Pharmaceuticals and Medical Devices Agency, Japan

ANNUAL REPORT FY 2015

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(in the event of inconsistency, the Japanese text shall prevail).

THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2015 (April 2015 - March 2016)

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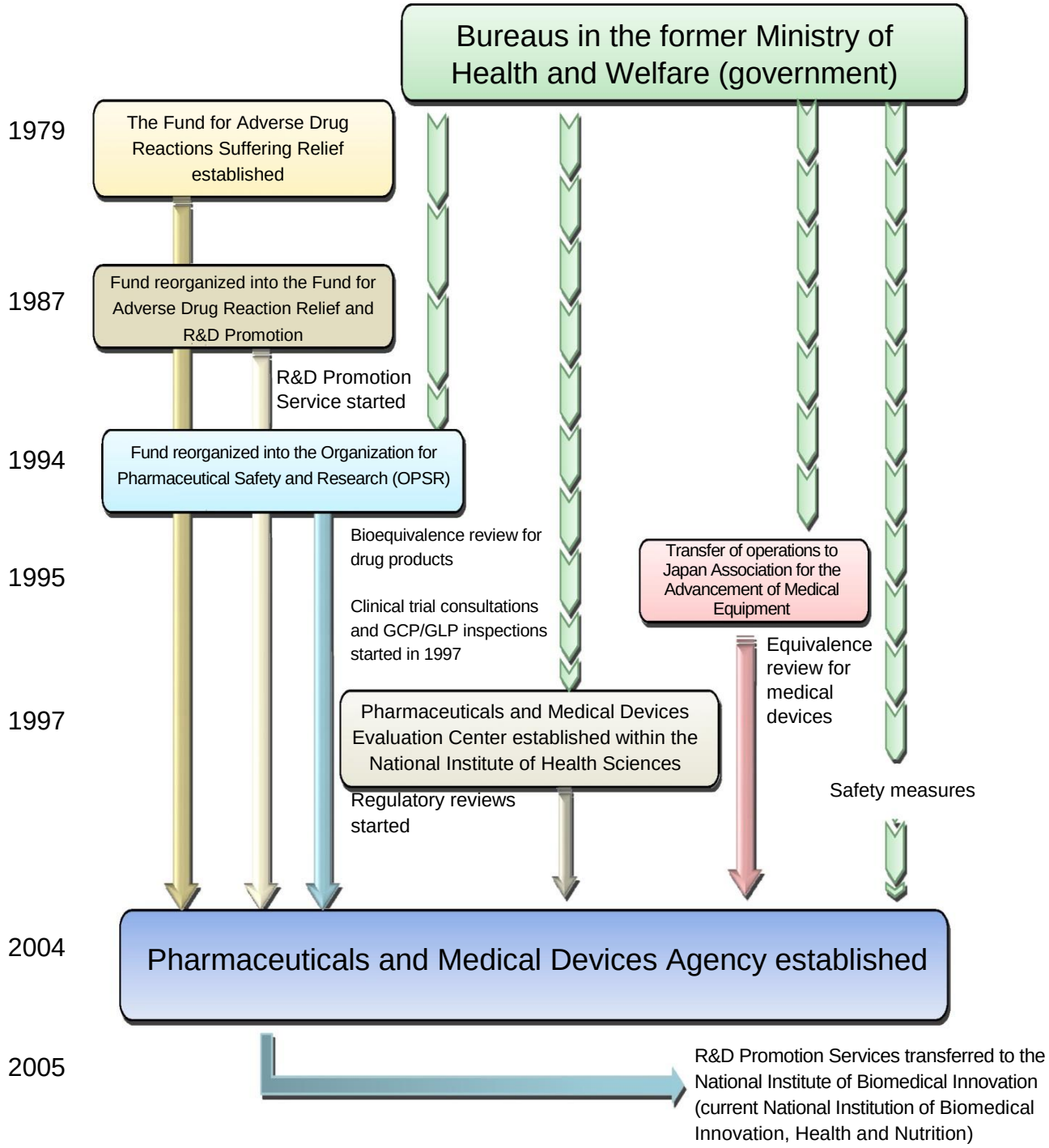
I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1 History and Objectives of the PMDA

- In response to lessons learned from incidents involving drug-induced health damage, 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 for the purpose of providing prompt relief to patients suffering from adverse drug reactions (ADRs), pursuant to the provisions of the Adverse Drug Reaction Suffering Relief Fund Act (Act No. 55 of 1979). In 1987, the Fund began implementation of R&D-promoting activities, using the name, “The Fund for Adverse Drug Reaction Relief and R&D Promotion.” This fund was later reorganized into the Organization for Pharmaceutical Safety and Research (OPSR) in 1994 to play the additional role of conducting bioequivalence reviews of generic drug products. Subsequently, in 1997, this organization began providing advice related to clinical trials and conducting GCP/GLP inspections as part of the review process for new drug applications.
- In 1997, the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) was established at the National Institute of Health Sciences (NIHS) in order to develop a full-scale regulatory review system and to increase the sophistication of review activities. It was decided that reviews conducted at the Center should be conducted in teams comprised of experts specializing in the pharmaceutical and medical sciences, biostatistics, and other related fields. In addition, the Japan Association for the Advancement of Medical Equipment (JAAME) was established in 1995 as a designated investigative body under the Pharmaceutical Affairs Act tasked with conducting equivalence reviews of medical devices.
- Between 1997 and 1999, there was a systematic and drastic increase in the number of the staff involved with product review 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 members 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 should be dissolved and that the Pharmaceuticals and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to PMDEC, OPSR, and JAAME in order to further enhance reviews and post-marketing safety measures. In 2002, a bill for the Act on the Pharmaceuticals and Medical Devices Agency (PMDA) was discussed and passed at the 155th extraordinary session of the Diet, resulting in the establishment of PMDA on April 1, 2004, in accordance with the Act on the Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002).
- PMDA’s mission is to contribute to the improvement in public health by providing prompt relief to people who have suffered health damage caused by adverse drug reactions or infections from biological products (Relief for Adverse Health Effects); providing guidance and reviews regarding the quality, efficacy, and safety of drugs and medical devices through a system that integrates the entire process from pre-clinical research to approval (Reviews); and collecting, analyzing, and providing post-marketing safety information (Safety Measures).

  Previously, one of the objectives of PMDA was to promote basic research and the 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 (now renamed to the National Institutes of Biomedical Innovation, Health and Nutrition) in April 2005, in order to allow PMDA to focus exclusively on reviews, safety measures, and relief services for harm caused by adverse events related to healthcare product use.


Bureaus in the former Ministry of Health and Welfare (government)
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)
1995
Bioequivalence review for drug products
Clinical trial consultations and GCP/GLP inspections started in 1997
Transfer of operations to Japan Association for the Advancement of Medical Equipment
Equivalence review for medical devices
1997
Pharmaceuticals and Medical Devices Evaluation Center established within the National Institute of Health Sciences
Regulatory reviews started
Safety measures
2004
Pharmaceuticals and Medical Devices Agency established
2005
R&D Promotion Services transferred to the National Institute of Biomedical Innovation (current National Institution of Biomedical Innovation, Health and Nutrition)

PART 2 Outline of Operations

2.1. Relief Services for Adverse Health Effects

- As a role inherited from the OPSR, PMDA provides benefits for medical expenses, disability pensions, and bereaved family pensions to the sufferers of illnesses or disabilities caused by adverse drug reactions (Relief Service for Adverse Drug Reaction).
- Since April 2004, PMDA has provided benefits to sufferers of adverse health effects caused by infections from drugs and medical devices manufactured using ingredients and materials of biological origin (Relief Service for Infections Acquired through Biological Products).
- Since January 2008, PMDA has also provided benefits to patients infected with drug-induced hepatitis C virus, in accordance with the Act on Special Measures concerning the Payment of Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus (Act No. 2 of 2008) (Specified Relief Service).
- In November 2014, PMDA began providing relief disbursements to sufferers of adverse health effects caused by regenerative medical products (as a part of Relief Service for Adverse Drug Reactions and Relief Service for Infections Acquired through Biological Products).
- PMDA is commissioned by the government of Japan and pharmaceutical companies to pay healthcare allowances and nursing care expenses to patients with SMON (Service for Healthcare Allowances). PMDA is also commissioned by the Yu-ai Welfare Foundation to make payments for healthcare expenses for patients with HIV infection or AIDS (Service for Healthcare Allowances).

2.2. Reviews

- In accordance with the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145 of 1960, PMD Act) and based on current scientific and technological standards, PMDA evaluates the efficacy, safety, and quality of drugs and medical devices for which applications have been submitted for regulatory approval. In addition, PMDA conducts re-examinations/re-evaluations of drugs and regenerative medical products, medical device use-result survey, and reviews of applications for confirmation of clinical use of genetically modified biological entities pursuant to the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Act No. 97 of 2003, Cartagena Law) (Reviews).
- In response to requests from clinical trial sponsors, PMDA provides guidance and advice through face-to-face consultations on clinical trials of new drugs, new medical devices, and new regenerative medical products as well as on clinical trials for re-examinations/re-evaluations of approved products (Consultations).
- For products submitted for approval or re-examinations (use results survey for medical devices)/re-evaluations, on-site and document-based inspections are conducted to determine whether application data comply with Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Post-marketing Surveillance Practice (GPSP), and the data integrity standards for product applications (GLP/GCP/GPSP Inspections).
- PMDA conducts on-site and document-based inspections to determine whether manufacturing facilities and manufacturing control methods for drugs, medical devices, and regenerative medical products, etc., are in compliance with the requirements set forth in the Ministerial Ordinance on Good Manufacturing Practices/Quality Management System, whereby products of appropriate quality can be manufactured.

PMDA also inspects manufacturing sites of regenerative medical products to determine whether their manufacturing facilities as well as manufacturing process and quality management system comply with the Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (Act No. 85 of 2013) (GMP/QMS/GCTP Inspections).

- PMDA conducts research and organizes various standards, such as the Japanese Pharmacopoeia (JP), which is set forth in the PMD Act (Research for Standards Development).

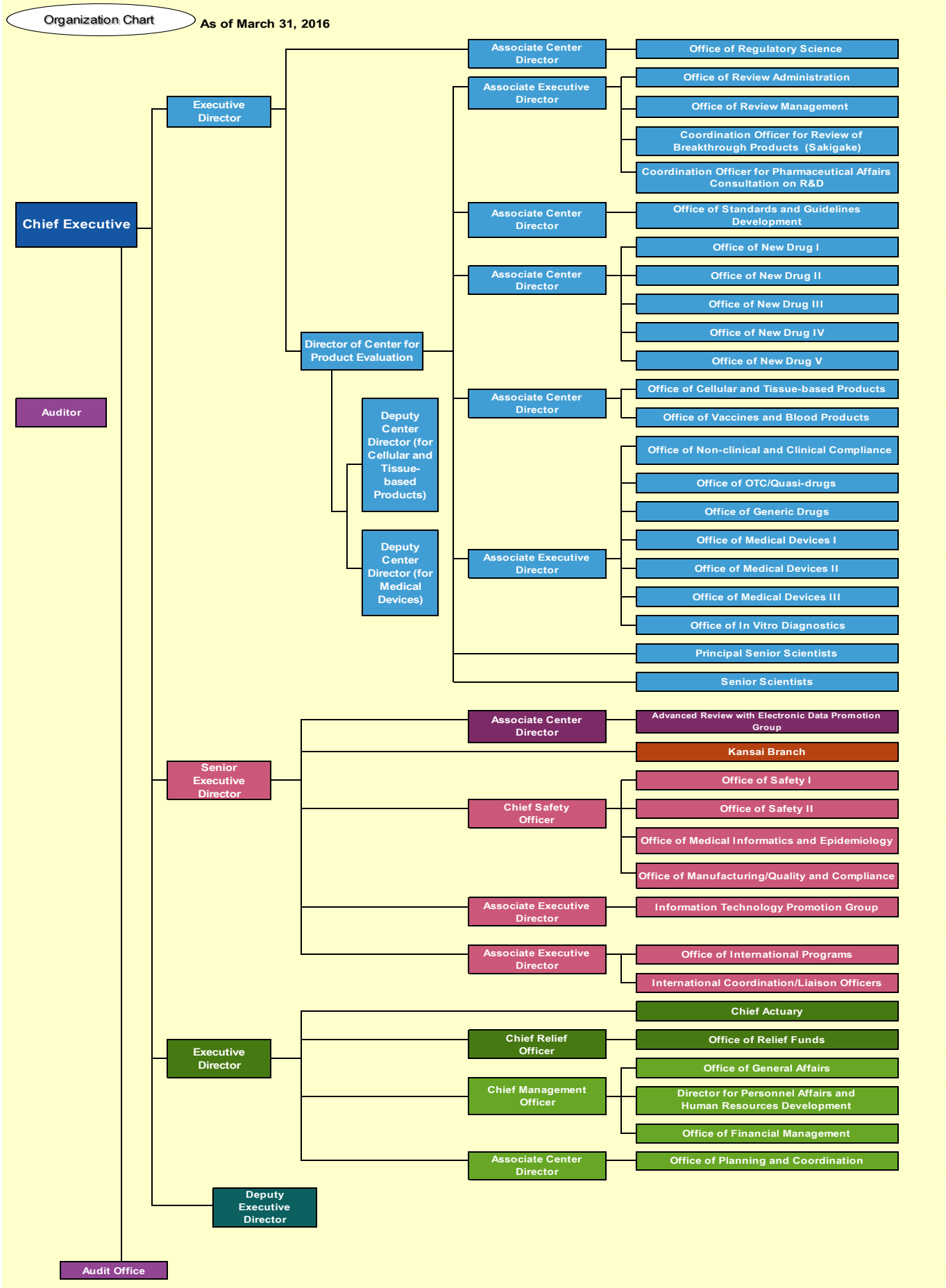
2.3. Safety Measures

- PMDA cooperates with the Ministry of Health, Labour and Welfare (MHLW) to provide the following services designed to improve the safety of marketed drugs, medical devices, and regenerative medical products, and also to ensure that patients and healthcare professionals can properly use drugs, medical devices, and regenerative medical products, with peace of mind.

(i) Centrally collecting and organizing information on the safety of drugs, medical devices, and regenerative medical products from a broad range of sources, such as reports from companies, information from medical institutions, information from foreign regulatory agencies, and reports presented at academic conferences, relating to adverse drug reactions, device malfunctions, and infections (Collection and Organization of Information).
(ii) Conducting research and reviews relating to safety measures based on the information collected in (i) above (Research and Reviews).
(iii) Giving guidance and advice to marketing authorization holders (MAHs) as well as providing consultations to consumers upon request (Consultations).
(iv) Providing safety information on drugs, medical devices, and regenerative medical products widely to healthcare professionals, patients, companies, etc., in a timely manner (Information Provision).

- PMDA also utilizes electronic medical records to conduct quantitative assessments of the risk of adverse events, assess impact on safety measures, investigate the real-world implications of prescription drug use, and to develop medical information databases, for the purpose of establishing a systematic approach to conducting safety measures based on pharmacoepidemiological methods.

PMDA Organizational Structure (as of March 31, 2016)



II. OPERATING PERFORMANCE FOR FY 2015

PART 1 Development of the 2015 Fiscal Year Plan

1.1. Development and Implementation of the 2015 Fiscal Year Plan

- PMDA, an incorporated administrative agency (incorporated administrative agency with non-civil service status), 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 Ministerial approval for the plan (effective period of the Third Mid-term Targets: April 2014 to March 2019). In order to realize the objectives of the Mid-term Plan, PMDA is required to develop a plan to govern the management of its operations for each fiscal year (fiscal year plan), submit these plans to the Minister, and announce these plans to the public.
- Also for FY 2015, the fiscal year plan was developed at the end of FY 2014 based on the Third Mid-term Targets and Mid-term Plan, the results of the evaluation of operating performance for FY 2013 provided by the Evaluation Committee for Incorporated Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW), and the opinions by the Commission on Policy Evaluation and Evaluation of Incorporated Administrative Agencies of the Ministry of Internal Affairs and Communications (MIC). The plan was submitted to the Minister of Health, Labour and Welfare and operations were performed in line with the plan.

1.2. Results of the Evaluation on Operating Performance for FY 2014

- It is stipulated that the incorporated administrative agencies with non-civil service status should undergo an evaluation conducted by the Minister after the end of each fiscal year with regard to the results of the operating performance during the relevant fiscal year. (Article 32 of the Act on General Rules for Incorporated Administrative Agencies [Act No. 103 of 1999])
- As for the operating performance results for FY 2014, the Minister of Health, Labour and Welfare released the “Results of the Evaluation of Operating Performance for FY 2014” on September 14, 2015 based on the expert committee’s interviews on the evaluation of incorporated administrative agencies as of July 9, 2015. PMDA received an “A” rating for 7 items and a “B” rating for 8 items among the 15 items to be rated. Of the 15 items, 6 “A”-rated items and 2 “B”-rated items were items with a “high” level of importance. No events causing a rating decrease were included. Therefore, the overall rating was “A: Showing overall outcomes exceeding the expected targets in the Mid-term Plan.”

  Note: List of rating criteria

  Assessment criteria for individual items

  If quantitative indices have been established:

  S: Showing remarkable outcomes exceeding the expected targets in the Mid-term Plan quantitatively and qualitatively as a result of agency activities (For the quantitative indices, showing values 120% or greater than the values in the Mid-term Plan [or the annual plan] and qualitatively remarkable achievements)

  A: Showing outcomes exceeding the expected targets in the Mid-term Plan as a result of agency activities (For quantitative indices, showing values 120% or greater than the values in the Mid-term Plan [or the annual plan])

  B: Showing outcomes achieving the expected targets in the Mid-term Plan (For quantitative indices, showing values of 100% or greater and less than 120% of the values in the Mid-term Plan [or the annual plan])

  C: Showing outcomes below the expected targets in the Mid-term Plan and improvement is required (For quantitative indices, showing values 80% or greater and less than 100% of the values in the Mid-term Plan [or the annual plan])

D: Showing outcomes below the expected targets in the Mid-term Plan and drastic improvement, including discontinuation of the services, is required (For quantitative indices, showing values less than 80% of the values in the Mid-term Plan [or the annual plan], or in the case where the competent minister finds it necessary to issue an order to improve operations or to take other necessary measures)

In the case where it is difficult to establish quantitative indices:

S: -
A: Meeting the target level for highly difficult targets
B: Meeting the target level (excluding the items categorized into “A”)
C: Not meeting the target level (excluding the items categorized into “D”)
D: Not meeting the target level and drastic revision of the services, including the case where the competent minister finds it necessary to issue an order to improve operations or to take other necessary measures

Overall assessment criteria

S: Showing remarkable overall outcomes that exceed the expected targets in the Mid-term Plan quantitatively and qualitatively as a result of agency activities
A: Showing overall outcomes that exceed the expected targets in the Mid-term Plan as a result of agency activities
B: Showing overall outcomes that generally achieve the expected targets in the Mid-term Plan
C: Showing overall outcomes below the expected targets in the Mid-term Plan and improvement is required
D: Showing overall outcomes below the expected targets in the Mid-term Plan and drastic improvement, including discontinuation of the services, is required

- The "Results of the Evaluation on Operating Performance for FY 2014" was published on the PMDA website and reported to Advisory Council Meeting held on November 5, 2015.

