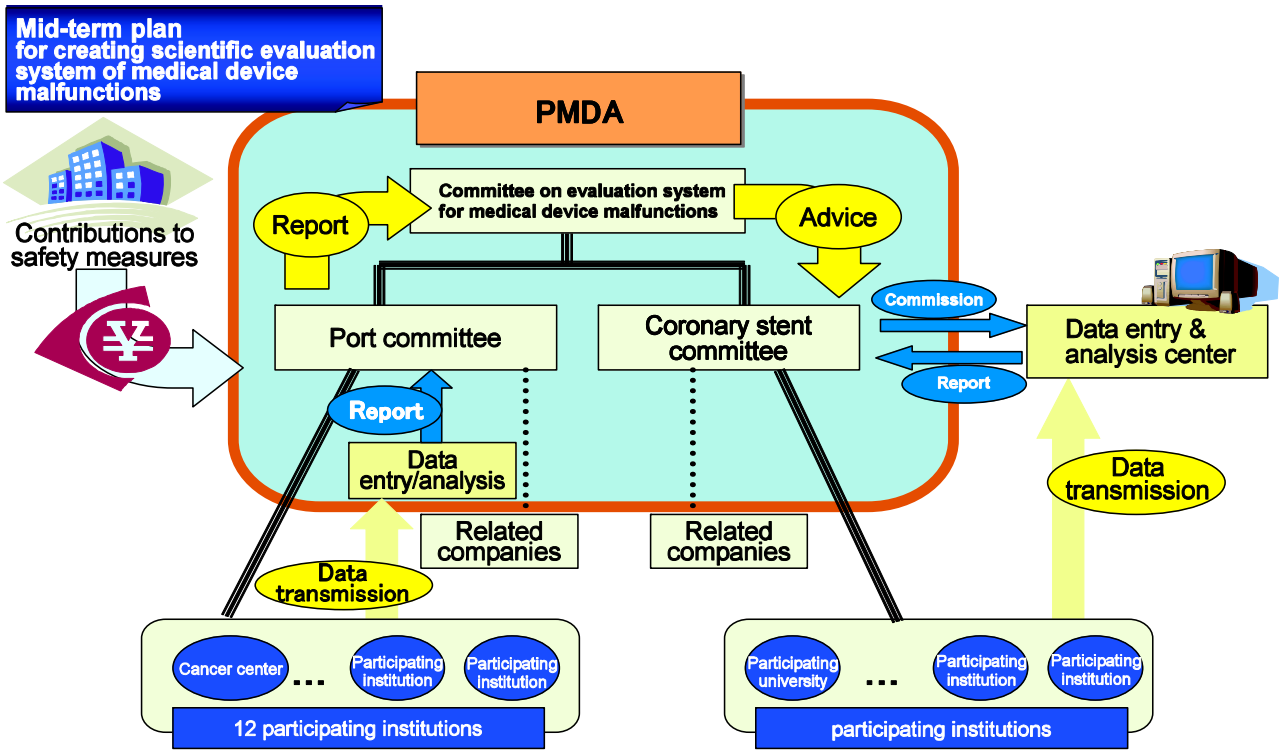
information on specific adverse drug reactions associated with specific drugs. Therefore, PMDA withdrew the project to establish the sentinel medical institution network, and decided to work on the use of electronic medical data for post-marketing safety measures.

(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 2008 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 February 2009.

  The status of implementation in FY 2008 was as follows:

  a) Implantable ports: With regard to the study on malfunctions of implantable ports started in FY 2006, a follow-up investigation (1 year) in all enrolled patients was completed in May 2008. After inquiries on collected data and data cleaning were made, the data were fixed in September 2008, and the final analysis was finished in November 2008. In 13 of the 112 patients enrolled from 12 institutions, a total of 21 malfunctions 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 committee in December 2008. After an additional analysis, the results of the examination were published on the PMDA website in April 2009.
  b) Coronary stents: In FY 2008, data from a study (26 institutions; planned sample size: more than 16,000 patients; 5-year follow-up period) in patients who underwent the first percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) have continued to be collected through an external contracted organization since 2007. In an interim evaluation, the development of stent thrombosis was evaluated using data collected up to September 2008 (more than 2,000 patients with PCI only from 9 institutions) (nondisclosed), and the results were examined at the stent committee in January 2009. The study will be continued the next fiscal year and thereafter.



- Cardiac pacemakers and tracking other medical devices: In FY 2008, the "Committee for an Implantable Artificial Heart Assist System" which was established under the "Discussion Group for Construction of the System for Collection and Evaluation of Data for Tracking Medical Devices," examined the protocol (draft) for the registry of an implantable artificial heart assist system (patient registration system) and its implementation structure based on the existing registry in the US (INTERMACs). In parallel, a consulting company, to which the supporting operation was contracted out, investigated Japanese medical institutions planning to participate in the study and the US INTERMACs and submitted the specifications (draft) for the system establishment to the PMDA in March 2009.

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 investigation on reports of adverse drug reactions and medical device malfunctions

- Adverse drug reaction reports, medical device malfunction reports, infection reports, research reports, etc., from marketing authorization holders of drugs and medical devices under the Pharmaceutical Affairs Law have been required to be submitted directly to PMDA since April 2004. These reports are input into the 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 the Minster of Health, Labour and Welfare

are input into the PMDA database and managed so that information can be shared with MHLW.

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

- The number of reports (the number of active ingredients for drugs, and the number of generic names for medical devices) made to MHLW on items for which measures were necessary (such as for revision of package inserts) in FY 2008 is as follows:

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Drugs	133	240	131	204	151
Medical devices	15	18	4	10	37
Medical safety*	2	2	2	1	4

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

- Post-marketing safety measures taken by MHLW in FY 2008 based on reports from PMDA are as follows (includes duplicated measures):

		FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Drugs	Instructions for revision to precautions in package insert	149	212	131	202	141
	Posting articles and cases on the Pharmaceuticals and Medical Devices Safety Information	33	26	24	86	20
Medical Devices	Instructions for revision to precautions in package insert or notifications to instruct self-check	7	7	0	8	4
	Posting articles on the Pharmaceuticals and Medical Devices Safety Information	6	7	0	3	2

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

- In FY 2008, PMDA 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. Updated the master files consisting of drug product and company names

c. Encouraged staff members to attend academic conferences (total of 68 participants attended) and gathered information through the academic conferences that they participated in
d. Regularly held liaison meetings on both drugs and medical devices every week with MHLW

(vi) Digitization of reporting of adverse drug reactions and medical device malfunctions

- In FY 2008, as part of effectively and efficiently collecting safety information through utilizing IT, PMDA 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, PMDA requested for cooperation from the private sector and aimed to secure an online reporting rate of 90%.

- For this purpose, in addition to releasing data input tools on the Web and developing an environment that allows for easy data transmission, PMDA monitored the electronic reporting rate monthly and directly asked major companies that had not yet implemented online reporting to implement such a system. PMDA 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 92.3% on a full-year basis was achieved in FY 2008, exceeding the target of 90%.

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

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Electronic reporting rate (full year)	69.1%	86.4%	90.4%	91.1%	92.3%

* *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 2008 plan: Ensuring the 90% of electronic reporting rate

Status of Online Reporting for Malfunction Reports

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Electronic reporting rate (full year)	36.8%	86.9%	53.6%	22.1%	73.4%

* *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 feedback 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, PMDA 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, PMDA disclosed all of the information on adverse drug reactions reported by the private sector in and after FY 2004. Since January 2006, PMDA has sequentially released information as line lists.

- At the end of March 2009, PMDA disclosed 110,879 adverse drug reaction reports and 42,405 medical device malfunction reports that had been submitted up to the end of

September 2008. The time from receiving reports to disclosure was decreased to 6 months so that the target period was achieved.

2) Responses to consultations from the private sector

- In order to contribute to the improvement of post-marketing safety measures in the private sector, PMDA responded to various consultations (on drugs, 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 drugs to prevent medical accidents, and improvements in products to prevent medical accidents based on analyses of near-incident cases.

- The number of consultations by category for FY 2008 is shown below:

	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Drugs	513	557	567	486	559
Medical devices	722	553	292	260	283
Medical safety	46	46	44	166	172

- 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. In FY 2008, the number of consultations became stable to some extent so that there was no great change from the previous fiscal year. In contrast, the increase in the number of consultations on medical safety is attributed to the sudden rise in the number of pre-application consultations on new application of change or replacement of brand name of drugs in 2007, as a preventive measure against medical accidents for drugs whose names are similar to those of other products, or whose brand names do not contain the quantity of the active ingredient. This tendency was also slightly noted in FY 2008, and the number of consultations on the names of new drugs and packaging/labeling increased. PMDA handled all cases in an appropriate and speedy manner.

b. Feedback to healthcare professionals

During FY 2008, PMDA took the following approaches to provide post-marketing safety information on drugs and medical devices to the public as well as healthcare professionals by using the Internet.

1) Prompt posting of information on the PMDA website

- PMDA posted information on revisions to package inserts of prescription drugs, etc., on its website within two days after receiving such information.

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

- To prepare for the revision of the Pharmaceutical Affairs Law in June 2009, PMDA commenced posting package inserts of OTC drugs on the PMDA website in March 2007, and there were 8,356 package inserts presented on the site as of the end of March 2008. The purpose of this initiative is to ensure information supply and consultation systems

according to the degree of risk associated with the drugs, ensure qualifications of professionals engaged in selling drugs, and develop an environment that can respond appropriately to consultations as well as provide appropriate information.

3) Preparation of information on *in vitro* diagnostics package inserts for posting it on the PMDA website

- Information on package inserts of prescription drugs, medical devices, and OTC drugs are provided on the Medical Product Information site of the PMDA website to ensure their correct usage. Package insert information for *in vitro* diagnostics was also started to be posted. A total of 2,237 package inserts were put on the site as of the end of March 2008.

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

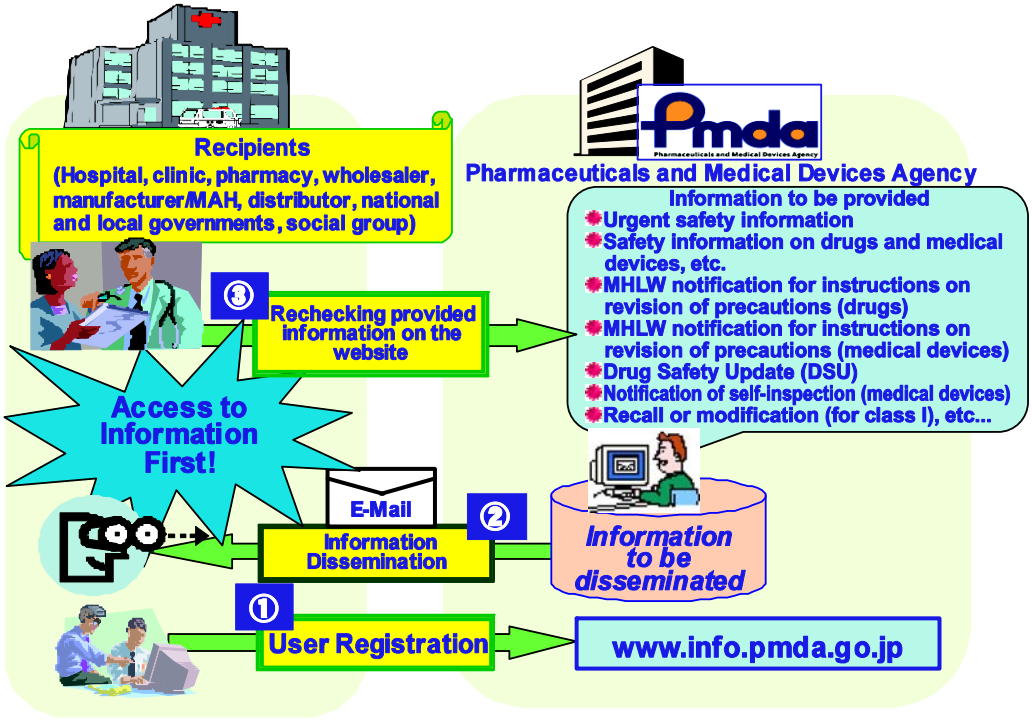
- The manuals for management of individual serious adverse drug reactions made by MHLW have been made available on the PMDA website since November 2006. In FY 2008, manuals for 13 diseases were added to the website (total number of diseases, 38).

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

5) Pharmaceuticals and medical devices information e-mail service

- The information delivery service for drugs 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 20,707 e-mail addresses were registered as of March 2009. 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 others.

Pharmaceuticals and Medical Devices Information E-mail Service



Number of Push E-mail Service by Subscription Content in FY 2008

Subscription content	Number
Recalls (Class I)	41
Pharmaceuticals and Medical Devices Safety Information	11
Drug Safety Update (DSU)	10
Revision of PRECAUTIONS of drugs	12
Revision of PRECAUTIONS of medical devices	2
Notification on self-check (medical devices)	2
PMDA Medical Safety Information	6
Others	23
Total	107

6) Provision of medical safety information

- PMDA has been extracting, evaluating, and examining near-incident cases associated with drugs and medical devices from the Project to Collect Information on Medical Incident Reports published by the Japan Council for Quality Health Care. In FY 2008, 276 cases associated with drugs and 343 cases associated with medical devices were evaluated, and the results were reported to MHLW. For 428 cases for which deliberations by MHLW were completed, the details of the cases were posted on the Medical Product Information site of the PMDA website.

Items	Drugs	Medical devices
Total applicable cases: 428 cases	242	186
1) Cases in which safety measures for the use of drugs/medical devices taken by the marketing authorization holders etc. were considered necessary or possible.	3	1
2) Cases in which measures have already been taken, or are currently being investigated, by the marketing authorization holder etc.	8	4
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.	231	181

- In addition, in November 2007, PMDA 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 malfunction reports stating much the same events repeatedly or with issuance of notification on revisions to package inserts, 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 2008, the following six issues of PMDA Medical Safety Information were posted on the Medical Product Information site of the PMDA website.

Volume No.	Month and year published	PMDA Medical Safety Information titles
No.4	June 2008	Precautions against smoking and use of fire in Long-term Oxygen Therapy (LTOT)
No.5	June 2008	Handling of lancing devices for obtaining blood samples
No.6	October 2008	Precautions against misuse (overdose) of anti-rheumatic methotrexate preparations
No.7	January 2009	Precautions in artificial respiration (No.1)
No.8	February 2009	Compatibility between a "Type A" needle and a insulin pen
No.9	February 2009	Recall of Jackson Rees Circuit

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, PMDA has disclosed information on fiscal year reported, sex, age, primary disease, suspected drug, adverse event, suspected concomitant drug, and outcome on the Medical Product Information site of the PMDA website, since January 2006. By the end of March 2009, PMDA posted 110,879 reports submitted up to October 2008.

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, PMDA has disclosed information on fiscal year reported, sex, age, outcome, generic name, condition of the medical device, and patient adverse event on the Medical Product Information site of the PMDA website designed to provide information on drugs and medical devices, since March 2006. By the

end of March 2009, PMDA posted 42,405 reports submitted up to September 2008.

9) Support for disclosing relevant information for companies

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

- PMDA translated into English the Pharmaceuticals and Medical Devices Safety Information 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 drugs and medical devices safely and securely, PMDA offers 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. Consultation services for consumers regarding medical devices were launched in July 2005.

- In FY 2008, there were 12,533 consultation requests for drugs and 902 requests for medical devices. Furthermore, PMDA set up its booth at the Forum on Eradication of Drug-induced Sufferings held in November and conducted a face-to-face consultation on drugs.

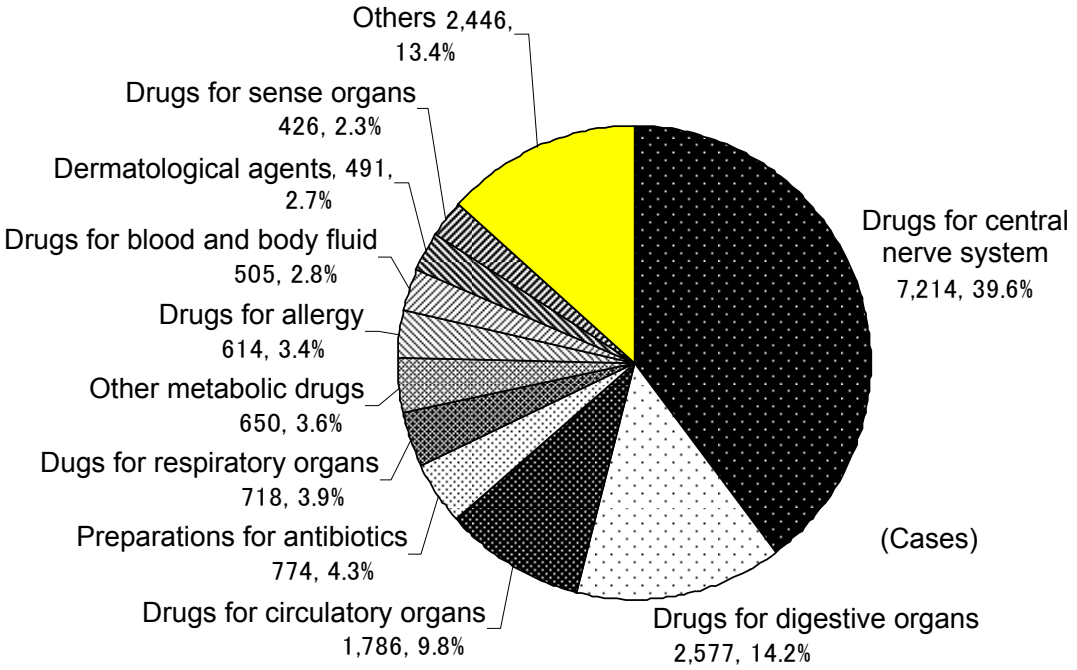
Contents of Consultations on Drugs

Contents of Consultation	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
(1) Safety	4,211 (47.9%)	5,968 (56.8%)	5,697 (48.7%)	5,731 (45.9%)	6,347 (50.6%)
(2) Indications	1,194 (13.6%)	1,132 (10.8%)	1,175 (10.0%)	1,175 (9.4%)	954 (7.6%)
(3) Administration and Dosage	669 (7.6%)	771 (7.3%)	828 (7.1%)	1,072 (8.6%)	836 (6.7%)
(4) Interaction	611 (7.0%)	628 (6.0%)	691 (5.9%)	715 (5.7%)	732 (5.8%)
(5) Active ingredients	205 (2.3%)	161 (1.5%)	219 (1.9%)	236 (1.9%)	214 (1.7%)
Other	1,900 (21.6%)	1,845 (17.6%)	3,086 (26.4%)	3,548 (28.4%)	3,450 (27.5%)
Total	8,790 (100.0%)	10,505 (100.0%)	11,696 (100.0%)	12,477 (100.0%)	12,533 (100.0%)

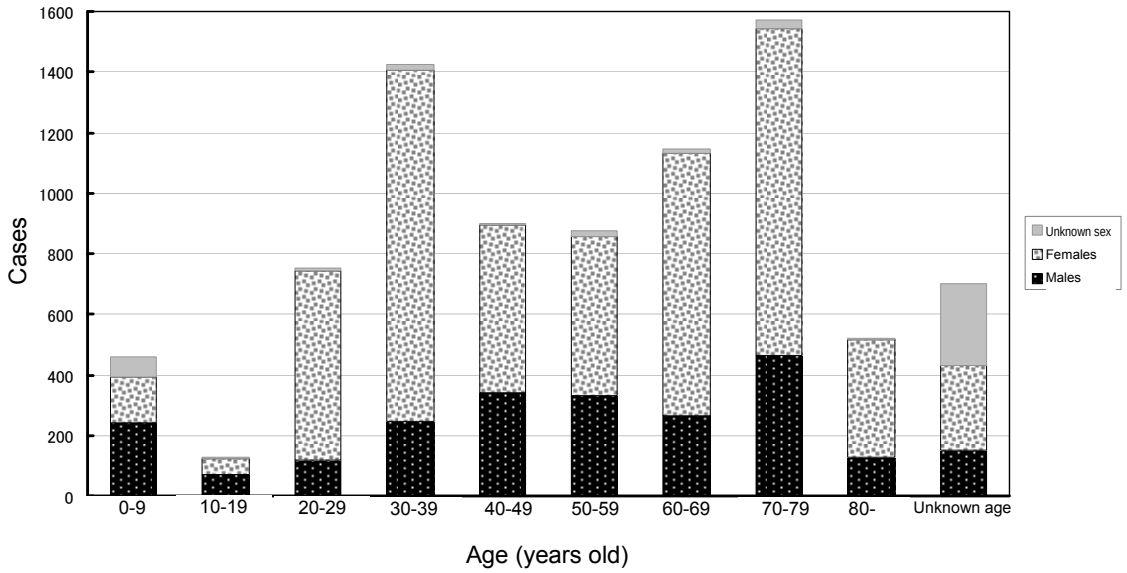
Number of Consultations on Drugs

	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Number of phone calls	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)	8,479 (34.9 cases/day)
Number of consultations	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)	12,533 (51.6 cases/day)

Number of Consultations by Major Classification of Therapeutic Category (Total of Top 10 Categories) in FY 2008



Number of Patients (Receiving a Drug) by Age and by Sex in FY 2008



Number of Consultations on Medical Devices with Consumers

	FY 2005*	FY 2006	FY 2007	FY 2008
Number of phone calls	166 (1.0 cases/day)	376 (1.5 cases/day)	564 (2.3 cases/day)	639 (2.6 cases/day)
Number of consultations	323 (1.9 cases/day)	581 (2.4 cases/day)	824 (3.4 cases/day)	902 (3.7 cases/day)

* *The consultation service has been provided since July 2005.*

Contents of Consultations on Medical Devices with Consumers

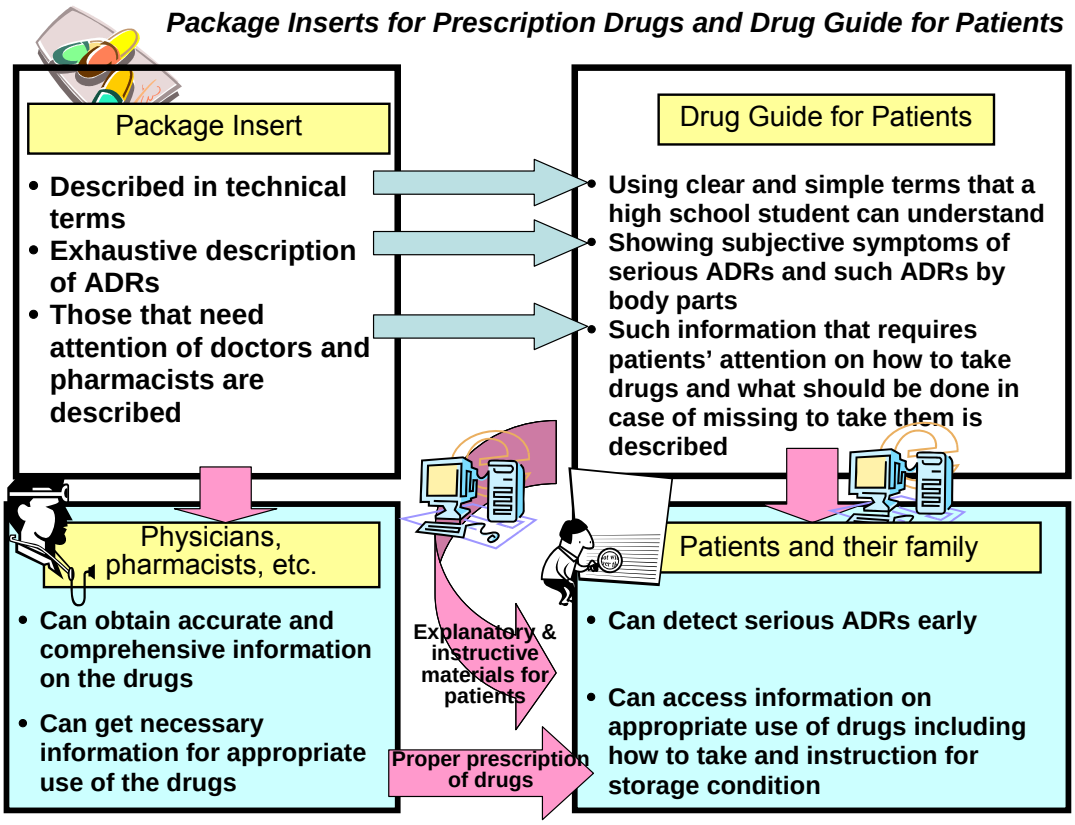
Contents of consultation	FY 2005	FY 2006	FY 2007	FY 2008
(1) Safety	32 (9.9%)	62 (10.7%)	91 (11.0%)	96 (10.6%)
(2) Indications	64 (19.8%)	101 (17.4%)	85 (10.3%)	90 (10.0%)
(3) Performance	25 (7.7%)	45 (7.7%)	37 (4.5%)	46 (5.1%)
(4) Directions for use	12 (3.7%)	16 (2.8%)	12 (1.5%)	17 (1.9%)
Others	190 (58.8%)	357 (61.4%)	599 (72.7%)	653 (72.4%)
Total	323 (100.0%)	581 (100.0%)	824 (100.0%)	902 (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 PMDA website since January 2006. In FY 2008, the Guide contained an additional 24 active ingredients in 391 items (which were newly designated or newly marketed), and 294 active ingredients in 1,958 items were posted by the end of March 2009.

