

Mid-term Plan of the Pharmaceuticals and Medical Devices Agency <sup>\*</sup> (Provisional Translation)

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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.

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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.

<sup>\*</sup> 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)	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 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 (EMA).
- 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.

## Budget for the Mid-term Plan (FY 2009 - 2013)

(Unit: million yen)

Classification	Amount						Total
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	
<b>Income</b>							
Administrative subsidies			2,717				2,717
Governmental subsidies	843	89	2,443				3,375
Contributions	20,410	3,160	12,144	20,255			55,969
User fees			49,448				49,448
Commissioned operations			242		7,140	3,521	10,903
Management income	1,843	266					2,108
Miscellaneous income	7	1	180	0	6	6	200
<b>Total</b>	<b>23,103</b>	<b>3,514</b>	<b>67,174</b>	<b>20,256</b>	<b>7,146</b>	<b>3,527</b>	<b>124,720</b>
<b>Expenditure</b>							
Operating expenses	14,788	520	57,107	24,429	7,079	3,481	107,404
Personnel expenses	1,142	125	26,005	88	186	118	27,665
Administrative expenses	13,646	395	31,102	24,341	6,893	3,363	79,740
General administrative expenses	664	74	13,011	19	68	45	13,881
Personnel expenses	288		3,149		19	9	3,465
Non-personnel expenses	376	74	9,862	19	49	36	10,416
<b>Total</b>	<b>15,452</b>	<b>594</b>	<b>70,119</b>	<b>24,448</b>	<b>7,146</b>	<b>3,527</b>	<b>121,286</b>

&lt;Note&gt;

In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

## Income and Expenditure Plan for the Mid-term Plan (FY 2009 - 2013)

(Unit: million yen)

Classification	Amount						Total
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	
Expenditure	24,497	780	67,313	24,470	7,147	3,525	127,732
Ordinary expenses	24,497	780	67,313	24,470	7,147	3,525	127,732
Operating expenses	14,623	489	53,782	24,429	7,073	3,456	103,851
Relief benefits	11,619	180					11,799
Operating expenses for health and welfare	171						171
Operating expenses for reviews			20,594				20,594
Operating expenses for safety measures			7,395				7,395
Specified relief benefits				24,080			24,080
Benefits (healthcare allowances, etc.)					6,802		6,802
Benefits (special allowances, etc.)						1,317	1,317
Operating expenses for research and study						1,919	1,919
Administrative expenses	1,696	185		261	86	101	2,329
Personnel expenses	1,136	124	25,792	88	186	118	27,444
General administrative expenses	599	65	10,986	20	69	46	11,786
Personnel expenses	287		3,152		19	9	3,467
Non-personnel expenses	311	65	7,834	20	51	37	8,319
Depreciation expenses	270	46	2,540	21	0	18	2,894
Provision for liability reserve	9,002	175					9,177
Miscellaneous losses	5	5	5		5	5	25
Income	23,103	3,516	67,303	24,470	7,145	3,526	129,064
Ordinary income	23,103	3,516	67,303	24,470	7,145	3,526	129,064
Governmental subsidies	843	89	2,443				3,375
Contributions	20,410	3,160	12,144				35,714
User fees			49,448				49,448
Commissioned operations			242		7,140	3,521	10,903
Other governmental grants				184			184
Administrative subsidies			2,717				2,717
Reversal of asset offset subsidies	1			21			22
Reversal of asset offset administrative subsidies			283				283
Reversal of asset offset gifts received			2				2
Financial income (no operating income)	1,849	268	2				2,119
Gain on reversal of specified relief fund deposit received				24,264			24,264
Miscellaneous income	0	0	22		5	5	32
Net income (net loss)	△1,394	2,737	△10	0	△2	1	1,331
Reversal of appropriated surplus							-
Gross income (△gross loss)	△1,394	2,737	△10	0	△2	1	1,331

&lt;Note 1&gt;

Administrative subsidies are assumed to be the financial resource for retirement allowances for staff members in charge of operations financed by administrative subsidies under the review account. However, this excludes the amount arranged through administrative subsidies as retirement allowances equivalent to tenure, as provided for in Article 8-2 of the supplementary provisions in the Law for Pharmaceuticals and Medical Devices Agency.

&lt;Note 2&gt;

In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.

## Cash Flows Plan for the Mid-term Plan (FY 2009 - 2013)

(Unit: million yen)

Classification	Amount						Total
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commission payment account	
<b>Cash Outflows</b>							
Cash outflows from operating activities	15,423	557	65,157	24,450	7,178	3,520	116,286
Relief benefits	11,564	178					11,743
Operating expenses for health and welfare	171						171
Operating expenses for reviews			20,739				20,739
Operating expenses for safety measures			7,468				7,468
Specified relief benefits				24,080			24,080
Benefits (healthcare allowances, etc.)					6,827		6,827
Benefits (special allowances, etc.)						1,317	1,317
Operating expenses for research and study						1,919	1,919
Administrative expenses	1,986	193		264	105	119	2,668
General administrative expenses	303	64	8,792	19	49	36	9,264
Personnel expenses	1,398	122	28,159	86	197	128	30,091
Cash outflows from investing activities	11,547	2,536	4,975			20	19,078
Payments for purchases of investment in securities	11,320	2,500	676				14,496
Payments for purchases of intangible fixed assets	154	25	2,749			20	2,948
Payments of deposit money and guarantee money	74	11	1,549				1,634
Cash outflows from financial activities							-
Amount carried forward to the next mid-term plan period	3,840	668	2,496	287	39	137	7,466
<b>Total</b>	<b>30,810</b>	<b>3,761</b>	<b>72,628</b>	<b>24,737</b>	<b>7,217</b>	<b>3,677</b>	<b>142,830</b>
<b>Cash Inflows</b>							
Cash inflows from operating activities	23,354	3,514	66,980	20,256	7,167	3,527	124,797
Governmental subsidies	843	89	2,443				3,375
Administrative subsidies			2,717				2,717
Contributions	20,410	3,160	12,144	20,255			55,969
User fees			49,410				49,410
Commissioned operations			242		7,161	3,521	10,924
Miscellaneous income	2,100	266	24	0	6	6	2,402
Cash inflows from investing activities	5,848						5,848
Cash inflows from financial activities							-
Amount brought forward at the beginning of the mid-term plan period	1,609	247	5,648	4,481	50	150	12,185
<b>Total</b>	<b>30,810</b>	<b>3,761</b>	<b>72,628</b>	<b>24,737</b>	<b>7,217</b>	<b>3,677</b>	<b>142,830</b>

&lt;Note&gt;

In principle, all figures have been rounded off; therefore, individual totals shown may not coincide with the actual totals.