Results of the Evaluation on Operating Performance for FY 2014

Mid-term Plan (Mid-term Targets)	Evaluation for each fiscal year				
Assessment of individual items	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
I. Improvement in the quality of PMDA services (e.g., services to the public)					
1. Provision of information on the Relief System and strengthening of the consultation system	B				
2. Expeditious operation and improvement of the system (Relief service)	A○				
3. Conduct of cross-functional collaboration and health and welfare services	B				
4. Provision of healthcare allowances for patients with SMON and patients infected with HIV through blood products	B				
5. Expeditious operation and improvement of the system (services related to drugs)	A○				
6. Expeditious operation and improvement of the system (services related to medical devices and regenerative medical products)	A○				
7. Support of the initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products	B○				
8. Reinforcement of collecting, and systematization of organizing, assessing and analyzing information on adverse drug reactions/malfunctions	A○				
9. Provision of safety information to companies/healthcare professionals and follow-up, and provision of safety information to patients and consumers	B○				
10. Promotion of international activities, etc.	A○				
II. Increased efficiency of operations					
11. Operation through target management and top management, ensuring transparency by establishing deliberative bodies, strengthening the consultation system, and announcement of the Agency's services.	B				
12. Cost control efforts	A				
13. Collection and management of contributions	B				
III. Fiscal improvement					
14. Budget, income and expenditure plan, and financial plan	B				
IV. Others					
15. Personnel matters and establishment of security	A○				
Overall assessment	A				

*For items with a "high" level of importance, the mark "○" is added besides the rating.

* For items with a "high" level of difficulty, the rating is underlined.

PART 2 Improvement in Overall Management of PMDA Operations and Quality of Services

2.1. Efficient and Flexible Management of Operations

2.1.(1) Operation through target management

- In managing operations, PMDA clarifies the objectives and responsibilities of operations for each department, and strives to identify and resolve problems through managing its operational progress on a daily basis.
- In conjunction with the development of PMDA's annual plan for FY 2015, each office and division formulated their operating plans for segregation of duties. PMDA has operated through management of the targets set in the operating plans.

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

- PMDA intends to reinforce its function of strategy planning for overall operations, as well as a system for managing operations (e.g., risk management, inspection of operations), and also plans to build an organizational system in which management decisions by the Chief Executive are promptly reflected in operations.
- To this end, the highest decision-making organ, the “Executive Directors’ Meeting” (consisting of executives, and employees at a level above associate center directors) that reviews the basic policy on management of operations, establishment and dissolution of the organization, and important matters regarding the management of operations was held more frequently on a periodic basis (every other week, in principle).
- In addition, PMDA regularly (once a week, in principle) held "Board of Directors meetings," attended by executives and office directors, to ensure that the Chief Executive directly comprehends operational progress and provides necessary direction.
- With the focus on discussion about security measures triggered by the information leakage affair in the Japan Pension Service, PMDA held 3 meetings of Headquarters of Information Systems Management (headed by the Chief Executive) and 8 meetings of the Committee on Investment in Information Systems. In addition, related office directors received explanations as necessary.

  In the Committee on Investment in Information Systems, the investment decision process was formulated so that decisions on investments with high investment effectiveness, determination of budget implementation, and evaluation of investment outcomes can be performed, according to such factors as the magnitude of all systems including their operation and maintenance, and the degree to which PMDA is affected.
- In order to regularly monitor the financial conditions to maintain sound financial performance and effective operations, the "Financial Management Committee," headed by the Chief Executive, held 12 meetings. The following information was reported to the meetings: user fees paid and cash flow analysis for each division for each month; and the declared amount of contributions.
- During the third Mid-term Plan period, personnel expenses associated with a larger workforce, as well as system development expenses and depreciation expenses will be increased in the situation where incomes including user fees for review fail to grow, resulting in a fundamental deficit. PMDA should therefore execute its operations efficiently during and after the period of the fourth Mid-term Plan. To this end, PMDA has established a project team to achieve fiscal soundness allowing PMDA to discuss short- or medium-to-long-term measures, reflect the outcomes of discussions in

the budget each fiscal year as part of the Plan-Do-Check-Action (PDCA) cycle, and achieve fiscal soundness by reviewing fiscal expenditure, strengthening the fiscal base, and ensuring effective budget implementation.

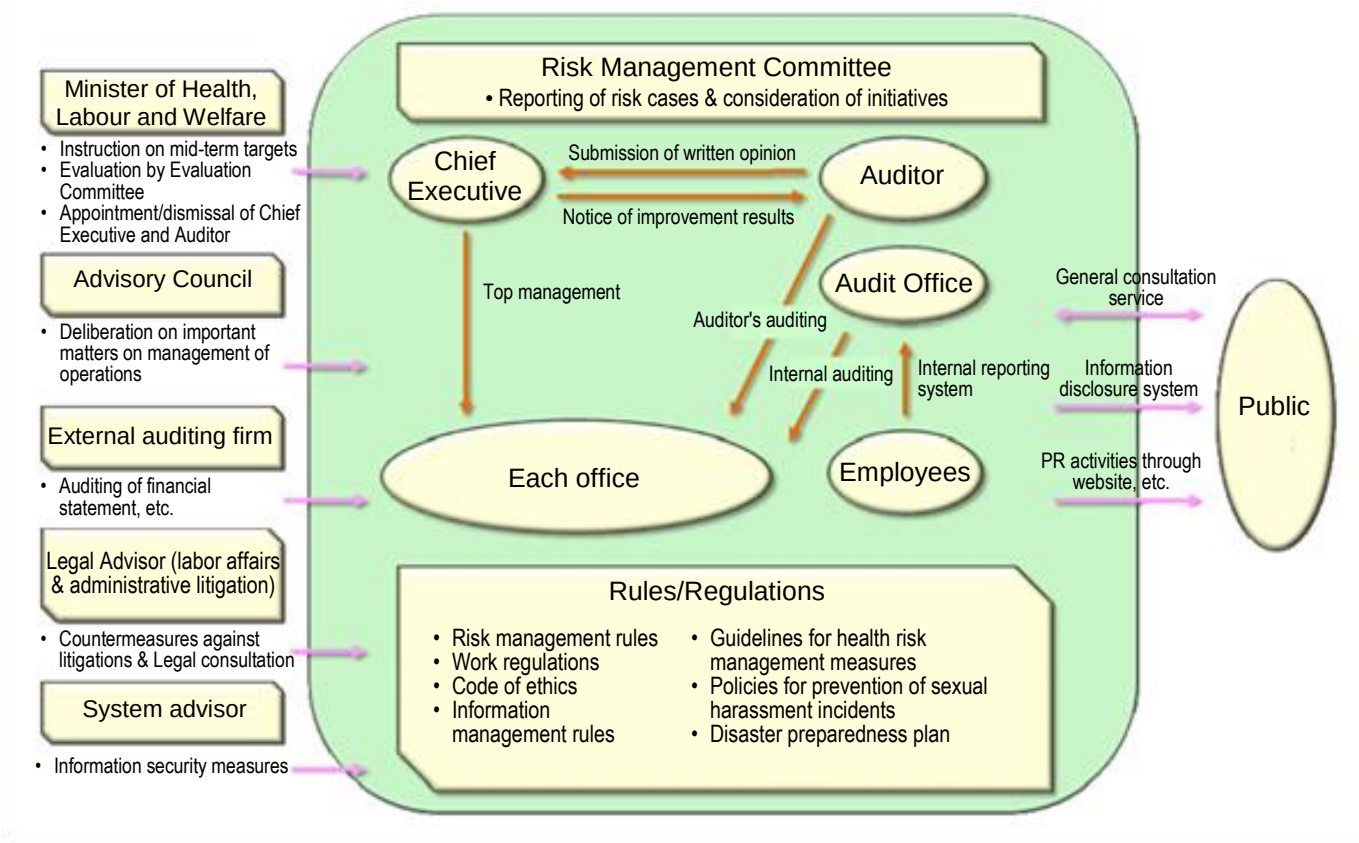
The project team carefully examined the fiscal outlook and discussed short- or medium-to-long-term measures.

- In March 2016, a "Meeting to Hear from Employees" was held, and policies to deal with opinions, requests, etc., from employees were examined.
- Meetings of the health committee were held every month to discuss various measures for maintaining and promoting the health of employees.
- PMDA held idea exchange sessions with members of the pharmaceutical industry concerning new drugs (held in November 2015) and on drug safety (held in October 2015).

  As for medical devices and *in vitro* diagnostics, PMDA also cooperated with MHLW to hold regular idea exchange forums focusing on medical device regulatory affairs issues (July 2015).
- "Risk Management Committee" meetings were held once a month to allow the directors to discuss PMDA's risks.

  PMDA has created a new page in its intranet for the Risk Management Committee and has continued its efforts to familiarize its executives and employees with risk management in accordance with the risk management rules and risk management manual.
- The Office of Audit, which reports directly to the Chief Executive, has continued to conduct internal auditing and management of PMDA’s internal reporting systems.
- In order to ensure readiness to respond to hazards and safety risks resulting from natural disasters such as earthquakes and fires, PMDA duly informed all executives and employees of its disaster preparedness plan.

Risk Management System at PMDA



★ Risks PMDA may face:

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

B. Risks that PMDA should address as part of its tasks
   - Risks relating to PMDA's operations which might cause or expand serious adverse health effects due to drugs, medical devices, etc. (including drugs, medical devices, quasi-drugs, cosmetics, and regenerative medical products, as well as agents, etc., subject to clinical trials)

- In order to systematically promote public relations (PR) activities in consideration of the public needs and international perspectives, PMDA developed the "PMDA Public Relations Strategic Plan" (July 11, 2008) as a basic policy for its overall PR activities. The Agency is striving to proactively provide information in line with the strategic plan. Further, in consideration of the development of PMDA's philosophy, changing socioeconomic circumstances, etc., PMDA revised the Strategic Plan in April 2015 and established the PR Committee to develop a PR plan, adjust the policies, and undertake progress management so that PMDA will be able to implement PR activities more effectively.
- PMDA has received high international recognition as a result of resolving the review lag for drugs and medical devices through the periods of the first and second Mid-Term Plan but is under pressure to make additional international contributions. Given this situation, PMDA developed and released the "PMDA International Strategic Plan 2015" in June 2015, based on expectations in and

outside Japan. Based on the strategy, PMDA is proactively promoting activities such as reinforcing collaboration with Western and Asian countries, participating in and contributing to international regulatory harmonization, and providing information to foreign countries. In addition, to promote a better understanding of Japanese regulatory systems for drugs and medical devices in Asian countries, PMDA has prepared to establish an educational organization for personnel employed by the regulatory authorities of Asian countries, namely, the “Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs” (established on April 1, 2016) within PMDA.

- In response to a request for promotion of the "Kansai Innovation Comprehensive Global Strategic Special Zone," PMDA established a Kansai Branch Office in Osaka in October 2013. This office has conducted Pharmaceutical Affairs Consultation on R&D Strategy, and also GMP on-site inspections etc., from April 2014. Both operations are intended to target mainly users residing in the western region of Japan (known as the Kansai region). Aiming for the "enhancement of PMDA operations in the Kansai region," the request was submitted to the national government by the local governments of Kyoto, Osaka, and Hyogo Prefectures as well as the municipal governments of the cities of Kyoto, Osaka, and Kobe.

2.1.(3) Advisory Council meetings

- In order to facilitate the exchange of ideas and opinions between knowledgeable individuals in various fields, PMDA convenes meetings of the "Advisory Council" (chaired by Masataka Mochizuki, Professor, Faculty of Pharmaceutical Sciences, Tokyo University of Science), which are open to the public. The Council consists of academic experts, healthcare professionals, and representatives from relevant industries, consumers, and the people who have suffered from adverse health effects caused by drugs, etc. By seeking opinions on operations and the management system, the Council serves to secure fairness and transparency of PMDA's operations, in addition to contributing to streamlining the efficiency of its operations. Under the "Advisory Council," the "Committee on Relief Services" (chaired by Hideaki Mizoguchi, Professor Emeritus, Tokyo Women's Medical University) and the "Committee on Review and Safety Operations" (chaired by Masataka Mochizuki, Professor, Faculty of Pharmaceutical Sciences, Tokyo University of Science) were also formed to discuss specialized operational issues. The dates of the meetings and specific agenda for FY 2015 were as follows.

Advisory Council (FY 2015)

Agenda for the 1st Meeting (June 24, 2015)

(1) Annual Report FY 2014
(2) Financial Report FY 2014
(3) Status of recent major initiatives
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions.
(6) Others

Agenda for the 2nd Meeting (November 5, 2015)

(1) Results of evaluation of operating performance for FY 2014
(2) Status of recent major initiatives
(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions
(5) Others

Agenda for the 3rd Meeting (March 8, 2016)

(1) FY 2016 plan (draft)
(2) Budget for FY 2016 (draft)
(3) Employment status and extension of interim measures for restrictions on employment of personnel from the private sector
(4) Status of recent major initiatives
(5) Status of PMDA's responses to opinions etc., given by members at the Advisory Council meetings for the past one year
(6) Cash contributions, etc., received by external experts commissioned for Expert Discussions
(7) Others

Committee on Relief Services (FY 2015)

Agenda for the 1st Meeting (June 24, 2015)

(1) Annual Report FY 2014
(2) FY 2015 plan
(3) PR on the Relief System for Adverse Health Effects
(4) Others

Agenda for the 2nd Meeting (December 18, 2015)

(1) Results of the evaluation of operating performance for FY 2014
(2) Operating performance so far in FY 2015 and current situation of recent major initiatives
(3) Others

Committee on Review and Safety Operations (FY 2015)

Agenda for the 1st Meeting (June 22, 2015)

(1) Annual Report FY 2014
(2) Status of recent major initiatives
(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions
(5) Others

Agenda for the 2nd Meeting (December 16, 2015)

(1) Results of the evaluation of operating performance for FY 2014
(2) Operating performance so far in FY 2015 and issues to be addressed in the future
(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions
(5) Others

- The above meetings were open to the public, and the minutes and materials for the meetings of the Advisory Council and its sub-committees were published on the PMDA website.

2.1.(4) Approaches for an efficient operation management 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 the review divisions that require particularly flexible processes, PMDA continued the group system where review teams are led by Review Directors who report to the Office Director.

- PMDA has regularly invited commissioned external experts to speaking and consultation events in order to benefit from their professional opinions relating to scientifically significant matters on reviews and safety measures. (1,385 external experts are commissioned as of March 31, 2016.)
- PMDA also has commissioned external experts to seek their opinions on the relief service for health damage caused by adverse drug reactions and infections acquired through biological products. (125 external experts are commissioned as of March 31, 2016.)
- The list of commissioned external experts is available on the PMDA website.
- Based on the need to secure impartiality and transparency of judgments offered by external experts, PMDA developed the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (December 25, 2008). The establishment of these rules enables PMDA to ensure the transparency by releasing review reports and information on conflict of interest of commissioned external experts, and also allows outside parties to check the decision making process at Expert Discussions. Cash contributions and contract payments received by external experts are disclosed immediately after confirmation of approval of designated products, implementation of safety measures, or development of approval standards for drugs or review guidelines, and are reported to the Advisory Council and the Committee on Review and Safety Operations.

  In addition, PMDA started a scheme on a trial basis from June 2015 to ensure that cash contributions and contract payments received by external experts are declared by using the information disclosed by companies.
- In carrying out operations, PMDA has also commissioned lawyers and accountants as advisors to handle operations that require legal and tax expertise. In addition, the Agency has made use of private companies for operational management of information systems and minimized the increase in the number of its regular staff.
- PMDA has continued to appoint a specialist with advanced expertise in information systems and knowledge of pharmaceutical affairs as an information system advisor, to ensure consistency and coordination of services across the Agency's information systems.

2.1.(5) Standardization of operating procedures

- In order to effectively utilize non-regular staff and limit the number of regular staff, PMDA has developed standard operating procedures (SOPs) for its major tasks. The contents of these SOPs have been examined and inspected, and, as necessary, revised. PMDA also used non-regular staff for routine operations.

2.1.(6) Development of databases

- As part of the development of system infrastructure, PMDA took an inventory of hardware and software of the system and prepared a management list to create a database that will support PMDA’s system management.

  In the review system, PMDA promoted digitalization of documents using the document management function of the new review system (Pegasus) and made it possible to confirm and manage the location of documents using the paper document management function of Pegasus.
- Among the notifications etc., issued by the MHLW and PMDA, those that are relevant to the Agency's operations or those that should be broadly disseminated to the public are posted on the PMDA website.

2.1.(7) Promotion of the optimization of operations and systems

- In FY 2015, PMDA created a management list of IT devices, etc. for centralized management regarding support period, lease period, maintenance contract period, and operation contract period of hardware and software used by PMDA to enhance management and make it more effective.

  In addition, to prepare the system environment in the Relief Department, PMDA reformed the infrastructural environment for the contribution system and that for specified hepatitis C system. PMDA standardized and unified the document forms in the review system by integrating the system. Other than this, to ensure that the individual systems are operated stably and to ascertain and classify the functions that should be further enhanced, PMDA checked the improvement status of the systems and the details of monthly reports obtained from the operation support company, and took actions in so far as possible within the scope of the current contract.

2.2. Cost Control through Increased Efficiency of Operations

2.2.(1) Retrenchment of general and administrative expense

- The Mid-term Plan set a target that the Mid-term Plan budget relating to general administrative expenses, covered by administrative subsidies, should be reduced by at least 15% from FY 2014 to the end of the effective period of the Mid-term Plan/Targets (FY 2018). To achieve the target, PMDA has been making ongoing efforts to improve operations and increase management efficiency.
- In FY 2015, PMDA promoted streamlining of efficiency of its services, such as optimization of systems and reduction of unnecessary expenditure. As in the previous fiscal year, PMDA made efforts to reduce procurement costs by conducting, in principle, general competitive bidding, resulting in a 51.1% reduction against budget for FY 2014.

2.2.(2) Cost control of operating expenses

- The Mid-term Plan set a target that Mid-term Plan budget relating to operating expenses, covered by administrative subsidies, should be reduced by at least 5% from FY 2014 to the end of the effective period of the Mid-term Plan/Targets (FY 2018). To achieve the target, PMDA has been making ongoing efforts to improve operations and increase management efficiency
- In FY 2015, PMDA promoted streamlining of efficiency of its services, such as optimization of systems, promotion of computerization, and reduction of unnecessary expenditure. Similarly to the measures taken for general administrative expenses, PMDA made efforts to reduce procurement costs by concluding contracts through, in principle, general competitive bidding, resulting in a 18.1% reduction against budget for FY 2014.

2.2.(3) Competitive bidding

- In FY 2015, however, the ratio of competitive contract schemes, including competitive requests for proposals and invitations to bid, to total contracts decreased by 11.2% in terms of number of bids and increased by 46.0% in terms of monetary amount compared to the preceding fiscal year.

  The ratio of competitive contract in number decreased from FY 2014 to FY 2015 (-11.2%). This was due to a decrease of 29 competitive contracts and an increase of 13 non-competitive optional contracts. Other than contracts for office leases, there was an increase of 10 non-competitive optional contracts regarding procurement contracts for software, etc. with the specified contract party.

Since FY 2014 was the first year of the effective period of the Third Mid-term Plan, PMDA entered into multi-year contracts for office leases, starting in FY 2014. As the total contract amount for the multi-year contracts was included in the first fiscal year, the monetary amount for non-competitive operational contracts in FY 2015 decreased by 8,103 million yen compared to the previous fiscal year, resulting in an increased ratio in terms of the monetary amount for competitive contracts.

		FY 2014	FY 2015	Change
General competitive bidding (including competitive planning competition and invitations to bids)		130 bids (87.8%)	101 bids (76.6%)	-29 bids (-11.2%)
		6,240 million yen (41.3%)	5,285 million yen (87.3%)	-955 million yen (46.0%)
Non-competitive optional contracts		18 bids (12.2%)	31 bids (23.5%)	13 bids (11.3%)
		8,869 million yen (58.7%)	766 million yen (12.7%)	-8,103 million yen (-46.0%)
	Excluding contracts in relation to office lease	12 bids (8.1%)	22 bids (16.7%)	10 bids (8.6%)
		321 million yen (2.1%)	537 million yen (8.9%)	216 million yen (6.8%)
Total		148 bids 15,109 million yen	132 bids 6,051 million yen	-16 bids 9,058 million yen

Note: Since the figures are rounded off to the nearest number, the figures in "Total" may not equal to the sum of the individual figures.

2.2.(4) Contract Review Committee meetings, etc.