- In accordance with the Guidelines for Developing the Drug Guide for Patients (Notification of the Director-General of the Pharmaceutical and Food Safety Bureau, MHLW dated June 30, 2005), PMDA has reviewed and revised the Drug Guide for Patients while continuously obtaining advice from experts (a study supported by the Health Labour Sciences Research Grant titled “Research on how to provide patients and people with drug safety information”).

Package Inserts for Prescription Drugs and Drug Guide for Patients



3) Upgrading Medical Product Information site of PMDA website

- In FY 2008, referring to opinions given by the website users, PMDA added icons on the upper part of the top page for linking to content such as Information Related to Drugs, Information Related to Medical Devices, and Information for the General Public, and also added icons for links to new information, thereby continuing to improve its website to provide the purpose-oriented user interface.

4) Implementation of post-marketing safety measures workshops

- Workshops on the effective use of information on safety measures recommended by PMDA were co-hosted with the Japan Pharmacists Education Center on the theme of "Information on Pharmaceuticals for Appropriate Use – Toward Early Detection of Adverse Drug Reactions." They were held in 4 regions in Japan (August 2008, Kyoto; November 2008, Sapporo; January 2009, Fukuoka; and March 2009, Tokyo). PMDA also gave presentations on the recent revision of precautions in package inserts, the effective use of the Medical Product Information site of the PMDA website, and PMDA's consultation services at workshops held by others and at academic conferences.

Number of Posted Items on the Medical Product Information Site of PMDA Website as of March 2009

Types of provided information	Number of posted information						
	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008
Package insert information *1							
Prescription drugs	11,380 sheets	11,516 sheets	11,706 sheets	11,819 sheets	12,341 sheets	13,090 sheets	13,287 sheets
Medical devices	—	—	—	1,524 sheets	3,995 sheets	5,462 sheets	8,164 sheets
OTC drugs	—	—	—	—	3,306 sheets	7,437 sheets	8,356 sheets
In vitro diagnostics							2,237 sheets
Drug Guide for Patients *1	—	—	—	23 active ingredients (150 items)	237 active ingredients (1,240 items)	270 active ingredients (1,567 items)	294 active ingredients (1,958 items)
Safety information issued by MHLW - Instruction of revisions of package inserts - Pharmaceuticals and Medical Devices Safety Information - Press release	153 cases	192 cases	231 cases	267 cases	294 cases	323 cases	350 cases
Urgent safety information (by pharmaceutical companies)	20 cases	23 cases	23 cases	23 cases	24 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	51 cases
Notification of safety measures for medical devices							
Notification of self-check	—	—	42 cases	45 cases	45 cases	45 cases	47 cases
Notification of revisions of labeling	—	—	10 cases	20 cases	21 cases	28 cases	30 cases
Notification of self-check	—	—	2 cases	33 cases	35 cases	54 cases	57 cases
Information about case reports on suspected ADR	—	—	—	3,884 cases	48,584 cases	84,094 cases	110,879 cases
Information about case reports on suspected malfunction	—	—	—	1,750 cases	17,345 cases	34,226 cases	42,405 cases
Notification related to preventive measures for medical accidents	1 cases	11 cases	14 cases	18 cases	21 cases	26 cases	44 cases
PMDA Medical Safety Information	—	—	—	—	—	3 cases	9 cases
Manuals for management of individual serious adverse drug reactions	—	—	—	—	9 cases	25 cases	38 cases
Information about approved new drugs - Review reports, summary of application dossiers	127 active ingredients (311 items)	114 active ingredients (268 items)	137 active ingredients (308 items)	203 active ingredients (435 items)	261 active ingredients (559 items)	308 active ingredients (642 items)	373 active ingredients (763 items)
A list of prescription drugs on which Quality Information Package (Orange Book) was published	190 active ingredients/ formulation (1,971 items)	358 active ingredients/ formulation (3,083 items)	427 active ingredients/ formulation (3,513 items)	481 active ingredients/ formulation (3,737 items)	481 active ingredients/ formulation (3,737 items)	811 active ingredients/ formulation (3,900 items)	811 active ingredients/ formulation (3,900 items)
Information about withdrawals of drugs or medical devices *2	2,150 cases	1,329 cases	1,295 cases	1,453 cases	2,128 cases	2,777 cases	3,448 cases
Pharmaceuticals and medical devices information e-mail service							
E-mails issued *3	—	—	—	92 cases	93 cases	87 cases	107 cases
Subscribers	—	—	—	2,892 cases	6,762 cases	11,965 cases	20,707 cases
Number of visitors to the website *4	87 million	107 million	233 million	289 million	391 million	497 million	642 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. FY 2008 List of Approved Products: New Drugs

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Apr. 16, 2008	1	Exjade Dispersible Tablets 125 mg Exjade Dispersible Tablets 500 mg (Novartis Pharma K.K.)	Approval Approval	Deferasirox	Drugs with a new active ingredient indicated for the treatment of chronic iron overload due to blood transfusions (In patients for whom injection of iron chelating agents is inappropriate). [Priority review]
1	Jun. 6, 2008	2	Simulect I.V. Injection 10 mg for Pediatric (Novartis Pharma K.K.)	Approval	Basiliximab (genetical recombination)	A drug with a new dosage and in a new dosage form indicated for supression of acute organ rejection after renal transplantation. [Orphan drug]
1	Jul. 16, 2008	3	Irribow Tablets 2.5 μg Irribow Tablets 5 μg (Astellas Pharma Inc.)	Approval Approval	Ramosetron hydrochloride	Drugs with a new indication and new dosages for the treatment of diarrhea-predominant irritable bowel syndrome in men.
1	Jul. 16, 2008	4	Graceptor Capsules 0.5 mg Graceptor Capsules 1 mg Graceptor Capsules 5 mg (Astellas Pharma Inc.)	Approval Approval Approval	Tacrolimus hydrate	Drugs in a new dosage form indicated for suppression of organ rejection in renal, liver, heart, lung, and pancreatic transplantation, as well as for suppression of graft rejection and graft versus host disease (GVHD) in bone marrow transplantation.
1	Jul. 16, 2008	5	Differin Gel 0.1% (Galderma S.A.)	Approval	Adapalene	A drug containing a new active ingredient indicated for the treatment of acne vulgaris.
1	Oct. 16, 2008	6	Sumiferon 300 Sumiferon 600 Sumiferon DS 300 Sumiferon DS 600 (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change Change	Interferon alfa (NAMALWA)	Drugs with a new indication and a new dosage for the treatment of viremia in patients with compensated cirrhosis type C (excluding patients with high blood levels of serogroup 1 HCV-RNA).
1	Oct. 16, 2008	7	Fosrenol Chewable Tablets 250 mg Fosrenol Chewable Tablets 500 mg (Bayer Yakuhin Ltd.)	Approval Approval	lanthanum carbonate hydrate	Drugs containing a new active ingredient indicated for the treatment of hyperphosphatemia in dialysis patients with chronic renal failure.
1	Oct. 16, 2008	8	Kenketu Glovenin-I-Nichiyaku (Nihon Pharmaceutical Co., Ltd.)	Change	Freeze-dried polyethylene glycol treated human normal immunoglobulin	A drug with a new indication and a new dosage for the treatment of pemphigus (for use when steroid drugs are not sufficiently effective).
1	Nov. 25, 2008	9	Oxarol Ointment 25 μg/g Oxarol Lotion 25 μg/g (Chugai Pharmaceutical Co., Ltd.)	Change Change	Maxacalcitol	Drugs with a new indication for the treatment of palmoplantar pustulosis.
1	Dec. 22, 2008	10	Pentasa Tablets 250 Pentasa Tablets 500 (Nisshin Kyorin Pharmaceutical Co., Ltd. (currently Kyorin Pharmaceutical Co., Ltd.))	Change Change	Mesalazine	Drugs with a new dosage indicated for the treatment of ulcerative colitis (excluding severe cases).
2	Apr. 16, 2008	11	Irbetan Tablets 50 mg Irbetan Tablets 100 mg (Shionogi & Co., Ltd.) Avapro Tablets 50 mg Avapro Tablets 100 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval Approval Approval Approval	Irbesartan	Drugs containing a new active ingredient indicated for the treatment of hypertension.
2	May 20, 2008	12	Arixtra Injection 1.5 mg Arixtra Injection 2.5 mg (GlaxoSmithKline K.K.)	Change Change	Fondaparinux sodium	Drugs with a new indication for prophylaxis of venous thromboembolism in patients undergoing abdominal surgery who are at a high risk of developing venous thromboembolism. [Priority review]
2	Jul. 16, 2008	13	INOflo for Inhalation 800 ppm (INO therapeutics LLC)	Approval	Nitric oxide	A drug containing a new active ingredient indicated for the treatment of hypoxic respiratory failure (HRF) with concurrent pulmonary hypertension in neonates. [Orphan drug]
2	Jul. 16, 2008	14	Novastan HI Inj. 10 mg/2mL (Mitsubishi Tanabe Pharma Corporation) Slonnon HI Injection 10 mg/2mL (Daiichi Sankyo Co., Ltd.)	Change Change	Argatroban hydrate	Drugs with a new indication and a new dosage for prophylaxis of thrombosis in patients with heparin-induced thrombocytopenia (HIT) type II. [Orphan drug]
2	Oct. 16, 2008	15	Bepricor Tablets 50 mg Bepricor Tablets 100 mg (Schering-plough K.K.)	Change Change	Bepridil hydrochloride hydrate	Drugs with a new indication for the treatment of persistent atrial fibrillation in patients in whom other antiarrhythmic drugs are contraindicated or who have not responded to other antiarrhythmic drugs. [Priority review]
2	Jan. 21, 2009	16	Trerief Tablets 25 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Approval	Zonisamide	A drug with a new indication and a new dosage for the treatment of Parkinson's disease (in patients who have been treated with other anti-Parkinson drugs in combination with a levodopa-containing agent, but sufficient therapeutic effect was not obtained).
2	Jan. 21, 2009	17	Co-Dio Combination Tablets MD Co-Dio Combination Tablets EX (Novartis Pharma K.K.)	Approval Approval	Valsartan/ hydrochlorothiazide	New combination drugs indicated for the treatment of hypertension.
2	Jan. 21, 2009	18	Ecard Combination Tablets LD Ecard Combination Tablets HD (Takeda Pharmaceutical Company Limited)	Approval Approval	Candesartan cilexetil/hydrochlorothiazide	New combination drugs indicated for the treatment of hypertension.
2	Feb. 23, 2009	19	Clexane Subcutaneous Injection Kit 2000 IU (Sanofi-Aventis K.K.)	Change	Enoxaparin sodium	A drug with a new additional indication for prophylaxis of venous thromboembolism in patients undergoing abdominal surgery who are at a high risk of developing venous thromboembolism.

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	Feb. 23, 2009	20	Norvasc Tablets 2.5 mg Norvasc Tablets 5 mg Norvasc OD Tablets 2.5 mg Norvasc OD Tablets 5 mg (Pfizer Japan Inc.) Amlodin Tablets 2.5 mg Amlodin Tablets 5 mg Amlodin OD Tablets 2.5 mg Amlodin OD Tablets 5 mg (Dainippon Sumitomo Pharma Co., Ltd.)	Change Change Change Change Change Change Change Change	Amlodipine besilate	Drugs with a new dosage indicated for the treatment of hypertension and angina pectoris.
3	Apr. 16, 2008	21	Popscaine 0.75% Inj. 75 mg/10 mL Popscaine 0.75% Inj. 150 mg/20 mL Popscaine 0.25% Inj. 25 mg/10 mL Popscaine 0.25% Inj. Bag 250 mg/100 mL Popscaine 0.75% Inj. Syringe 75 mg/10 mL Popscaine 0.25% Inj. Syringe 25 mg/10 mL (Maruishi Pharmaceutical Co., Ltd.	Approval Approval Approval Approval Approval Approval	Levobupivacaine hydrochloride	Drugs containing a new active ingredient. The 0.25% formulation is indicated for postoperative analgesia, and the 0.75% formulation is indicated for epidural anaesthesia.
3	Jul. 16, 2008	22	AtvagoReverse Intravenous Injection Syringe 3 mL AtvagoReverse Intravenous Injection Syringe 6 mL (Terumo Corporation)	Approval Approval	Neostigmine methylsulfate/ atropine sulfate hydrate	New combination drugs indicated for reversal of nondepolarizing muscle relaxants.
3	Jul. 16, 2008	23	Macugen Ivt Inj. Kit 0.3 mg (Pfizer Japan Inc.)	Approval	Pegaptanib sodium	A drug containing a new active ingredient indicated for treatment of age-related macular degeneration with concurrent choroidal neovascularization. [Orphan drug]
3	Oct. 16, 2008	24	Lamictal Tablets 2 mg for Children Lamictal Tablets 5 mg for Children Lamictal Tablets 25 mg Lamictal Tablets 100 mg (GlaxoSmithKline K.K.)	Approval Approval Approval Approval	Lamotrigine	Drugs containing a new active ingredient indicated for use as adjunctive treatment with other antiepileptic drugs for partial seizures (including secondary generalized seizures), tonic-clonic seizures, and generalized seizures associated with Lennox-Gastaut syndrome in patients with epilepsy for whom other antiepileptic drugs are not sufficiently effective.
3	Oct. 16, 2008	25	Tapros Ophthalmic Solution 0.0015% (Santen Pharmaceutical Co., Ltd.)	Approval	Tafluprost	A drug containing a new active ingredient indicated for the treatment of glaucoma and ocular hypertension.
3	Oct. 16, 2008	26	Noberbar 250 mg for Injection (Nobelpharma Co., Ltd.)	Approval	Phenobarbital sodium	A drug with a new route of administration indicated for the treatment of 1) neonatal seizures and 2) status epilepticus. [Orphan drug: 1]
3	Jan. 21, 2009	27	Remitch Capsules 2.5 μg (Toray Industries, Inc.)	Approval	Nalfurafine hydrochloride	A drug containing a new active ingredient indicated for the treatment of pruritus in hemodialysis patients (for use only when conventional therapies are not sufficiently effective).
3	Jan. 21, 2009	28	Lucentis Solution for Intravitreal Injection 2.3 mg/0.23 mL (Novartis Pharma K.K.)	Approval	Ranibizumab (genetical recombination)	A drug containing a new active ingredient indicated for treatment of age-related macular degeneration with concurrent choroidal neovascularization. [Orphan drug]
3	Jan. 21, 2009	29	Botox Vista Injection 50 Units (GlaxoSmithKline K.K.)	Approval	Botulinum toxin type A	A drug with a new indication and a new dosage for the temporary improvement in the appearance of glabellar lines between the brows in adults aged under 65 years.
3	Feb. 23, 2009	30	Botox Injection 50 Botox Injection 100 (GlaxoSmithKline K.K.)	Change	Botulinum toxin type A	Drugs with a new additional indication and a new dosage for the treatment of equinus deformity associated with lower limb spasticities in juvenile cerebral palsy in patients 2 years or older.
4	Apr. 16, 2008	31	Famvir Tab. 250 mg Famciclovir (Asahi Kasei Pharma Corporation)	Approval Approval	Famciclovir	A drug containing a new active ingredient indicated for the treatment of herpes zoster.
4	Jul. 16, 2008	32	Zosyn 2.25 g for Intravenous Injection Zosyn 4.5 g for Intravenous Injection (Taiho Pharmaceutical Co., Ltd.)	Approval Approval	Tazobactam/ piperacillin hydrate	New combination drugs indicated for the treatment of septicemia, pneumonia, pyelonephritis, and complicated cystitis.
4	Jul. 16, 2008	33	Mycobutin Capsules 150 mg (Pfizer Japan Inc.)	Approval	Rifabutin	A drug containing a new active ingredient indicated for the treatment of 1) tuberculosis, 2) non-tuberculous mycobacteriosis including mycobacterium avium complex (MAC) infections, and 3) prophylaxis of disseminated MAC infections in patients with HIV disease.
4	Aug. 29, 2008	34	Clarith Tab. 200 (Taisho Pharmaceutical Co., Ltd.) Klaricid Tablets 200 mg (Abbott Japan Co., Ltd.)	Change Change	Clarithromycin	Drugs with a new indication and a new dosage for non-tuberculous mycobacteriosis including mycobacterium avium complex (MAC) infections.
4	Sep. 24, 2008	35	Hepsera Tablets 10 (GlaxoSmithKline K.K.)	Change	Adefovir dipivoxil	A drug with a new indication for inhibition of hepatitis B virus replication in patients with type B chronic liver disease in whom abnormal hepatic function was observed in association with proliferation of hepatitis B virus.
4	Jan. 21, 2009	36	Zithromac SR Dry Syrup 2 g for Adults (Pfizer Japan Inc.)	Approval	Azithromycin hydrate	A drug with a new additional indication for Neisseria gonorrhoeae infections, with a new dosage in a new dosage form. Conversion from an immediate release formulation of azithromycin to a sustained release formulation.

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
5	Apr. 16, 2008	37	Julina Tablets 0.5 mg (Bayer Yakuhin, Ltd.)	Approval	Estradiol	A drug with a new route of administration indicated for the treatment of vasomotor symptoms (hot flushes and sweating) and vaginal atrophy symptoms associated with climacteric disturbance and ovarian deficiency symptoms.
5	Apr. 16, 2008	38	Lunabell Tablets (Nobelpharma Co., Ltd.)	Approval	Norethisterone/ ethinylestradiol	A new combination drug indicated for the treatment of dysmenorrhea associated with endometriosis.
5	Jul. 16, 2008	39	Ganirest Subcutaneous 0.25 mg Syringe (Nippon Organon K.K.)	Approval	Ganirelix acetate	A drug containing a new active ingredient indicated for prevention of premature ovulation during controlled ovarian stimulation.
5	Sep. 1, 2008	40	Gonatropin 5000 (ASKA Pharmaceutical. Co., Ltd.)	Change	[JP] Human chorionic gonadotrophin (extract from human urine)	A drug with a new route of administration and a new indication for induction of spermatogenesis in male hypogonadotropic hypogonadism. [Expedited review]
5	Oct. 16, 2008	41	Menoaid Combipatch (ASKA Pharmaceutical. Co., Ltd.)	Approval	Estradiol/norethisterone acetate	A new combination drug indicated for the treatment of vasomotor symptoms (hot flushes and sweating associated with climacteric disturbance and ovarian deficiency symptoms.
5	Mar. 31, 2009	42	Elneopa No. 1 Injection Elneopa No. 2 Injection (Otsuka Pharmaceutical Factory, Inc.)	Approval Approval	N/A for this combination drug	A combination drug similar to other products indicated for the supplementation of water, electrolytes, calories (a calorie source), amino acids, vitamins, Zn, Fe, Mn, and I in patients in whom peroral or enteral nutrition is impossible or insufficient, and who have to rely on parenteral nutrition.
6-1	Apr. 16, 2008	43	Actemra 80 mg for Intravenous Infusion Actemra 200 mg for Intravenous Infusion Actemra 400 mg for Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Approval Change Approval	Tocilizumab (genetical recombination)	Drugs with a new indication and a new dosage in a new dosage form for the treatment of rheumatoid arthritis (including prevention of structural damage of joint) that cannot be treated sufficiently with conventional therapies, active juvenile idiopathic arthritis in multiple joints, and systemic juvenile idiopathic arthritis. [Priority review] [Expedited review]
6-1	Apr. 16, 2008	44	Humira 40mg for S.C. Injection (Abbott Japan Co., Ltd.)	Approval	Adalimumab (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of rheumatoid arthritis (for use only when conventional therapies are not sufficiently effective).
6-1	Jul. 16, 2008	45	Nasonex Nasal Suspension 50 μg 56 spray Nasonex Nasal Suspension 50 μg 112 spray (Schering-Plough K.K.)	Approval Approval	Mometasone furoate hydrate	Drugs containing a new active ingredient indicated for the treatment of allergic rhinitis.
6-1	Sep. 24, 2008	46	Rheumatrex Capsules 2 mg (Wyeth K.K.) Trexamette Capsules 2 mg (Shiono Chemical Co., Ltd.) Methotrexate Cap. 2 mg “Sawai” (Sawai Pharmaceutical Co., Ltd.) Methotrexate Capsules 2 mg “Towa” (Towa Pharmaceutical Co., Ltd.) Methotrexate Cap. 2 mg “Mylan” (Mylan Seiyaku Ltd.) Metolate Tablets 2 mg (Santen Pharmaceutical Co., Ltd.) Methotrexate Tablets 2 mg "Tanabe" (Mitsubishi Tanabe Pharma Corporation)	Change Change Change Change Change Change Change	Methotrexate	Drugs with a new indication and a new dosage for the treatment of juvenile idiopathic arthritis accompanied by articular symptoms. [Expedited review]
6-1	Oct. 16, 2008	47	Neoral solution Neoral 10 mg Capsules Neoral 25 mg Capsules Neoral 50 mg Capsules (Novartis Pharma K.K.)	Change Change Change Change	Cyclosporine	Drugs with a new indication and a new dosage for the treatment of atopic dermatitis (in patients in whom conventional therapies are not sufficiently effective).
6-1	Oct. 16, 2008	48	Pirespa Tablets 200 mg (Shionogi & Co., Ltd.)	Approval	Pirfenidone	A drug containing a new active ingredient indicated for the treatment of idiopathic pulmonary fibrosis. [Orphan drug]
6-1	Jan. 21, 2009	49	Xolair for S.C. Injection (Novartis Pharma K.K.)	Approval	Omalizumab (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of bronchial asthma (for use only in patients with intractable bronchial asthma whose asthmatic responses are uncontrollable with conventional therapies).
6-1	Jan. 21, 2009	50	Adoair 250 Diskus (GlaxoSmithKline K.K.)	Change	Salmeterol xinafoate/fluticasone propionate	A drug with a new additional indication and a new dosage for the alleviation of various symptoms associated with chronic obstructive pulmonary disease (chronic bronchitis and emphysema) (for use when concomitant use of inhaled corticosteroid and long-acting β2-agonist is required).
6-1	Jan. 21, 2009	51	Adoair 100 Diskus Adoair 50 Air 120 puffs (GlaxoSmithKline K.K.)	Change Approval	Salmeterol xinafoate/fluticasone propionate	A drug with a new additional pediatric dosage in a new dosage form indicated for the treatment of bronchial asthma (for use when concomitant use of inhaled corticosteroid and long-acting β2-agonist is required). [Expedited review]

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Apr. 16, 2008	52	Aroglycem Capsules 25 mg (Schering-plough K.K.)	Approval	Diazoxide	A drug containing a new active ingredient indicated for the treatment of hyperinsulinemic hypoglycemia. [Priority review]
6-2	Jul. 16, 2008	53	Biopten Granules 2.5% (Asubio Pharma Co., Ltd.)	Change	Sapropterin hydrochloride	A drug with a new indication and a new dosage for reduction of serum phenylalanine levels in patients with hyperphenylalaninemia (tetrahydrobiopterin-responsive hyperphenylalaninemia) caused by tetrahydrobiopterin-responsive phenylalanine hydroxylase deficiency. [Orphan drug]
6-2	Jul. 16, 2008	54	Actonel Tab. 17.5 mg (Ajinomoto Co., Inc.) Benet Tablets 17.5 mg. (Takeda Pharmacdeutical Co., Ltd.)	Change Change	Risedronate sodium hydrate	Drugs with a new indication and a new dosage for the treatment of Paget's disease of bone. [Orphan drug]
6-2	Oct. 16, 2008	55	1) Wellnara Combination Tablets (Bayer Yakuhin, Ltd.) 2) Julina 0.5 mg (Bayer Yakuhin, Ltd.)	Approval Change	1) Estradiol/levonorgestrel 2) Estradiol	1) A new combination drug and 2) a drug with a new indication and a new dosage for the treatment of postmenopausal osteoporosis.
6-2	Oct. 16, 2008	56	Genotropin 5.3 mg Genotropin MiniQuick S.C. Inj. 0.4 mg Genotropin MiniQuick S.C. Inj. 0.6 mg Genotropin MiniQuick S.C. Inj. 0.8 mg Genotropin MiniQuick S.C. Inj. 1.0 mg Genotropin MiniQuick S.C. Inj. 1.4 mg Genotropin Inj. 12 mg (Pfizer Japan Inc.)	Change Change Change Change Change Change Change	Somatropin (genetical recombination)	Drugs with a new indication and a new dosage for the treatment of dwarfism with no epiphyseal closure in patients born small-for-gestational age (SGA).
6-2	Dec. 22, 2008	57	Seibule Tablets 25 mg Seibule Tablets 50 mg Seibule Tablets 75 mg (Sanwa Kagaku Kenkyusho Co., Ltd.)	Change Change Change	Miglitol	Drugs with a new indication for the treatment of postprandial hyperglycemia in Type 2 diabetes mellitus (for use only in patients who have not benefitted sufficiently from taking insulin preparations in conjunction with dietary and exercise regimens) and the treatment of postprandial hyperglycemia in Type 1 diabetes mellitus (for use only in patients who have not benefited sufficiently from dietary and exercise regimens or from taking sulfonylurea or insulin preparations in conjunction with dietary and exercise regimens).
6-2	Dec. 22, 2008	58	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 additional indication for the treatment of postprandial glucose excursions in Type 2 diabetes mellitus (for use only when treatment with thiazolidines in conjunction with dietary and exercise regimens is not sufficiently effective).
6-2	Dec. 22, 2008	59	Actos Tablets 15 Actos Tablets 30 (Takeda Pharmaceutical Company Limited)	Change Change	Pioglitazone hydrochloride	Drugs with a new additional indication for the treatment of Type 2 diabetes mellitus (for use only in patients in whom treatment with biguanides in conjunction with dietary and exercise regimens is not sufficiently effective, and insulin resistance is suspected).
6-2	Jan. 21, 2009	60	Recalbon Tablets 1 mg (Ono Pharmaceutical Co., Ltd.) Bonoteo Tablets 1 mg (Astellas Pharma Inc.)	Approval Approval	Minodronic acid hydrate.	Drugs containing a new active ingredient indicated for the treatment of osteoporosis.
6-2	Feb. 23, 2009	61	Glufast Tab. 5 mg Glufast Tab. 10 mg (Kissei Pharmaceutical Co., Ltd.)	Change Change	Mitiglinide calcium hydrate	Drugs with a new additional indication for the treatment of postprandial glucose excursions in Type 2 diabetes mellitus in patients who have not benefited sufficiently from taking thiazolidines in conjunction with dietary and exercise regimens.
6-2	Mar. 24, 2009	62	Actos Tablets 15 Actos Tablets 30 (Takeda Pharmaceutical Company Limited)	Change Change	Pioglitazone hydrochloride	Drugs with a new indication and a new dosage for the treatment of Type 2 diabetes mellitus in patients who have not benefitted sufficiently from taking insulin preparations in conjunction with dietary and exercise regimens in whom insulin resistance is suspected.
Oncology drugs	Apr. 16, 2008	63	Sutent Capsule 12.5 mg (Pfizer Japan Inc.)	Approval	Sunitinib malate	A drug containing a new active ingredient indicated for the treatment of imatinib-resistant gastrointestinal stromal tumors, and unresectable or metastatic renal cell carcinomas. [Priority review]
Oncology drugs	May 20, 2008	64	Fludara for IV Inj.50 mg (Bayer Yakuhin, Ltd.)	Change	Fludarabine phosphate	A drug with a new indication and a new dosage for use as a conditioning prior to allogeneic hematopoietic stem cell transplantation in the following diseases: acute myeloid leukemia, myelodysplastic syndrome, chronic myeloid leukemia, chronic lymphocytic leukemia, malignant lymphoma, and multiple myeloma.
Oncology drugs	Jul. 16, 2008	65	Erbitux Injection 100 mg (Merck KGaA)	Approval	Cetuximab (genetical recombination)	A drug containing a new active ingredient indicated for the treatment of EGFR-expressing, unresectable and advanced/recurrent colorectal carcinomas. [Priority review]
Oncology drugs	Aug. 29, 2008	66	Taxotere Injection (Sanofi-Aventis K.K.)	Change	Docetaxel hydrate	A drug with a new indication and a new dosage for the treatment of prostate cancer. [Priority review]