- Based on "Inspection/Review of the Contract Status of Incorporated Administrative Agencies" (adopted by the Cabinet on November 17, 2009), PMDA established the "Contract Review Committee" in the Agency. The Committee consists of external knowledgeable experts as well as internal auditors. In the Committee meetings, PMDA underwent a pre-inspection of procurement cases etc., for which contracts were planned to be concluded in FY 2015, regarding the appropriateness of the contract schemes and of corrective measures for ensuring the competitiveness. The Committee held 5 meetings in FY 2015 and disclosed the summary of review on the website. In addition, PMDA established the Committee for Discussion on Rationalization of Procurements, etc., within PDMA, based on "Promotion of Rationalization of Procurements, etc. in Incorporated Administrative Agencies" (adopted by the Minister of Internal Affairs and Communications, dated May 25, 2015). The Committee was convened to address urgent procurement cases where there were rational reasons, and where these cases had previously been investigated from a viewpoint similar to that of the Contract Review Committee and reported to the Contract Review Committee after the fact.

2.2.(5) Collection and management of contributions

- Contributions from marketing authorization holders (MAHs) of the industry enable PMDA to secure the major part of financial resources for relief services for adverse health effects (e.g., adverse reactions to drugs and regenerative medical products, infections acquired through biological products and regenerative medical products) and other operations to improve the quality, efficacy, and safety of drugs and medical devices. Specifically, contributions to the adverse drug reaction fund ("ADR contributions") are declared and made by MAHs of approved drugs or approved regenerative medical products related to adverse reaction relief benefits. Contributions to the relief fund for infections acquired through biological products ("infection contributions") are declared and made by MAHs of approved biological products or approved regenerative medical products related

to infection relief benefits. Contributions to post-marketing safety measures are declared and made by MAHs of drugs, medical devices, regenerative medical products, and *in vitro* diagnostics.

- Basic data such as those concerning newly approved products and money transfers are automatically processed by the contribution collection management system, which is able to manage these contributions in an integrated fashion. Thus, PMDA was able to efficiently collect and manage these contributions through various methods, such as the calculation of products' transaction value which constitutes the basis of the contribution amount and the management of data concerning unpaid contributions. PMDA also maintained contributors' convenience through continuing consignment contracts with five major banks for receipt of contributions, resulting in the prompt transfer of funds.
- In its Mid-term Plan, PMDA set its target collection rates for owed contributions related to ADRs, infections, and post-marketing safety measures to be no less than 99%. In FY 2015, the collection rates achieved for ADR, infection, and post-marketing safety measure-related contributions were 99.7%, 100%, and 99.7%, respectively.

FY 2015 Contribution Collection Results

Category		Number of parties obligated to make contributions	Number of parties who made contributions	Collection Rate	Contribution amount (Million yen)
ADR contributions	MAHs of approved drugs, etc.	688	688	100%	3,841
	MAHs of pharmacy-compounded drugs	5,542	5,439	99.7%	5
	Total	6,140	6,127	99.7%	3,847
Infection contributions	MAHs of approved biological products, etc.	96	96	100%	93
Post-marketing Safety measures etc., contributions	MAHs of drugs, etc.	3,149	3,139	99.6%	2,952
	MAHs of pharmacy-compounded drugs	5,452	5,439	99.7%	5
	Total	8,601	8,578	99.7%	2,958

Note: Since the figures for contribution amount are rounded off to the nearest million yen, the figures in "Total" may not equal to the sum of the individual figures.

- PMDA exerted the following efforts in order to efficiently improve contribution collection rates:

  1) PMDA continued to commission the Japan Pharmaceutical Association (JPA) to collect contributions from MAHs of pharmacy-compounded drugs.

  2) PMDA placed advertisements on websites and relevant trade journals, and tried to make the procedure known to all the parties obligated to make contributions by preparing and distributing a handbook on the procedure. Also, PMDA sent out written requests to all the contributors who have not yet made contributions.

(i) Collected ADR contributions and trends in the liability reserve

a. ADR contributions

- In order to fund the relief service for adverse drug reactions, PMDA has collected ADR contributions from MAHs of approved drugs, etc. In FY 2015, the contribution rate applied to such MAHs was set at 0.27/1000 and the collected amount was 3,847 million yen.

(Million yen)

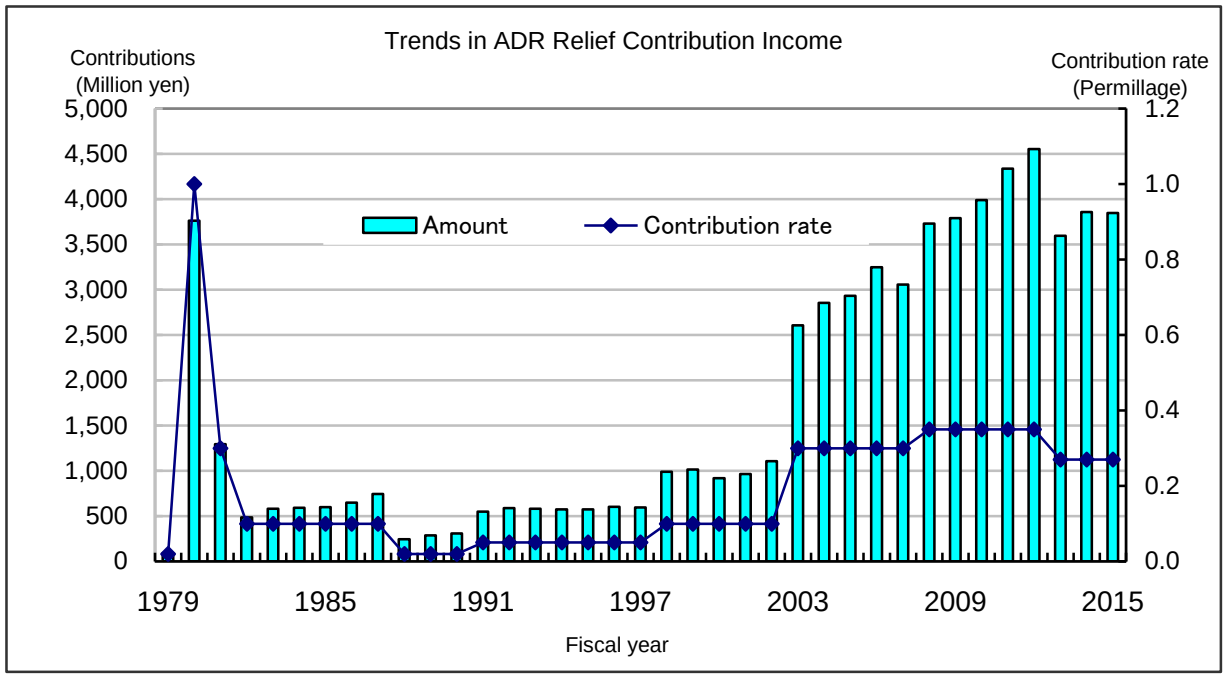
Fiscal year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Contributions from MAHs of approved drugs*	4,330 [713]	4,548 [688]	3,590 [688]	3,852 [692]	3,841 [688]
Contributions from MAHs of pharmacy-compounded drugs	7 [6,694]	6 [6,186]	6 [5,866]	6 [5,658]	5 [5,439]
Total amount	4,337	4,554	3,596	3,857	3,847
Contribution rate	0.35/1000	0.35/1000	0.27/1000	0.27/1000	0.27/1000

Note: Figures in brackets represent the numbers of contributors.

Since the figures for contribution amount are rounded off to the nearest million yen, the figures in "Total" may not equal to the sum of the individual figures.

**Representing MAHs of drugs in and before FY 2014 and representing MAHs of approved drugs and MAHs of approved regenerative medical products related to ADR contributions in FY 2015.*

- The ADR contribution income and the contribution rate since the establishment of this service are shown below.



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

- In order to fund the relief service for infections acquired through biological products, PMDA has collected infection contributions from MAHs of approved biological products, etc. In FY 2015, the contribution rate applied to such MAHs was set at 0.1/1000 and the collected amount was 93 million yen.

(Million yen)

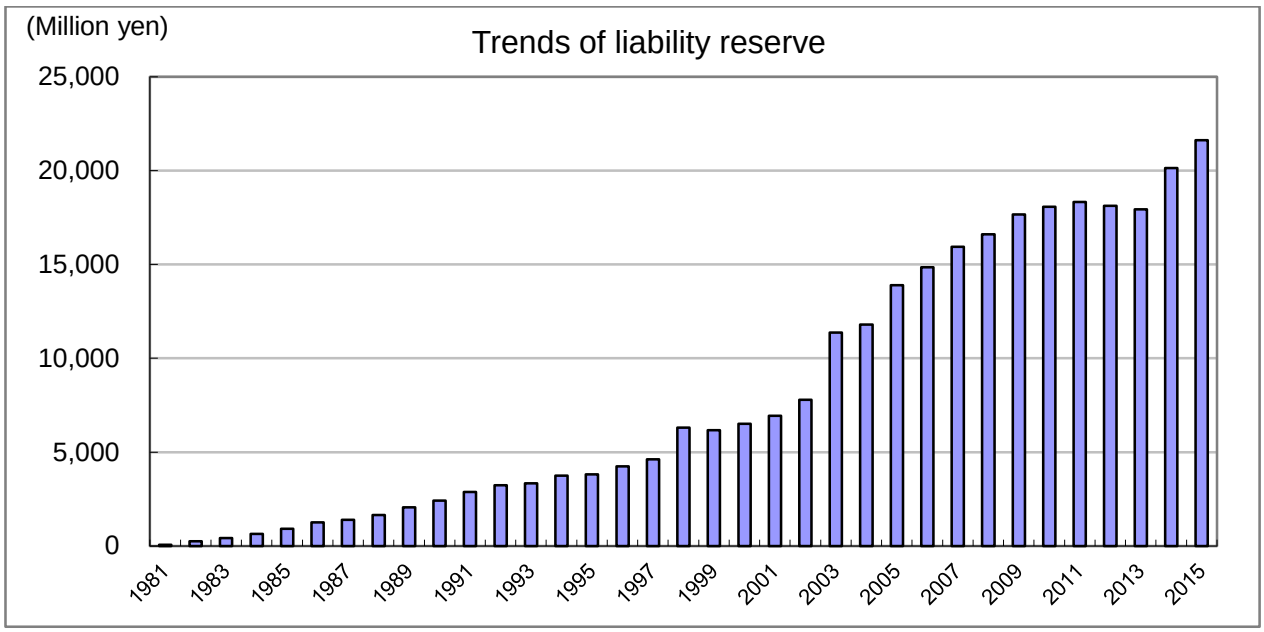
Fiscal year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Contributions from MAHs of approved biological products, etc.*	785 [92]	866 [92]	869 [94]	93 [92]	93 [96]
Contribution rate	1/1000	1/1000	1/1000	0.1/1000	0.1/1000

Note: Figures in brackets represent the numbers of contributors.

** Representing MAHs of approved biological products in and before FY 2014 and representing MAHs of approved biological products and MAHs of approved regenerative medicines related to infection contributions in FY 2015.*

c. Liability reserve

- In order to cover the estimated costs for relief benefits that eligible persons will receive in the future, PMDA calculates the amount that the Agency should possess at the end of every fiscal year and accumulates funds accordingly. The liability reserve at the end of FY 2015 was 21,617 million yen



(ii) Collected contributions for post-marketing safety measures

- In order to fund services for improvements in the quality, efficacy, safety of drugs, etc., PMDA has collected contributions to post-marketing safety measures from MAHs of drugs, medical devices, regenerative medical products, and *in vitro* diagnostics. In FY 2015, the contribution rate applied to such MAHs was set at 0.22/1000 for drugs excluding *in vitro* diagnostics and 0.11/1000 for *in vitro* diagnostics, medical devices, and regenerative medical products, and the collected amount was 2,958 million yen.

(Million yen)

Fiscal year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
MAHs of drugs/ medical devices	2,596 [2,974]	2,768 [2,970]	2,810 [3,023]	2,972 [3,099]	2,952 [3,139]
MAHs of pharmacy-compounded drugs	7 [6,694]	6 [6,186]	6 [5,866]	6 [5,658]	5 [5,439]
Total amount	2,603	2,774	2,816	2,977	2,958
Contribution rate	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices and *in vitro* diagnostics)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices, *in vitro* diagnostics, and regenerative medical products)

Note: Figures in brackets represent the numbers of contributors.

Since the figures for contribution amount are rounded off to the nearest million yen, the figures in "Total" may not equal to the sum of the individual figures.

**The figures from FY 2011 to FY 2014 represent the amount of contributions paid by MAHs of drugs (including in vitro diagnostics) and medical devices. The figures in FY 2015 represent the amount of contributions paid by MAHs of drugs, medical devices, regenerative medical products, and in vitro diagnostics.*

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

- To steadily implement measures for "Reinforcement of efforts to reduce unnecessary expenditures" (formulated in FY 2014), PMDA promoted efforts for cost-cutting, along with "Standard practice for taking more efficient cost-cutting measures" (formulated in FY 2009).

2.3. Improvement of Services to the Public

2.3.(1) General inquiry service

- Based on the "General Inquiry Guidelines" that specifies how to handle inquiries directed to PMDA and how to make use of comments and opinions to improve its operations, PMDA provides a general inquiry service and makes questionnaires available at the reception desk, enabling the collection of comments and opinions of visitors regarding its overall operations. In addition, PMDA receives opinions etc., via telephone, facsimile, and the website.
- Since June 2010, PMDA has disclosed the "Public Voices" sent to the Agency on its website on a weekly basis to make use of it to improve management of its operations.
- Among the 2,529 inquiries that PMDA received in FY 2015, 743 or approximately 30% of the total inquiries received were those relating to applications and consultations for drugs, medical devices, etc.

	Inquiry	Complaint	Opinion/ request	Others	Total
FY 2015	2,405 (713)	5 (1)	119 (29)	0 (0)	2,529 (743)

Note 1: Figures in parentheses represent the number of cases related to consultations and applications for approval of drugs, medical devices, etc. They are included in the total numbers above.

Note 2:The Office of Review Administration also accepts inquiries on consultations and applications for approval of drugs, medical devices, etc. separately from this general inquiry service.

2.3.(2) Responses to inquiries, complaints, and claims of dissatisfaction from companies regarding product reviews and product safety operations

- In addition to responding to inquiries and complaints from general consumers, PMDA also handles complaints from relevant companies regarding product reviews and product safety operations.
- In FY 2004, PMDA established a system where, if an applicant files claims of dissatisfaction etc., regarding product reviews and product safety operations, the responsible office director (the Director of the Center for Product Evaluation or the Chief Safety Officer, if the second claim of dissatisfaction has been filed in the same case) is to directly conduct an investigation and respond to the applicant within 15 working days. PMDA continued to operate the system in FY 2015.
- In addition, PMDA developed a consultation manual to handle complaints from relevant companies. From among the complaints received, PMDA selects and reviews those that would be helpful in improving its operations.

2.3.(3) Enrichment of the PMDA website

- PMDA has enhanced the content of its website. For example, new information and updates of existing content are sequentially posted on the website in order of requests from relevant departments.
- Based on requests about the PMDA website which was completely redesigned in March 2015, PMDA has improved its functionality, such as facilitating accessibility to the search page for package inserts, etc.

2.3.(4) Proactive PR activities

- The PMDA Public Relations Strategic Plan (July 11, 2008; revised on April 1, 2015) was developed from the perspective of systematically promoting PR activities of the Agency as a whole. In line with the Plan, PMDA intends to promote information provision proactively by implementing PR activities that are effective for individual stakeholders and improve services to the public. In FY 2015, the following activities were implemented based on the Strategic Plan.

  In FY 2015, PMDA distributed leaflets, which are designed to introduce PMDA to the general public, at events in various locations. In addition, PMDA notified patient groups of the distribution of leaflets etc., and provided them to the groups that requested.

  For the occasion of "Drug and Health Week," PMDA conducted PR activities for the general public by distributing brochures/leaflets on PMDA's services, brochures on relief systems, give-away goods, etc., and giving lectures and running booths at events held in various regions, in cooperation with pharmaceutical associations in 18 prefectures.

  In addition, PMDA introduced its operations to researchers and healthcare professionals by making booth exhibitions at academic conferences.

  PMDA also held a press conference in September 2015 and introduced PMDA’s role and recent actions to media representatives.

  PMDA also issued monthly PMDA newsletters (e-mail magazines for prospective employees) and released them on its website. In addition, the Chief Executive delivered speeches etc., 20 times in Japan and 4 times overseas.

2.3.(5) Disclosure requests for agency documents

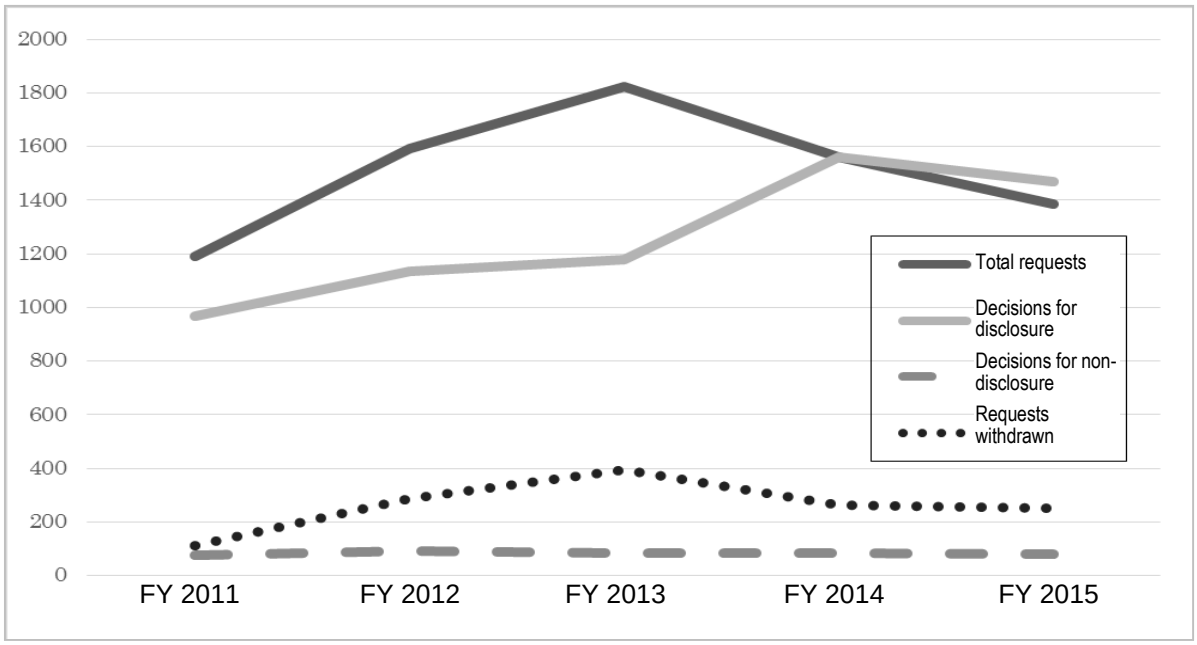
- The status of requests (over the last 5 years) for disclosure of documents under the Act on Access to Information Held by Incorporated Administrative Agencies is shown below. In FY 2015, the number of requests decreased by 11.3% and the number of disclosures decreased by 5.8% compared to the previous fiscal year. PMDA appropriately processed requests in accordance with the relevant laws and regulations.

Number of Requests for Disclosure of Agency Documents

	Total requests	Requests withdrawn	Decisions*					Objections made	Carry-over into FY 2016**
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2011	1,192	112	138	831	1	74	0	1	0
FY 2012	1,593	287	147	988	0	81	10	5	0
FY 2013	1,823	394	73	1,104	7	72	4	0	0
FY 2014	1,562	262	176	1,384	0	82	1	0	0
FY 2015	1,385	249	66	1,404	0	70	2	5	223

** A single request does not necessarily receive a single decision for disclosure etc., but may receive multiple decisions on separate occasions. The figures show the number of decisions, not the number of requests.*

*** "Carry-over into FY 2016" includes requests made at the end of the fiscal year and requests for which the deadline for decision of disclosure was extended because of large amounts of relevant documents or other reasons, in accordance with applicable laws and regulations.*



Note 1:The number of decisions for disclosure includes full and partial disclosure.

Note 2:The number of decisions for non-disclosure includes cases of non-existing documents and refusals to answer whether the documents exist.

Number of Requests for Disclosure of Agency Documents by Operational Category of Document

Operational category/FY	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Examples
Product application Review	1,046	1,410	1,675	1,457	1,295	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post-marketing Safety	139	176	131	97	82	ADR reports etc.,
Others	7	7	17	8	8	
Total	1,192	1,593	1,823	1,562	1,385	

Note: The figures include requests withdrawn, requests rejected (decision for non-disclosure), requests for non-existing documents, or requests for which PMDA refused to answer whether the requested document exists.

2.3.(6) Disclosure requests for personal information

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

Number of Requests for Disclosure of Personal Information

	Total requests	Requests withdrawn	Decisions					Objections made	Carry-over into FY 2016
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2011	1	0	0	2	0	0	0	0	0
FY 2012	3	1	0	2	0	0	0	0	0
FY 2013	6	0	0	4	0	0	0	0	0
FY 2014	8	1	0	9	0	0	0	0	0
FY 2015	8	0	2	4	0	0	0	0	2

2.3.(7) Auditing

- PMDA undergoes audits conducted by an accounting auditor in accordance with the general rules for incorporated administrative agencies and by the Agency's Auditors. 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 2015, PMDA conducted internal audits on the management status of documents, articles, cash and cash equivalents, status of salary and bonus payments, status of management competitive research funds, etc., and the status of compliance with rules restricting work assignments of personnel who had been working in the private sector.

2.3.(8) Report on the financial standing

- To ensure the transparency of expenditures, PMDA disclosed its financial standing for FY 2014, including the use of user fees and contributions, in government gazettes and on its website. PMDA also released the budget for FY 2015 on the website.

2.3.(9) Development and release of "Plan to Rationalize Procurement, etc."

- Based on “Promotion of Rationalization of Procurements, etc. in Incorporated Administrative Agencies” (adopted by the Minister of Internal Affairs and Communications, dated May 25, 2015), the Committee for Discussions on Rationalization of Procurements, etc. developed “Plan to Rationalize Procurement, etc. in the Pharmaceuticals and Medical Devices Agency for FY 2015,” in order to secure fairness and transparency through the PDCA cycle considering the characteristics of the clerical and business operations and to address the rationalization of procurements, etc. autonomously and continuously. The plan was posted on the website in July 2015.

2.4. Personnel Matters

2.4.(1) Personnel evaluation system

- According to the Mid-term Plan Targets, PMDA is required to evaluate personnel fairly and consistently by taking factors related to the performance of individual employees into consideration. Moreover, in the Third Mid-term Plan (FY 2014 to FY 2018), PMDA also intends to manage a personnel evaluation system in which the results of the evaluation and the attainment of individual goals are properly reflected in remuneration, pay raises, and promotions, to enhance the morale of employees.
- To this end, PMDA appropriately reflected the results of personnel evaluation during the period from April 2014 to March 2015 in pay raises etc., as of July 2015. In order to ensure the proper implementation of this personnel evaluation system, PMDA provided briefing sessions for all employees, and explained the "personnel evaluation system" to the new recruits as a subject of their training course.
- In FY 2013, evaluators (managerial staff) started to receive training programs given by external trainers, to enhance their evaluation capability and allow the personnel evaluation to contribute to more effective development of human resources and employee potential.
- In FY 2013, secondary evaluators started to conduct interviews with evaluatees so that the evaluators can know daily working conditions and evaluators and evaluates can communicate with each other to establish a favorable relationship.

2.4.(2) Systematic implementation of staff training

- In the operations for reviews, safety, and relief service conducted by PMDA, highly specialized expertise is required. In addition, rapid strides are constantly being made in the advancement of technology for developing drugs, medical devices, etc.
- Thus, to improve the quality of operations, PMDA must systematically provide training opportunities tailored to the objectives of each operation, for not only technical employees but also administrative employees who support organizational management. PMDA’s training programs are divided into two courses: the General Training Course on important topics in light of the specialized nature of PMDA’s services (e.g., information technology and business manners) that employees must

understand and address to fulfill their roles; and the Specialized Training Course to develop expertise in quality, efficacy, safety evaluation, and other matters related to drugs, medical devices, etc. Employees systematically participate in both courses to learn about the knowledge and expertise.

In addition, to provide efficient and effective training tailored to services, PMDA has actively utilized external institutions and experts, thereby enriching training content in order to improve the quality and capabilities of employees. PMDA also encouraged employees to participate in academic conferences etc., both in Japan and overseas to improve their knowledge and technical expertise.

To conduct each training course, the Training Committee formulated plans based on the needs of the employees. Various training programs, as listed below, have been implemented. Each of these training programs were evaluated and each earned high scores pertaining to participant satisfaction and acquisition of knowledge/skills.

1) General Training Course programs

(i) New personnel training sessions were conducted between April and May 2015. The major subjects are as follows:
- Operations of each office, related systems/procedures
- Human skills (e.g., business manner, communications, motivation)
- Document management, reduction of unnecessary expenditures, etc.

(ii) Training programs for skill and knowledge reinforcement, mid-level employees and management-level employees, as part of training programs by job level.

(iii) One-on-one English conversation lessons (e.g. practical business English for international conferences) and correspondence courses in English language, etc. were subsidized and TOEIC tests were administered to improve employees' English language skills.

(iv) Legal compliance training for all executives and employees to promote awareness of legal compliance obligations and protection of personal information.

(v) Lecturers invited from support groups for patients or adverse drug reaction sufferers gave presentations in three training sessions.

(vi) In order to utilize electronic documents more efficiently, 57 employees received IT literacy training (in Microsoft Office applications) through e-learning.

2) Specialized Training Course programs

(i) Training programs concerning the basic knowledge needed for review, safety, and relief services (case studies, medical writing training, etc.) were provided mainly for new recruits.

(ii) On-site training programs, such as visits to drug/medical device manufacturing facilities (4 facilities) and IRBs of medical institutions were provided. Hands-on training on medical devices was provided.

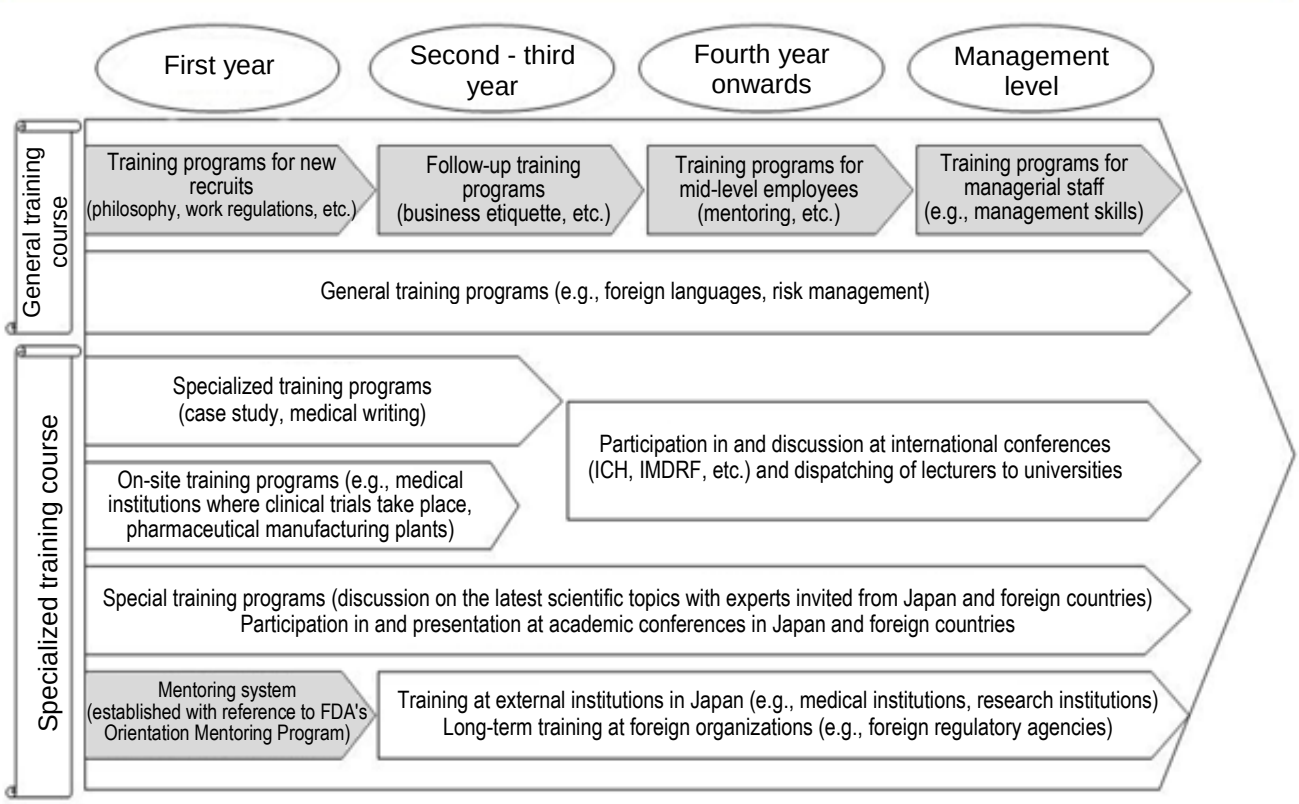
(iii) Experts invited from Japanese or overseas regulatory authorities, corporations, and universities provided special training in technical issues (14 sessions) and training in the regulatory system including the PMD Act (1 session). Training in clinical study design to learn biostatistics (12 sessions) and in pharmacoepidemiology to learn features of pharmacoepidemiological study design (5 sessions) were also provided.

(iv) A total of 13 employees were dispatched to technical training programs conducted by external institutions (e.g., Pharmaceuticals Promotion Association's Regular Course, National Institute of Public Health, and Union of Japanese Scientists and Engineers). For the acquisition of basic knowledge about medical devices, class I and II ME (Biomedical Engineering) technical trainings were also provided (16 employees).

(v) Seven employees were dispatched to 2 medical institutions for practical training with pharmacists and 2 employees were dispatched to 2 medical institutions for practical training with clinical engineers at hospitals to learn clinical practice.

(vi) One employee was dispatched to an accounting training course and another employee to a contract training course provided by the Accounting Center, Ministry of Finance, to improve administrative processing skills. In addition, 1 employee attended Grade 3 bookkeeping courses. Also, 4 employees attended either an external logical thinking course, a management course, a labor management course, or a course regarding preparation for Japanese business law examinations, as training for administrative staff members who are on main career tracks.

Training and Human Resource Development



Note: Training courses indicated in color are mandatory for all eligible employees.

2.4.(3) Appropriate personnel allocation

- In order to secure the expertise of staff members, operational continuity, and the most effective and efficient use of limited resources, PMDA seeks to conduct appropriate personnel allocation practices in line with the basic policy of the Third Mid-term Plan.
  To achieve this target, PMDA deploys personnel while taking into consideration the knowledge and work experience of individual staff members. PMDA conducts medium- and long-term rotation of personnel upon overall adjustment.
- Also, in FY 2015, personnel changes were implemented in line with the basic policies for the PMDA Career Paths that were developed in March 2011.

2.4.(4) Securing of human resources through open recruitment

- It is an important task to recruit capable persons with professional expertise while paying due attention to the neutrality and impartiality of PMDA, in order to conduct its operation of reviews and post-marketing safety measures promptly and accurately.
- In the Third Mid-term Plan, in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act, which reflects the content of the Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the final recommendations of the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Drug-induced Suffering, the target number of regular employees at the end of the period (end of FY 2018) is set to be up to 1,065. PMDA is required to recruit capable persons in relevant areas, based on the recruitment plan for each job category. Therefore, PMDA held information sessions on career opportunities, and conducted open recruitment of regular technical employees twice in FY 2015 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2015 *(as of April 1, 2016)*

1)	Technical (specialist) employees [open recruitment conducted twice]	
	Number of applicants	493
	Number of employments	48
2)	Administrative staff members who are on main career track [open recruitment conduced once]	
	Number of applicants	203
	Number of employments	10

FY 2015 Recruitment Activities

- Information sessions on career opportunities
  - April to June 2015: Four sessions in Tokyo and one session each in Osaka, Nagoya, Sapporo, Sendai, Kyoto, Hiroshima, and Fukuoka (total 575 participants)
  - September 2015: Two sessions in Tokyo and one session in Osaka (total 64 participants)
- Activities performed in collaboration with directors/employees
  - Lectures at universities etc., and a business introduction during the lectures given by directors/employees
  - Encouragement of alumni-student visit activities by young PMDA employees
- Tools for recruitment activities
  - Brochures for recruitment, posters for recruitment
  - The brochures and posters were sent out to approximately 500 institutions including medical schools of universities, medical institutions such as university hospitals, faculties of pharmaceutical science of universities, pharmacy departments of hospitals, faculties relevant to biostatistics and veterinary science, and research institutions. Also, the brochures were distributed at recruitment information sessions etc.

- Information to be posted on job information websites
  - Websites presenting job offers for new graduates in 2017 ("My Navi 2017" and "Rikunavi 2017")
  - Websites presenting job offers for persons in mid-career (“Rikunavi NEXT”)

- Staff were recruited as needed for 10 job categories: toxicology, IT systems, clinical medicine, biostatistics, epidemiology, clinical pharmacology/pharmacokinetics, GLP, GMP/QMS, foreign language (English), and data management. As a result, 17 individuals were employed on an as-needed basis.

Numbers of Executives and Regular Employees

	FY 2009 April 1	FY 2010 April 1	FY 2011 April 1	FY 2012 April 1	FY 2013 April 1	FY 2014 April 1	FY 2015 April 1	FY 2016 April 1	At the end of the effective period of Third Mid-term Plan (end of FY 2018)
Total	521	605	648	678	708	753	820	873	1,065
Review Department	350	389	415	438	460	492	532	560	
Safety Department	82	123	133	136	140	152	165	185	
Relief Department	32	34	34	33	33	33	36	37	

Note 1: The "Total" includes 6 executives (including one part-time auditor). However, the number of executives is 5 as of April 1, 2014.

Note 2: The Review Department consists of the Director for Center for Product Evaluation, Director of Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, Associate Executive Directors (excluding the one responsible for the Information Technology Promotion Group), Associate Center Directors (excluding the ones responsible for Office of Regulatory Science and for Office of Planning and Coordination), Advanced Review with Electronic Data Promotion Group, Office of International Programs, Office of International Cooperation, International Liaison Officers, Office of Review Administration, Office of Review Management, Coordination Officer for Review of Breakthrough Products (SAKIGAKE), Coordination Officer for Pharmaceutical Affairs Consultation on R&D, Office of Standards and Guidelines Development, Offices of New Drugs I to V, Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products, Office of OTC/Quasi-Drugs, Office of Generic Drugs, Offices of Medical Devices I to III, Office of In Vitro Diagnostics, Office of Non-clinical and Clinical Compliance, Chief of Kansai Branch, Consultation Division of Kansai Branch, Principal Senior Scientists, and Senior Specialists.

Note 3:The Safety Department consists of the Chief Safety Officer, Offices of Safety I and II, Office of Medical Informatics and Epidemiology, Office of Manufacturing/Quality and Compliance, and Inspection Division of Kansai Branch.

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

- PMDA carefully manages its personnel appropriately in order to mitigate any suspicion of impropriety or inappropriate ties with pharmaceutical companies. PMDA accomplishes this by imposing certain restraints on recruitment and allocation of executives and employees as well as on employment with other organizations after resignation from PMDA.
- For this purpose, PMDA's work regulations prescribe the requirement of submission of a written oath for newly-employed staff members, rules for personnel allocation, restrictions regarding re-employment after resignation, and work restrictions for employees whose family members work in the pharmaceutical industry. PMDA conducts appropriate personnel management by making a handbook which provides outlines of related regulations, Q&A, and other information and distributing it to executives and employees and by keeping its staff members informed of these regulations through training sessions for new employees.
- Also, PMDA encouraged relevant employees to submit reports on donations etc., under the code of ethics, and also reviewed the details of the submitted reports.

- As a set of countermeasures against bullying and harassment in the workplace, a structure for efficient prevention and resolution of workplace bullying and harassment has been developed, involving measures such as placing a counseling staff member in each office, based on the regulations relating to prevention of harassment and a manual on how to deal with workplace bullying and harassment.

2.4.(6) Optimization of standards for remuneration

- PMDA compared its personnel remuneration system for FY 2014 against that for national government employees in order to facilitate public understanding of its remuneration levels, and released the results on its website.
- Based on the recommendations of the National Personnel Authority in FY 2015, PMDA revised the overall remuneration system, including narrowing the disparities in remuneration standards between PMDA and the private sector, etc., in addition to reviewing regional differences and remuneration standards for older employees.

2.4.(7) Development of better workplace

- A questionnaire survey was administered to employees in September 2015 because PMDA should promote the efficiency of all its services to bring about environmental improvement in order to support work-life balance.

  Based on the results of the questionnaire given to employees, the Work-Life Balance Promotion Committee has been discussing measures to improve services and putting them into practice in order of feasibility.

2.5. Ensuring Security

2.5.(1) Entry/exit access control

- To ensure security and protect confidential information, PMDA has installed a door access control system for each office to reinforce the internal security control.
- Specifically, the ID card based-"access control system" installed at each office can log every entry through designated doors and prevent outsiders from freely entering

  In May 2010, in order to reinforce security, PMDA set up non-stop floors at which elevators do not stop unless the passengers (PMDA executives and employees, etc.) have appropriate ID cards.
- In order to ensure further strict access control, PMDA has also prescribed rules on its access control, and has made maximum efforts to thoroughly inform its staff members of these rules through the intranet and during new recruit training.

2.5.(2) Security measures for information systems

- Based on the FY 2015 plan, PMDA strove to maintain and improve the security of information in its information systems and changed and amended the setting of systems compatible with the results of an IT audit and the information provided by the National center of Incident readiness and Strategy for Cybersecurity (NISC). In order to strengthen security measures, PMDA also evaluated the current security measures for shared local area network (LAN) systems, systems in the Review

Department and the Safety Department, and logically separated the Internet environment from the service systems in the shared LAN.

- In addition, PMDA ensured that the persons concerned received cautionary advice (information on suspicious mail) from NISC via MHLW and took security measures as necessary.
- PMDA prepared the PMDA Information Security Policy in accordance with the MHLW security policy, based on "Actions for 'Promotion of Information Security Measures in Incorporated Administrative Agencies' (Administrative notice from the Counsellor [in charge of promotion of general measures for governmental organizations], National Information Security Center, Cabinet Secretariat dated July 2, 2014)".
- 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 make it possible to use secure e-mails in the audio transcription processes of records of consultations because of expanded use of secure e-mails in such processes, PMDA initiated further strengthening of its security service, "Electronic certificate issuance service for PMDA secure e-mail ID," which became available from January 2016.

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

		Number of registered companies	Cumulative total of issued certificates
Electronic certificate issuance service for PMDA secure e-mail ID Class 1 plus	Outside PMDA	75	837
	Within PMDA		1,517
Electronic certificate issuance service for PMDA secure e-mail ID	Outside PMDA	12	32
	Within PMDA		44

Note: The numbers of registered companies and issued certificates as of the end of FY 2015

PART 3 Improvements in Operations Management and Quality of Services Offered by Division

3.1. Relief Services for Adverse Health Effects

PMDA, as part of its relief services, conducts various activities to provide adequate and swift relief to victims of adverse health effects caused by drugs and regenerative medical products as well as infections contracted as a result of use of biological products and regenerative medical products, in order to ensure public awareness of the Relief System for Sufferers from Adverse Drug Reactions and the Relief System for Infections Acquired through Biological Products (collectively, the “Relief Systems”). These activities are detailed below.