Category	Approval Date		Brand Name (Applicant Company)	Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Oct. 16, 2008	67	Thaled Capsule 100 (Fujimoto Pharmaceutical Corporation)	Approval	Thalidomide	A drug containing a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Nov. 25, 2008	68	Gemzar Injection 200 mg Gemzar Injection 1 g (Eli Lilly Japan K.K.)	Change	Gemcitabine hydrochloride	Drugs with a new additional indication for the treatment of urothelial carcinoma.
Oncology drugs	Jan. 21, 2009	69	Tasigna Capsules 200 mg (Novartis Pharma K.K.)	Approval	Nilotinib hydrochloride hydrate	A drug containing a new active ingredient indicated for the treatment of imatinib-resistant, chronic phase and accelerated phase chronic myelogenous leukemia. [Orphan drug]
Oncology drugs	Jan. 21, 2009	70	Sprycel Tablets 20 mg Sprycel Tablets 50 mg (Bristol-Myers K.K.)	Approval Approval	Dasatinib hydrate	Drugs containing a new active ingredient indicated for the treatment of 1) imatinib-resistant chronic myelogenous leukemia and 2) recurrent or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia. [Orphan drug]
Oncology drugs	Mar. 24, 2009	71	Leustatin Injection 8 mg (Janssen Pharmaceutical K.K.)	Change	Cladribine	A drug with a new additional dosage indicated for the treatment of recurrent, relapsing, or refractory indolent B-cell non-Hodgkin's lymphoma including follicular lymphoma, and mantle cell lymphoma.
AIDS drugs	Jun. 24, 2008	72	Isentress Tablets 400 mg (Banyu Pharmaceutical Co., Ltd.)	Approval	Raltegravir potassium	A drug containing a new active ingredient indicated for the treatment of HIV infection. [Orphan drug]
AIDS drugs	Dec. 25, 2008	73	Intelence Tablets 100 mg (Janssen Pharmaceutical K.K.)	Approval	Etravirine	A drug containing a new active ingredient indicated for the treatment of HIV-1 infection. [Orphan drug]
AIDS drugs	Dec. 25, 2008	74	Celsentri Tablets 150 mg (Pfizer Japan Inc.)	Approval	Maraviroc	A drug containing a new active ingredient indicated for the treatment of CCR5-tropic HIV-1 infection. [Orphan drug]
In vivo Diagnostics	Oct. 16, 2008	75	Thyrogen IM Injection 0.9 mg (Sato Pharmaceutical Co., Ltd.)	Approval	Thyrotropin human alfa (genetical recombination)	A drug containing a new active ingredient indicated for use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine scintigraphy in patients with differentiated thyroid cancer who have undergone near total or total thyroidectomy. [Orphan drug]
In vivo Diagnostics	May 20, 2008	76	Iomeron 350 Iomeron 350 Syringe (Bracco-Eisai Co., Ltd.)	Change Change	Iomeprol	A drug with a new dosage (Iomeron 350) and a drug with a new dosage in a new dosage form (Iomeron 350 Syringe) indicated for use in angiocardiography, thoracic angiography, abdominal angiography, angiography of the extremities, intravenous digital angiography, arterial digital angiography, computed tomography, and intravenous urography.
In vivo Diagnostics	Feb. 23, 2009	77	Patch test tapes "Nickel sulfate" 160 µg "Potassium dichromate" 19 µg "Cobalt chloride" 16 µg "Mercaptobenzothiazole" 61 µg "Formaldehyde" 150 µg "Thimerosal" 6.5 µg (Sato Pharmaceutical Co., Ltd.)	 Approval Approval Approval Approval Approval Approval	 Nickel sulfate Potassium dichromate Cobalt chloride Mercaptobenzothiazole N-hydroxymethyl succinimide Thimerosal	Drugs indicated for use in patch tests to identify allergens in patients with allergic dermatitis.
Biologicals	Feb. 23, 2009	78	Jebik V (Research Foundation for Microbial Diseases of Osaka University)	Approval	Inactivated Japanese encephalitis virus (Beijing strain)	A drug containing a new active ingredient indicated for prophylaxis against Japanese encephalitis.
Blood products	Jul. 16, 2008	79	Thymoglobuline for Intravenous Infusion 25 mg (Sanofi-Aventis K.K.)	Approval	Anti-human thymocyte immunoglobulin, Rabbit	A drug containing a new active ingredient indicated for the treatment of moderate to very severe aplastic anemia, for use as pretreatment prior to hematopoietic stem cell transplantation, and for the treatment of acute graft-versus-host disease after hematopoietic stem cell transplantation. [Orphan drug]

Table 2. FY2008 List of Approved Products: New Medical Devices

Category	Approval Date Review time	Date Approved in US Clinical study results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Apr. 9, 2008 Total review time: 1107 days Regulatory review time: 320 days	Aug. 11, 2006 Domestic clinical study results	1	Excimer Laser System MEL80 (Carl Zeiss Meditec 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	Jun. 25, 2008 Total review time: 56 days Regulatory review time: 46 days	May 23, 2003 No clinical study results	2	Star S4 IR Excimer Laser (AMO Manufacturing USA, LLC)	Change	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia or astigmatism and remove corneal opacities by laser ablation of corneal tissue. The addition of the manufacturing site. (A partial change during the reexamination period)
1	Dec. 22, 2008 Total review time: 574 days Regulatory review time: 162 days	Apr. 14, 2000 (For myopia) Oct. 11, 2006 (For hyperopia) Domestic and overseas clinical study results	3	Excimer Laser Corneal Surgery System EC-5000 (Nidek Co., Ltd.)	Change	Instrument & apparatus 31 Ophthalmic laser corneal surgical instrument	An excimer laser surgical system used in ophthalmology to correct myopia, hyperopia or astigmatism, remove corneal surface opacities, and smooth corneal irregularities by laser ablation of corneal tissue. A partial change for the objectives including the addition of correction of hyperopia to the indications.
3-1	Sep. 26, 2008 Total review time: 1276 days Regulatory review time: 601 days	Jul. 21, 2005 Overseas clinical study results	4	ONYX Liquid Embolic System LD (ev3, K.K.)	Approval	Instrument & apparatus 51 Other tube and catheter related auxiliary devices (vascular embolization system)	The first liquid embolic material in Japan used to occlude the flow of blood as pretreatment for surgical resection of arteriovenous malformations(bAVM's). [Priority review]
3-1	Jan. 28, 2009 Total review time: 303 days Regulatory review time: 195 days	Oct. 10, 2008 Overseas clinical study results	5	Taxus Libertè Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with paclitaxel coating to be used for dilating and holding a stenotic site of the coronary artery in symptomatic ischemic heart disease. (The original product is in a reexamination period)
3-1	Mar. 24, 2009 Total review time: 685 days Regulatory review time: 367 days	Feb. 1, 2008 Domestic and overseas clinical study results	6	Endeavor Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A drug-eluting coronary stent system with zotarolimus coating to be used for dilating and holding the stenotic site of the coronary artery in symptomatic ischemic heart diseases.
3-2	Jul. 22, 2008 Total review time: 481 days Regulatory review time: 421 days	Dec. 20, 2002 No clinical study results	7	Excluder Bifurcated Stent Graft System (Japan Gore-Tex Inc.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft for abdominal aortic aneurysm to be deployed in the lesion in order to prevent the enlargement and rupture of aneurysm by blocking the blood flow into the aneurysm. A change of the manufacturing site and the addition of the applicable size. (A partial change during the reexamination period)
3-2	Dec. 26, 2008 Total review time: 848 days Regulatory review time: 517 days	May 14, 2003 Amplatzer Duct Occluder Amplatzer Delivery System Apr. 25, 2007 Amplatzer TorqVue Delivery System Overseas clinical study results	8	PDA Occlusion Set (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	The first device in Japan dedicated for the closure of patent ductus arteriosus (PDA) by the deployment of the duct occluder in the PDA site percutaneously using the delivery system.
4	Apr. 4, 2008 Total review time: 175 days Regulatory review time: 137 days	May 12, 2006 No clinical study results	9	Concerto C154DWK (Medtronic Japan Co., Ltd)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT (treatment method to improve cardiac failure symptoms, which synchronizes ventricular contraction by stimulating cardiac muscles of bilateral ventricles electrically for a long time), with the function of a defibrillator. (A partial change during the reexamination period)
4	May 7, 2008 Total review time: 138 days Regulatory review time: 117 days	Mar. 17, 2008 Overseas clinical study results	10	Consulta CRT-D (Medtronic Japan Co., Ltd)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT, with the function of a defibrillator. (The original product is in a reexamination period)
4	Jul. 1, 2008 Total review time: 489 days Regulatory review time: 79 days	Dec. 9, 1997 (12 Fr) Sep. 4, 1998 (14 Fr/16 Fr) Jan. 25, 2002 (16 Fr SLSⅡ) May 2, 2002 (12/14 Fr SLSⅡ) Overseas clinical study results	11	Excimer Laser Cardiac Lead Removal System (DVx Inc.)	Approval	Instrument & apparatus 7 Pacemaker / defibrillator lead extraction kit	The first extraction laser sheath in Japan used at removal of chronically implanted pacing or defibrillator leads to ablate binding tissue around the circumference of leads using the laser energy delivered from the dedicated excimer laser system. [Priority review]

Category	Approval Date Review time	Date Approved in US Clinical study results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Jan. 26, 2009 Total review time: 395 days Regulatory review time: 353 days	− No clinical study results	12	Intravascular OCT ImageWire (Goodman Co., Ltd.)	Change	Instrument & apparatus 51 Intravascular optical tomographic catheter	A catheter utilizing optical coherence tomography (OCT) for monitoring of the vascular lumen and the vascular wall surface in the coronary artery. A change in the shape of the joint with the dedicated OCT diagnostic imaging instrument. (A partial change during the reexamination period)
4	Jan. 26, 2009 Total review time: 395 days Regulatory review time: 351 days	− No clinical study results	13	Intravascular OCT Imaging System (Goodman Co., Ltd.)	Change	Instrument & apparatus 12 OCT diagnostic imaging instrument	An optical coherence tomography (OCT) diagnostic imaging instrument for monitoring of the vascular lumen and the vascular wall surface in the coronary artery. The addition of a unit for connection with the dedicated catheter, and a change in the pullback speed. (A partial change during the reexamination period)
5	Sep. 2, 2008 Total review time: 1257 days Regulatory review time: 267 days	− Domestic clinical study results	14	Adacolumn (JIMRO Co., Ltd.)	Change	Instrument & apparatus 7 Adsorption apheresis device	The Adacolumn is an adsorptive type extracorporeal leukocyte apheresis device. An indication is added for the promotion of remission in patients with moderate to severe active Crohn's disease who are refractory to conventional treatment methods. [Orphan device]
5	Sep. 8, 2008 Total review time: 602 days Regulatory review time: 266 days	Sep. 14, 2007 Domestic clinical study results	15	Olympus Capsule Endoscope System (Olympus Medical Systems Corp.)	Approval	Instrument & apparatus 25 Capsule electronic endoscope system	An endoscopic system comprised of a capsule endoscope (26 x 11 mm) and a monitoring unit. To be used for monitoring and diagnosis of the small bowel. (The original product is in a reexamination period)
6	Dec. 22, 2008 Total review time: 208 days Regulatory review time: 71 days	Aug. 18, 2004 Overseas clinical study results	16	VEPTR System (Synthes K. K.)	Approval	Medical products 4 Internal fixation system	An implantable device made of standard medical grade titanium to be used in patients with thoracic insufficiency syndrome to stabilize their thorax while correcting chest wall malformations in order to help the growth of their thorax and lungs. [Priority review]

Table 3. FY 2008 List of Approved Products: Medical Devices Approved with Clinical Data (Not Classified as New Medical Devices)

Category	Approval Date Review Time	Date Approved in US Clinical study results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
1	Sep. 8, 2008 Total review time: 992 days Regulatory review time: 343 days	Mar. 22, 2004 Domestic clinical study results	1	Bausch & Lomb Microkeratome System (Bausch & Lomb Japan Co., Ltd.)	Approval	Instrument & apparatus 34 Electric keratome	An electric keratome used in ophthalmic surgeries such as laser *in-situ* keratomileusis (LASIK) for lamellar corneal incisions. A clinical study was conducted to evaluate the safety of this product in LASIK.
1	Aug. 5, 2008 Total review time: 594 days Regulatory review time: 228 days	Sep. 14, 2005 (Colorless); Dec. 16, 2005 (Yellow) Overseas clinical study results	2	Alcon AcrySof Toric Single Piece (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Posterior chamber lens	An intraocular lens with its posterior face having a cylindrical optical power for correcting corneal astigmatism. Clinical studies were conducted to evaluate the efficacy and safety of this astigmatic (toric) intraocular lens.
1	Aug. 5, 2008 Total review time: 461 days Regulatory review time: 209 days	- Domestic clinical study results	3	Tecnis Multifocal IOL (AMO JAPAN K. K.)	Approval	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal intraocular lens with its anterior face having an aspheric mechanism and the posterior face having a diffractive multifocal mechanism. Clinical studies were conducted to evaluate the efficacy and safety of this multifocal intraocular lens.
1	Oct. 31, 2008 Total review time: 283 days Regulatory review time: 251 days	Nov. 22, 2006 Domestic clinical study results	4	Proclear 1 Day (CooperVision Japan, Inc.)	Approval	Instrument & apparatus 72 Single use colored contact lenses for correcting visual acuity	A daily disposable soft contact lens for myopia, hyperopia, astigmatism, or presbyopia. A copolymer of HEMA and MPC is used as lens material. A clinical study was conducted to evaluate the efficacy and safety of this product.
1	Nov. 28, 2008 Total review time: 561 days Regulatory review time: 264 days	Oct. 30, 2007 Overseas clinical study results	5	Tecnis 1-Piece IOL (AMO Japan K. K.)	Approval	Instrument & apparatus 72 Posterior chamber lens	An one-piece intraocular lens utilizes the raw materials of the optical zone of the existing intraocular lens in the haptic zone as well. Clinical studies were conducted to evaluate the efficacy and safety of this product including the performance of the haptic zone.
2	Jan. 29, 2009 Total review time: 427 days Regulatory review time: 331 days	- Domestic clinical study results	6	µ-one HA Implant (Yamahachi Dental MFG, Co.)	Approval	Medical products 4 Intraosseous dental implant	An intraosseous dental implant made of titanium with a hydroxyapatite (HA) coating (1 - 2 µm). Clinical studies were conducted to evaluate the efficacy and safety of this product coated with HA.
3-1	Jul. 4, 2008 Total review time: 463 days Regulatory review time: 334 days	Sep. 10, 2004 Overseas clinical study results	7	MULTI-LINK Mini Vision Coronary Stent System (Abbott Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A coronary stent for reference vessel diameters ranging from 2.25 mm to 2.5 mm.Clinical trials were conducted to evaluate the efficacy and safety of the stent for bailout use in small vessels.
3-1	Mar. 26, 2009 Total review time: 1945 days Regulatory review time: 553 days	- Domestic clinical study results	8	Coroflex (B. Braun Aesculap Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Stent	A stainless-steel balloon-expandable coronary stent. Clinical studies were conducted to evaluate the clinical performance (e.g. restenosis rate) of the stent.
3-2	Aug. 25, 2008 Total review time: 858 days Regulatory review time: 599 days	Sep. 26, 2006 Overseas clinical study results	9	Arista AH (Senko Medical Trading Co.)	Approval	Medical products 4 Bioresorbable local hemostatic device	An absorbable hemostat consisting of microporous polysaccharide hemospheres (MPHs) to be used for the local management of bleeding wounds. Clinical studies were conducted to evaluate the hematostatic ability and safety of this product compared with a similar product.
4	Jul. 11, 2008 Total review time: 280 days Regulatory review time: 150 days	Nov. 21, 2007 Overseas clinical study results	10	Medtronic Reveal DX (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 21 ECG monitor	An insertable cardiac monitor to be implanted under the skin in patients for whom the diagnosis was not made from the test(s) the physician considered necessary. The device is intended for use in patients with unexplained syncope for the purpose of recording and storing the ECGs for diagnosis. The documents on clinical evaluation were submitted concerning the efficacy and safety of electrocardiography using this product.
4	Jul. 16, 2008 Total review time: 610 days Regulatory review time: 140 days	Feb. 10, 2000 Domestic clinical study results	11	INOvent (Air Water Inc.)	Approval	Instrument & apparatus 6 Nitric oxide management system	A device to be used for patients with respiratory failure to allow the dilution of nitric oxide inhalant to a certain concentration and its stable supply to the patient. Clinical studies were conducted to compare the predefined concentration of nitric oxide and the concentration of inhaled nitric oxide and to evaluate the concentration of inhaled nitrogen dioxide.

Category	Approval Date Review Time	Date Approved in US Clinical study results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Jul. 16, 2008 Total review time: 181 days Regulatory review time: 141 days	Apr. 7, 2009 Overseas clinical study results	12	Attain Ability Lead (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	Over-the-wire (OTW) type of left ventricular lead used with implantable pulse generators such as cardiac resynchronization therapy defibrillator (CRT-D). The documents on clinical studies were submitted for evaluation of the efficacy and safety of this product.
4	Jul. 16, 2008 Total review time: 166 days Regulatory review time: 121 days	Dec. 7, 2006 Overseas clinical study results	13	Lumax 300 HF-T (BIOTRONIK Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers cardiac resynchronization therapy (CRT), with the function of a defibrillator. The documents on clinical studies were submitted for evaluation of the efficacy and safety of this product.
4	Jul. 16, 2008 Total review time: 166 days Regulatory review time: 121 days	Dec. 7, 2006 Overseas clinical study results	14	Lumax 340 HF-T (BIOTRONIK Japan, Inc.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT, with the function of a defibrillator. The documents on clinical studies were submitted for evaluation of the efficacy and safety of this product.
4	Oct. 14, 2008 Total review time: 459 days Regulatory review time: 316 days	Nov. 17, 2004 (V-343) Jun. 30, 2004 (V-340) Overseas clinical study results	15	Atlas + HF (St. Jude Medical Japan CRMD)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT (treatment method to improve cardiac failure symptoms, which synchronizes ventricular contraction by stimulating cardiac muscles of bilateral ventricles electrically for a long time), with the function of a defibrillator. Optimization of interventricular timing of biventricular pacing therapy was evaluated in the clinical studies.
4	Oct. 14, 2008 Total review time: 459 days Regulatory review time: 316 days	Nov. 17, 2004 (V-337) Jun. 30, 2004 (V-338) Overseas clinical study results	16	Epic HF (St. Jude Medical Japan CRMD)	Change	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	An implantable pulse generator that delivers CRT, with the function of a defibrillator. Optimization of interventricular timing of biventricular pacing therapy was evaluated in the clinical studies.
4	Dec. 15, 2008 Total review time: 410 days Regulatory review time: 227 days	Nov. 5, 2004 Overseas clinical study results	17	Navistar Thermocool (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An electrode catheter used in myocardium with radiofrequency current and for the electrophysiological study of the heart to treat type I atrial flutter. Clinical studies were conducted to evaluate the novel irrigation feature of this product that allows saline flushing from the tip electrode to aviod increasing tip electrode-tissue interface temperature.
4	Jan. 29, 2009 Total review time: 482 days Regulatory review time: 353 days	Jul. 25, 2007 Overseas clinical study results	18	QuickFlex (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An over-the-wire (OTW) type of left ventricular lead used with implantable pulse generators such as CRT-D for CRT. The documents on clinical studies were submitted for evaluation of the efficacy and safety of this product.
4	Feb. 10, 2009 Total review time: 215 days Regulatory review time: 166 days	Jun. 13, 2008 Overseas clinical study results	19	Attain StarFix Lead (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	An over-the-wire (OTW) type of left ventricular lead used with implantable pulse generators such as CRT-D for CRT. The documents on clinical studies were submitted for evaluation of the efficacy and safety of this product.
4	Mar. 17, 2009 Total review time: 404 days Regulatory review time: 251 days	Zephyr DR: Mar. 29, 2007 Zephyr XL DR: Mar. 29, 2007 Overseas clinical study results	20	Zephyr DR (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual-chamber implantable cardiac pacemaker. Its ventricular autocapture algorithm was modified to reduce the possibility of the misdetection of electrochemical polarization voltage that occurs in the conventional product. Clinical studies were conducted chiefly to evaluate the modified algorithm.
4	Mar. 17, 2009 Total review time: 404 days Regulatory review time: 251 days	Zephyr SR: Mar. 29, 2007 Zephyr XL SR: May 9, 2007 Overseas clinical study results	21	Zephyr SR (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	A single-chamber implantable cardiac pacemaker. Its ventricular autocapture algorithm was modified to reduce the possibility of the misdetection of electrochemical polarization voltage that occurs in the conventional product. Clinical studies were conducted chiefly to evaluate the modified algorithm.
4	Mar. 24, 2009 Total review time: 358 days Regulatory review time: 260 days	Apr. 29, 2005 Overseas clinical study results	22	Frontier II (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable pulse generator that delivers CRT. Optimization of interventricular timing of biventricular pacing therapy was evaluated in the clinical studies.
4	Mar. 30, 2009 Total review time: 364 days Regulatory review time: 264 days	Apr. 29, 2005 Overseas clinical study results	23	Frontier CRT-P (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator without defibrillator function	An implantable pulse generator that delivers CRT. Optimization of interventricular timing of biventricular pacing therapy was evaluated in the clinical studies.