3.1.(1) Expansion and review of dissemination of information regarding the Relief Systems

(i) Disclosure of information (e.g., payment cases) on the PMDA website

- PMDA promptly discloses the results of reviews of claims for relief benefits with due care for the protection of claimants’ personal information. Every month, claims approved or rejected during the previous month are posted on the PMDA website.
  When posted on the website, information on claims approved or rejected is also publicized through the “PMDA Medi-Navi,” PMDA’s free E-mail notification service.
- PMDA calls users' attention to the cases of drug-related health damage using information obtained from claims submitted for relief benefits with respect to adverse events that have occurred repeatedly despite precautions that were already provided in package inserts. Information concerning such cases is posted on PMDA’s website (on a web page entitled “PMDA Request for Proper Use of Drugs”) and is distributed through the "PMDA Medi-Navi" to further promote the proper use of drug products.
- The PMDA website contains a trial web page entitled "Patient Reports of Adverse Drug Reactions.” The web page is aimed at identifying trends in occurrence of adverse drug reactions and collect other information, and to improve safety measures for drugs. The web page has a link to the "Relief Systems for Adverse Health Effects" web page.
- To make the administration of the Relief Systems more transparent, PMDA has disclosed details related to operating performance through the end of September 2015 on its website.

(ii) Improvement of PR materials, etc.

- In order to deepen public understanding of the Relief Systems and promptly offer relief benefits, PMDA has made the following efforts:

  a) The leaflet on the Relief Systems features the tagline “This is a system that all drug users should be familiar with.” with the goal of attracting the attention of both patients and healthcare professionals. In addition, the back of the leaflet provides answers to basic questions about the Relief Systems in a Q&A format. This helps readers who pick up the leaflet to understand the outline of the Relief Systems.

     Further, the design of the leaflet was improved to highlight the name of the system by increasing its visual impact, by using Mincho typeface across 3 columns, and by displaying in red the Japanese characters meaning “sufferers from adverse reactions” in the middle column.

In addition, the poster for the Relief Systems with the same design (in PDF format) is available on the PMDA website for users' convenience.

b) PMDA has been making efforts to inform the general public that claim forms can be downloaded from its website. To further improve claimants' ease of use, PMDA has completely revised the format of the claim forms, including medical certificate for medical expenses/allowances, and amended the instructions for how to fill out the forms. The revised forms and instructions are available on PMDA's website.

http://search.pmda.go.jp/fukusayo_dl/ (Japanese only)

c) The guidance for claims and the checklists for claimants were revised, in accordance with the revision of amounts of payment as of April 1, 2015. (The guidance and checklists are enclosed with the claim forms sent from PMDA to users.) This aims to reduce the claimants' burden by clearly showing how to fill in the claim forms and what documents should be submitted with the claim forms.

3.1.(2) Proactive PR activities of the Relief Systems

PMDA implemented the following activities for proactive and efficient PR for the Relief Systems.

Major activities conducted in FY 2015

(i) PMDA renewed the design of the Relief System name, etc. and posted TV commercial videos on the special website for the Relief Systems. The website uses PMDA's original character "Doctor Q."

(ii) As a PR campaign on TV, a 30- and 15-second commercial was aired through 30 nationwide TV stations to familiarize the general public with the Relief Systems in accordance with the "Drugs and Health Week" from October 17 to 30, 2015.

(iii) A 1/6 page monochrome advertisement was placed in 50 morning newspapers on October 17, 2015 (5 national papers, 5 multi-regional newspapers, and 40 regional papers) (including 1 newspaper on October 20, 2015 and 1 evening newspaper).

(iv) Web advertisements were placed on the display network advertisement[*1] of Yahoo! Japan and Google for three months from October 17, 2015 to January 17, 2016.

(v) As transit advertising, B2-size posters were displayed at 700 major stations nationwide for one week (10 days or one month at some stations).

(vi) A 30-second commercial was shown 90 times a day on TV monitors in 518 dispensing pharmacies nationwide from November 1 to 30, 2015.

(vii) A 30-second commercial was aired an average of 8 times a day from November 1 to 30, 2015 on the Hospital Channel. The Hospital Channel is broadcast on TV monitors in the waiting rooms of 738 medical institutions nationwide.

(viii) A 30-second commercial was aired on TV monitors placed in areas accessible exclusively by healthcare professionals in 119 medical institutions nationwide (an average of 516 times a day per institution) from November 1 to 30, 2015. (A total of 4 to 112 TV monitors were set up in each institution.)

(ix) An advertisement was placed in 18 medical newspapers/journals (one advertisement per newspaper/journal) during the period from November 1, 2015 to January 1, 2016. In FY 2015, PMDA expanded its advertising to journals for medical students, student nurses, and pharmacy students.

(x) Advertorials were printed in medical journals (Nikkei Medical, Medical Asahi, Nikkei Drug Information) to publicize PMDA's activities.

(xi) PMDA placed a banner advertisement on special websites for doctors, pharmacists, nurses, and student nurses (m3.com, Cocoyaku, Nurse Senka) or distributed banner ads by e-mail during the period from November 2 to December 1, 2015. In addition, PMDA placed search advertising[*2] on Yahoo! JAPAN and Google, targeting healthcare professionals.

[*1] A banner advertisement was placed on the websites of major Internet media/content providers such as Yahoo! JAPAN or Google, and also including newspaper or magazine companies.

[*2] Search advertising is a method of placing online advertisements on web pages that match keywords an Internet user has entered on a search engine. Search advertising is mostly text-type.

On-site Activities

(i) Dispatching lecturers to employee training workshops held by medical institutions and other organizations

In order to encourage healthcare professionals to support the utilization of the Relief Systems and to promote public awareness, PMDA proactively dispatches members of its staff to serve as lecturers at employee training courses organized by medical institutions or other organizations.

In FY 2015, in response to requests from medical and related institutions, PMDA dispatched staff to give lectures at 30 medical institutions and 32 related organizations to explain the Relief Systems. PMDA also sent PR materials to 134 medical institutions.

In FY 2015, PMDA began to distribute questionnaires to medical institutions receiving lecture presentations from PMDA staff. These questionnaires included a questionnaire designed to gather information concerning the degree to which the Relief Systems are recognized and to collect comments and suggestions for improvements to PMDA staff lectures (administered at training sessions); and another questionnaire concerning how this awareness and systems in place at medical institutions have been changed in reaction to training sessions (administered 3 months after training sessions).

(ii) Lectures delivered at training sessions for designated mental health doctors

PMDA gave lectures and distributed information materials on the Relief Systems and the proper use of antipsychotic drugs at 11 training sessions for designated mental health doctors (for new doctors and for those renewing their certification) held in 4 cities/prefectures (Tokyo, Osaka, Hyogo, and Fukuoka).

(iii) Academic conferences

PMDA conducted PR activities at academic conferences as listed below:

- Booth presentations
  - Annual Meeting of the Japanese Society of Neurology
  - Annual Meeting of the Japanese Society of Hematology
  - Annual Meeting of the Japanese Society of Pharmaceutical Health Care and Sciences
  - Annual Congress of Japanese Society for Quality and Safety in Healthcare
  - Annual Meeting of the Japanese Society for AIDS Research
  - Meetings of other scientific societies

- Distribution of booklets and brochures
  - Annual Meeting of the Japanese Association for Infectious Diseases
  - Annual Meeting of Japanese Society of Allergology

- Annual Meeting of the Japanese Society of Psychiatry and Neurology
- Meetings of other scientific societies

(iv) Requests for cooperation to government bodies, relevant organizations, etc.

PMDA informed 17 government bodies and relevant organizations of the current level of awareness of the Relief System, and requested their cooperation on PR-related activities.

(v) Others

PMDA opened a consultation desk for the Relief Systems and distributed leaflets at the 17th Forum on Eradication of Drug-induced Suffering (sponsored by the Japan Federation of Drug-Induced Sufferers Organizations).

Others

(i) PMDA maintained a special website for the Relief System, featuring its original mascot character "Doctor Q."

(ii) PMDA ran a PR campaign using a brochure aimed at healthcare professionals, urging them to "Know it better than anyone else and pass it on to other people: Relief System for Sufferers from Adverse Drug Reactions." The brochure in PDF format is available on the PMDA website.

(iii) PMDA updated its presentation slides entitled “What is the Relief System for Sufferers from Adverse Drug Reactions?” to accelerate the use of the slides in lectures, training sessions, etc., on the Relief System at universities and hospitals.

(iv) PMDA posted the following images of its publicity materials on its website: a poster for the Relief Systems to be displayed in pharmacies and a medicine envelope printed with information on the Relief Systems.

(v) PMDA published the “Summary of the Relief System for Sufferers from Adverse Drug Reactions and Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs” in the “Pharmaceuticals and Medical Devices Safety Information No. 328 (December 2015).”

(vi) In cooperation with the Federation of Pharmaceutical Manufacturers’ Associations of Japan, PMDA sent leaflets to pharmaceutical companies so that medical representatives could distribute them to doctors to promote their knowledge and understanding of the Relief System.

(vii) With cooperation of the Federation of Pharmaceutical Manufacturers' Associations of Japan, PMDA published information on the Relief Systems in the Federation’s journal “Drug Safety Updates” and distributed the journal to medical institutions nationwide.

(viii) In collaboration with MHLW, PMDA enclosed the leaflet on the Relief Systems in the brochure "Pharmaceuticals and Medical Devices Safety Information Reporting System." The leaflets enclosed in the brochures were distributed to relevant organizations etc.

(ix) Information on the Relief Systems was provided in a brochure "Useful Information on Medicines" for the "Drug and Health Week." (The brochure is published by MHLW and the Japan Pharmaceutical Association.)

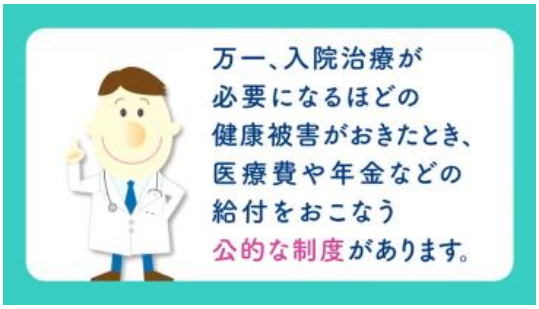
(x) PMDA requested the Japan Pharmaceutical Association (JPA) to retain the banner ad for the Relief Systems on a JPA’s web page for the general public, to make the system known to many people.

(xi) The Relief System’s website address was printed on the educational material entitled “Learn Yakugai (Drug-Induced Sufferings)” prepared by MHLW. The educational material, together with the poster for the Relief Systems, was distributed to junior high schools, boards of education, etc., nationwide.

(xii) PMDA surveyed the level of awareness of the Relief Systems among the general public and healthcare professionals, to understand how well the system is recognized and to make PR activities more effective.
Survey period: December 22, 2015 to January 8, 2016.

Home page of the special website

TV commercial



Newspaper Ad

Promoting the Relief Systems through TV monitors in hospitals and pharmacies

Promoting the Relief Systems through TV monitors in areas accessible by healthcare professionals only

Advertorials in healthcare journals

◆Promoting the Relief Systems through interview articles posted in Nikkei Medical, Nikkei DI, and Medical Asahi

医薬品
副作用被害
救済制度

正しい理解で有効な活用を

医薬品副作用被害救済制度により守られるわが国の医療制度

新百合ヶ丘総合病院　皮膚疾患研究所 所長　飯島 正文 氏

医薬品を適正に使用すれば
処方責任が問われることなく
救済される制度

PR

判定部会では「疑わしきは救済」
という考え方で審議

コンセンサスがとれている使い方であれば
適正な使用として判定

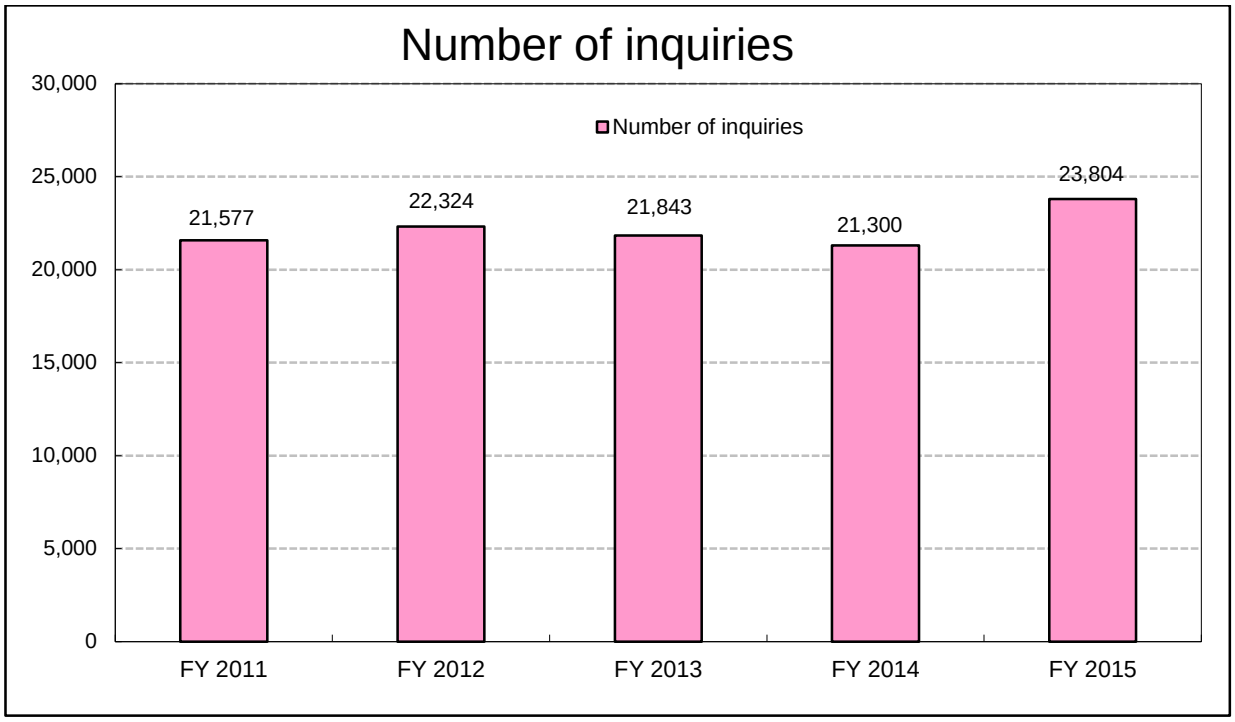
0120-149-931

独立行政法人
医薬品医療機器総合機構

3.1.(3) Maintaining efficient management of the inquiry service

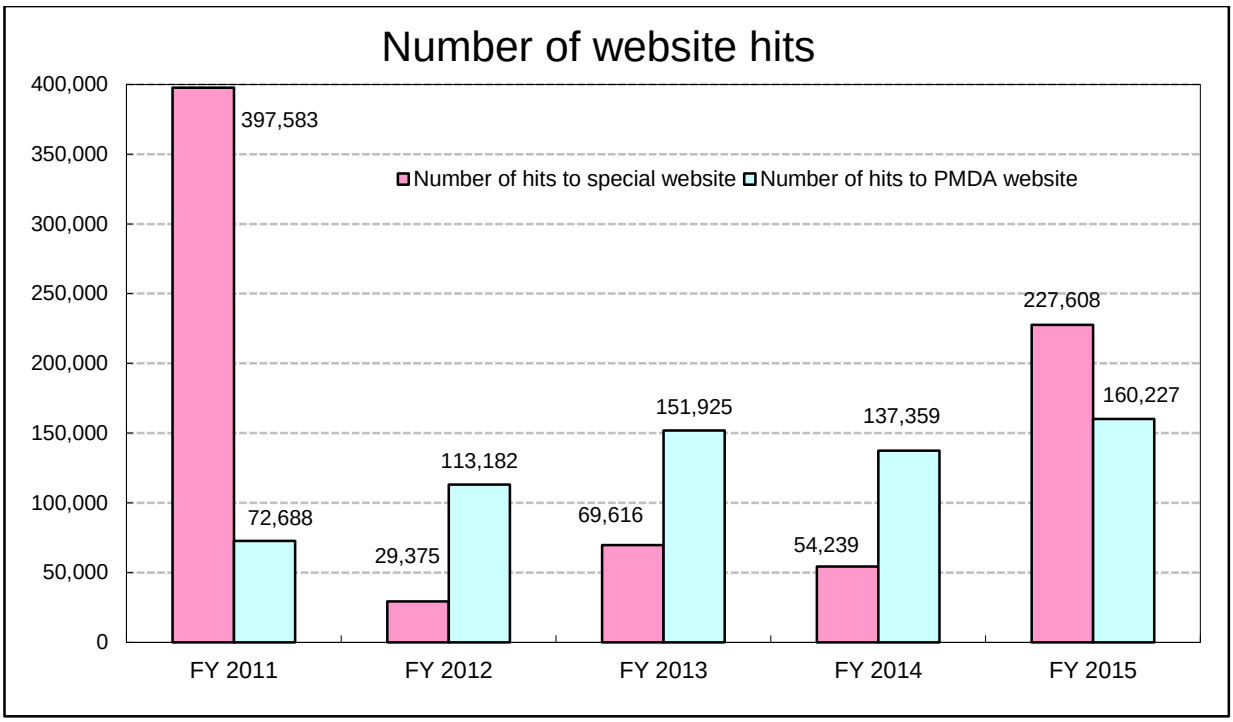
- In FY 2015, the Relief System Inquiry Service received 23,804 inquiries, an 11.8% increase over the previous fiscal year (21,300 inquiries).

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Versus FY 2014
Number of inquiries	21,577	22,324	21,843	21,300	23,804	111.8%



- In FY 2015, the PMDA website was accessed 160,227 times, a 16.6% increase over the previous fiscal year (137,359 hits).
- In FY 2015, the special website for the Relief Systems was accessed 227,608 times, a 319.6% increase over the previous fiscal year (54,239 hits).

Fiscal year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Versus FY 2014
Access to PMDA website	72,688	113,182	151,925	137,359	160,227	116.6%
Access to special website	397,583	29,375	69,616	54,239	227,608	419.6%



<Relief System Inquiry Service>

- ♦ Toll-free number: 0120-149-931
  (Office hours: Monday - Friday [except public holidays and New Year holidays] 9:00 -17:00)
- ♦ Relief System Inquiry Service E-mail address: kyufu@pmda.go.jp

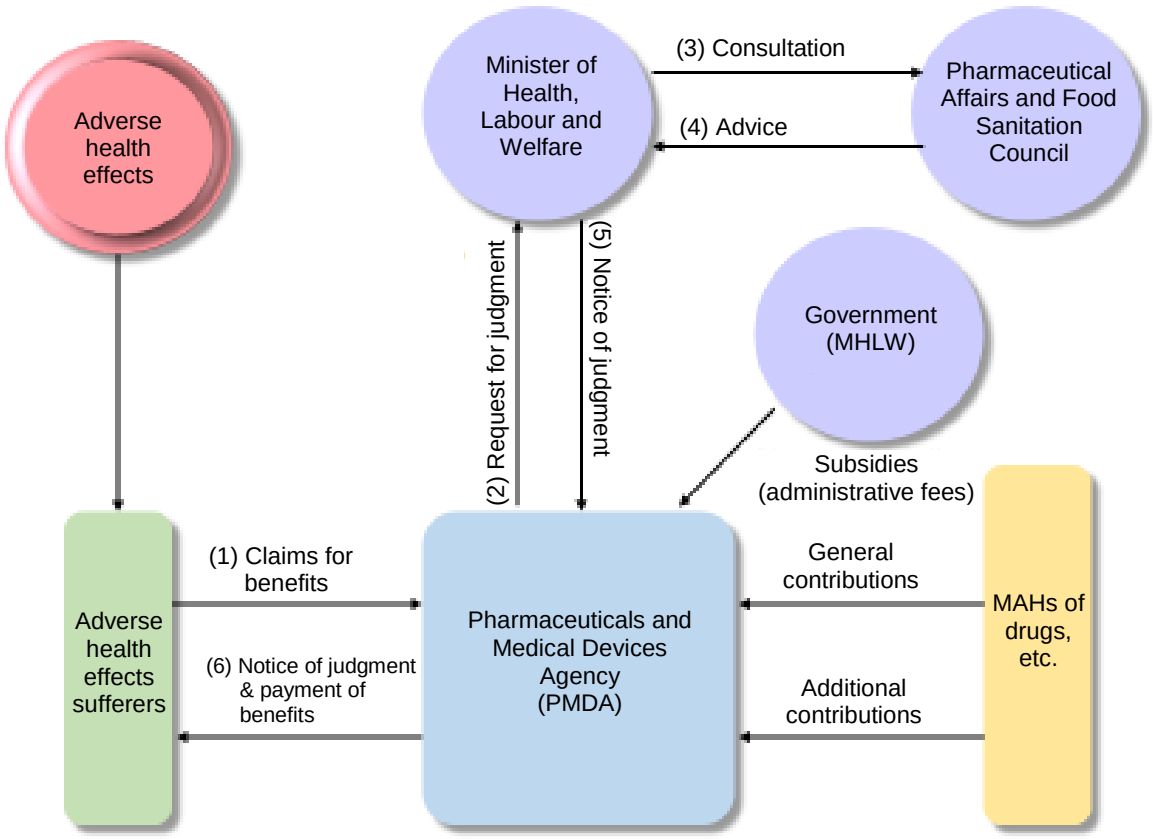
3.1.(4) Promotion of efficient services using databases

- Information on relief benefit services for adverse reactions was collected on a database and used to expedite relief benefit services based on past cases.

3.1.(5) Promotion of expeditious processing of relief benefit claims

- Upon receiving a claim for relief benefits, PMDA investigates and analyzes related facts and processes paperwork (e.g., investigation of relevant facts, preparation of case narrative summaries and investigation reports). The agency then submits a request to the Minister of Health, Labour and Welfare to make a judgment on the medical and pharmaceutical matters associated with the claim. This process flow helps ensure that claimants receive relief benefits without delay.

Process Flow for Adverse Health Effect Relief Services



* Claimants who are not satisfied with the outcome of the judgment regarding their claim(s) for relief benefits may submit a request to the Minister of the MHLW to review the judgment.

- Although the number of claims is expected to increase, the Third Mid-term Plan specifies that PMDA maintain the following numerical goals for the administrative processing times: between filing a claim and a decision on approval/rejection (at least 60% of claims should be judged within 6 months of filing). In FY 2015, PMDA endeavored to promptly process claims so that at least 60% of the claims are judged within 6 months of filing.

  The number of claims filed greatly increased from 1,412 in FY 2014 to 1,566 in FY 2015. The number of claims judged also increased from 1,400 in FY 2014 to 1,510 in FY 2015. Of these 1,510 claims, 915 were judged within 6 months of filing. These 915 claims account for 60.6% of all claims filed, exceeding the annual target for FY 2015, and far exceeding 867 in FY 2014.

  In total, the 39 claims filed in FY 2014 were associated with human papillomavirus (HPV) (mean annual number of claims in past 5 years: 16.6 claims). HPV-associated claims increased sharply in FY 2015 (152 claims). Of all HPV-associated claims filed to date, 75 have been processed and judged.

  HPV-associated claims

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FT 2014	FY 2015	Total
Number of claims	2	10	7	25	39	152	235
Number of claims judged	0	5	9	8	4	75	101

(i) Relief Service for adverse drug reactions

PMDA provides benefits to victims of diseases, disabilities, and deaths occurring on or after May 1, 1980 that were determined to have been the result of adverse reactions to drugs (and regenerative medical products on or after November 25, 2014) that were used appropriately. These benefits consist of medical expenses, medical allowances, disability pensions, pensions for raising handicapped children, bereaved family pensions, lump-sum benefits for bereaved families, and funeral expenses.

a. Performance of the Relief Service for adverse drug reactions

The performance for FY 2015 is shown below.

Fiscal Year			FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of claims filed			1,075	1,280	1,371	1,412	1,566
Number of claims judged			1,103	1,216	1,240	1,400	1,510
	Approved		959	997	1,007	1,204	1,279
	Rejected		143	215	232	192	221
	Withdrawn		1	4	1	4	10
	Within 6 months	Number of claims	534	553	754	867	915
		Achievement rate[*1]	48.4%	45.5%	60.8%	61.9%	60.6%
Claims in progress[*2]			715	779	910	922	978
Median processing time (months)			6.1	6.2	5.8	5.7	5.6

*[*1] Percentages of claims judged within 6 months of filing, of the total number of claims judged in each fiscal year.*

*[*2] The numbers of claims for which reviews remained in progress at the end of each fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2015 by type of benefit are shown below.

Fiscal Year		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of claims filed		1,075	1,280	1,371	1,412	1,566
Types of benefit	Medical expenses	909	1,101	1,200	1,221	1,341
	Medical allowances	964	1,168	1,252	1,290	1,428
	Disability pensions	77	83	88	95	109
	Pensions for raising handicapped children	4	1	7	12	7
	Bereaved family pensions	47	46	49	41	37
	Lump-sum benefits for bereaved families	63	53	54	65	61
	Funeral expenses	107	98	105	103	100

Note: A single claim may be classified under more than one type of benefit.

c. Approval by type of benefit

The number of approved cases and amounts of benefits paid in FY 2015 by type of benefit are shown below.

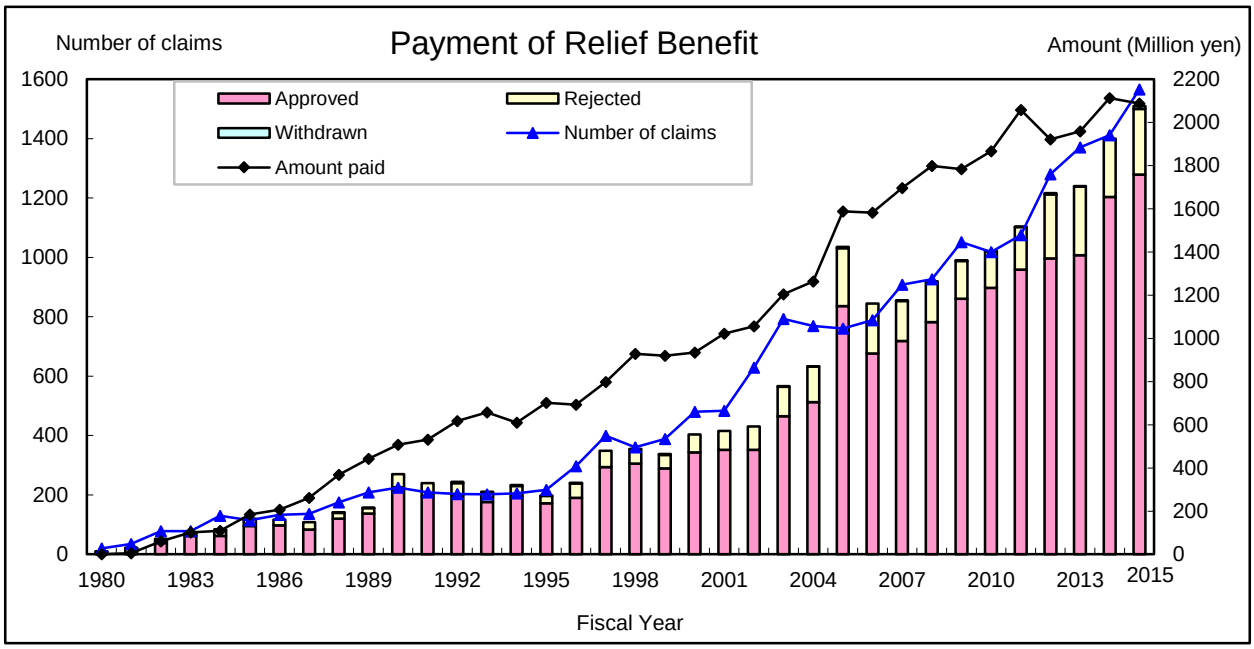
(Unit: Thousand yen)

Type	FY 2011		FY 2012		FY 2013	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	836	93,284	892	97,905	886	95,025
Medical allowances	895	75,198	947	75,326	945	82,730
Disability pensions	28	881,885	28	861,595	39	905,233
Pensions for raising handicapped children	6	49,906	0	43,744	3	40,785
Bereaved family pensions	35	614,318	32	602,068	31	603,130
Lump-sum benefits for bereaved families	47	328,093	32	227,696	32	220,032
Funeral expenses	80	16,006	62	12,438	59	12,249
Total	1,927	2,058,389	1,993	1,920,771	1,995	1,959,184

Type	FY 2014		FY 2015	
	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	1,108	123,987	1,146	118,235
Medical allowances	1,151	95,457	1,220	112,040
Disability pensions	37	943,939	47	1,002,305
Pensions for raising handicapped children	2	38,965	8	43,675
Bereaved family pensions	31	585,626	23	580,934
Lump-sum benefits for bereaved families	45	310,806	32	218,891
Funeral expenses	72	14,507	53	10,822
Total	2,446	2,113,286	2,529	2,086,902

Note 1: "Number of cases" is the number of approved cases. "Amount paid" is the amounts of the benefits paid for both new and existing cases.

Note 2: Since the amounts are rounded off to the nearest thousand yen, the figures in "Total" may not equal to the sum of the individual figures.



(ii) Relief service for infections acquired through biological products

PMDA provides benefits to victims of diseases, disabilities, or deaths occurring on or after April 1, 2004, due to infections caused by biological products (and regenerative medical products on or after November 25, 2014) that were used properly. The benefits consist of medical expenses, medical allowances, disability pensions, pensions for raising handicapped children, bereaved family pensions, lump-sum benefits for bereaved families, or funeral expenses.

a. Performance of relief service for infections

The performance for FY 2015 is shown below.

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of claims filed	9	4	7	3	6
Number of claims judged	7	6	4	7	2
Approved	3	4	4	6	1
Rejected	4	2	0	1	1
Withdrawn	0	0	0	0	0
Claims in progress*1	4	2	5	1	5
Achievement rate*2	100.0%	83.3%	100.0%	42.9%	50.0%
Median processing time (months)	4.4	4.7	4.3	6.3	7.5

*[1] *Claims yet to be judged at the end of each fiscal year.*

*[2] *Percentages of claims judged within 6 months of filing, of the total number of claims judged in each fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2015 by type of benefit are shown below.

Fiscal Year		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of claims		9	4	7	3	6
Types of benefit	Medical expenses	6	2	6	2	5
	Medical allowances	8	4	7	3	5
	Disability pensions	0	0	0	0	0
	Pensions for raising handicapped children	1	0	0	0	0
	Bereaved family pensions	0	0	0	1	2
	Lump-sum benefits for bereaved families	0	0	1	1	0
	Funeral expenses	0	0	1	2	2

Note: A single claim may be classified under more than one type of benefit.

c. Approval by type of benefit

The number of approved cases and amounts of benefits paid in FY 2015 by type of benefit are shown below.

(Unit: Thousand yen)

Type	FY 2011		FY 2012		FY 2013		FY 2014		FY 2015	
	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid	Number of cases	Amount paid
Medical expenses	3	213	2	83	3	258	5	336	1	0
Medical allowances	3	282	4	282	4	356	6	566	1	170
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,370	–	2,362	–	2,353	–	2,338	–	2,393
Lump-sum benefits for bereaved families	–	–	–	–	–	–	–	–	–	–
Funeral expenses	–	–	–	–	–	–	–	–	–	–
Total	6	2,865	6	2,726	7	2,967	11	3,239	2	2,563

Note: As benefit amounts are rounded to the nearest thousand yen, the figures in "Total" may not equal the sum of the individual figures.

3.1.(6) Promotion of collaboration between the review and safety offices

- Office of Relief Funds and Offices of Safety conducted joint meetings approximately once a month to promote information sharing.
- In accordance with the PMD Act, after appropriate measures have been taken to safeguard personal information, the Office of Relief Funds periodically provides the Office of Safety with the following information: information on diseases, disorders, and/or death in relation to persons who filed claims for relief benefits for adverse reactions and/or infections; and information on the decision on approval/rejection of the claim.

- The Office of Relief Funds provides the Office of Safety with detailed information concerning adverse reactions not listed in package inserts (unknown adverse reactions) and on adverse events that have been repeatedly reported despite warnings in package inserts.
- PMDA calls users' attention to the cases of drug-related health damage using information obtained from claims submitted for relief benefits with respect to adverse events that have occurred repeatedly despite precautions that were already provided in package inserts. Information concerning such cases is posted on PMDA's website (on a web page entitled "PMDA Request for Proper Use of Drugs"). This document clearly explains to healthcare professionals PMDA's recommended precautions for safe use of drugs in order to further promote the proper use of drugs.

  Reference: "PMDA Request for Proper Use of Drugs" is disseminated to healthcare professionals, etc. through the "PMDA Medi-Navi," the agency's E-mail notification service.
- The Office of Relief Funds and the Office of Safety work in tandem through their defined roles and responsibilities related to the "Relief System Inquiry Service" and "Drugs and Medical Devices Inquiry Service."

3.1.(7) Appropriate management of health and welfare services

- In accordance with the PMD act, to provide more immediate relief from health damage due to adverse drug reactions, PMDA offers health and welfare services to victims of adverse health effects if it is determined that such services are required in addition to relief benefits.

(i) Investigative research to improve the quality of life of sufferers from serious and rare adverse health effects caused by drug products

As part of its health and welfare services, PMDA established an Investigative Research Team for Improvements in the Quality of Life (QOL) of Sufferers from Serious and Rare Adverse Health Effects Caused by Drug Products in April 2006. The team launched an investigative research initiative to examine methods for offering necessary services and how to improve the QOL of victims of serious and rare adverse health effects who are unable to obtain adequate support from general assistance programs for disabled people. This research project was carried out based on the results of a survey on adverse health effects due to adverse drug reactions (March 2006).

In FY 2015, PMDA summarized the operating performance for FY 2014, prepared an investigative research report, and conducted investigative research targeting 77 individuals presenting with serious adverse health effects, including Stevens Johnson syndrome, Reye's syndrome, and symptoms similar to Reye's syndrome.

Research Method

Sufferers from adverse health effects were asked to provide detailed data on their daily living by completing a survey form. The data are analyzed and evaluated (77 volunteers in FY 2015).

Research Team

Team Leader: Atsushi Ozawa, Professor, Graduate School of Comprehensive Human Sciences, University of Tsukuba
(Master's Program in Lifespan Developmental Science)
Takao Takahashi, Professor, School of Medicine, Keio University
(Department of Pediatrics)
Kazuo Tsubota, Professor, School of Medicine, Keio University
(Department of Ophthalmology)

Chieko Matsunaga, Professor, School of Health and Welfare, International University of Health and Welfare

(ii) Consultation services to address mental health problems etc.

The survey on adverse health effects due to adverse drug reactions showed the necessity of care for persons presenting with deep mental trauma due to diseases and disabilities caused by adverse drug reactions, as well as the importance of consultation support for persons with remarkable restrictions in daily living due to such adverse health effects. PMDA therefore held many discussions with support groups for adverse drug reaction sufferers and other organizations on how to offer support services to persons who have received benefits under the Relief Systems. Accordingly, PMDA initiated "Consultation Services to Address Mental Problems etc." in January 2010.

Through these consultation services, qualified experts in social work provided advice on mental health care and on the use of welfare services to persons and their families who are suffering from adverse health effects caused by adverse drug reactions or infections acquired through biological products. In FY 2015, 43 consultations were performed.

(iii) Distribution of benefit recipient cards

In January 2010, PMDA began issuing by request credit card sized certificates to beneficiaries of adverse reaction relief benefits for their convenience. The card displays specific information including the name of the drug(s) that were determined or suspected to have caused the adverse reaction to the card holder. In FY 2015, cards were issued to 704 persons.

(iv) Investigative research concerning improvements to the QOL of patients with hepatitis C caused by treatment for congenital diseases

As part of its health and welfare-related services, PMDA established an Investigative Research Group for Improvements in the QOL of Patients with Hepatitis C Caused by Treatment for Congenital Diseases in August 2010. The group initiated research to study the actual living conditions of sufferers from infections acquired through biological products and thereby obtain information to examine how to improve the QOL of sufferers and provide necessary services to them.

In FY 2015, PMDA summarized the operating performance for FY 2014, prepared an investigative research report, and conducted research in 159 subjects.

Research Method

Among individuals with hepatitis C caused by treatment for congenital diseases, those with serious infections are asked to provide detailed data on their daily living by completing a survey form. The data are analyzed and evaluated (159 volunteers in FY 2015).

Research Team

Team Leader: Kugahisa Teshima, Professor, Graduate School of Social Service, Japan College of Social Work
Namiki Izumi, Deputy Director, Musashino Hospital, Japanese Red Cross Society
Midori Shima, Professor, Department of Pediatrics, Nara Medical University
Akira Terashima, Professor, Faculty of General Welfare, Urawa University

(v) Questionnaire survey to ascertain claimants' needs related to Relief System operations

PMDA distributed a questionnaire to 1,056 new beneficiaries of relief benefits and 483 pension beneficiaries. The questionnaire aimed to publicize the Relief Systems, promote the use of the system,

and improve the relief services by improving the operations of the system, and to obtain information (e.g., the needs of claimants) that would help accelerate the provision of relief benefits. A total of 1,126 beneficiaries (73.2%) answered the questionnaire.

◆Questionnaire results (excerpted)

(i) How (or from whom) did you know that your symptoms were an adverse drug reaction(s)? (Multiple responses allowed)

Doctor	Pharmacist	Others	No response	Total
958	46	160	4	1,168

(ii) How (or from whom) did you learn about the Relief Systems? (Multiple responses allowed)

Medical institutions						Advertising media			Word-of-mouth		
Doctor	Office staff	Pharmacist	Nurse	Dentist	(Subtotal)	Internet	Newspaper/ advertisement	(Subtotal)	Family	Friend/ acquaintance	(Subtotal)
475	73	63	9	2	(622)	182	87	(269)	87	84	(171)

Governmental office				Pharmacy	Others	No response	Total
City, ward, town, and village	Health center	Medical safety support center	(Subtotal)				
20	16	5	(41)	27	158	2	1,290

(iii) Have you ever used or would use the consultation service for mental issues? (Single response only)

Using / Have used	28
May use if I had the opportunity	410
Never used / Will not use	456
Total*	894

*Those who did not respond to the questionnaire were excluded.

(iv) Have you ever used or would use the Benefit Recipient Card? (Single response only).

Using / Have used	46
May use if I had the opportunity	137
Never used / Will not use	218
Total*	401

*Those who did not respond to the questionnaire were excluded.