Category	Approval Date Review Time	Date Approved in US Clinical study results: Domestic/Overseas		Brand Name (Applicant Company)	Approval/ Partial Change	Classification Generic Name	Notes
4	Mar. 24, 2009 Total review time: 397 days Regulatory review time: 257 days	- Overseas clinical study results	24	Emprise SR+ (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	A single chamber implantable cardiac pacemaker. Its ventricular autocapture algorithm was modified to reduce the possibility of the misdetection of electrochemical polarization voltage that occurs in the conventional product. Clinical studies were conducted chiefly to evaluate the modified algorithm.
4	Mar. 24, 2009 Total review time: 397 days Regulatory review time: 257 days	- Overseas clinical study results	25	Emprise DR+ (Fukuda Denshi Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	A dual chamber implantable cardiac pacemaker. Its ventricular autocapture algorithm was modified to reduce the possibility of the misdetection of electrochemical polarization voltage that occurs in the conventional product. Clinical studies were conducted chiefly to evaluate the modified algorithm.
5	May 7, 2008 Total review time: 894 days Regulatory review time: 489 days	- Domestic clinical study results	26	Asahi Hollow Fiber Hemodiafilter (Asahi Kasei Medical Co., Ltd.)	Approval	Instrument & apparatus 7 Hemodiafilter	A hemodialfilter using hollow fibers made of polysulfone resin to remove metabolites in blood during hemodiafiltration for patients with acute and chronic renal failure. Clinical studies were conducted because it was the first time to use polysulfone resin as a raw material of hollow fibers for hemodialfilter, although it had been approved for hemodialyzer.
5	Dec. 18, 2008 Total review time: 875 days Regulatory review time: 519 days	- Domestic clinical study results	27	Flow Star (JMS Co., Ltd.)	Approval	Instrument & apparatus 7 Slow continuous hemofilter	A hemofilter used for treatment and purification of body fluid in patients with acute renal failure accompanying acute hepatic insufficiency, acute on chronic renal failure, perioperative period, sepsis, multiple organ failure, acute respiratory failure, or acute circulation failure. Clinical studies were conducted because it was the first time to use polyethersulfone (PES) as a raw material of hollow fibers.
6	May 22, 2008 Total review time: 2586 days Regulatory review time: 376 days	Mar. 1, 1996 Overseas clinical study results	28	Integra Dermal Regeneration Template (Century Medical, Inc.)	Approval	Medical products 4 Other surgical or orthopedic materials (dermal regeneration graft)	A two-layered matrix consisting of a cross-linking layer of bovine-derived collagen and shark-derived glycosaminoglycan and a silicone layer. To be indicated for the postexcisional treatment of full-thickness or partial-thickness thermal injuries. The product contains glycosaminoglycan, which is a novel feature unseen in existing products. Clinical studies were conducted to evaluate the efficacy and safety of this product.
6	Sep. 17, 2008 Total review time: 504 days Regulatory review time: 253 days	Mar. 14, 2007 Domestic clinical study results	29	Super Fixsorb MX30 (Takiron Co., Ltd.)	Change	Medical products 4 Absorbable internal fixation screw	Absorbable screws composed of poly L-lactide and hydroxyapatite. A partial change for the addition of the skull to the target site of Super Fixsorb MX30. Clinical studies were conducted to evaluate the efficacy and safety concerning the added target site.
6	Sep. 17, 2008 Total review time: 37 days Regulatory review time: 28 days	Mar. 14, 2007 No clinical study results	30	Osteotrans Plus 30 Screw (Takiron Co., Ltd.)	Change	Medical products 4 Absorbable internal fixation screw	A partial change for application of another brand name of Super Fixsorb MX30.
6	Sep. 17, 2008 Total review time: 491 days Regulatory review time: 240 days	Mar. 14, 2007 Domestic clinical study results	31	Super Fixsorb MX40 (Takiron Co., Ltd.)	Change	Medical products 4 Absorbable internal fixation plate	Absorbable plate composed of poly L-lactide and hydroxyapatite. A partial change for the addition of the skull to the target site of Super Fixsorb MX40. Clinical studies were conducted to evaluate the efficacy and safety concerning the added target site.
6	Sep. 17, 2008 Total review time: 37 days Regulatory review time: 28 days	Mar. 14, 2007 No clinical study results	32	Osteotrans Plus 40 Plate (Takiron Co., Ltd.)	Change	Medical products 4 Absorbable internal fixation plate	A partial change for application of another brand name of Super Fixsorb MX40.
6	Mar. 23, 2009 Total review time: 682 days Regulatory review time: 509 days	- Domestic clinical study results	33	Neobone X (MMT Co., Ltd.)	Approval	Medical products 4 Artificial bone implant	A composite type of synthetic hydroxyapatite bone substitute made of interconnected porous and solid parts. The product is used with the inner and outer fixation devices at the load bearing site. Clinical studies were conducted to evaluate its efficacy and safety in patients with cortical bone defect.

Table 4. Post-marketing safety Measures Implemented by MHLW and Revision of PRECAUTIONS for Drugs, etc. in FY 2008

Post-marketing safety measures implemented by MHLW in FY 2008

	Drugs	Medical devices
Instructions for revision of PRECAUTIONS	151	4
Publishing information on the Pharmaceuticals and Medical Devices Safety Information	20	6

Note: Including the issuance of notification on self-check of medical devices.

Revision to PRECAUTIONS in the Package Inserts of Drugs, instructed by MHLW in FY 2008

Date	Drug name
Apr. 25, 2008	1. Carbamazepine 2. Bromocriptine mesilate 3. Chlorphenesin carbamate 4. Doripenem hydrate
May 30, 2008	1. Bepridil hydrochloride
Jun. 16, 2008	1. Irinotecan hydrochloride
Jul. 4, 2008	1. Tiotropium bromide hydrate 2. Bucillamine 3. Darunavir ethanolate 4. Varenicline tartrate 5. Over-the-counter Drugs Products containing dextromethorphan hydrobromide or phenolphthalinate dextromethorphan 6. Over-the-counter Drugs Cold medicines (oral dosage form) [products with a dosage for patients aged less than 2 years (products with a dosage for patients aged less than 1 year)] Antitussive/expectorant drugs (oral dosage form) [products with a dosage for patients aged less than 2 years (products with a dosage for patients aged less than 1 year)] Oral rhinitis medicines [products with a dosage for patients aged less than 2 years (products with a dosage for patients aged less than 1 year)] 7. Over-the-counter Drugs Cold medicines (oral dosage form) [products with a dosage for patients aged less than 2 years (products without a dosage for patients aged less than 1 year)] Antitussive/expectorant drugs (oral dosage form) [products with a dosage for patients aged less than 2 years (products without a dosage for patients aged less than 1 year)] Oral rhinitis medicines [products with a dosage for patients aged less than 2 years (products without a dosage for patients aged less than 1 year)]
Aug. 8, 2008	1. Gefitinib
Aug. 8, 2008	1. Peg-interferon alpha-2a (genetical recombination) 2. Salicylamide/Acetaminophen/Anhydrous caffeine/Promethazine methylenedisalicylate 3. Alacepril Imidapril hydrochloride Captopril Quinapril hydrochloride Cilazapril Temocapril hydrochloride Delapril hydrochloride Trandolapril Perindopril erbumine Lisinopril 4. Enalapril maleate 5. Benazepril hydrochloride 6. Tacrolimus hydrate (ointment for adult use)

Date	Drug name
	7. Tacrolimus hydrate (ointment for pediatric use) 8. Amoxicillin hydrate 9. Lansoprazole/Amoxicillin hydrate/Clarithromycin 10. Garenoxacin mesilate hydrate 11. Interferon alpha (BALL-1) Interferon alpha (NAMALWA) Interferon alpha-2b (genetical recombination) Interferon alfacon-1 (genetical recombination) Interferon beta Peg-interferon alpha-2b (genetical recombination)
Sep. 19, 2008	1. Bromocriptine mesilate 2. Azelnidipine 3. Dihydroergotoxine mesilate 4. Magnesium oxide 5. Cabergoline 6. Talipexole hydrochloride Pramipexole hydrochloride hydrate Levodopa Levodopa-carbidopa Levodopa-benserazide hydrochloride Ropinirole hydrochloride 7. Pergolide mesilate 8. Modafinil 9. Carvedilol 10. Estradiol preparations (oral dosage form, injectable dosage form) (Products with the indication of climacteric disturbance) Estriol preparations (products with the indication of climacteric disturbance) Androgen/estrogen combination product 11. Estradiol preparations (external medications) (products with the indication of climacteric disturbance) 12. Conjugated estrogen 13. Bortezomib 14. Clarithromycin 15. Amphotericin B (injectable dosage form) 16. Lansoprazole/Amoxicillin hydrate/Clarithromycin
Oct. 24, 2008	1. Amantadine hydrochloride 2. Everolimus 3. Ciclosporin (oral dosage form, injectable dosage form)
Nov. 17, 2008	1. Insulin kit, insulin cartridge as part of structure of an insulin pen
Nov. 28, 2008	1. Lornoxicam 2. Elental Elental P Twinline 3. Ensure H Ensure Liquid Harmonic-F Harmonic-M Racol 4. Ergotamine tartrate/Anhydrous caffeine Ergotamine tartrate/Anhydrous caffeine/Isopropylantipyrine Dihydroergotamine mesylate 5. Acetazolamide Acetazolamide sodium

Date	Drug name
	6. Diltiazem hydrochloride (oral dosage form) 7. Enterued 8. Ethambutol hydrochloride 9. Octocog alfa (genetical recombination) 10. Freeze-dried human coagulation factor VIII concentrate Rurioctocog alfa (genetical recombination) 11. Freeze-dried human coagulation factor IX concentrate Freeze-dried human blood-coagulation factor IX complex
Dec. 19, 2008	1. Sorafenib tosilate
Jan. 9, 2009	1. Etanercept (genetical recombination) 2. Temozolomide 3. Rituximab (genetical recombination) 4. Aripiprazole 5. Oxypertine Pipamperone hydrochloride 6. Olanzapine 7. Carpipramine hydrochloride Carpipramine maleate Clocapramine hydrochloride Chlorpromazine hydrochloride Chlorpromazine hydrochloride/Promethazine hydrochloride/Phenobarbital Chlorpromazine hibenzate Chlorpromazine phenolphthalinate Spiperone Sultopride hydrochloride Sulpiride Zotepine Timiperone Trifluoperazine maleate Nemonapride Haloperidol Pimozide Fluphenazine decanoate Fluphenazine maleate Prochlorperazine maleate Prochlorperazine mesilate Propericiazine Bromperidol Perphenazine Perphenazine hydrochloride Perphenazine fendizoate Perphenazine maleate Mosapramine hydrochloride Moperone hydrochloride Levomepromazine hydrochloride Levomepromazine maleate 8. Quetiapine fumarate 9. Haloperidol decanoate 10. Blonanserin 11. Perospirone hydrochloride 12. Infliximab (genetical recombination) 13. Dienogest 14. Garenoxacin mesilate hydrate 15. Efavirenz 16. Over-the-counter Drugs

Date	Drug name
	Magnesium oxide
Feb. 13, 2009	1. Tocilizumab (genetical recombination) 2. Hydroxyzine hydrochloride (injectable dosage form)
Mar. 19, 2009	1. Naproxen 2. Bucolome 3. Entacapone 4. Telmisartan 5. Losartan potassium/Hydrochlorothiazide 6. Exemestane 7. Voriconazole 8. Entecavir hydrate

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

Table 5. Revision of PRECAUTIONS and Instructions for Self-check of Medical Devices in FY 2008

Revision of PRECAUTIONS for Medical Devices in FY 2008

Date	Title
Oct. 6, 2008	Instructions, etc. on the revision of package inserts of ureteral stents
Nov. 17, 2008	Revision of PRECAUTIONS for the combined use of an insulin pen/syringe, etc. and injection needle

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

Instructions for Self-check of Medical Devices in FY 2008

Date	Title
Sep. 11, 2008	Self-check of package inserts regarding the combined use of an artificial nose and warmer/humidifier in a ventilator circuit
Oct. 31, 2008	Self-check of indications of a self-monitoring blood glucose meter when exceeding the measurement range

Note: Detailed information is available at the PMDA's Medical Product Information site

Table 6. FY 2008 Pharmaceuticals and Medical Devices Safety Information (No. 246-256)

Date	No.	Contents
May 22, 2008	246	1. Revision of PRECAUTIONS (No. 196) (a) Desmopressin acetate (products with the indication for nocturnal enuresis) (and 4 others) (b) Drug-eluting coronary stent 2. List of products subject to Early Post-marketing Phase Vigilance (Reference) 1. Manuals for management of individual serious adverse drug reactions 2. Expansion of collaborating hospitals in operations of Pregnancy and Medicine Information Center
Jun. 26, 2008	247	1. Revision of PRECAUTIONS (No. 197) Carbamazepine (and 3 others) 2. List of products subject to Early Post-marketing Phase Vigilance (Reference) 1. Heparin sodium preparations, etc.
Jul. 23, 2008	248	1. Revision of PRECAUTIONS (No. 198) Bepridil hydrochloride (and 1 other) 2. List of products subject to Early Post-marketing Phase Vigilance
Aug. 28, 2008	249	1. Important Safety Information [1] Tiotropium bromide hydrate 2. Revision of PRECAUTIONS (No. 199) Bucillamine (and 5 others) 3. List of products subject to Early Post-marketing Phase Vigilance
Sep. 25, 2008	250	1. Interstitial pneumonia induced by interferon products (products with the indication of the “improvement of viremia in patients with chronic hepatitis C”) 2. Revision of PRECAUTIONS (No. 200) Gefitinib (and 9 others) 3. List of products subject to Early Post-marketing Phase Vigilance (Reference) 1. Results of the Japanese phase III study of gefitinib and opinion on the use, etc. of gefitinib
Oct. 30, 2008	251	1. Adverse Drug Reaction Relief System and the Relief System for Infections derived from Biological Products 2. Obstruction of artificial nose caused by the combined use with a warmer/humidifier 3. List of products subject to Early Post-marketing Phase Vigilance (Reference) 1. Reports of the adverse drug reactions of influenza vaccines in FY 2007 (Results of Review Committee for Adverse Reactions to Vaccines)
Nov. 27, 2008	252	1. Hypermagnesemia associated with magnesium oxide 2. Important Safety Information [1] Azelnidipine 3. Revision of PRECAUTIONS (No. 201) (a) Bromocriptine mesilate (and 13 others) (b) Ureteral stent 4. List of products subject to Early Post-marketing Phase Vigilance
Dec. 18, 2008	253	1. Revision of PRECAUTIONS (No. 202) (a) Amantadine hydrochloride (and 3 others) (b) Insulin pen 2. List of products subject to Early Post-marketing Phase Vigilance

Date	No.	Contents
Jan. 29, 2009	254	1. Pharmaceuticals and Medical Devices Information E-mail Alert Service 2. Important Safety Information [1] Enteral nutrition (Elental, Elental P, Ensure H, Ensure Liquid, Enterued, Twinline, Harmonic-F, Harmonic-M and Racol) [2] Lornoxicam 3. Revision of PRECAUTIONS (No. 203) Ergotamine Tartrate/Anhydrous Caffeine (and 6 others) 4. List of products subject to Early Post-marketing Phase Vigilance
Feb. 26, 2009	255	1. Important Safety Information [1] Sorafenib tosilate [2] Etanercept (genetical recombination) [3] Temozolomide [4] Rituximab (genetical recombination) 2. Revision of PRECAUTIONS (No. 204) Aripiprazole (and 13 others) 3. List of products subject to Early Post-marketing Phase Vigilance (Reference) 1. Precautions for abnormal behaviors in patients infected with influenza
Mar. 26, 2009	256	1. Injection site necrosis/skin ulcer, etc. caused by hydroxyzine hydrochloride (injectable dosage form) 2. Important Safety Information [1] Tocilizumab (genetical recombination) 3. List of products subject to Early Post-marketing Phase Vigilance

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

Table 7. PMDA Medical Safety Information

No.	Date published	Title
1	Jun. 2008	Precautions against smoking and use of fire in long-term oxygen therapy (LTOT)
2	Jun. 2008	Handling of lancing devices for obtaining blood samples
3	Oct. 2008	Precautions against misuse (overdose) of antirheumatic methotrexate preparations
4	Jan. 2009	Precautions in artificial respiration (No.1)
5	Feb. 2009	Compatibility between a “Type A” needle (JIS T 3226-2) and a insulin pen (JIS T 3226-1)
6	Feb. 2009	Recall of Jackson-Rees circuits

Note: Detailed information is available at the PMDA’s Medical Product Information site.

Table 8. Lists of User Fees (partially revised on April 1, 2008; see the Attachments for comparison with the revision implemented on April 1, 2009.)

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 expenses	133,300 + travel expenses
				Article 16 (2) 1-a	
		Document		58,100	58,100
				Article 16 (2) 1-b	
Change/Addition of classification		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 2-a	
		Document		39,700	39,700
				Article 16 (2) 2-b	
Renewal of existing accreditation		On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 3-a	
		Document		39,700	39,700
				Article 16 (2) 3-b	
Approval review of drugs (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	Switch to OTC status, etc.	First application items	1,291,600		1,291,600
			Article 17 (1) 1-a (10)		
		Applications with different dosage, etc.	1,291,600		1,291,600
			Article 17 (1) 1-a (10)		
	Others		110,300		110,300
			Article 17 (1) 1-a (11)		
In vitro diagnostics (without approval standards)			584,100		584,100
			Article 17 (1) 1-a (14)		
In vitro diagnostics (with approval standards)		Basic	282,900		282,900
			Article 17 (1) 1-a (13)		
		Addition of series	60,300		60,300
			Article 17 (1) 1-a (12)		
Quasi-drugs/cosmetics			63,500		63,500
			Article 17 (1) 1-b, c		
New application of change or replacement of brand name			35,600		35,600
			Article 17 (1) 1-e		

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
Approval review of drugs (approval for partial changes to approved matters)							
	New drug 1 (non-orphan drugs)	Changes in indications	First application items		10,190,500 Article 17 (1) 2-a (1)	2,463,200 Article 17 (2) 2-a	12,653,700
			Applications with different dosage, etc.		1,057,400 Article 17 (1) 2-a (2)	615,900 Article 17 (2) 2-b	1,673,300
		Others			205,100 Article 17 (1) 2-a (3)	120,700 Article 17 (2) 2-c	325,800
	New drug 1 (orphan drugs)	Changes in indications	First application items		8,434,300 Article 17 (1) 2-a (4)	1,232,500 Article 17 (2) 2-d	9,666,800
			Applications with different dosage, etc.		875,600 Article 17 (1) 2-a (5)	310,100 Article 17 (2) 2-e	1,185,700
		Others			132,700 Article 17 (1) 2-a (6)	109,800 Article 17 (2) 2-f	242,500
	New drug 2 (non-orphan drugs)	Changes in indications	First application items		10,190,500 Article 17 (1) 2-a (1)	2,463,200 Article 17 (2) 2-a	12,653,700
			Applications with different dosage, etc.		1,057,400 Article 17 (1) 2-a (2)	615,900 Article 17 (2) 2-b	1,673,300
		Others			205,100 Article 17 (1) 2-a (3)	120,700 Article 17 (2) 2-c	325,800
	New drug 2 (orphan drugs)	Changes in indications	First application items		8,434,300 Article 17 (1) 2-a (4)	1,232,500 Article 17 (2) 2-d	9,666,800
			Applications with different dosage, etc.		875,600 Article 17 (1) 2-a (5)	310,100 Article 17 (2) 2-e	1,185,700
		Others			132,700 Article 17 (1) 2-a (6)	109,800 Article 17 (2) 2-f	242,500
	Generic drugs (with conformity audit)	Changes in indications	First application items		10,190,500 Article 17 (1) 2-a (1)	2,463,200 Article 17 (2) 2-a	12,653,700
			Applications with different dosage, etc.		1,057,400 Article 17 (1) 2-a (2)	615,900 Article 17 (2) 2-b	1,673,300
		Changes based on guidelines			35,600 Article 17 (1) 2-a (7)		35,600
		Others			205,100 Article 17 (1) 2-a (3)	120,700 Article 17 (2) 2-c	325,800
	OTC drugs	Switch to OTC status, etc.	Changes in indications	First application items	10,190,500 Article 17 (1) 2-a (1)		10,190,500
				Applications with different dosage, etc.	1,057,400 Article 17 (1) 2-a (2)		1,057,400
		Changes based on guidelines			35,600 Article 17 (1) 2-a (7)		35,600
		Others			56,400 Article 17 (1) 2-a (8)		56,400
	In vitro diagnostics (without approval standards)				295,800 Article 17 (1) 2-a (11)		295,800
	In vitro diagnostics (with approval standards)			Basic	143,500 Article 17 (1) 2-a (10)		143,500
				Addition of series	31,900 Article 17 (1) 2-a (9)		31,900
	Quasi-drugs and cosmetics				35,600 Article 17 (1) 2-b, c		35,600
GMP inspection of drugs							
	Approval, partial change and manufacture for export	New drugs		Domestic		739,800 Article 17 (4) 1-b (1)	739,800
				Overseas		933,500 + travel expenses Article 17 (4) 1-b (2)	933,500 + travel expenses
		Biological drugs/ Radiopharmaceuticals		Domestic		666,100 Article 17 (4) 1-a (1)	666,100
				Overseas		844,400 + travel expenses Article 17 (4) 1-a (2)	844,400 + travel expenses
		Sterilized drugs/ sterilized quasi-drugs		Domestic		201,300 Article 17 (4) 1-c (1)	201,300
				Overseas		229,800 + travel expenses Article 17 (4) 1-c (2)	229,800 + travel expenses
		Other drugs/quasi-drugs		Domestic		141,200 Article 17 (4) 1-d (1)	141,200
				Overseas		155,400 + travel expenses Article 17 (4) 1-d (2)	155,400 + travel expenses
		Package, labeling, storage, external testing, etc.		Domestic		63,800 Article 17 (4) 2-a, Article 17 (5) 1-a	63,800
				Overseas		84,800 + travel expenses Article 17 (4) 2-b, Article 17 (5) 1-b	84,800 + travel expenses

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
Renewal of the above	Biological drugs/ Radiopharmaceuticals	Basic	Domestic			436,000	436,000
						Article 17 (4) 3-a (1)	
			Overseas			554,200 + travel expenses	554,200 + travel expenses
						Article 17 (4) 3-a (2)	
		Addition of 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 expenses	480,000 + travel expenses
						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)	
	Other drugs/quasi-drugs	Basic	Domestic			336,500	336,500
						Article 17 (4) 3-c (1)	
			Overseas			409,400 + travel expenses	409,400 + travel expenses
						Article 17 (4) 3-c (2)	
		Addition of 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 expenses	338,100 + travel expenses
						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 (inspection) of drugs							
		Domestic				2,062,400	2,062,400
						Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
		Overseas				2,282,600 + travel expenses	2,282,600 + travel expenses
						Article 17 (3) 1-b, Article 17 (9) 2-a (2)	
GCP audit (inspection) of drugs							
	New GCP	First application items	Domestic			2,723,200	2,723,200
						Article 17 (3) 2-a	
			Overseas			3,011,900 + travel expenses	3,011,900 + travel expenses
						Article 17 (3) 2-b	
		Applications with different dosage, etc.	Domestic			720,800	720,800
						Article 17 (3) 2-c	
			Overseas			751,800 + travel expenses	751,800 + travel expenses
						Article 17 (3) 2-d	
	GCP audit (inspection) of generic drugs		Domestic			645,200	645,200
						Article 17 (3) 2-e	
			Overseas			950,200 + travel expenses	950,200 + travel expenses
						Article 17 (3) 2-f	
Re-examination of drugs							
	Confirmation/ examination	First application items			806,600	2,673,700	3,480,300
					Article 17 (8) 1-a	Article 17 (9) 1-a	
		Applications 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 expenses	2,409,600 + travel expenses
						Article 17 (9) 2-b (2)	
		Applications with different dosage, etc.	Domestic			752,600	752,600
						Article 17 (9) 2-b (3)	
			Overseas			772,300 + travel expenses	772,300 + travel expenses
						Article 17 (9) 2-b (4)	

List of user fees for reviews etc. of medical devices under 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 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 expenses	133,300 + travel expenses
				Article 16 (2) 1-a	
		Document		58,100	58,100
				Article 16 (2) 1-b	
	Change/Addition of classification	On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 2-a	
		Document		39,700	39,700
				Article 16 (2) 2-b	
	Renewal of existing accreditation	On-site		64,600 + travel expenses	64,600 + travel expenses
				Article 16 (2) 3-a	
		Document		39,700	39,700
				Article 16 (2) 3-b	
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)		

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
QMS inspection 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 expenses	933,500 + travel expenses
						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 expenses	844,400 + travel expenses
						Article 17 (4) 1-a (2)	
	Sterilized medical devices		Domestic			201,300	201,300
						Article 17 (4) 1-c (1)	
			Overseas			229,800 + travel expenses	229,800 + travel expenses
						Article 17 (4) 1-c (2)	
	Other medical devices		Domestic			141,200	141,200
						Article 17 (4) 1-d (1)	
			Overseas			155,400 + travel expenses	155,400 + travel expenses
						Article 17 (4) 1-d (2)	
	Package, labeling, storage, external testing, etc.		Domestic			63,800	63,800
						Article 17 (4) 2-a, Article 17 (5) 1-a	
			Overseas			84,800 + travel expenses	84,800 + travel expenses
						Article 17 (4) 2-b, Article 17 (5) 1-b	
Renewal of the above	Biological medical devices, specially controlled medical devices (class IV), etc	Basic	Domestic			436,000	436,000
						Article 17 (4) 3-a (1)	
			Overseas			554200 + travel expenses	554200 + travel expenses
						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 expenses	480,000 + travel expenses
						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)	
	Other medical devices	Basic	Domestic			336,500	336,500
						Article 17 (4) 3-c (1)	
			Overseas			409,400 + travel expenses	409,400 + travel expenses
						Article 17 (4) 3-c (2)	
		Addition of 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 expenses	338,100 + travel expenses
						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 (inspection) of medical devices							
	GLP		Domestic			2,062,400	2,062,400
						Article 17 (3) 1-a, Article 17 (9) 2-a (1)	
			Overseas			2,282,600 + travel expenses	2,282,600 + travel expenses
						Article 17 (3) 1-b, Article 17 (9) 2-a (2)	
GCP audit (inspection) of medical devices							
	GCP		Domestic			635,300	635,300
						Article 17 (3) 3-a	
			Overseas			918,400 + travel expenses	918,400 + travel expenses
						Article 17 (3) 3-b	