3.1.(8) Appropriate provision of healthcare allowances for patients with SMON and patients infected with HIV through contaminated blood products

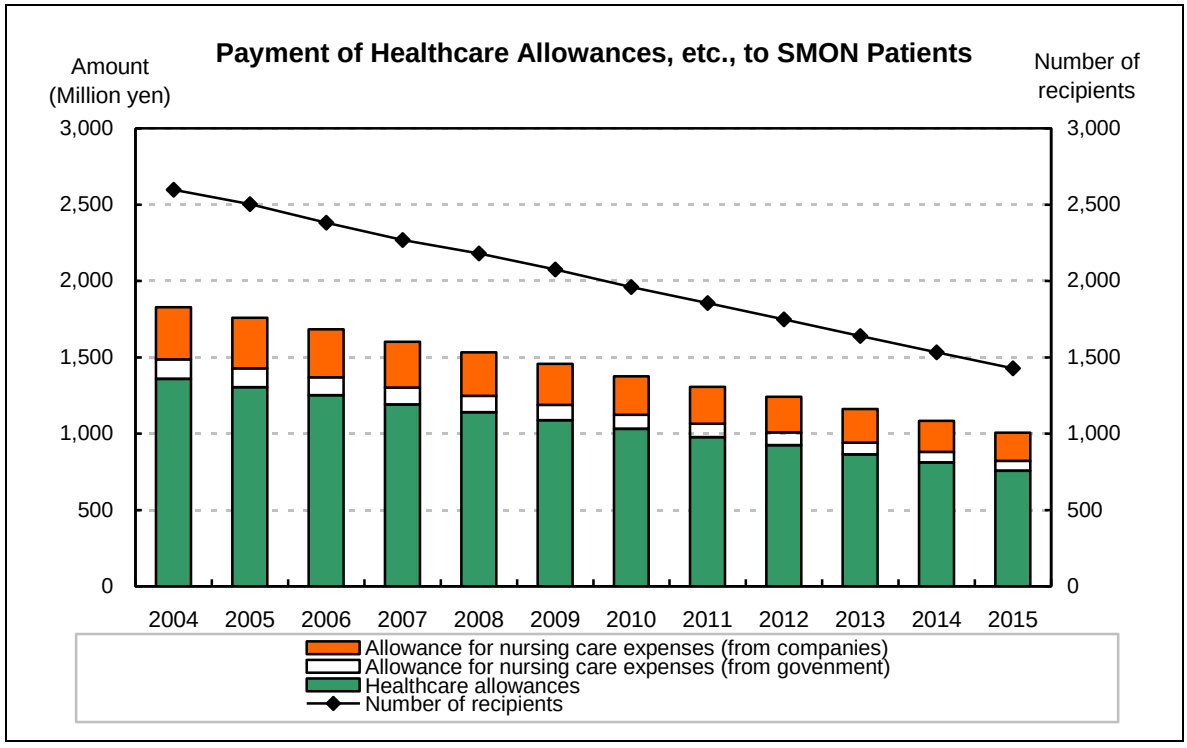
- PMDA has been commissioned to provide healthcare allowances to patients with SMON and patients infected with HIV through contaminated blood products, giving due consideration to the confidentiality of personal information.

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

- PMDA provides healthcare allowances and nursing care expenses to patients with SMON for whom an out of court settlement was reached. In FY 2015, a total of 1,006 million yen was paid to 1,428 patients.

Fiscal Year		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of recipients		1,855	1,748	1,639	1,533	1,428
Amount paid (thousand yen)		1,306,329	1,241,368	1,160,994	1,082,992	1,006,135
Break down	Healthcare allowances	975,567	924,669	864,462	811,727	757,285
	Allowance for nursing care expenses (from companies)	241,890	233,050	219,630	201,919	185,319
	Allowance for nursing care expenses (from government)	88,872	83,650	76,902	69,346	63,532

Note: As benefit amounts are rounded to the nearest thousand yen, the figures in "Amount paid" may not equal the sum of the individual figures in "Breakdown."



(ii) HIV-related services (commissioned payment of healthcare allowances)

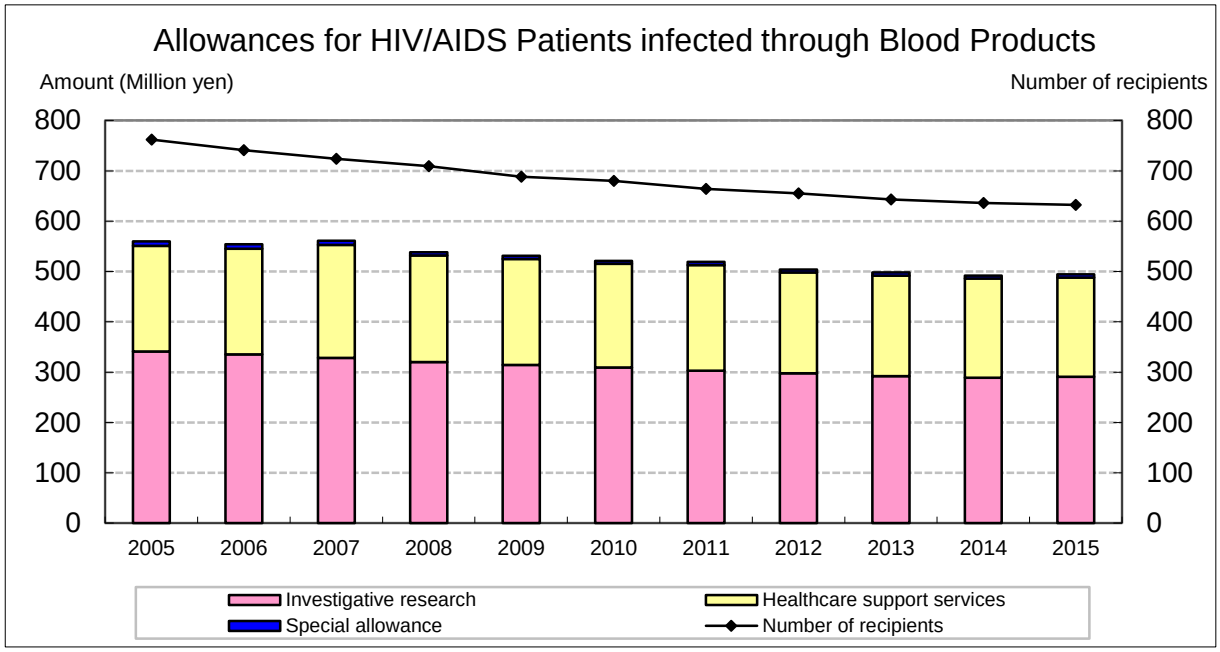
- PMDA provides allowances for patients infected with HIV through blood products under three types of services (see below). In FY 2015, 520 HIV-positive patients received allowances under the investigative research, 110 patients with AIDS under the healthcare support service, and two patients with AIDS received special allowances. In total, 635 patients received allowances under the three services (495 million yen in total).

  a. Payment of healthcare allowances for HIV-positive patients without AIDS, as part of the investigative research
  b. Payment of healthcare allowances for patients with AIDS for whom a settlement has been reached in court, as the healthcare support service
  c. Payment of special allowances etc., for patients with AIDS for whom a settlement has not been reached in court

Fiscal Year	FY 2011		FY 2012		FY 2013	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	547	302,763	540	297,790	529	292,349
Healthcare support services	115	210,000	112	199,500	112	199,650
Special allowance	2	6,276	3	6,362	2	6,232
Total	664	519,039	655	503,652	643	498,230

Fiscal Year	FY 2014		FY 2015	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	524	288,736	520	290,935
Healthcare support services	110	197,400	110	197,400
Special allowance	2	6,190	2	6,336
Total	636	492,325	632	494,671

Note: As benefit amounts are rounded to the nearest thousand yen, the figures in "Total" may not equal the sum of the individual figures.



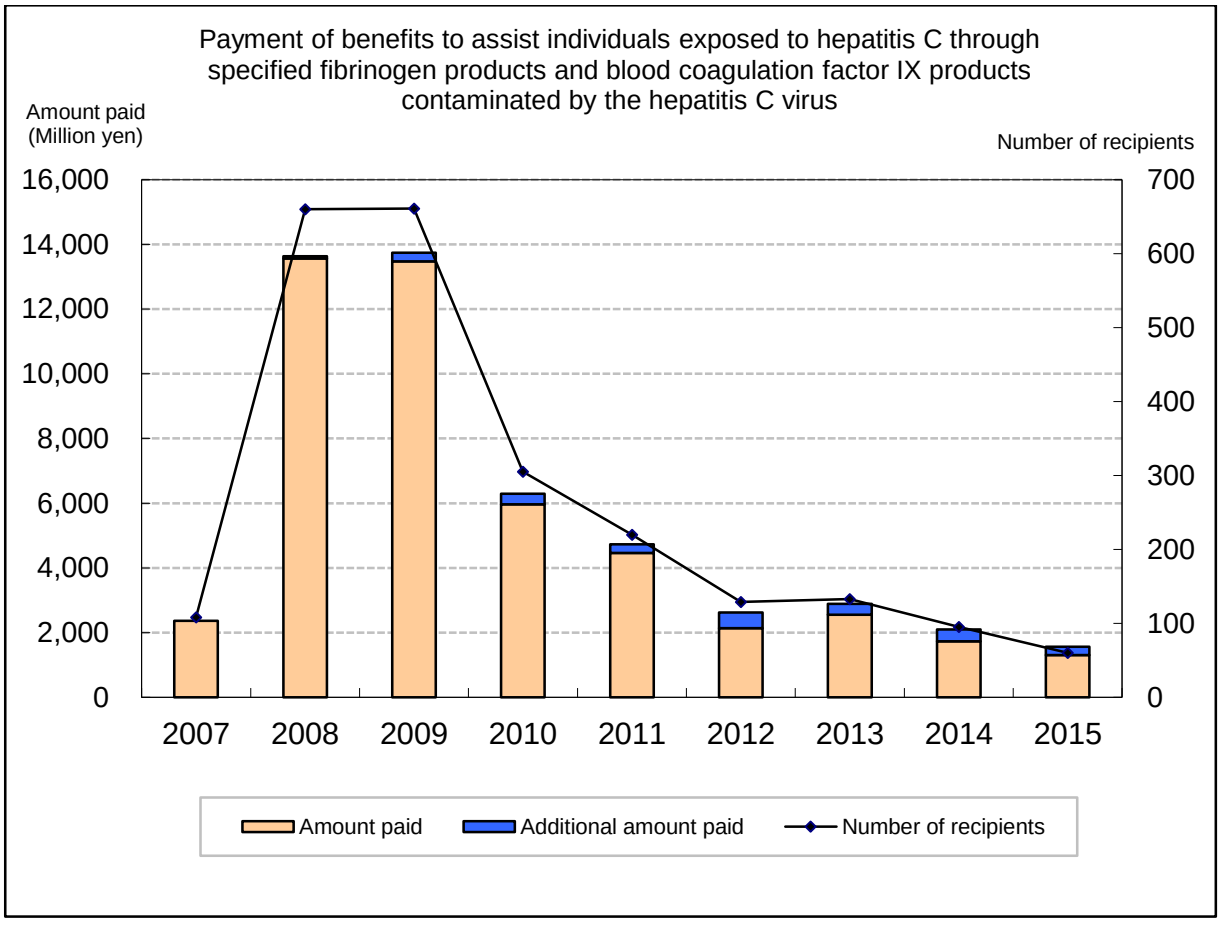
3.1.(9) Appropriate provision of benefits to individuals with hepatitis C caused by specified fibrinogen products and specified blood coagulation factor IX products

- On January 16, 2008, PMDA began to provide benefits to individuals with hepatitis C, in accordance with the Act on Special Measures concerning the Payment of Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus.* In FY 2015, 60 patients received benefits (1,300 million yen in total).

* A revised Act went into effect on September 14, 2012, and thereby the time frame for claiming benefits was extended by 5 years (until January 15, 2018).

	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011
Number of recipients	108	660	661	305	220
(Number of these recipients receiving additional payment)	(0)	(4)	(22)	(20)	(20)
Amount paid (thousand yen)	2,360,000	13,632,000	13,748,000	6,293,000	4,732,000
(Amount of additional payment)	(0)	(68,000)	(272,000)	(324,000)	(268,000)
Number of inquiries	16,814	3,607	894	1,286	674

	FY 2012	FY 2013	FY 2014	FY 2015
Number of recipients	129	133	95	60
(Number of these recipients receiving additional payment)	(28)	(18)	(20)	(14)
Amount paid (thousand yen)	2,624,000	2,888,000	2,100,000	1,308,000
(Amount of additional payment)	(488,000)	(332,000)	(368,000)	(252,000)
Number of inquiries	982	473	660	834



3.2. Reviews and Related Services

Based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14, 2013), etc., Healthcare and Medical Strategy (adopted by the Cabinet on July 22, 2014), the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Act), and Act on the Safety of Regenerative Medicine, etc., PMDA took the following actions in order to accelerate the review process, achieve "zero" review lag*; and upgrade the quality of reviews by investigating drugs, medical devices, and regenerative medical products according to their respective characteristics, as well as to support the elimination of development lag* by pharmaceutical affairs consultations on R&D strategy and to promote first-in-the-world practical application of innovative drugs, etc. by utilizing the SAKIGAKE designation system.

*Drug lag and device lag are roughly classified into two types of lag: "review lag," caused by the difference in the review time (from application to approval) between the US and Japan; and "development lag," caused by the difference in time which medical companies apply to regulatory agencies in the US and Japan (quoted from the "Japan Revitalization Strategy"). Resolution of the issues associated with review lag and development lag will lead to the overall elimination of lag during the approval process.

The Science Board, consisting of external experts in the areas of medicine, dentistry, pharmaceutical sciences, engineering, etc., was established in FY 2012 to more appropriately manage products employing advanced scientific techniques and technologies. In FY 2015, PMDA focused on continuously improving the quality of its operations ranging from reviews/consultations to post-marketing safety measures.

3.2.(1) Accelerated access to drugs and medical devices

New drugs

- Various measures were implemented or reviewed with the aim of increasing the number of reviewers and improving the quality of reviews, based on the “Japan Revitalization Strategy - JAPAN is BACK” and “Healthcare and Medical Strategy,” etc.

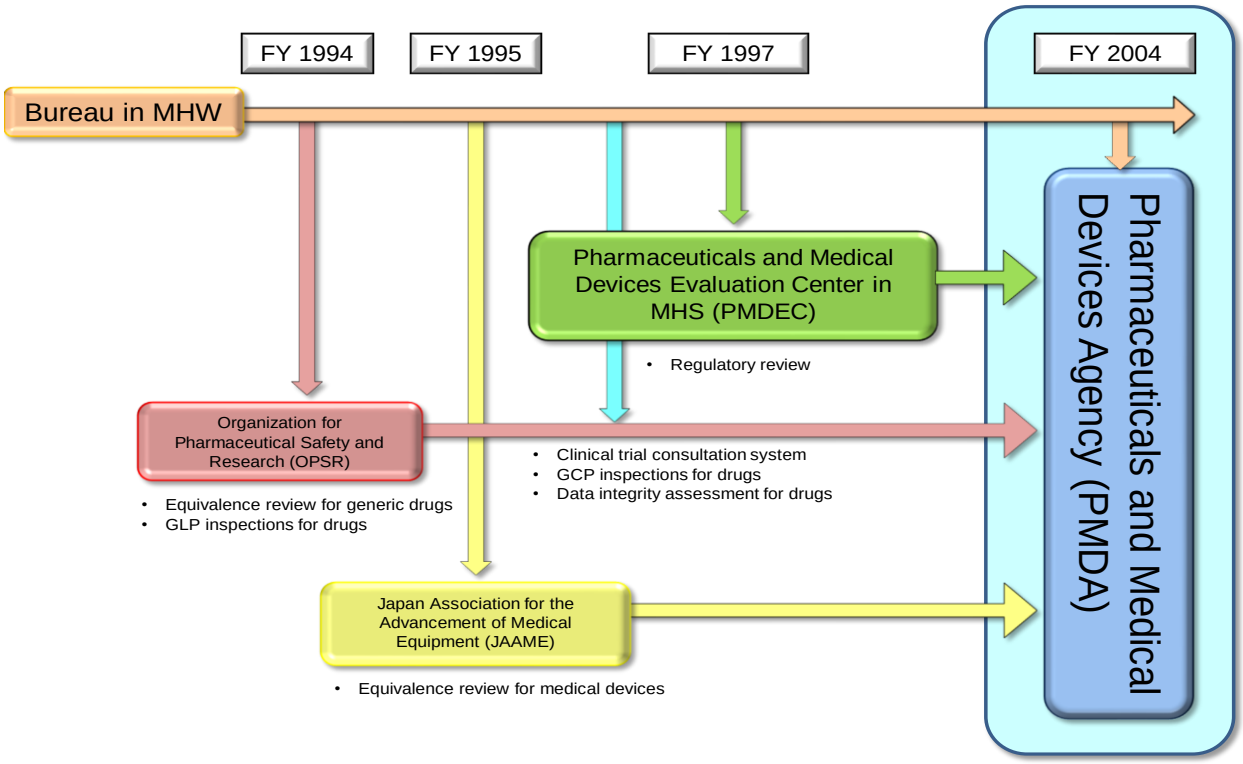
(i) Appropriate and prompt reviews

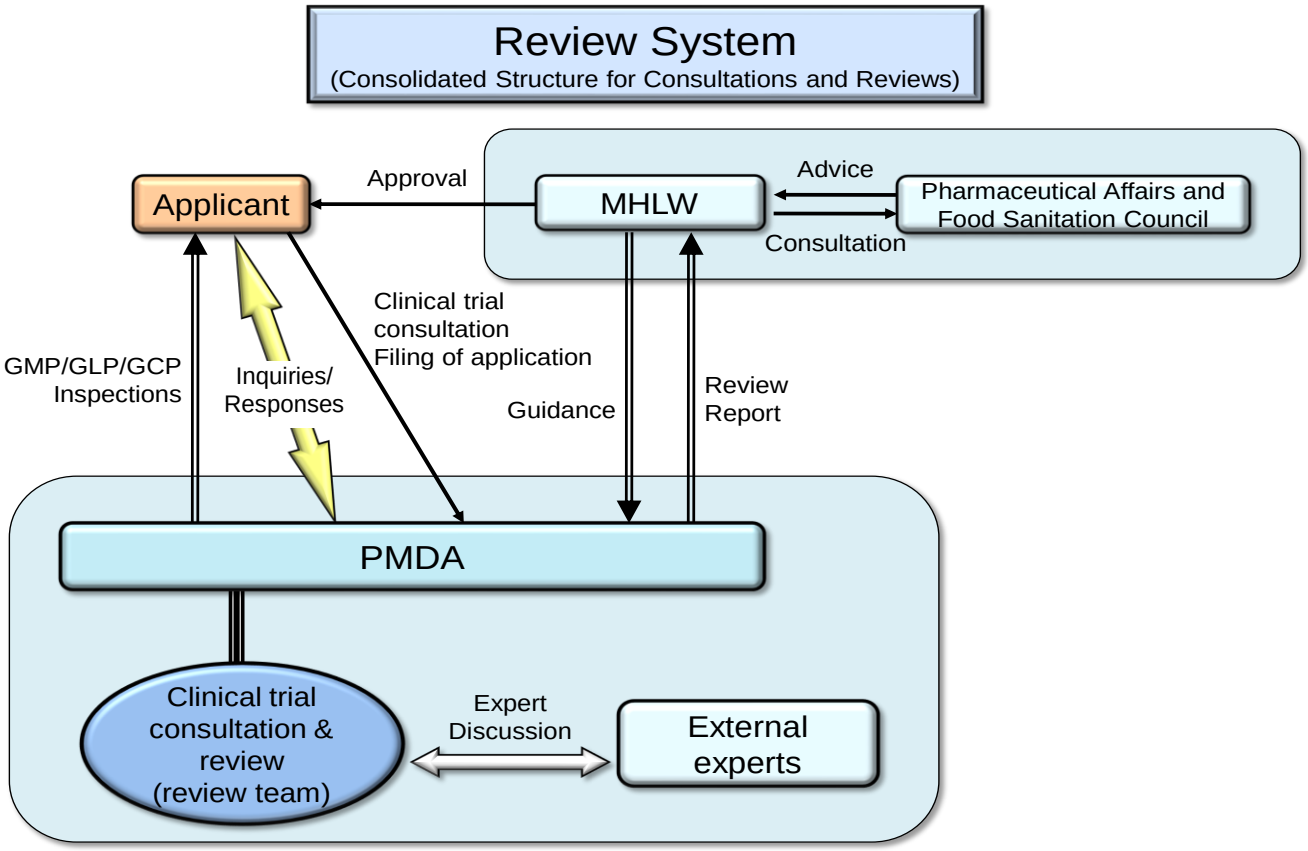
a. Structure for clinical trial consultations and reviews