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
Re-examination of medical devices					
	New medical devices		502,600	624,600	1,127,200
			Article 17 (8) 2-a	Article 17 (9) 1-c	
	Medical devices other than new ones		51,600		51,600
			Article 17 (8) 2-b		
	GPSP	Domestic		610,700	610,700
				Article 17 (9) 2-b (5)	
		Overseas		949,000 + travel expenses	949,000 + travel expenses
				Article 17 (9) 2-b (6)	

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

Attachment 1

Comparison of former and revised user fees (revision implemented on April 1, 2009)

(Yen)

[Before revision] User fees		
Classification	PMDA	
	Review	Conformity
Approval review of medical devices (new approval)		
Medical devices (with clinical data)	3,077,000 Article 17 (1) 1-d (1)	664,500 Article 17 (2) 1-j
Medical devices (with approval standards, without clinical data)	282,900 Article 17 (1) 1-d (2)	68,500 Article 17 (2) 1-k
Medical devices (without approval standards, without clinical data)	1,164,300 Article 17 (1) 1-d (3)	68,500 Article 17 (2) 1-l
Approval review of medical devices (approval for partial changes to approved matters)		
Medical devices (with clinical data)	1,538,000 Article 17 (1) 2-d (1)	664,500 Article 17 (2) 2-g
Medical devices (with approval standards, without clinical data)	143,500 Article 17 (1) 2-d (2)	37,100 Article 17 (2) 2-h
Medical devices (without approval standards, without clinical data)	584,100 Article 17 (1) 2-d (3)	37,100 Article 17 (2) 1-i

[Revised] User fees		
Classification	PMDA	
	Review	Conformity
Approval review of medical devices (new approval)		
Class IV: New medical devices	8,705,500 Article 17 (1) 1-d (1)	664,500 Article 17 (2) 1-j
Class IV: Improved medical devices (with clinical data)	6,213,000 Article 17 (1) 1-d (2)	664,500 Article 17 (2) 1-j
Class III or II: New medical devices	6,213,000 Article 17 (1) 1-d (3)	664,500 Article 17 (2) 1-j
Class III or II: Improved medical devices (with clinical data)	3,721,200 Article 17 (1) 1-d (4)	664,500 Article 17 (2) 1-j
Class IV: Improved or generic medical devices (with approval standards)	429,200 Article 17 (1) 1-d (5)	68,500 Article 17 (2) 1-k
Class III or II: Improved or generic medical devices (with approval standards)	344,100 Article 17 (1) 1-d (6)	68,500 Article 17 (2) 1-k
Class IV: Improved medical devices	2,355,400 Article 17 (1) 1-d (7)	68,500 Article 17 (2) 1-l
Class IV: Generic medical devices	1,767,700 Article 17 (1) 1-d (8)	68,500 Article 17 (2) 1-l
Class III or II: Improved or generic medical devices	1,409,900 Article 17 (1) 1-d (9)	68,500 Article 17 (2) 1-l
Approval review of medical devices (approval for partial changes to approved matters)		
Class IV: New medical devices	4,357,500 Article 17 (1) 2-d (1)	664,500 Article 17 (2) 2-g
Class IV: Improved medical devices (with clinical data)	3,109,900 Article 17 (1) 2-d (2)	664,500 Article 17 (2) 2-g
Class III or II: New medical devices	3,109,900 Article 17 (1) 2-d (3)	664,500 Article 17 (2) 2-g
Class III or II: Improved medical devices (with clinical data)	1,872,400 Article 17 (1) 2-d (4)	664,500 Article 17 (2) 2-g
Class IV: Improved or generic medical devices (with approval standards)	217,600 Article 17 (1) 2-d (5)	37,100 Article 17 (2) 2-h
Class III or II: Improved or generic medical devices (with approval standards)	173,600 Article 17 (1) 2-d (6)	37,100 Article 17 (2) 2-h
Class IV: Improved medical devices	1,181,200 Article 17 (1) 2-d (7)	37,100 Article 17 (2) 2-i
Class IV: Generic medical devices	884,200 Article 17 (1) 2-d (8)	37,100 Article 17 (2) 2-i
Class III or II: Improved or generic medical devices	709,500 Article 17 (1) 2-d (9)	37,100 Article 17 (2) 2-i

Attachment 2

Comparison of former and revised user fees (revision implemented on April 1, 2009)

(Yen)

Classification			[Before revision] User fees	[Revised] User fees
Face-to-face consultations				
Clinical trial consultations	Drugs	Procedural consultation for drugs	139,800 yen per consultation	139,800 yen per consultation
		Consultation on bioequivalence testing, etc. for drugs	556,000 yen per consultation	556,000 yen per consultation
		Safety consultation for drugs	1,782,800 yen per consultation	1,782,800 yen per consultation
		Quality consultation for drugs	1,478,300 yen per consultation	1,478,300 yen per consultation
		Consultation before start of phase I study for drugs	4,239,400 yen per consultation	4,239,400 yen per consultation
		Consultation before start of early phase II study for drugs	1,623,000 yen per consultation	1,623,000 yen per consultation
		Consultation before start of late phase II study for drugs	3,028,400 yen per consultation	3,028,400 yen per consultation
		Consultation after completion of phase II study for drugs	6,011,500 yen per consultation	6,011,500 yen per consultation
		Pre-application consultation for drugs	6,011,400 yen per consultation	6,011,400 yen per consultation
		Consultation on the protocols of clinical trials for reevaluation and re-examination of drugs	3,320,600 yen per consultation	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	3,319,400 yen per consultation
		Additional consultation for drugs	2,675,600 yen per consultation	2,675,600 yen per consultation
		Consultation on compliance with conformity criteria for drugs	2,875,500 yen per consultation	2,875,500 yen per consultation
		Prior assessment consultation for drugs (quality)		3,049,300 yen per consultation
		Prior assessment consultation for drugs (non-clinical: toxicity)		2,061,100 yen per consultation
		Prior assessment consultation for drugs (non-clinical: pharmacology)		2,061,100 yen per consultation
		Prior assessment consultation for drugs (non-clinical: pharmacokinetics)		2,061,100 yen per consultation
		Prior assessment consultation for drugs (phase I study)		3,484,700 yen per consultation
		Prior assessment consultation for drugs (phase II study)		4,497,400 yen per consultation
		Consultation on pharmacogenomics/ biomarker		3,028,400 yen per consultation
		Pre-application consultation for new OTC drugs	445,100 yen per consultation	445,100 yen per consultation
	Devices and *in vitro* diagnostics	Pre-development consultation for medical devices	135,200 yen per consultation	135,200 yen per consultation
		Safety consultation for medical devices (excluding biological devices)	675,100 yen per consultation	822,100 yen per consultation
		Safety consultation for biological medical devices	754,400 yen per consultation	910,100 yen per consultation
		Quality consultation for medical devices (excluding biological devices)	650,500 yen per consultation	775,400 yen per consultation
		Quality consultation for biological medical devices	753,500 yen per consultation	921,400 yen per consultation
		Performance testing consultation for medical devices	690,900 yen per consultation	845,900 yen per consultation
		Clinical evaluation consultation for medical devices	854,100 yen per consultation	1,026,600 yen per consultation
		Exploratory clinical trial consultation for medical devices	903,700 yen per consultation	1,105,300 yen per consultation
		Clinical trial/Pre-application consultation for medical devices	1,594,700 yen per consultation	2,413,000 yen per consultation
		Clinical trial/Pre-application consultation for *in vitro* diagnostics	1,594,700 yen per consultation	1,594,700 yen per consultation
		Application procedure consultation for medical devices	135,200 yen per consultation	135,200 yen per consultation
		Application procedure consultation for *in vitro* diagnostics	135,200 yen per consultation	135,200 yen per consultation
		Additional consultation for medical devices	927,500 yen per consultation	1,130,100 yen per consultation
		Additional consultation for *in vitro* diagnostics	927,500 yen per consultation	927,500 yen per consultation
		Consultation on compliance with conformity criteria for medical devices	650,300 yen per consultation	772,900 yen per consultation
		Consultation on preparation of documents for cell- and tissue-based products	223,500 yen per consultation	223,500 yen per consultation
Confirmation of certification on drugs, etc.				
GMP certification on investigational products (with on-site inspection)				739,800 yen per site per product
GMP certification on investigational products (without on-site inspection)				15,100 yen per site per product
Certification of drug products			15,100 yen per product	15,100 yen per product
Other certifications			8,400 yen per matter of one product	8,400 yen per matter of one product

Mid-term Targets of the Pharmaceuticals and Medical Devices Agency*

(Provisional Translation)

Instruction No. 0227068 issued by the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, Dated February 27, 2009

Targets related to the management of operations to be achieved by the Pharmaceuticals and Medical Devices Agency shall be as follows, based on the provision of Article 29-1 of the Law on General Rules of Incorporated Administrative Agency (Law No. 103, 1999).

February 27, 2009

Yoichi Masuzoe
Minister of Health, Labour and Welfare

Part 1 Effective Period for Mid-term Targets

The effective period for the Mid-term targets according to Article 29-2-1 of the Law on General Rules of Incorporated Administrative Agency (Law No. 103, 1999; hereinafter referred to as "General Rules") shall be 5 years from April 2009 to March 2014.

Part 2 Items Related to Improvement in the Overall Management of Operations and the Quality of Services and Other Operations Rendered to the Public

With regard to targets related to efficiency improvement in the management of operations in accordance with Article 29-2-2 of the General Rules and targets related to improvement in the quality of services and other operations rendered to the public in accordance with Article 29-2-3 of said law, targets related to the Agency as a whole shall be as follows.

<1> Efficient and Flexible Management of Operations

(a) The Agency shall establish an efficient and flexible system for managing operations, confirm the way of operational control and methods for implementing operations through external evaluation, and improve the management of operations based on the following points:

- Improve internal control on the way of implementation of operations and other matters by obtaining instructions from accounting auditors, and proactively disclose measures taken.
- Examine the way of internal control by making use of the professional knowledge of third parties.

(b) The Agency shall promote computerization in operations and increase efficiency in the system for managing operations.

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* *This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail).*

(c) The Agency shall reduce systems costs, ensure transparency in systems procurement, streamline the management of operations, and reduce expenses by reviewing the overall system configuration and the procurement method, based on the results of re-examination of information systems management services that are common throughout the Agency, and review services.

To achieve this goal, the Agency shall integrate individual review systems, based on the Optimization Plan for Operations and Systems that was developed at the end of FY 2007, and promote activities to optimize operations and systems by constructing systems for advancing information sharing among review services, safety measures services, and adverse health effects relief services.

<2> Cost Control through Increased Efficiency of Operations

(a) By increasing efficiency in the management of operations, the Agency shall reduce general administrative expenses (excluding expenses for office relocation and retirement allowances) by the end of the effective period for the Mid-term targets, through the following specific measures:

(1) Approximately 15% reduction in comparison with FY 2008

(2) General administrative expenses to be incurred starting in FY 2009 shall be reduced by approximately 12% in comparison with FY 2013 and FY 2009 for the increase, due to efforts to speed up approval reviews in accordance with the report issued by the Council for Science and Technology Policy, entitled “Revision of Structures Aimed at the Promotion of Science and Technology and Return of Achievements to Society” (dated December 25, 2006; hereinafter referred to as “Report of the Council for Science and Technology Policy”).

(3) General administrative expenses shall be as follows in consideration of activities to speed up approval reviews based on the “Action Program to Accelerate Reviews of Medical Devices” (dated December 11, 2008):

- General administrative expenses to be incurred starting in FY 2009 shall be reduced by approximately 12% in comparison with FY 2013 and FY 2009 for the increase.
- General administrative expenses to be incurred starting in FY 2010 shall be reduced by approximately 9% in comparison with FY 2013 and FY 2010 for the increase.
- General administrative expenses to be incurred starting in FY 2011 shall be reduced by approximately 6% in comparison with FY 2013 and FY 2011 for the increase.
- General administrative expenses to be incurred starting in FY 2012 shall be reduced by approximately 3% in comparison with FY 2013 and FY 2012 for the increase.

(4) General administrative expenses to be incurred in FY 2009 will be reduced by approximately 12% in comparison with FY 2013 and FY 2009 for the increase due to efforts to strengthen and enhance safety measures in accordance with the Interim Report of the Committee for Verification of

Drug-induced Hepatitis Cases and for Examination of Drug Administration to Prevent Similar Diseases, entitled “How Drug Administration Should Function to Prevent Similar Drug-induced Diseases” (dated July 31, 2008; hereinafter referred to as “Interim Report of the Verification Committee on Drug-induced Hepatitis”).

(b) By increasing operational efficiency, the Agency shall reduce operating expenses (excluding expenses for office relocation and benefit payments and single-year expenses due to new project launches) by the end of the effective period for the mid-term targets, through the following specific measures:

(1) Approximately 5% reduction in comparison with FY 2008

(2) Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase due to efforts to speed up approval reviews in accordance with the Report of the Council for Science and Technology Policy.

(3) Operating expenses shall be as follows in consideration of activities to speed up approval reviews based on the “Action Program to Accelerate the Reviews of Medical Devices.”

- Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase.
- Operating expenses to be incurred starting in FY 2010 shall be reduced by approximately 3% in comparison with FY 2013 and FY 2010 for the increase.
- Operating expenses to be incurred starting in FY 2011 shall be reduced by approximately 2% in comparison with FY 2013 and FY 2011 for the increase.
- Operating expenses to be incurred starting in FY 2012 shall be reduced by approximately 1% in comparison with FY 2013 and FY 2012 for the increase.

(4) Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase through efforts to strengthen and enhance safety measures in accordance with the Interim Report of the Verification Committee on Drug-induced Hepatitis.

At the end of the effective period for the Mid-term targets, administrative subsidies excluding the amount for office relocation, which is scheduled during this Mid-term target period, are to be reduce by approximately 18% (or approximately 15% if subsidies are added to administrative subsidies for each year to partially cover expenses for office relocation) in comparison with FY 2013 and FY 2008 for the increase. The Agency expects to develop the next Mid-term targets on the assumption of a reduction of about 18% in comparison with FY 2008.

(c) The Agency shall promote improvement in operational efficiency by centrally managing approved item data in each company on adverse drug reaction (ADR) contributions, infection contributions and safety measures contributions.

(d) The Agency shall have reduced total personnel expenses by 5% or more in comparison with FY 2005 over a 5-year period starting from FY 2006, based on the "Law Concerning Promotion of Administrative Reforms to Realize a Streamlined and Efficient Government" (Law No. 47 dated June 2, 2006).

The Agency shall also continue to work to reform personnel expenses up to FY 2011 in accordance with the "Basic Policy 2006 for Economic and Fiscal Management and Structural Reforms" (approved in a cabinet meeting on July 7, 2006) and based on reforms in respect of national government employees.

Moreover, the Agency shall verify its remuneration standard from the following perspective, and shall publicly announce its verification results and activities.

(1) Whether or not the remuneration standard for Agency staff is higher than that for government employees, taking into account factors, such as office locations and the academic qualification of employees

(2) Whether or not it is possible to eliminate causes for the high remuneration standard for Agency staff, such as the high proportion of employees dispatched from the national government

(3) Whether or not the appropriateness of the current remuneration standard can be satisfactorily explained, taking into account the large financial expenditure of the national government, the accumulated losses, the remuneration standards of private companies that are engaged in similar services, etc.

(4) Whether or not explanation of the remuneration standard can gain full public understanding

(e) The Agency shall, in principle, conclude contracts through open competitive bidding, and shall promote appropriate optional contracts by taking the following measures:

(1) Steadily implement and disclose activities based on the Plan for the Review of Optional Contracts.

(2) Choose methods that can fully secure competitiveness and transparency, especially in planning competition and open recruitment, even where contracts are concluded through open competitive bidding.

(3) In audits by auditors and accounting auditors, the appropriateness of bidding and contracts shall be thoroughly checked.

(f) The Agency shall examine the feasibility of relocating the head office and shall take the necessary measures during the effective period for the Mid-term targets, based on the "Reorganization and

Rationalization Plan for Incorporated Administrative Agency" (approved in a cabinet meeting on December 24, 2007).

<3> Improvement of Services to the Public

The Agency shall comprehensively inform the public about its services and roles, strengthen consultation systems for the public, ensure transparency in the management of operations and the contents of services, and improve the quality of services for the public.

Part 3 Items Related to Improvement in the Management of Operations in Each Division and the Quality of Services and Other Operations Rendered to the Public

1 Relief Fund Services for Adverse Health Effects

With regard to the relief fund services, it is important not only to fully inform more people of the Adverse Drug Reaction Relief System and the Relief system for Infections Derived from Biological Products (hereinafter collectively referred to as "relief system") and appropriately operate them but also adequately and promptly provide relief for those suffering from adverse drug reactions and infections derived from biological products.

Based on this concept, the Agency shall achieve the following targets:

<1> Expansion and Review of the Provision of Information Concerning the Relief Systems

(a) The Agency shall increase transparency in system management by improving the content of information provided concerning the relief systems.

(b) The Agency shall increase operational efficiency by minimizing factors that extend processing time, such as incomplete application documents, etc.

<2> Proactive Public Relations Activities to Broadly Inform the Public About Relief Systems

The Agency shall broadly and comprehensively publicize the relief systems.

<3> Expansion of Consultation Services

The Agency shall improve the system for accepting consultations concerning procedures for benefit payment based on the relief systems by expanding consultation services.

<4> Central Management of Information Through Databases

The Agency shall promote operational efficiency by upgrading information databases on relief fund services in order to make them easier to use.

<5> Prompt Processing of Relief Benefit Claims Through Fact-finding Investigations

(a) The Agency shall promptly process relief benefit claims.

(b) The Agency shall improve operations by setting time-reduction targets within the standard administrative processing time. (This includes the period for medical and pharmaceutical judgments by the Ministry of Health, Labour and Welfare. However, the period during which administrative processing cannot be conducted because of the need for additional or supplementary documents and investigations, which are required in respect of claimants and medical institutions for the purposes of making medical and pharmaceutical judgments, shall be excluded from administrative processing time.)

<6> Promotion of Appropriate Information Provision Through Interdivisional Cooperation

Through interdivisional cooperation, the Agency shall appropriately provide information on relief payments in particular to both review divisions and safety measures divisions.

<7> Examination of Appropriate Implementation of Health and Welfare Services

In respect of health and welfare services, the Agency shall progressively implement services based on the results of a survey on the actual states of suffering of relief beneficiaries.

<8> Appropriate Implementation of Healthcare Allowances for SMON Patients and HIV-positive Patients Affected Through Blood Products

The Agency shall appropriately pay healthcare allowances to SMON patients and HIV-positive patients who have been adversely affected as a result of use of blood products.

<9> Appropriate Implementation of Benefit Payment Services to Assist Individuals Affected by Hepatitis C Through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

The Agency shall appropriately implement benefit payment services to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus.

2 Reviews and related Services and Safety Measures Services

With regard to reviews and related services and safety measures services, it is important not only to provide improved pharmaceuticals and medical devices to medical institutions more promptly and safely in order to enable the public to confidently make use of pharmaceuticals and medical devices that are of world class, but also to prevent the occurrence of health hazards, appropriately and promptly respond in the event that any such hazard occurs, and to make the pharmaceuticals and medical devices can fulfill their purposes over longer periods of time.

Based on this concept, the Agency shall reinforce systems for consultations, reviews and post-marketing safety measures, organically link such operations, and work to attain the targets listed below.

The Agency shall also accelerate approval reviews and strengthen and improve safety measures based on the

Report of the Council for Science and Technology Policy, the Action Program to Accelerate Reviews of Medical Devices, and the Interim Report of the Verification Committee on Drug-induced Hepatitis.

<1> Faster Access to the Latest Pharmaceuticals and Medical Devices

The Agency shall make efforts to enable both the public and healthcare professionals to gain early and timely access, to the maximum extent possible, to the benefits of advanced and safe pharmaceuticals and medical devices that meet their needs.

(a) Based on action plans for expediting reviews in order to solve the drug lag, the Agency shall take all appropriate measures, evaluate and verify progress, and initiate additional measures where necessary.

Following completion of the target period for the action plans, in FY 2011, the Agency shall promptly verify the results.

(b) To achieve this goal, the Agency shall improve services by setting time-reduction targets (targets under ordinary conditions, excluding exceptional cases such as significant institutional changes and changes in social conditions) in relation to the review service processing time for applications on and after April 1, 2004 (“the processing time on the reviewer side for items approved for the year”). The Agency shall also establish an efficient review system.

(c) In cooperation with the United States, the European Union and Asian countries, the Agency shall proactively promote international activities aimed at improving medical services, and thereby establish its international status.

(d) The Agency shall improve pre-application consultations, and give priority to conducting consultations on clinical trials for pharmaceuticals and medical devices that are expected to be highly effective, in order to shorten approval times.

(e) In light of the rapid development of new technologies, such as biotechnology, genomics, and regenerative medicine, the Agency shall improve the level of guidance and review technologies in these areas, and shall take necessary measures for consultations and reviews in response to the development of new drugs and new medical devices based on the latest technologies.

(f) The Agency shall take measures to accelerate reviews on over-the-counter drugs and generic drugs, as in the case of new drugs.

(g) With regard to medical devices, as in the case of new drugs, the Agency shall take all appropriate measures to accelerate reviews based on the Action Program to Accelerate Reviews of Medical Devices, in order to solve the device lag.

(h) The Agency shall appropriately and efficiently conduct conformity audits.

(i) The Agency shall construct a system for appropriately conducting on-site GMP/QMS audits by the end of the effective period for the Mid-term targets.

<2> Improvement of Reliability of Review Services and Safety Measures Services

The Agency shall provide pharmaceuticals and medical devices that the public and healthcare professionals can use with a sense of security, by further improving the reliability of review services and safety measures services.

(a) In respect of review services and safety measures services, the Agency shall work to improve staff skills in order to foster a group of technical experts who are in no way inferior to their overseas counterparts. The Agency shall also further strengthen cooperation with regulatory agencies in the United States, the European Union and Asian countries, as well as domestic and overseas research institutes and researchers.

(b) The Agency shall provide support for efficient implementation of clinical trials on pharmaceuticals and medical devices that can provide patients with the most effective and safest medical care, by focusing on the individual characteristics of patients.

(c) The Agency shall further promote transparency in review services and safety measures services such as by disclosing review reports.

(d) The Agency shall develop information system infrastructures to ensure reliability and further increase efficiency in review services and safety measures services.

<3> Strengthening and Improvement of Safety Measures Services

Based on the Interim Report of the Verification Committee on Drug-induced Hepatitis, the Agency shall work to prevent risks of adverse drug reactions in the use of pharmaceuticals and medical devices, and shall further strengthen the risk management system among relevant parties in order to foster rapid response to occurrences of adverse drug reactions and malfunctions.

(a) In order to precisely respond to the sophisticated and specialized evaluation of adverse drug reaction information, the Agency shall significantly improve and strengthen the system for organizing, evaluating and analyzing such information, and shall comprehensive evaluate adverse drug reaction information systematically and regularly. The Agency shall also identify new correlations between adverse drug data by utilizing IT technologies, construct a system to efficiently and effectively evaluate safety information by studying and making use of methods to locate and analyze new safety information, and make improvements on an as-needed basis.

(b) The Agency shall expand both the use of information feedback to healthcare professionals and companies, such as analysis results on collected safety information, and the means to provide information on proper use to patients, and shall strengthen the system for providing detailed safety information, which

contributes to improvement of safety measures at medical institutions. At the same time, from the perspective of making it easier for the public to understand the achievements of safety measures services, the Agency shall set indices to enable more precise ascertainment of achievements.

(c) The Agency shall appropriately evaluate safety through linkage with relief services and review services.

(d) With regard to the safety measures that have been taken, the Agency shall construct a system for confirming the states of implementation and effectiveness within companies and medical institutions.

Part 4 Matters Related to Financial Improvement

The target in relation to financial improvement as provided for in Article 29-2-4 of the General Rules shall be as follows.

With regard to matters determined in <1> and <2> of Part 2 of the Mid-term targets, the Agency shall develop the Mid-term budget plan in anticipation of cost reductions and conduct management based on this budget.

Part 5 Other Important Matters Related to the Management of Operations

Important targets related to the management of other operations provided in Article 29-2-5 of the General Rules shall be as follows.

<1> Personnel Matters

(a) To improve the expertise of staff members, the Agency shall appropriately develop their abilities through exchanges with external organizations and conduct personnel evaluation in consideration of their achievements. The Agency shall also aim to enhance staff motivation through these measures.

(b) Based on the Report of the Council for Science and Technology Policy, the Action Program to Accelerate Reviews of Medical Devices, and the Interim Report of the Verification Committee on Drug-induced Hepatitis, the Agency shall secure the workforce required for necessary reviews and safety measures.

In employing human resources, the Agency shall be fully cognizant of its neutral status.

(c) The Agency shall take appropriate measures for the employment, allocation, and post-retirement reemployment of executives and employees in order to avoid any suspicion of inappropriate operational ties with pharmaceutical companies.

<2> Ensuring Security

To thoroughly protect personal and corporate information, the Agency shall ensure security for each office and take all possible measures to securely manage information.

Mid-term Plan of the Pharmaceuticals and Medical Devices Agency*

(Provisional Translation)

Authorization No. 0331002 issued by the Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare
Dated March 31, 2009

February 27, 2009

To achieve the mid-term targets of the Pharmaceuticals and Medical Devices Agency in accordance with the instruction of the Minister of Health, Labour and Welfare as of February 27, 2009, based on the provisions of Article 29-1 of the Law on General Rules of Incorporated Administrative Agency (Law No. 103 of 1999), the Agency has developed the following mid-term plan based on the provisions of Article 30-1 of said law.

Tatsuya Kondo (M.D., Ph.D)
Chief Executive
Pharmaceuticals and Medical Devices Agency

Development toward global PMDA based on the PMDA Philosophy

In order to carry out its mission of more promptly providing the public with more effective and safer pharmaceuticals and medical devices, the Pharmaceuticals and Medical Devices Agency (PMDA) has, since its establishment in April 2004, been dedicated to improving systems for review services, safety measures services, and adverse health effects relief services. However, given the wide variety of issues that the Agency must address while continuing to maintain high levels of expertise, it is necessary to further strengthen and enhance those systems.

With respect to securing safety and efficacy, the Agency is committed to two major objectives: 1. Proactively contributing to improvement of public health and safety through comprehensive risk management based on a safety triangle, which is the first of its kind anywhere in the world and focuses on review, safety measures and adverse health effects relief services in relation to pharmaceuticals and medical devices; 2. To further enhance public health service quality not only in Japan but also internationally by promoting cooperation with the United States, the European Union, and Asian nations to address a wide variety of issues from a global perspective, based on the Agency's organizational action philosophy (PMDA Philosophy), which was developed in September 2008 and embodies the following principles:

(1) We pursue the development of medical science while performing our duty with greater transparency based on our mission to protect public health and the lives of our citizens.
(2) We will be the bridge between the patients and their wishes for faster access to safer and more effective drugs and medical devices.
(3) We make science-based judgments on quality, safety, and efficacy of medical products by training personnel to have the latest technical knowledge and wisdom in their field of expertise.
(4) We play an active role within the international community by promoting international harmonization.
(5) We conduct services in a way that is trusted by the public based on our experiences from the past

To achieve these goals, the Agency has developed and will implement the following Mid-term Plan.

* *This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail).*

Target Points of the PMDA Second Mid-term Plan

1. — Proactive Operational Development from a Fresh Perspective —

The Agency shall:

- Complete the PMDA safety triangle by strengthening cooperation among review divisions, safety divisions and relief divisions.
- Promote international cooperation based on the "PMDA International Strategic Plan."
- Promulgate regulatory science by promoting joint graduate school program, research exchange, information provision, etc.
- Make concerted efforts to appropriately evaluate state-of-the-art technologies, such as biotechnology, genomics, and regenerative medicine, to utilize the data mining method, and to respond to Super Special Consortia.

2. — Activities to Improve Services and Conduct Effective Management of Operations —

The Agency shall:

- Seek recommendations and opinions on improvements from third-party review institutions in order to develop an internal control process and to increase transparency and efficiency (in terms of cost control) in the management of operations, and examine the feasibility of relocating the office with a view to managing operations more effectively and efficiently.
- Promote optimization of operations and systems based on the Optimization Plan for Operations and Systems.
- Improve services to the public by providing information based on the PMDA Public Relations Strategic Plan.

3. — Promotion of Relief Services for Adverse Health Effects —

The Agency shall:

- Inform the public of the relief system for adverse health effects and promote understanding of the system by conducting effective public relations activities directed toward patients and healthcare professionals respectively, and by making use of in-school educational opportunities.
- Further reduce the administrative processing period between application for relief benefits and approval decision-making.

(First-term Plan)		(Second-term Plan)
60% of all applications should be processed within 8 months	→	60% of all applications should be processed within 6 months.

- Initiate consultation services to address mental issues of sufferers of adverse health effects caused by adverse drug reactions, as part of health and welfare services.

4. — Activities to Provide Better Pharmaceuticals and Medical Devices More Promptly and Safely —

The Agency shall:

- Set and achieve targets for solving the drug lag by steadily implementing the project management system, introducing a new evaluation system from the development stage, strengthening the approval review system, and promoting efficiency improvement.

Total review time for new pharmaceuticals (priority review items) (median)		
At the end of the First-term Plan (end of FY 2008) 12 months	→	At the end of the Second-term Plan (end of FY 2013) 9 months

- Promote not only international harmonization by strengthening cooperation with the United States, the European Union, Asian countries, and relevant international organizations, but also proactive participation in Global Clinical Trials.
- Provide high-quality clinical trial consultations and develop a system to respond to all consultations.
- Set targets for shortening review times for over-the-counter (OTC) drugs and generic drugs.
- Set and achieve targets for solving the device lag based on action plans, by introducing the three-track system, strengthening other systems for approval review of medical devices, and promoting efficiency improvement.

Total review time for new medical devices (priority review items) (median)		
At the beginning of the Second-term Plan (end of FY 2009) 16 months	→	At the end of the Second-term Plan (end of FY 2013) 10 months

- Efficiently conduct reliability and conformity audits by gradually introducing document-based inspection at sponsor site, and promote the implementation of efficient GMP/QMS audits by proactively conducting on-site inspections at overseas manufacturing sites in Asian countries, etc.

5. — Prevention of Occurrence and Expansion of Adverse Drug Reactions by Enhancing Post-marketing Safety Measures —

The Agency shall:

- Organize assessment teams in individual fields to appropriately respond to the sophisticated and specialized evaluation of information on adverse drug reactions of pharmaceuticals, and improve the system for collecting, analyzing, and evaluating safety information.
- Enhance safety measures by developing infrastructures to access clinical information

databases, including Receipt data, by FY 2013.

- Develop a consistent system for managing the safety of pharmaceuticals from the clinical trial stage through the post-marketing stage, thereby making it possible to take more effective and reasonable safety measures.

Part 1 Measures to Achieve Targets with Regard to Items Related to Improvement in the Overall Management of Operations and the Quality of Services and Other Operations Rendered to the Public

— Conduct More Efficient and Flexible Management of Operations and Proactively Promote Information Provision to the Public —

Below are the measures that the Agency should take to achieve targets for efficiency improvement in the management of operations, as stipulated in Article 30, Paragraph 2, Item 1 of the Law on General Rules of Incorporated Administrative Agency, and to achieve targets for improvement in the quality of services and other operations rendered to the public, as stipulated in Article 30, Paragraph 2, Item 2 of said law.

<1> Efficient and Flexible Management of Operations

(a) Transparent and appropriate management of operations based on thorough compliance risk management

The Agency shall:

- Clarify operational targets and responsibilities of individual divisions and identify and resolve problems by managing operational progress on a daily basis.
- Develop and appropriately utilize an internal control process to secure the efficacy and efficiency of operations and the reliability of financial reports, to ensure compliance with laws in relation to operational activities, and to preserve assets, and shall proactively disclose details of measures that have been taken.
- Gather opinions on operational performance for each year and make use of them in the management of operations.
- Establish deliberative bodies to create opportunities for exchange of opinions with experts in a wide range of fields, and increase operational efficiency and secure operational fairness and transparency by seeking recommendations and improvement measures for operations and the management system from such bodies.
- Conduct efficient management through flexible personnel allocation tailored to specific situations and effective use of external experts.
- Appropriately utilize manuals for emergency management by reviewing them from time to time in response to particular situations, in order to thoroughly manage risks in the management of operations.

(b) Development of materials and information databases

The Agency shall:

- Make the most of part-time staff and control the number of full-time staff by advancing standardization in each operating process.
- Utilize electronic records to the greatest possible extent and promote the establishment of databases to make it possible to systematically organize and store all kinds of documentary information and to collect and analyze information.

(c) Promotion of systems optimization to enhance operational efficiency

The Agency shall:

- Develop basic policies for improvement in the systems environment of the Agency.
- Integrate by FY 2011 individual review systems which have been constructed in a fragmentary manner, based on the Optimization Plan for Operations and Systems that was developed at the end of FY 2007, and promote activities for optimizing operations and systems by constructing systems to advance information sharing in relation to review services, safety measures services and adverse health effects relief services.
- Increase operational efficiency by adding functions to information systems based on the actual status of operations of individual divisions, in parallel with implementation of the Optimization Plan for Operations and Systems.

<2> Cost Control through Increased Efficiency of Operations

(a) Retrenchment of general administrative expenses (Management divisions)

- By continuously improving operations and increasing the efficiency of management, the Agency is expected to make the following reductions in the budget for the Mid-term Plan relating to general administrative expenses (excluding expenses for office relocation and retirement allowance) at the end of the effective period for the mid-term targets.

  (1) Approximate 15% reduction in comparison with FY 2008.

  (2) General administrative expenses to be incurred starting in FY 2009 are to be reduced by approximately 12% compared with FY 2013 and FY 2009 for the increase, due to efforts to speed up approval reviews in accordance with the report issued by the Council for Science and Technology Policy, entitled “Revision of Structures Aimed at the Promotion of Science and Technology and the Return of Achievements to Society” (dated December 25, 2006; hereinafter referred to as the “Report of the Council for Science and Technology Policy”).

(3) Reductions in general administrative expenses with respect to activities to speed up approval reviews based on the "Action Program to Accelerate Reviews of Medical Devices" (dated December 11, 2008) are as follows:

- General administrative expenses to be incurred starting in FY 2009 shall be reduced by approximately 12% in comparison with FY 2013 and FY 2009 for the increase.
- General administrative expenses to be incurred starting in FY 2010 shall be reduced by approximately 9% in comparison with FY 2013 and FY 2010 for the increase.
- General administrative expenses to be incurred starting in FY 2011 shall be reduced by approximately 6% in comparison with FY 2013 and FY 2011 for the increase.
- General administrative expenses to be incurred starting in FY 2012 shall be reduced by approximately 3% in comparison with FY 2013 and FY 2012 for the increase.

(4) General administrative expenses to be incurred in FY 2009 shall be reduced by approximately 12% in comparison with FY 2013 and FY 2009 for the increase through efforts to strengthen and enhance safety measures in accordance with the Interim Report of the Committee for Verification of Drug-induced Hepatitis Cases and for Examination of Drug Administration to Prevent Similar Diseases, entitled "How Drug Administration Should Function to Prevent Similar Drug-induced Diseases" (dated July 31, 2008; hereinafter referred to as the "Interim Report of the Verification Committee on Drug-induced Hepatitis").

(b) Cost control of operating expenses based on efficient management of operations

- By increasing operational efficiency through the promotion of computerization, the Agency is expected to make the following reductions in the budget for the Mid-term Plan relating to operating expenses (excluding expenses for office relocation and benefit payments, and single-year expenses due to new project launches) at the end of the effective period for the Mid-term targets.

(1) Approximate 5% reduction in comparison with FY 2008

(2) Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase to speed up approval reviews in accordance with the Report of the Council for Science and Technology Policy.

(3) Reductions in operating expenses in consideration of activities to speed up approval reviews based on the "Action Program to Acceleration the Reviews of Medical Devices" are as follows:

- Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase
- Operating expenses to be incurred starting in FY 2010 shall be reduced by approximately

3% in comparison with FY 2013 and FY 2010 for the increase

- Operating expenses to be incurred starting in FY 2011 shall be reduced by approximately 2% in comparison with FY 2013 and FY 2011 for the increase

- Operating expenses to be incurred starting in FY 2012 shall be reduced by approximately 1% in comparison with FY 2013 and FY 2012 for the increase

(4) Operating expenses to be incurred starting in FY 2009 shall be reduced by approximately 4% in comparison with FY 2013 and FY 2009 for the increase through efforts to strengthen and enhance safety measures in accordance with the Interim Report of the Verification Committee on Drug-induced Hepatitis.

- At the end of the effective period for the Mid-term targets, administrative subsidies, excluding the amount for the office relocation which is scheduled during this Mid-term target period, are to be reduced by approximately 18% (or approximately 15% if subsidies are added to administrative subsidies for each year to partially cover expenses for office relocation) in comparison with FY 2013 and FY 2008 for the increase. The Agency is expected to set the next Mid-term targets based on the assumption of an approximate 18% reduction in comparison with FY 2008.

(c) Efficient collection of contributions

- The Agency shall efficiently conduct collection management in administrative processing related not only to the collection of ADR (adverse drug reaction) contributions, infection contributions, and safety measures contributions, but also to review of contribution rates for financial recalculation, by making use of the contribution collection management system.

- The collection rate for ADR contributions, infection contributions, and safety measures contributions should be no less than 99%.

(d) Ongoing reform in personnel expenses

- The Agency shall conduct efficient management based on the Law Concerning Promotion of Administrative Reforms to Realize a Streamlined and Efficient Government (Law No. 47 dated June 2, 2006) and reduce personnel expenses by at least 5% over the 5-year period commencing FY 2006, in comparison with the initial personnel expenses at the beginning of the reform in accordance with the Mid-term target 2-(2)-d.

* Standard value after corrections

"Initial personnel expenses at the beginning of the reform in accordance with the Mid-term target 2-(2)-d" are calculated by multiplying 709 (people) by personnel expenses per person for FY 2005.

- The Agency shall also continue to work to reform personnel expenses by FY 2011 in accordance with the Basic Policy 2006 for Economic and Fiscal Management and Structural Reforms (approved in a cabinet meeting on July 7, 2006) and based on reforms relating to government employees.

  * Standard value after corrections if the reform in personnel expenses is continued until FY 2011.

    "Initial personnel expenses at the beginning of the reform in accordance with the Mid-term target 2-(2)-d" are calculated by multiplying 723 (people) by personnel expenses per person for FY 2005.

- Moreover, the Agency shall verify its remuneration standard from the following perspectives. If there is no reasonable cause to maintain the standard, the Agency shall take the necessary measures to promptly realize a reasonable remuneration standard and publicly announce its verification results and activities:

  (1) Whether or not the remuneration standard for Agency staff is higher than that for government employees, taking into account factors such as office locations and the academic qualifications of employees

  (2) Whether or not it is possible to eliminate causes for the high remuneration standard for Agency staff, such as the high proportion of employees dispatched from the national government

  (3) Whether or not the appropriateness of the current remuneration standard can be satisfactorily explained, taking into account the large financial expenditure of the national government, the accumulated losses, the remuneration standards of private companies that are engaged in similar services, etc.

  (4) Whether or not explanation of the remuneration standard can gain full public understanding

(e) Securing of contract competitiveness and transparency

- The Agency shall in principle conclude contracts through open competitive bidding and shall promote appropriate optional contracts by taking the following measures:

  (1) Steadily implement and disclose activities based on the Plan for the Review of Optional Contracts.

  (2) Choose methods that can fully secure competitiveness and transparency, especially in planning competition and open recruitment, even where contracts are concluded through open competitive bidding.

  In audits by auditors and accounting auditors, the appropriateness of bidding and contracts shall be thoroughly checked.

(f) Examination of office relocation aimed at contributing to effective and efficient management of operations

- In consideration of convenience for applicants, the need for close cooperation with the Ministry of Health, Labour and Welfare, and the need to secure additional space in response to an increased workforce, and from the perspective of more effective and efficient management of operations, the Agency shall examine the feasibility of relocating its office to an appropriate site and shall then take the necessary measures during the effective period for the Mid-term targets.

<3> Improvement of Services to the Public

- The Agency shall take all appropriate measures, including those listed below, to steadily implement the PMDA Public Relations Strategic Plan, which was formulated in FY 2008:

(1) Public relations through Agency newsletters

(2) Regular provision and disclosure of information concerning the Agency to popular, high-consumption TV and print media

(3) Creation of English newsletters and provision of information to the Foreign Correspondents' Club of Japan and overseas media

(4) Strengthening and improvement of the system for responding to inquiries, suggestions, and complaints from of the public

The Agency also shall:

- Properly disclose information concerning its operations and activity results on its website, and enhance information provision to the general public by means of announcements through public relations journals, in order to enhance understanding of not only safety considerations regarding pharmaceuticals and medical devices but also the overall operations of the Agency.

- Conduct external audits in accordance with the system for incorporated administrative agencies, together with systematic internal audits and accounting audits, and disclose the results.

- Disclose its overall financial standing and the financial standing by account and by segment, in order to ensure transparency of its expenditures.

Part 2 Measures to Achieve Targets with Regard to Items Related to Improvement in the Management of Operations in Each Division and the Quality of Services and Other Operations Rendered to the Public

—Make effort to promote the safety triangle of review, safety, and relief as a mission of PMDA—

1 Relief Fund Services for Adverse Health Effects

Relief fund services for adverse health effects are based on a system unique to Japan in which the services make up a “safety triangle” that contributes to appropriate implementation of reviews and safety measures. To further promote these services, it is necessary not only to inform more people of the Adverse Drug Reaction Relief System and the Relief System for Infections Derived from Biological Products (hereinafter collectively referred to as “relief systems”) and appropriately operate them but also to adequately and promptly provide relief for those suffering from adverse drug reactions and infections derived from biological products. Based on this necessity, the Agency shall take the following measures.

<1>Expansion and Review of the Provision of Information Concerning the Relief Systems

(a) Disclosure of benefit payment cases

- The Agency shall continue to seek to gain understanding by the public, healthcare professionals and marketing authorization holders as to the reality of benefit payments and to broadly inform them of the relief systems by disclosing benefit payment cases, operational statistics and other similar data on its website.

(b) Provision of information concerning the relief systems

- The Agency shall review methods of providing information from the perspectives of user-friendliness and understandability for information receivers, including the need for improvement of brochures and instruction manuals relating to application for relief benefit payments and improvement in the content of information provided via the Internet.

<2>Proactive Public Relations Activities to Broadly Inform the Public about the Relief Systems

The Agency shall:

- Examine and proactively implement effective public relations activities in relation to the relief systems.

- Continue to expand the reach of information on the relief systems by making use of media such as websites and newspaper publicity.

- Promote existing measures, such as information provision in cooperation with concerned bodies, in order to realize more widespread awareness among the public, healthcare professionals and marketing authorization holders of the systems and to gain deeper understanding among such groups; improve visibility by the end of the effective period for the Mid-term targets by intensively implementing the measures listed below; and conduct annual visibility surveys, and verify the results.

(1) Promote public relations by making use of medicine bag to provide patients with comprehensive information about the systems.

(2) Promote public relations to intern clinicians and students attending pharmaceutical sciences faculties and nursing training facilities in order to comprehensively inform healthcare professionals about the systems.

(3) Promote public relations by making use of opportunities to educate and train medical representatives (MRs) in order to comprehensively inform them about the systems.

(4) Inform students nationwide about the systems by supporting the provision of documents that can be used as educational materials for pharmaceutical education at junior high schools, etc.

<3>Securing of Efficient Operation of Consultation Services

- The Agency shall allocate full-time staff for consultation services and ensure the provision of a system designed exclusively for acceptance of consultations in relation to use of the systems and procedures for benefit payments for adverse drug reactions and infections.

<4> Promotion of Improvement in Operational Efficiency by Making Use of Databases

The Agency shall:

- Promote the accumulation of information related to relief benefit services for adverse drug reactions (especially information related to offending drugs and adverse health effects) on databases, statistically process and analyze the accumulated data from all perspectives, and operate a system for prompt and efficient payment of relief benefits based on the analysis results.

- Upgrade the systems and develop operation support tools in response to increases in relief benefit claims and operational situations.

<5> Promotion of Prompt Processing of Relief Benefit Claims

(a) Investigation and organization of the facts supplied in the contents of claims

- In order to promptly process relief benefit claims, the Agency shall, upon receiving a claim for relief benefit services, investigate and organize the facts supplied in the contents of such claim and request the Minister of Health, Labour and Welfare to make medical and pharmaceutical judgments on such claim.

(b) Prompt administrative processing within standard administrative processing time

- With regard to administrative processing time from claim submission to payment approval/rejection judgments, the Agency processed more than 60% of total claims within 8 months during the First Mid-term Plan period through the prompt investigation and organization mentioned above in (a) in

cooperation with the Ministry of Health, Labour and Welfare. By further promoting prompt administrative processing, the Agency aims to process more than 60% of all annual total payment approval/rejection judgments within 6 months, by FY 2013.

- However, the period during which administrative processing cannot be conducted because of the need for additional or supplementary documents and investigations, which are required in respect of claimants and medical institutions for the purposes of making medical and pharmaceutical judgments, shall be excluded from administrative processing time.

<6> Promotion of Cooperation with Review Divisions and Safety Measures Divisions

- The Agency shall appropriately provide review divisions and safety measures divisions with information in cooperation with internal divisions, with paying attention to personal information, especially in relief payment cases.

<7> Appropriate Implementation and Expansion of Health and Welfare Services

The Agency shall:

- Continue to conduct investigative research in order to obtain information for the examination of QOL improvement measures for sufferers of severe and rare adverse health effects caused by pharmaceuticals based on the results of a survey on the actual status of adverse health effects stemming from adverse drug reactions.

- Progressively provide mental consultation services from FY 2009.

<8> Appropriate Implementation of Healthcare Allowances for SMON Patients and HIV-positive Patients Affected Through Blood Products

- In providing healthcare allowances for SMON patients and HIV-positive patients affected through blood products, the Agency shall appropriately implement operations based on the contents of consignment contracts, while giving due consideration to the confidentiality of personal information.

<9> Appropriate Implementation of Benefit Payment Services to Assist Individuals Affected by Hepatitis C Through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

- In implementing benefit payment services to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus, the Agency shall appropriately implement operations, while giving due consideration to the confidentiality of personal information.

2 Reviews and Related Services and Safety Measures Services

With regard to reviews and related services and safety measures services, the Agency shall provide improved pharmaceuticals and medical devices to medical institutions more promptly and safely in order to enable the public to confidently make use of pharmaceuticals and medical devices that are of world class. In addition, the Agency shall ensure the proper use of such pharmaceuticals and medical devices, work to prevent the occurrence of health hazards, and appropriately and promptly respond in the event that any such hazard occurs. The Agency shall take the following measures to reinforce the system for consultations and reviews, and for post-marketing safety measures, and to organically link the operations so that pharmaceuticals and medical devices can fulfill their purposes over longer periods of time.

<1> Faster Access to the Latest Pharmaceuticals and Medical Devices

<New drugs>

Based on the 5-year Strategic Plan to Generate Innovative Pharmaceuticals and Medical Devices (dated April 26, 2007) and action plans for expediting reviews, the Agency shall take the following measures with the aim of shortening the time between first approval of new drugs in the United States and the European Union and approval in Japan by 2.5 years by FY 2011.

With regard to the action plans for expediting reviews, including review times for new drugs, the Agency shall evaluate and verify progress annually, shall take additional measures where necessary, and shall verify the results after the action plans end in FY 2011.

(a) Implementation of precise and prompt reviews

The Agency shall:

- Accelerate the review process by approximately doubling the number of review teams for new drugs and biological drugs compared with the current situation.
- Enhance the progress management function in review services and increase transparency for applicants in the progress and forecasting of reviews, by steadily implementing the project management system.
- Promote standardization of the process for review services by not only fully informing the public of the “Points to Be Considered by the Review Staff Involved in the Evaluation Process for New Drugs” but also promoting and disclosing manuals for the process for review services, in order to promote transparency and efficiency in review services.
- Strengthen cooperation with academia and medical experts, provide consultations and conduct reviews based on up-to-date medical care trends and needs, and advance cooperation on proper use of pharmaceuticals.

- Precisely and promptly conduct reviews and provide consultations by flexibly organizing teams and maintaining linkage between consultations and reviews, in order to realize consistency in contents between clinical trials and reviews.

- Precisely and promptly conduct reexamination for new drugs, and appropriately respond to reevaluation.

- Promote computerization in clinical trial consultations and review procedures, and improve staff IT literacy.

- Promote submission of electronic application documents for new drugs by further developing an environment for eCTD.

- Precisely and promptly conduct reviews by promoting the development of standards for the quality of pharmaceuticals, such as the Japanese Pharmacopoeia.

(b) Introduction of a new review method, etc.

The Agency shall:

- Further strengthen linkage among clinical trial consultations, review services, and safety measures services for new drugs, gradually seek to introduce a system for evaluating the safety and efficacy of new drugs from the development stage, starting FY 2009, and conduct necessary reviews from time to time.

- Gradually seek to introduce a system for consistently managing the safety of new drugs from the stage of clinical trials through the post-marketing stage, starting FY 2009.

(c) Target-setting to solve the drug lag

- Targets shall be as follows with regard to the total review time (from application date to approval date; same below) for pharmaceutical approval applications submitted on and after April 1, 2004, the administrative review time (including the review time for the Ministry of Health, Labour and Welfare; same below) and the applicant elapsed time, and both the government and applicants shall make efforts to achieve the targets.

  (1) Review times for new drugs, i.e. priority review items designated by the Minister of Health, Labour and Welfare (hereinafter referred to as “priority items”)

  50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	11 months	6 months	5 months
2010	10 months	6 months	4 months
2011	9 months	6 months	3 months
2012	9 months	6 months	3 months
2013	9 months	6 months	3 months

(2) Review time for new drugs (standard items)

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	19 months	12 months	7 months
2010	16 months	11 months	5 months
2011	12 months	9 months	3 months
2012	12 months	9 months	3 months
2013	12 months	9 months	3 months

(d) Promotion of international harmonization and Global Clinical Trials

Based on the PMDA International Strategic Plan, the Agency aims to improve medical services and establish its international status by proactively promoting international activities in association with the Ministry of Health, Labour and Welfare and in cooperation with the United States, the European Union and Asian countries, and is implementing a range of measures, including the following:

(1) Strengthening of cooperation with the United States, the European Union, Asian countries, and relevant international organizations

The Agency shall:

- Promote bilateral talks and information sharing based on confidentiality agreements, in cooperation with the U.S. Food and Drug Administration (FDA), the European Commission and the European Medicines Agency (EMEA).

- Develop cooperative relationships with other Western and Asian countries, and relevant international organizations.

- Strengthen cooperation with other countries on conducting investigations into standards for implementing non-clinical tests relating to the safety of pharmaceuticals (hereinafter referred to as Good Laboratory Practice: GLP), standards for implementing clinical trials for pharmaceuticals (hereinafter referred to as Good Clinical Practice: GCP), and standards for manufacturing control and quality control of drugs and quasi-drugs (hereinafter referred to as Good Manufacturing Practice: GMP), and develop an environment for exchange of investigation reports.

(2) Strengthening of activities for international harmonization

The Agency shall:

- Promote harmonization of Japanese standards with international guidelines, such as standards for developing application data for approval, which were agreed upon among Japan, the United States and the European Union at the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (hereinafter referred to as "ICH"), and promote international harmonization of pharmacopoeia in the Pharmacopoeial Discussion Group (PDG).

- Proactively express Japan's opinions at international conferences such as ICH and contribute to the establishment of international standards.

- Participate in international harmonization activities led by WHO, OECD and other relevant international organizations, and contribute to such activities.

(3) Promotion of personnel exchanges

The Agency shall:

- Proactively send staff members to international meetings and conferences and increase opportunities to send personnel to the FDA and the EMEA, in order to promote the establishment of networks with overseas regulatory agencies.

- Promote personnel exchanges with countries, including China and South Korea, and international organizations, and establish a system for regular exchange of information related to reviews and safety measures.

(4) Fostering of internationally minded human resources with communication skills

The Agency shall:

- Develop and implement staff training programs, including communications with overseas parties and attendance at international conferences, in order to foster the development of personnel who can actively participate in ICH and other international conferences.

- Help directors and staff members to improve their foreign language skills, such as English, by continuing and strengthening its foreign language training.

(5) Improvement and strengthening of international publicity and information provision

The Agency shall:

- Promote the disclosure of English translations concerning pharmaceutical regulations, details of

its services, product review reports, and safety information in order to strengthen and improve its English website.

- Give regular lectures and mount booth exhibits at international meetings.
- Promote information provision to overseas press.

(6) Promotion of Global Clinical Trials

The Agency shall:

- Promote proactive participation by Japan in Global Clinical Trials by appropriately responding to applications for Global Clinical Trial consultations based on test design guidance, in order to promote Global Clinical Trials.
- Proactively develop an environment for significantly increasing the number of Global Clinical Trials by FY 2013.

(e) Efficient implementation of clinical trial consultations

The Agency shall:

- Increase opportunities to provide guidance and consultations before applications for approvals are made through ongoing priority consultations and advance confirmation of application documents.
- Firmly maintain the current time from applications for clinical trial consultations to face-to-face consultations (approximately 2 months) with regard to clinical trial consultations for new drugs, and accelerate procedures for priority clinical trial consultations by accepting applications on an as-needed basis.
- Provide high-quality clinical trial consultation services for new drugs and respond to all consultations. Up to 1,200 cases shall be secured as processable cases by FY 2011.

(f) Promotion of evaluation of new technologies

The Agency shall:

- Utilize external highly knowledgeable experts during the effective period for the Mid-term targets, in order to evaluate the latest technologies, such as biotechnology, genomics, and regenerative medicine.
- Cooperate with the government to develop national guidelines for evaluating products to which the latest technologies have been applied, and proactively disclose points-to-consider for evaluation.
- Promptly conduct preliminary reviews on cell and tissue-derived pharmaceuticals and

pharmaceuticals for gene therapy before clinical trials are conducted. With regard to preliminary reviews based on the Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (hereinafter referred to as the "Cartagena Law"), the administrative review time shall be 6 months for approval of first-class use and 3 months for confirmation of second-class use, and a 50% median shall be targeted for each class.

- Develop a system for responding to pharmaceutical affairs consultations from an early stage in order to enable appropriate development of new pharmaceuticals based on the latest technologies, so that more effective and safer pharmaceuticals can be promptly provided to the public.

- Take necessary measures to respond to "special districts for development of advanced medical care" (hereinafter referred to as "Super Special Consortia") as presented in the 2008 Basic Policy for Economic and Financial Reform.

<Over-the-counter drugs and generic drugs>

The Agency shall take the following measures to promote self-medication and wide use of generic drugs.

(a) Implementation of precise and prompt reviews

The Agency shall:

- Strengthen cooperation with academia and medical experts, provide consultations and conduct reviews based on up-to-date medical care trends and needs, and shall advance cooperation on proper use of pharmaceuticals.

- Promote computerization in review procedures and improve staff IT literacy.

- Precisely and promptly conduct reviews by promoting not only the development of guidelines on the quality of pharmaceuticals, including the Japanese Pharmacopoeia, but also official determination of additive specifications.

- Enhance and increase efficiency in the review system for Chinese herbal medicine formulations and natural medicine formulations.

(b) Target-setting to shorten review times

- Targeted administrative review times for drug approval applications submitted on and after April 1, 2004, shall be as follows and the government shall make efforts to achieve the targets:

(1) Review time for generic drugs

By FY 2011, 50% (median) shall definitely be achieved for the review time determined in the following table.

Item	Administrative review time
Generic drugs	10 months

(2) Review time for over-the-counter drugs (OTC drugs)

By FY 2011, 50% (median) shall definitely be achieved for the review time determined in the following table.

Item	Administrative review time
OTC drugs	8 months

(3) Review time for quasi-drugs

By FY 2011, 50% (median) shall definitely be achieved for the review time determined in the following table.

Item	Administrative review time
Quasi-drugs	5.5 months

(c) Efficient implementation of clinical trial consultations

The Agency shall:

- Establish a pre-application consultation system for generic drugs, separately from simple consultations.
- Enhance consultations for OTC drugs by reviewing its consultation system so that consultations may be accepted from the pre-development stage until immediately prior to application.
- Improve pre-application consultations for quasi-drugs for which expert discussions are needed.

<Medical devices>

Based on the Action Program to Accelerate Reviews of Medical Devices, the Agency shall take the following measures with the aim of shortening the time between first approval of new medical devices in the United States and approval in Japan by 19 months.

(a) Implementation of precise and prompt reviews

The Agency shall:

- Strengthen cooperation with academia and medical experts, provide consultations, and conduct reviews based on up-to-date medical care trends and needs, and advance cooperation on proper use of medical devices.

- Gradually implement the three-track review system, starting from FY 2011, by establishing review teams exclusively for new medical devices, improved medical devices and generic medical devices, respectively, with the aim of increasing efficiency and speed in review services.

- Promote computerization in review procedures and increase staff IT literacy.

- Promote standardization of the process for review services by developing process manuals and informing the public of such documents in order to promote transparency of and increase efficiency in reviews, and strengthen management functions by enhancing the progress management function of each team in review services.

- Progressively examine and rationalize application documents for improved medical devices and generic medical devices (including application documents for approvals of partial changes), starting from FY 2009, in collaboration with the Ministry of Health, Labour and Welfare.

(b) Introduction of a new review method, etc.

The Agency shall:

- Further strengthen linkage among clinical trial consultations, review services, and safety measures services for new medical devices, develop guidance for the introduction of a system for evaluating the safety and efficacy of new medical devices from the clinical trial consultation stage within FY 2009, and introduce it in FY 2010.

- Partially introduce the short-term review method for approvals for partial changes in the specific contents of medical devices in FY 2009 and fully introduce it in FY 2010.

- Accelerate reviews through not only cooperation on development of the Medical Device Approval Standards, the Medical Device Certification Standards, and the Medical Device Review Guidelines, but also disclosure promotion on the Agency's website, and clarify the following points in particular:

  (1) The scope within which applications for approvals for partial changes related to minor changes are not required and the scope within which notifications for minor changes are required, within FY 2009.

  (2) Cases for which clinical trials are required, within FY 2009.

  (3) Start to examine clarification of not only the scope of one item but also procedures for similar changes in FY 2009, and clarify policies.

- Introduce the equivalence review method for generic medical devices, starting from FY 2009.

- Prioritize reviews for high-risk items, such as Class-III and Class-IV medical devices, in response to the transfer of all Class-II medical devices to the third-party certification system by FY 2011, in

principle.

(c) Target-setting to solve the device lag

- Targets shall be as follows with regard to the total review times for medical device approval applications submitted on and after April 1, 2004, administrative review times and applicant elapsed times, and both the government and applicants shall make efforts to achieve the targets.

(1) Review times for new medical devices (priority items)

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	16 months	8 months	9 months
2010	16 months	8 months	9 months
2011	15 months	7 months	8 months
2012	13 months	7 months	6 months
2013	10 months	6 months	4 months

(2) Review times for new medical devices (standard items)

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	21 months	8 months	14 months
2010	21 months	8 months	14 months
2011	20 months	8 months	12 months
2012	17 months	7 months	10 months
2013	14 months	7 months	7 months

(3) Review times for improved medical devices (approved with clinical data)

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	16 months	8 months	7 months
2010	16 months	8 months	7 months
2011	14 months	7 months	6 months
2012	12 months	7 months	5 months
2013	10 months	6 months	4 months

(4) Review times for improved medical devices (approved without clinical data)

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	11 months	6 months	5 months
2010	11 months	6 months	5 months
2011	10 months	6 months	5 months
2012	9 months	5 months	4 months
2013	6 months	4 months	2 months

(5) Review times for generic medical devices

50% (median) shall definitely be achieved for each review time determined in the following table.

Fiscal Year	Total review time	Administrative review time	Applicant elapsed time
2009	8 months	5 months	3 months
2010	6 months	4 months	2 months
2011	5 months	4 months	1 month
2012	4 months	3 months	1 month
2013	4 months	3 months	1 month

(d) Promotion of international harmonization and Global Clinical Trials

Based on the PMDA International Strategic Plan, the Agency aims to improve medical services and establish its international status by proactively promoting international activities in association with the Ministry of Health, Labour and Welfare and in cooperation with the United States, the European Union and Asian countries, and is taking a range of measures including the following:

(1) Strengthening of cooperation with the United States, the European Union, Asian countries, and relevant international organizations

The Agency shall:

- Promote bilateral talks, HBD activities and information sharing based on confidentiality agreements, in cooperation with the U.S. Food and Drug Administration (FDA).
- Develop cooperative relations with other Western and Asian countries, and relevant international organizations.
- Strengthen cooperation with other countries on conducting investigations into GLP standards, GCP standards, and standards for manufacturing control and quality control of medical devices and *in vitro* diagnostics (hereinafter referred to as Quality Management System: QMS), and develop an environment for exchange of investigation reports.

(2) Strengthening of activities for international harmonization

The Agency shall:

- Promote harmonization of Japanese standards with international standards, such as standards for developing application data for approval, which have been determined at the Global Harmonization Task Force (hereinafter referred to as “GHTF”), and other international standards, including ISO standards.

- Proactively express Japan’s opinions at international conferences such as GHTF and contribute to the establishment of international standards.

- Participate in international harmonization activities led by WHO, OECD, and other relevant international organizations, and contribute to such activities.

(3) Promotion of personnel exchanges

The Agency shall:

- Proactively send staff members to international meetings and conferences and increase opportunities to send personnel to the FDA, in order to promote the establishment of networks with overseas regulatory agencies.

- Promote personnel exchanges with countries, including China and South Korea, and international organizations, and establish a system for regular exchange of information related to reviews and safety measures.

(4) Fostering of internationally minded human resources with communication skills

The Agency shall:

- Develop and implement staff training programs, including communications with overseas parties and attendance at international conferences, in order to foster the development of personnel who can actively participate in GHTF and other international conferences.

- Help directors and staff members to improve their foreign language skills, such as English, by continuing and strengthening its foreign language training.

(5) Improvement and strengthening of international publicity and information provision

The Agency shall:

- Promote the disclosure of English translations concerning pharmaceutical regulations, details of its services, product review reports, and safety information, in order to strengthen and improve its English website.

- Give regular lectures and mount booth exhibits at international meetings.
- Promote information provision to overseas press.

(e) Efficient implementation of clinical trial consultations

The Agency shall:

- Increase opportunities to provide guidance and consultations before applications for approvals are made, through ongoing priority consultations and advance confirmation of application documents.
- Accelerate procedures for clinical trial consultations for new medical devices by shortening the time from consultation applications to face-to-face consultations, and the time until the first face-to-face priority clinical trial consultations.
- Provide high-quality clinical trial consultation services and respond to all consultations. Up to 200 cases shall be secured as processable cases by FY 2013.
- Review consultation classifications within FY 2009, and improve consultation services, including clinical trial consultations, qualitatively and quantitatively.

(f) Promotion of evaluation of new technologies

The Agency shall:

- Utilize external highly knowledgeable experts during the effective period for the Mid-term targets, in order to evaluate the latest technologies, such as biotechnology, genomics, and regenerative medicine.
- Cooperate with the government to develop national guidelines for evaluating products to which the latest technologies have been applied, and proactively disclose points-to-consider for evaluation.
- Promptly conduct preliminary reviews on cell and tissue-derived medical devices before clinical trials are conducted. With regard to preliminary reviews based on the “Cartagena Law,” the administrative review time shall be 6 months for approval of first-class use and 3 months for confirmation of second-class use, and 50% (median) shall be targeted for each class.
- Develop a system for responding to pharmaceutical affairs consultations from an early stage in order to enable appropriate development of new medical devices based on the latest technologies, so that more effective and safer medical devices can be promptly provided to the public.
- Take necessary measures to respond to the Super Special Consortia.

<All kinds of audits>

With regard to pharmaceuticals and medical devices, the Agency shall conduct a full range of audits and take the following measures to promote appropriate implementation of tests and clinical trials related to applications for approval, secure the reliability of application documents, and properly maintain and manage the manufacturing process and the quality management process.

(a) Efficient implementation of conformity audits for new drugs

- In consideration of further computerization of clinical trial materials and records in the future and the development of facilities for Global Clinical Trials (medical institutions and corporate bases for clinical trial operation and management systems) in Japan and abroad, the Agency shall review the current audit method, which was developed on the assumption of domestic clinical trials. With regard to conformity audits for new drugs, the Agency shall gradually introduce a method whereby its staff members visit companies and conduct audits (document-based inspection at sponsor site), starting from FY 2009, with a target of conducting 50% or more of audits based on this method by FY 2013.

- For the purpose of increasing efficiency in conformity audits that are conducted for individual application items, the Agency shall examine and verify the introduction of a GCP audit system to investigate the systems of companies, medical institutions and the Institutional Review Board, all of which implement clinical trials.

(b) Efficient implementation of reexamination conformity audits

- With regard to items on which post-marketing surveillances have already been conducted, the Agency shall increase efficiency by conducting GPSP on-site inspections and document-based inspections at more appropriate and effective times.

(c) Efficient implementation of GMP/QMS audits

The Agency shall:

- Examine and conduct efficient GMP/QMS audits.

- In consideration of risks, construct a system for conducting on-site GMP/QMS audits at the following frequencies by FY 2013:

  (1) Facilities approved by the Minister of Health, Labour and Welfare: basically once every 2 years

  (2) Facilities approved by governors (only manufacturing facilities for the Agency's audit items): basically once every 5 years

  (3) Overseas facilities (only manufacturing facilities for the Agency's audit items, excluding manufacturing facilities for items such as MRA): to be properly conducted based on past audit records

- Proactively conduct on-site inspections at manufacturing sites in overseas countries, including Asian countries.

- Promote linkage between audits and reviews and improve quality in both operations by allocating persons in charge of reviews to GMP/QMS audit teams, and persons in charge of GMP/QMS audits to review teams.

<2> Improvement of Reliability of Review Services and Safety Measures Services

(a) Improvement of training program

- The Agency shall evaluate the state of implementation of the pharmaceuticals review training program that was developed in FY 2007, improve its contents, and steadily implement it in order to improve the quality of review services and safety measures services.

- During FY 2009, the Agency shall develop an advanced training program that focuses on review services and safety measures services for medical devices, under which personnel will be sent to domestic and overseas universities and research institutes, and which will reference training methods employed by review organizations of the FDA (U.S.).

- Given the critical need for relevant clinical experience and knowledge when considering appropriate safety measures for pharmaceuticals and medical devices, as well as medical safety measures, the Agency shall provide its staff with training on clinical practice sites and inspection sites.

- The Agency shall work to improve understanding of manufacturing processes and quality management methodology with respect to medical devices, and to improve the quality of post-marketing safety measures services for medical devices.

(b) Promotion of cooperation with overseas regulatory agencies

- With regard to reviews and related services and safety measures services, the Agency shall strengthen cooperation with regulatory agencies in the United States, the European Union, and Asian Countries during the effective period for the Mid-term targets. In particular, the Agency shall develop a system to enable the gathering of more detailed information and the exchange of more detailed opinions in real-time with the FDA (U.S.) and the EMEA (EU).

(c) Promotion of exchanges with outside researchers and investigative research

The Agency shall:

- Cooperate on the development of infrastructures for clinical research and clinical trials practice sites, and diffusion of regulatory science, by promoting exchanges through acceptance of graduate students at joint graduate schools, while proactively ascertaining domestic and overseas research trends in regulatory science and providing information on research activities.

- Properly induct graduate students by developing internal regulations.

(d) Promotion of responses to pharmacogenomics

- The Agency shall cooperate to develop national guidelines for evaluating products to which new technologies have been applied during the effective period for the Mid-term targets.

- To promote the use of pharmacogenomics for the development of pharmaceuticals, the Agency shall cooperate on the development national guidelines for evaluating products, and shall consider how to contribute to the establishment of international methodology through the promotion of cooperation and information sharing with the overseas regulatory agencies, such as establishing a system to provide advice, in association with the FDA (U.S.) and the EMEA (EU).

(e) Promotion of appropriate clinical trials

- The Agency shall implement educational activities aimed at diffusing appropriate clinical trials based on on-site inspections at medical institutions, in order to secure the quality of clinical trials in Japan during the effective period for the Mid-term targets.

(f) Promotion of information provision such as product review reports

- To promote operational transparency, the Agency shall proactively promote activities to improve information disclosure, in cooperation with the Ministry of Health, Labour and Welfare, by promptly providing product review reports, which include the results of priority reviews, and other information related to review services in a more accessible form for the public and healthcare professionals, and by expanding the contents of review information.

- Both the government and applicants shall make efforts to release review reports on new drugs and new medical devices on the website of the Agency, immediately after approval, and shall appropriately deal with the disclosure of drug reexamination reports. The outlines of documents related to new drugs and new medical devices shall also be released on the website within 3 months after approval.

- The Agency shall consider how to respond to requests for disclosure of review information, in cooperation with the Ministry of Health, Labour and Welfare during the effective period for the Mid-term targets, and shall take appropriate measures based on the results.

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

- The Agency shall utilize external experts with appropriate knowledge. On such occasions, the Agency shall secure neutrality and fairness in review services and safety measures services based on fair rules, and shall review the rules as necessary.

(h) Enhancement in the quality of review and safety services by advancing information systems

- In review services and safety measures services with regard to which it is expected that the volume of information handling will increase and that the correlativity and the accuracy of information will improve, the Agency shall enhance the quality of the services by adding functionality to information systems in response to such changes.

<3> Strengthening and Improvement of Safety Measures Services

By developing a system for post-marketing safety measures, the Agency shall work with the Ministry of Health, Labour and Welfare to promptly and precisely take steps to prevent occurrence and expansion of suffering due to adverse drug reactions, in order to secure medical care for patients and to ensure that pharmaceuticals play effective roles in medical practices.

The Agency shall also strengthen cooperation between review divisions and safety measures divisions as a basis for the acceleration of approval reviews, in order to make it possible to consistently manage and evaluate risks and benefits, from pharmaceutical research and development through reviews to the post-marketing stage.

Staff members of the Agency shall understand the basic approaches to analyzing and evaluating adverse drug reactions. In other words, in implementing these services, they shall evaluate adverse drug reactions without prejudice, based on respect for life and the latest scientific knowledge. They shall also assume worst-case scenarios at all times, and shall develop and implement safety measures based on the precautionary principle, because progress in medical and pharmaceutical sciences occasionally reveals the uncertainty of preceding knowledge.

(a) Strengthening of information gathering on adverse drug reactions and malfunctions

The Agency shall:

- Take measures to increase the flow of reports from medical institutions, in cooperation with the Ministry of Health, Labour and Welfare.

- Construct a system to make use of adverse drug reactions from patients in the development of safety measures, in cooperation with the Ministry of Health, Labour and Welfare.

- Strengthen and refine the system for reporting on information related to adverse drug reactions and malfunctions based on the status of international system development, reflected ICH E2B guideline etc, and the development of information technologies, and promote efficient and effective collection of safety information.

- Computerize information on adverse drug reactions, such as drug use result survey, and build databases in order to make use of computerized information in the development of safety measures.

(b) Organization of information on adverse drug reactions and systemization of evaluation and analysis

<Organization and systemization of evaluation and analysis>

The Agency shall:

- Organize assessment teams by area (approximately 12 teams) by FY 2011 according to therapeutic categories and clinical fields in response to review divisions, in order to precisely respond to sophisticated and specialized evaluation of information on adverse drug reactions. The Agency shall significantly strengthen and improve the system for organizing, evaluating, and analyzing information on adverse drug reactions by gradually increasing the number of teams, and shall simultaneously take measures to make use of IT technologies and carefully examine all domestic reports on adverse drug reactions and infections.

- Proactively make use of the data mining method and make improvements on an as-needed basis by referring to overseas cases, in order to detect adverse drug reactions at an early stage and take measures to prevent expansion, by organizing, evaluating, and analyzing information on such reactions.

- Gradually develop a system for independently conducting follow-up investigations in relation to reports from medical institutions on adverse drug reactions, starting from FY 2009, and covering all reports by FY 2010.

- Standardize the process from the acquisition of information on adverse drug reactions to the planning of safety measures, including revision of package inserts, increase transparency in the process, and improve accuracy and speed in processing.

<Guidance and consultation system for companies>

The Agency shall:

- Reflect the latest knowledge in package inserts, even after approval reviews are conducted, recognizing the importance of the documents to companies as a means of providing medical institutions with the latest knowledge, and shall clarify a system for the official confirmation required, in association with the Ministry of Health, Labour and Welfare.

- Steadily speed up the process by setting targets for planning of safety measures and promoting standardization and operational efficiency in the process, and shall examine targets from various aspects, including shortening the time between first interviews with companies and notification of investigation results in terms of medians, as compared with the current period.

- Promptly respond to consultations from companies that voluntarily develop and revise package inserts for pharmaceuticals and medical devices, as well as information provision tools for healthcare professionals and patients.

- Promptly respond to medical safety consultations from companies so that pharmaceuticals and medical devices may be more safely used in medical practices.

<Sophistication of safety measures>

The Agency shall:

- Develop by FY 2013 infrastructures for access to clinical information databases that include Receipt data, conduct pharmaceutical and epidemiological analyses, and quantitatively evaluate pharmaceutical risks. Specifically, the Agency shall start to make use of the infrastructures on a trial basis in FY 2011, and shall by FY2013 establish a system for conducting investigations on the frequency of occurrence of adverse drug reactions, together with pharmaceutical and epidemiological analyses.

- Construct a system for gathering and evaluating data on the operational status of high-risk, implantable tracking medical devices (implantable ventricular-assist devices), such as the occurrence rate of malfunctions over time, and appropriately utilize such system in the development of safety measures.

- Ascertain the occurrence rate of malfunctions which occur at a constant rate, i.e., not due to structural failures but rather to the characteristics of medical devices, and develop scientific evaluation methods.

- Promote investigative research on the application of pharmacogenomics to post-marketing safety measures.

(c) Establishment of a post-marketing safety system through information feedback

The Agency shall:

- Double the number of accesses to the website for information services on pharmaceuticals and medical devices, by FY 2013.

- Make line lists of adverse drug reactions more user-friendly for relevant parties, and shorten the time between reporting on adverse drug reactions and disclosure to 4 months, starting from FY 2011.

- Promptly release reports from medical institutions on adverse drug reactions to be studied, in the line lists, starting from FY 2010.

- Post instructions relating to the revision of package inserts for ethical pharmaceuticals on its website within 2 days after written instructions are provided.

- Start in FY 2009 to consider utilization of adverse reaction report data and drug use result data by relevant parties for investigative research, starting from FY 2011.

- Improve the contents of the information delivery service concerning pharmaceuticals and medical devices, and strongly promote registration of both persons responsible for safety management of pharmaceuticals and those responsible for safety management of medical devices who work in this service are at medical institutions and pharmacies, in cooperation with relevant organizations. By taking these measures, the Agency shall register approximately 60,000 information service delivery personnel by FY 2011, and approximately 150,000 by FY 2013.

- Provide information on adverse drug reactions and malfunctions, such as cases used as bases for revising package inserts for ethical pharmaceuticals and medical devices.

- Provide consultation services on pharmaceuticals and medical devices for general consumers and patients so that they may make use of pharmaceuticals and medical devices with a sense of safety and security.

- More effectively inform patients about the availability Drug Guide for Patients and improve convenience in order to strengthen patient information provision.

- Improve the quality of drug administration guidance information provided to patients.

- Examine “Urgent Safety Information” and consider methods of providing information to medical institutions, during FY 2009, in cooperation with the Ministry of Health, Labour and Welfare, and properly deal with this issue based on the results.

- Completely review “Urgent Safety Information” and “Pharmaceuticals and Medical Devices Information,” and promote measures to enable medical institutions to more easily discern the urgency and importance of provided information, in cooperation with the Ministry of Health, Labour and Welfare.

- Provide improved information to promote the proper use of generic drugs.

- Regularly provide medical care safety information in order to foster safer use of pharmaceuticals and medical devices in medical practices.

- Provide better-quality information by collecting medical care safety information submitted by individual professional organizations.

- Explore other ways of providing higher-quality information to the general public.

(d) Cooperation with relief services and a consistent safety management system from review stage

The Agency shall:

- Utilize information on adverse health effects relief services in the development of safety measures services, giving due consideration to protection of personal information.

- Gradually introduce, from FY 2009, a consistent management system for the safety of pharmaceuticals from the clinical trial stage through post-marketing, under which persons in charge of review services and those in charge of safety measures services will jointly provide advice on new pharmaceuticals, and put this system into full-scale operation by FY 2011. The Agency shall also develop an information support system to facilitate efficient implementation of these services.

- Strengthen the management function for overall safety measures services so that individual teams can organically link with each another and implement services more precisely.

- Make post-marketing surveillance and safety measures required at the time of approval, more reasonable and effective, in response to pharmaceutical risks and in harmonization with international activities for post-marketing safety measures; appropriately and in a timely manner evaluate the status of implementation and the effects; and construct a system for conducting reviews as necessary, in cooperation with the Ministry of Health, Labour and Welfare. In FY 2009, the Agency shall begin considering how to achieve this goal with a view to introducing a new system by FY 2011.

- Appropriately and in a timely manner evaluate safety and efficacy information obtained through post-marketing surveillances on items approved under the condition of observational study of all cases, and promptly communicate the results to the public and healthcare professionals.

(e) Strengthening and improvement of follow-up on implemented safety measures

The Agency shall:

- Construct a system for independently investigating, confirming, and verifying the effects of safety measures, where necessary, starting from FY 2011, in parallel with evaluations conducted by companies.

- Confirm the state of implementation of safety measures by companies from the perspective of consistent information provision by companies to medical institutions, and progressively conduct investigations, starting from FY 2010, to verify the statuses of transmission and utilization of company-provided information within medical institutions.

- Conduct investigations on the status of utilization of information that the Agency has provided to general consumers and healthcare professionals in order to contribute to improvement of information provision services; analyze the needs and satisfaction levels of information recipients; and reflect the results in improvements to information provision services.

Part 3 Budget, Income and Expenditure Plan and Cash Flow Plan

1 Budget: See Attachment 1.
2. Income and Expenditure Plan: See Attachment 2.
3. Cash Flows Plan: See Attachment 3.

Part 4 Limit on Short-term Borrowing

<1> Limit on Borrowing

2.2 billion yen

<2> Reasons for Assuming Short-term Borrowing

(a) Shortage of funds due to delayed receipt of administrative subsidies, subvention, agent service fees, etc.

(b) Payment of retirement allowances to unscheduled retirees

(c) Shortage of funds due to other unforeseen contingencies

Part 5 Plan for Transferring or Mortgaging Important Property

No plan.

Part 6 Use of Surplus Funds

Surplus funds can be allocated in the review account for the following purposes:

- Resources for expenditure related to operational improvement
- Financial resources for training to improve personnel skill and knowledge levels

With regard to the adverse drug reactions relief account and the infection relief account, residues shall be organized as reserve funds in accordance with the provision of Article 31-4 of the Law on the Pharmaceuticals and Medical Devices Agency (Law No. 192, 2002).

Part 7 Other Issues Relating to Management of Operations Determined by Directions from the Competent Ministry

Matters relating to the management of operations determined by Article 4 of the Ministerial Ordinance Relating to the Management of Operations, Finance and Accounting of the Pharmaceuticals and Medical Devices Agency (MHLW Ministerial Ordinance No. 55 in FY 2004) shall be as follows:

<1> Personnel Matters

(a) The Agency shall:

- Systematically provide training opportunities in response to operational targets, and upgrade the skills, knowledge, and capabilities of personnel by improving training through cooperation with companies and exchanges with the Ministry of Health, Labour and Welfare, domestic and overseas universities, and research institutes, in order to improve overall quality of operations.

- Improve guidance for new staff in particular, and strengthen the system by expanding the workforce.
- Improve training programs for staff members who are on main career tracks in order to improve the skills, knowledge, and capabilities of clerical personnel who support organizational management.
- Implement a personnel evaluation system that is designed to help motivate staff, and appropriately reflect the results of personnel evaluation and the status of goal achievement in remuneration, pay raises, and promotions.
- Strategically allocate human resources in consideration of future career development, in order to maintain staff expertise and continuity of operations.

(b) In order to increase the permanent staff establishment, based on the Report of the Council for Science and Technology Policy, the Action Program to Accelerate Reviews of Medical Devices, and the Interim Report of the Verification Committee on Drug-induced Hepatitis, the Agency shall employ capable human resources with high levels expertise, mainly through open recruitment. In employing such human resources, the Agency shall be fully cognizant of its neutral status.

* Personnel Index

The upper limit of staff numbers at the end of the period shall be 108.1% of the numbers at the beginning of the period.

(Reference 1) Number of Agency permanent personnel at the beginning of the period: 695

Based on the Action Program to Accelerate the Reviews of Medical Devices,

Number of new permanent personnel in review divisions in FY 2010:	14
Number of new permanent personnel in review divisions in FY 2011:	14
Number of new permanent personnel in review divisions in FY 2012:	14
Number of new permanent personnel in review divisions in FY 2013:	14
Number of permanent personnel at the end of the period:	(up to) 751

(Reference 2) Total personnel expenses during the effective period for the Mid-term targets: 27,627 million yen (estimated)

However, the above-mentioned amount is equivalent to compensation for executives, basic pay for staff, various staff allowances, and overtime allowances.

(c) The Agency shall appropriately conduct personnel management by imposing certain constraints on the employment, allocation, and post-retirement reemployment of executives and employees, in order to avoid any suspicion of inappropriate relationships with pharmaceutical companies.

<2> Ensuring Security

The Agency shall:

- Continue to reinforce the internal security control system by effectively controlling entrances/exits, day and night, by means of entrance/exit control equipment for each office, in order to ensure security and protect confidential information.
- Ensure information security in respect of information systems.
- Maintain efficiency of the document management system based on the characteristics of stored documents.

July 11, 2008
Pharmaceuticals and Medical Devices Agency

PMDA Public Relations Strategic Plan

Introduction

Public relations activities conducted by the Pharmaceuticals and Medical Devices Agency (PMDA), such as the National Forum on Drugs and Medical Devices, did not receive high praise from the Evaluation Committee for Incorporated Administrative Agencies and the council members of the Advisory Council in fiscal year 2006. In order to increase recognition of PMDA among the public, its public relations activities need some improvement.

PMDA has developed a "PMDA Public Relations Strategic Plan," with the intention of advancing the PMDA's public relations activities through the Second Mid-term Plan period (FY 2009 through FY 2013) by considering public needs, with attention to international perspectives. The "PMDA Public Relations Strategic Plan" is a foundation policy for all of PMDA's public relations activities during this period, and reflects on the PMDA's decision to improve its public affairs, by pursuing information dissemination based on this strategic plan.

Framework of the Public Relations Strategic Plan

PMDA will implement public relations activities by applying the approaches stated in the "Public Relations Strategic Plan" based on the following three concepts. These activities will include public relations tailored to PMDA stakeholders, and the conscious raising of all staff members to their role as public relations representatives of PMDA.

(i) Realizing PMDA's Philosophy and Mission

The philosophy and mission of an organization are developed to foster a sense of internal unity, and engender a feeling of pride amongst staff members toward the work they do. They also act to clarify purpose for each staff member, and their way forward as contributors to the organization.

Cogent public relations activities based on the philosophy and mission of an organization will, externally, raise awareness for the organization in society and create an impression of reliability and familiarity. Internally, the organization strengthens its foundations and promotes a common set of values among its staff.

PMDA is determined to share its philosophy and mission with both public stakeholders (those coming into contact with PMDA either directly or indirectly) and staff members, accelerating these activities to as short a timeline as feasible, and to do this through use of public relations.

(ii) PMDA Globalization (Strengthening Cooperation with Overseas Partners)

In order to realize a societal role and fulfill public expectation, PMDA needs to act to further the information it provides to parties both inside Japan and all over the world, with the essential aim to become a globalized organization (on strengthening cooperation with overseas partners).

To carry out a role comparable with the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) of the European Union, and to deepen cooperation with these agencies, PMDA intends to improve and strengthen its systems with respect to review and safety, and further its activities to provide information.

To secure closer cooperation with Asian countries and to lead the way in future developments in Asia, PMDA will also further strengthen the means by which it promotes its information to Asian countries.

(iii) Information Provision Based on the Significance, Purpose, and Basic Philosophy of Public Relations

Public relations are communication made with the aim of building reliable relations with a variety of stakeholders including the public, society, and the media. The significance and purpose of public relations is to allow an organization to operate based on a relationship of trust.

To bring about such relationships with the public and society as a whole, PMDA needs to provide information that is facts-based. Such information should grasp the essence of events, and provide information that is factual, easy-to-understand, and tailored to the context and circumstances of its recipients.

The purpose of public relations conducted by PMDA thus lies in garnering a public understanding of its role, building better relations with society as a whole, and laying the groundwork for societal development within the public and social spheres. The PMDA's first-line policy on public relations should be to examine its public charter, its position in relation to the Ministry of Health, Labour and Welfare, and to endeavor to provide easy-to-understand facts-based information for true recognition of its activities.

PMDA will actively further its activities of providing information in order to fulfill its responsibility to society and the public, based on the purpose, significance, and basic philosophy of public relations.

Public Relations Plan 1: Public Relations Tailored to Stakeholders

The PMDA's operations consist of three pillars; "relief services for adverse health effects," "review services," and "post-marketing safety measures," for which the main respective audiences are patients and their families, relevant parties in the pharmaceuticals and medical devices industries, and healthcare professionals. PMDA stakeholders include the above-mentioned parties, in addition to relevant administrative parties and the general public.

The main intended audience of PMDA's public relations activities are the above-mentioned three parties, where each public relations exercise is tailored to each PMDA operation for each stakeholder group.

On the other hand, when PMDA intends to communicate its information as a whole beyond service boundaries, it is also very important to address the audience groups in an organized manner. But the approach is yet to be further examined, as PMDA has tended to separately address the above-mentioned three parties.

Thus, PMDA will determine its public relations targets before examining the means and methods to be used. Specifically, for each individual project, certain targets will be prioritized, and means of communicating examined and tailored for each stakeholder, while being conscious of to whom, what and how the information will be communicated.

By providing effective public relations services tailored to its stakeholder groups, PMDA will be able to construct relations with each group, and improve its standing in general.

Among PMDA stakeholders, the general public generally only come into contact with pharmaceuticals and medical devices when they come to use them. Therefore, public relations activities intended for the general public should be provided as easy-to-understand information specifically to meet this context. PMDA will provide easy-to-understand information in response to the following needs as examples:

- Needs to know more about a drug prescribed to them by a doctor
- Needs to know how a drug will interact with food/drinks
- Needs to know how a drug will interact with other drugs
- Needs to know whether a drug will interact with health food products (supplements, etc.)
- Needs to know about the latest medical devices

From the viewpoint of raising PMDA's profile among the general public, PMDA will make continuing and proactive efforts to provide both easy-to-understand and visible information, as below:

- As its legitimate name the Pharmaceuticals and Medial Devices Agency is too long for the general public to become familiar with. PMDA will continue to use its abbreviated name and logo proactively in its public relations activities.
- When the abbreviation "PMDA" is written, the pronunciation [pi:émdi:ei] will also be written by its side as often as possible, as it is hard to distinguish the correct pronunciation of "PMDA."
- PMDA will examine the possibility of changing its abbreviated name from "PMDA" to "PAMDA," or some similar name that is easier to pronounce.
- PMDA will include messages and information, such as its telephone number, URL, and QR code for consultation services on the envelopes/paper bags used to carry drugs.
- PMDA will consider creating newsletters describing its activities, and mascot characters that appeal to children.
- PMDA will distribute information regularly through television and magazine media (health magazines, magazines targeting middle-aged people, etc.) viewed by the general public.

The use of easy-to-understand means and methods is important for providing information on PMDA activities to schools, both in reflection of the increasingly important role PMDA plays in society, and to further spread understanding of this role throughout the general public.

In order to attract sufficient numbers of enthusiastic and highly-specialized new recruits as core future staff members, PMDA will need to provide better information to graduate students.

To achieve these goals, PMDA will distribute information through the school system in a way that is easy-to-understand, and in cooperation with the Ministry of Health, Labour and Welfare, and relevant parts of the Ministry of Education, Culture, Sports, Science and Technology.

PMDA will also build relationships of trust with pharmaceutical and medical devices industry experts and healthcare professionals, among others, by working together with specialists on the following activities:

- Having information on PMDA provided by opinion leaders in individual fields of specialization
- Preparing exhibition booths at pharmaceutical events hosted by academic societies with the aim of distributing PMDA brochures
- Regularly updating information on PMDA delivered by establishing information corners on the websites of various academic societies regularly accessed by specialists

To provide information on PMDA to international stakeholders, PMDA will also carry out the following activities:

- Improvements and enhancements on the PMDA's English website
- Translating information on PMDA, such as brochures and annual reports, into English
- Continuation of lectures and booth exhibits at international conferences
- Dispatching PMDA delegations to Europe, the United States, and Asian countries
- Preparation of newsletters in English

- Handing information to the Foreign Correspondents' Club of Japan and overseas media reporters

From the viewpoint of cost-effectiveness, the National Forum on Drugs and Medical Devices, held three times to date, is not thought an effective means of increasing awareness of PMDA among the general public in its current annual forum form. PMDA will use other means to extend its public relations activities, including distributing information at pharmaceutical events hosted by local governments or pharmaceutical and medical device organizations, through the following activities:

- Booth exhibitions with the aim of distributing brochures on PMDA
- Opening a consultation corner for enquiries on PMDA's operations
- Lectures by PMDA staff members

If the National Forum on Drugs and Medical Devices does continue, PMDA will examine new approaches including the following measures:

- Measures to enhance contact with participants
- Measures to produce external media content, such as video and newspaper articles reporting on the forum

Public Relations Plan 2: Every Staff Member is a PR Representative

All PMDA staff members must understand that they too are PR representatives of PMDA. Such awareness will work to bring a proper understanding of the PMDA's operations among the public, and gain their cooperation on future projects for societal development. All staff members should communicate information based on a full understanding of not just their individual duties, but also the PMDA's philosophy and mission, its general activities, while listening carefully to stakeholder voices.

To achieve these goals, in addition to other public relations activities, PMDA staff members will participate in symposia and other similar events organized for the general public, and provide information on the PMDA's activities at the grassroots level. PMDA will also take measures to involve staff members in public relations planning as follows:

- Creating opportunities for contact with the public realm at the individual staffing level by nominating those staff with an interest in public relations to become "PR representatives"
- Organizing public relations project teams consisting mainly of staff members with interest in public relations, which will propose public relations activities, and hold contests related to public relations, etc.

PMDA will reward members whose proposals are adopted, thus improving motivation among its staff.

PMDA will examine to change its business card designs to create a tool for increasing awareness of PMDA useful for day-to-day communication, by including the PMDA philosophy and mission, fully or partially, and its URL on its business cards.

Moreover, PMDA will review new measures to increase the profile of its staff members. This will involve them carrying not just business cards, but other card-style medium summarizing the PMDA's philosophy and mission.

With regard to the public relations activities of individual services (relief services for adverse health effects, review services, and post-marketing safety measures), PMDA will continue and improve on the activities in place. These activities may require the use of external communication consultants by PMDA where beneficially

synergistic results can be expected of a collaboration between staff members and external public relations experts, and advancements in the provision of easier-to-understand information.

Public Relations Plan 3: Building Beneficial Media Relations

To conduct effective public relations allowing the sharing of information with the public, PMDA must earn the media's trust and build mutually beneficial media relations. This relationship should be based on an understanding of the various functions of the media.

In order to build good media relations, PMDA recognizes the variety of media, and that correct information should be conveyed promptly, and in a way that is easy-to-understand. Instead of keeping its doors closed in fear of an unfavorable reaction, PMDA should respond to requests from the media with honesty. This has the added benefit of demonstrating to the public the openness of PMDA.

To gain sympathetic understanding from the media, PMDA needs to create contacts with persons in the media where accurate information on PMDA can be communicated.

Other possible approaches for beneficial media relations include the top management (Chief Executive of PMDA) releasing information to the media, and holding press conferences for news reporters.

Public Relations Plan 4: Practicing Risk Communication

PMDA recognizes a wide range of external risks (e.g., public health, safety and environment) and internal risks.

It is very important that PMDA appropriately manage these risks as a whole, while focusing on the important task of preventing external risks from occurring. PMDA must also provide information to increase awareness of crisis management among the public, even during ordinary times, so that persons of all levels may act promptly and adequately if such risks emerge.

As for information on unavoidable risks and benefits associated with the use of pharmaceuticals and medical devices in particular, such information needs to be provided based on the founding intentions of PMDA, so that people of any walk of life may understand the importance of the proper use of pharmaceuticals and medical devices.

To this end PMDA will play a public role in releasing crisis management information as often as possible, by conducting communications on pharmaceutical and medical device safety in relation to risk with people of all levels.

Public Relations Plan 5: Improving and Enhancing Information Provision Using IT Technologies

The Internet is characteristic for the immediacy and scale by which information can be spread. Anyone can obtain information while his/her workstation is connected to the Internet. PMDA will further improve information provision via the Internet by making it easy to search, and making its website both user-friendly and easy-to-understand.

For example, PMDA will carry out the following:

- Improving its visibility on Internet search engines by setting keywords tailored to stakeholders, so allowing immediate access to information relating to PMDA to someone who is searching for information on pharmaceuticals and medical devices

- Improving information content shown relating to PMDA on search engines
- Wider access to the PMDA's website from links on websites of relevant organizations
- Improvements to the website design, such as unified banner designs
- Setting up a system by which individual groups of stakeholders (experts, the general public, etc.) can evaluate whether a planned website upgrade is user-friendly, easy-to-understand or easy to search

Though the PMDA's website has been upgraded several times, the following information is still indistinct:

- Information required to describe the PMDA's accountability as a public organization
- Information for experts
- Information for the general public

PMDA will therefore make changes to the structure of the website itself, clearly separating information for experts and information for the general public by creating pages on independent domains (Internet addresses).

Public Relations Plan 6: Public Relations Based on the PDCA-Cycle

To achieve a level of understanding with the public and society, PMDA must focus not only on information provision (public relations) but also on information acquisition, by interactive communications and listening to the voices of its various stakeholder groups. Gaining a correct image of the public need and societal events through public hearings, and providing information to meet such needs is an important task for PMDA.

Understanding the needs of the public and society, both for implementation of beneficial public relations and its general operations is an imperative for PMDA. The PMDA's goal must be to accomplish organizational goals in response to such needs.

PMDA should be flexible with respect to the means and methods it uses for conducting public relations. Rather than continuing with a tried and tired format, effectiveness should be assessed, and measures taken to tailor-make its public relations to public needs.

To achieve this, PMDA will be conscious of the PDCA cycle (Plan-Do-Check-Act cycle: a process of creating a Plan, Doing the plan, Checking the results and Acting on the results in order to improve) while also listening to the public. In order to evaluate and learn from the effects of its public relations activities, PMDA will need to continuously evaluate and verify (monitor) its activities by conducting regular surveys on the needs of the general public, its visibility and public awareness of PMDA on the Internet, focusing such surveys on specific public relation events. While also taking the public relations aspect of conducting such public relations into consideration, PMDA now aims to create a program for continued development by dissemination of information relating to its public relations activities.

February 6, 2009

Pharmaceuticals and Medical Devices Agency

PMDA International Strategic Plan

—Objectives for the Second Mid-Term Plan—

Introduction

With the globalization of the development and distribution of pharmaceuticals and medical devices, Pharmaceuticals and Medical Devices Agency (PMDA) has been required to harmonize its services with the international community in order to provide people with more effective and safer pharmaceuticals and medical devices more quickly. Given this, PMDA has declared its determination, as part of its philosophy, to play an active role within the international community from a global point of view by promoting international harmonization. PMDA must implement international activities in a more organized and systematic manner in order to realize this philosophy during the coming second mid-term plan period (from FY2009 to 2013). To this end, PMDA has formulated the PMDA International Strategic Plan, which outlines the basic policies for overall international activities during this period. PMDA will appropriately meet the needs of the Japanese people for pharmaceuticals and medical devices by promoting proactive international operations in accordance with the strategic plan. In addition, PMDA will play the role expected of it within the international community by meeting the needs of people around the world for pharmaceuticals and medical devices.

Three targets to be achieved during the second mid-term plan period

1. **Strengthening of cooperation and building of collaborative relations with the United States (US), the European Union (EU), Asian countries, and relevant international organizations**
2. **Proactive participation in international harmonization activities and further contributions to such activities**
3. **Improvement and strengthening of information provision to overseas countries**

To achieve these targets, PMDA will steadily implement the following five strategies as its basic principles by establishing an internal office in charge of international affairs to improve and strengthen its system.

International Strategy 1

Strengthening of Cooperation with the US, the EU, Asian countries, and Relevant International Organizations

PMDA will play a full part in the review and safety of pharmaceuticals and medical devices in Japan—which together with the US and the EU is one of the main regions for new drug development—in

cooperation with the US Food and Drug Administration (FDA) and the European Commission and the European Medicines Agency (EMEA). To this end, PMDA will promote continuous bilateral talks based on confidentiality agreements, information sharing, and proactive personnel exchanges as required in conducting business with relevant parties. PMDA will deploy its staff members in the FDA and EMEA, regularly invite personnel from the two organizations to its offices, and establish a system under which detailed information can be gathered and opinions can be exchanged in real time. PMDA will swiftly analyze, evaluate, and translate important overseas information and communicate it to the relevant parties.

During the second mid-term plan period, PMDA will promote the building of collaborative relations with Asian countries, with the primary focus on China and South Korea. PMDA will also examine how to promote and strengthen information sharing as required in conducting business with the other Western and Asian countries and international organizations. PMDA will also build a system to enable it to flexibly respond to training requests from other countries.

Furthermore, PMDA will strengthen cooperation with foreign countries with respect to inspections and audits conducted to ensure compliance with Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Manufacturing Practice (GMP), and Quality Management System (QMS). PMDA will also develop an environment geared toward the exchange of inspection reports and other such cooperative activities, and make continued efforts to work with relevant international organizations toward the establishment of international standards.

International Strategy 2

Strengthening of activities for international harmonization

PMDA will enhance Japan's contribution to ongoing international harmonization activities such as the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the Global Harmonization Task Force (GHTF), the Harmonization By Doing (HBD), and the Pharmacopoeial Discussion Group (PDG) and maintain and strengthen favorable relations with relevant countries by continuing to proactively send directors and staff members to and proactively participating in these activities. In addition, PMDA will enhance Japan's contribution to and strengthen collaborative relations with the World Health Organization (WHO), the Organization for Economic Co-operation and Development (OECD), and other relevant international organizations by proactively sending directors and staff members to international harmonization activities led by those organizations.

International Strategy 3

Promotion of personnel exchanges

PMDA will proactively and continuously send its staff members to international meetings and conferences in a variety of specialized fields and promote the building of networks with overseas

regulatory agencies. PMDA will also work to increase its opportunities to send personnel to the FDA and EMEA and will promote personnel exchanges with relevant countries and international organizations.

To promote mutual understanding among Japan, China, and South Korea in particular, PMDA will promote personnel exchanges with the State Food and Drug Administration (SFDA, China) and the Korea Food and Drug Administration (KFDA) and will build a system under which information on product evaluation and safety measures can be steadily exchanged.

International Strategy 4

Fostering of internationally minded human resources with communication skills

To foster internationally minded human resources with communication skills, PMDA will promote the development of staff training programs—which will include communications with overseas parties, attendance and presentations at international conferences and meetings—and the implementation of these programs in an organized manner.

PMDA will also work to help relevant staff members improve their foreign language skills, such as English, by continuing and strengthening its foreign language training and daily educational activities for directors and staff members.

International Strategy 5

Improvement and strengthening of international publicity and information provision

To ensure that relevant overseas parties correctly understand its role and activities, PMDA will proactively implement activities such as the improvement and enhancement of its English website, which explains pharmaceutical regulations, PMDA's services, and so on. PMDA will also prepare and disclose English translations of product review reports, post-marketing safety information, legal notices, and other administrative documents. In addition, PMDA will proactively give lectures and have booth exhibits regularly at international meetings and conferences, distribute relevant information to and grant interviews to the Foreign Correspondents' Club of Japan and overseas media, and thus provide important information such as that concerning pharmaceutical regulations in Japan in an easy-to-understand and swift manner to overseas countries.