- The review system for drugs and medical devices, etc. has been significantly improved since 1997. In FY 2004, PMDA was founded to consolidate review functions while the final authority for approval of drugs and medical devices, etc. was left to the Ministry of Health, Labour and Welfare (MHLW). Further improvements in the review system were made by taking the following measures:

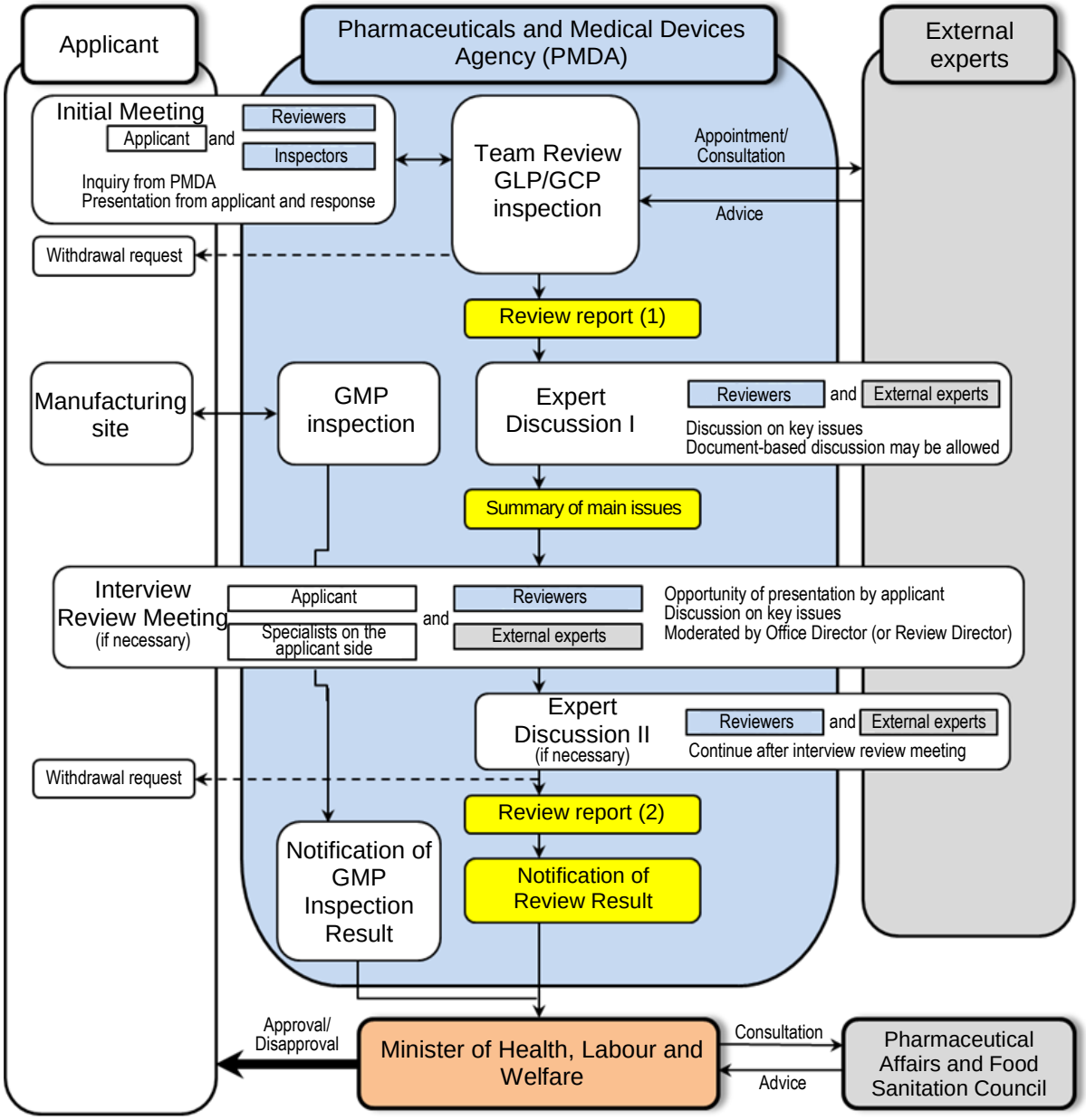
  1) In order to ensure the consistency and efficiency, the roles of three review-related agencies were re-examined thoroughly, and integrated into one agency as "incorporated administrative agency, the Pharmaceuticals and Medical Devices Agency."
  2) Substantial increase in the number of staff including reviewers.
  3) Introduction of a coherent system in which the process from clinical trial consultations until reviews is conducted by the same team with the same staff members.
  4) Enhancement of reviews of biological and biotechnology-derived products.
  5) Reinforcement of functions for reviewing medical devices.

Transition of approval review system on drugs and medical devices





Flowchart of review process



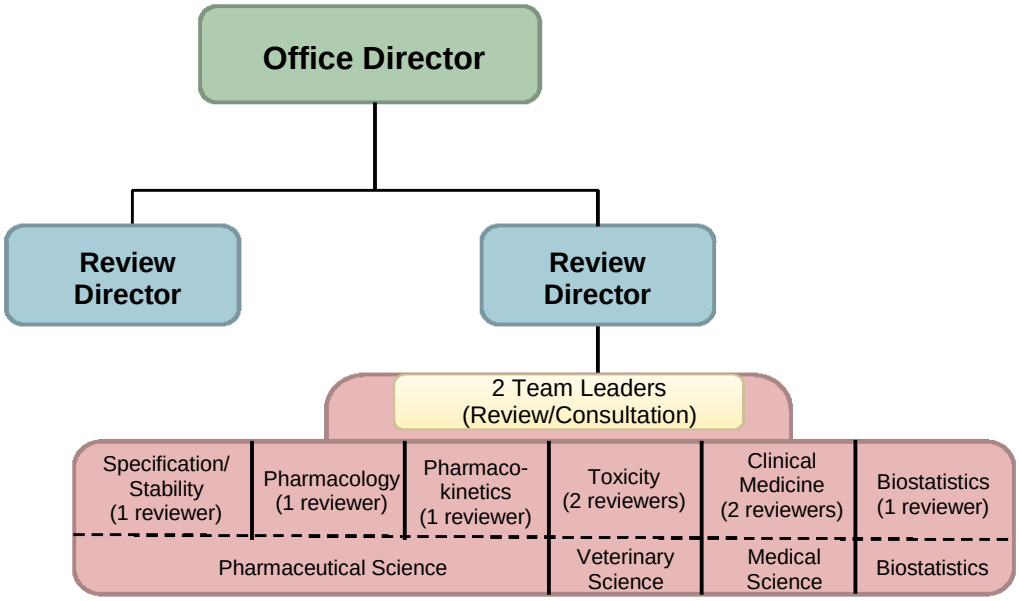
Review Performance for FY 2015 (drugs)

(1) Number of Expert Discussions conducted: 302 (240 document-based discussions, 62 meetings)

(2) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 81
Applications reported to the Drug Committees (under PAFSC): 34

- Reviews of new drugs were conducted by review teams under the guidance of an office director and a review director. As a general rule, each review team consists of experts who have academic degrees in pharmaceutical science, veterinary medicine, medicine, biostatistics, and other specialized courses. Each review team is typically comprised of team leader(s), deputy team leader(s), and reviewers specializing in quality, toxicology, pharmacology, pharmacokinetics, clinical medicine, or biostatistics.

Organization Chart for Reviews of New Drugs



- In order to strengthen the review system, PMDA increased the number of reviewers allocated to the categories where many new drug applications were being filed and the review process for them was likely to be prolonged.
- Reviews of new drug applications are shared among the responsible offices and teams according to the review categories by therapeutic area. The review categories are as follows:

Review Categories Covered by the Offices of New Drugs

Office	Review Categories	
Office of New Drug I	Category 1	Gastrointestinal drugs, dermatologic drugs, immunosuppressive drugs, and others (not classified as other categories)
	Category 6-2	Hormone drugs, drugs for metabolic disorders (including diabetes mellitus, osteoporosis, gout, and inborn errors of metabolism)
Office of New Drug II	Category 2	Cardiovascular drugs, antiparkinsonian drugs, anti-Alzheimer's drugs
	Category 5	Reproductive system drugs, drugs for urogenital system, combination drugs
	Radiopharmaceuticals	Radiopharmaceuticals
	In vivo diagnostics	Contrast agents, reagents for function tests (excluding *in-vitro* diagnostics)
Office of New Drug III	Category 3-1	Central/peripheral nervous system drugs (excluding anesthetic drugs)
	Category 3-2	Anesthetic drugs, sensory organ drugs (excluding drugs for inflammatory diseases), narcotics
Office of New Drug IV	Category 4	Antibacterial drugs, antiviral drugs (excluding AIDS drugs), antifungal drugs, antiprotozoal drugs, anthelmintic drugs
	Category 6-1	Respiratory tract drugs, anti-allergy drugs (excluding dermatologic drugs), sensory organ drugs (drugs for inflammatory diseases)
	AIDS drugs	Anti-HIV drugs
Office of New Drug V	Oncology drugs	Antineoplastic drugs
Office of Cellular and Tissue-based Products	Cellular and tissue-based products	Cell/tissue-processed products among regenerative medical products
	Gene therapy products	Gene therapy products among regenerative medical products, Cartagena
	Bio-CMC	Quality of biologics, biosimilars
	Biological devices (quality)	Biological devices (quality)
Office of Vaccines and Blood Products	Vaccines	Vaccines (only those to be used for prevention of infection), antitoxic serum, etc.
	Blood products	Blood products

- PMDA conducted clinical trial consultations for new drugs based on the team-reviewed guidance plan drafted by three staff members, i.e., the Review Director as well as the consultation leader and the deputy consultation leader in charge, who were appointed from among the review team members.

b. Reinforcement and improvement in the transparency of the progress management of reviews

- The project management system was introduced in FY 2008 for progress management and coordination of reviews of new drugs as an effort to further accelerate reviews and related services. In FY 2015, based on the experience accumulated so far, this scheme was further integrated into the review system.
- In order to conduct reviews and related services promptly and appropriately to achieve the target review times specified in the Mid-term Plan, PMDA's Progress Management Committee for Reviews and Related Services held meetings once every 3 months to ensure that the Chief Executive and other PMDA executives have an accurate understanding of the progress of reviews

and related services as well as the associated support improvement, as needed. In this way, operational progress was monitored, while particularly relevant information for new drugs was dealt with comprehensively and approaches for solving operational challenges were considered.

- The Review Segment Committee for Progress Management, with the Director of the Center for Product Evaluation as its head, met on multiple occasions throughout FY 2015 to manage the progress of reviews. In the meetings, opinions for the advancement of the review system were exchanged, as well as information on the overall review status for new drugs and associated issues including GCP and GMP inspections, were shared, measures addressing challenges and future approaches were examined, and the detailed review status of new drugs and other products under review were reported. (12 meetings were held in FY 2015.)

  Necessary guidance was provided on an ongoing basis by the Director of the Center for Product Evaluation and the Associate Center Director of the Review Segment Committee for Progress Management while taking into account reports from office directors of review divisions, and each review segment was notified of the results of discussions and of improvement measures for products requiring prolonged review.

- In accordance with the "Way of Explaining the Progress of Review of New Drug Applications" (PMDA Notification No. 1227001 dated December 27, 2010), the progress of the PMDA review is to be communicated to applicants in each review stage. The relevant office director appropriately held meetings with applicants upon their request to explain the progress and outlook of the review to them. If reviewing a new drug application is difficult, review-related issues including reasons for the difficulty and the possibility of approving the drug are to be provided in writing to the applicant, in order to increase the transparency of the review process. If applicants take time to respond to inquiries for approval review, such time should be excluded when calculating the total review time.

c. Standardization of review

- To clarify review standards, reviewers were informed of the "Points to be Considered by the Review Staff Involved in the Evaluation Process of New Drug" released in FY 2008, which provides basic considerations for review. The document is posted on the PMDA website. In addition, target review times for priority review products and standard review products were presented for each review process in “Timeline in the Standard Process of New Drug Application” (PFSB/ELD Administrative Notice of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Division, MHLW, dated January 30, 2015). This document is also posted on the PMDA website.

d. Consultations and reviews based on medical care needs

- PMDA actively exchanged opinions with healthcare professionals by participating in academic conferences etc., in and out of Japan, to comprehend their needs. The Agency conducted consultations and reviews, taking into account the information obtained in this manner.

- In order to request pharmaceutical companies to develop drugs and indications that have been approved in Europe and the U.S. but not approved in Japan, the Investigational Committee on Medically Necessary Unapproved Drugs and Off-Label Use Drugs (chaired by Dr. Tomomitsu Hotta, President of National Cancer Center) was established in the MHLW in February 2010, and has been active. PMDA continuously supports this Committee, and offers clinical trial consultations and reviews based on the results of the investigations by the Committee.

- In order to resolve the drug lag of unapproved drugs and off-label use drugs with high medical needs, PMDA promptly and timely grasped information on the approval status at FDA and EMA, and collected/organized evidence information etc., and then expanded the unapproved drug

database to compare the approval status between Japan and the US or Europe. Of drugs with a new active ingredient approved by FDA or EMA in or after April 2009, 113 (FDA) and 84 (EMA) have not been approved in Japan as of March 2015. The list of the unapproved drugs is available on the PMDA website.

e. Consistency between clinical trial consultations and reviews

- In order to ensure the consistency between clinical trial consultations and reviews, review team members are involved in all the clinical trial consultations for products falling under the category to which they are assigned. Coherence from consultations to reviews is maintained and teams are flexibly organized as necessary.

  To further secure the consistency of clinical trial consultations etc., efforts to provide feedback information on previous clinical trial consultations were continued in FY 2014.

f. Appropriate conduct of re-examination and re-evaluation

- When a certain period has passed since approval of new drugs, re-examinations are conducted to confirm the efficacy and safety, based on data of use-results surveys that have been conducted by marketing authorization holders (MAHs) etc.

  Already-approved drugs that have been designated by the Minister of Health, Labour and Welfare are re-evaluated for their efficacy and safety, in the light of the current standards of medical/ pharmaceutical sciences, based on the data submitted by MAHs. In addition, re-evaluations for quality are conducted to ensure that the dissolution of drugs in solid oral dosage forms meets the quality requirements. Once the quality has been assured, an appropriate dissolution specification is established to ensure that the quality of the drug in solid oral dosage forms is maintained at a certain level.

- In FY 2014, 86 products underwent re-examination; 139 products underwent re-evaluation for drug efficacy; and no product underwent re-evaluation for quality. Re-evaluation for drug efficacy had been completed for traditional Chinese medicines, non-steroidal anti-inflammatory agents, and antimetabolites by the end of FY 2014.

Concerning products for which applications for re-examination are filed in or after FY 2014, PMDA is aiming to complete re-examination within 18 months (median) by FY 2018. For 102 products for which applications were filed in FY 2014, no notice of re-examination results was issued in FY 2014.

Number of Re-examinations/Re-evaluations Conducted

		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Products that underwent re-examination		81	50	121	86	114
Re-evaluations	Products that underwent re-evaluation for drug efficacy	0	0	0	139	19
	Products that underwent re-evaluation for quality	0	0	0	0	0

Note: Number of products for which a notice of re-examination/re-evaluation results was issued in respective fiscal year.

g. Development of the Japanese Pharmacopoeia draft

- In FY 2015, the Japanese Pharmacopoeia (JP) Draft Committee held 83 meetings, and information was posted on the PMDA website to seek public comments regarding 32 official monographs (11 new articles, 21 amendments), 6 general tests and general information (4 new tests, 1 amendment,

1 deletion), 5 ultraviolet-visible reference spectra, and 5 infrared reference spectra as a draft of the 17th edition, Supplement I of the Japanese Pharmacopoeia (which will be notified in autumn 2017).

The number of drafts of official monographs reported to MHLW thus far was as follows:

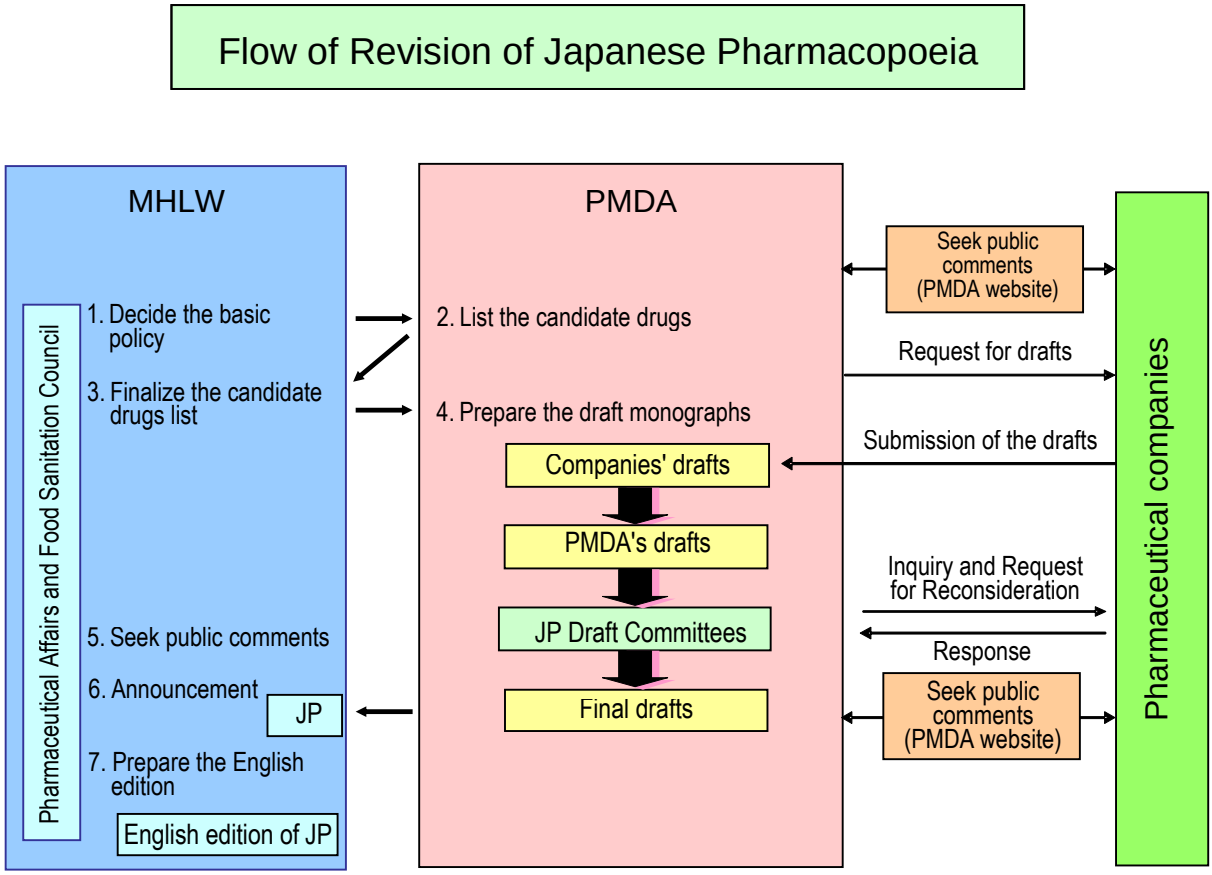
Month and year reported	Nov. 2008	Mar. 2009	Aug. 2009	Aug. 2010	Mar. 2012	Jan. 2013	Sep. 2013	Jul. 2015
New monographs	1	106	-	106	77	0	60	76
Amendments	1	122	2	330	176	1	172	471

Note: The JP drafts prepared by PMDA 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 usually provides those drafts to MHLW 6 months before the publication.

Ministerial Announcement on the Japanese Pharmacopoeia by MHLW

	15th edition	15th edition Supplement 1	Partial revision	15th edition Supplement 2	Partial revision	16th edition	16th edition Supplement 1	Partial revision	16th edition Supplement 2	17th edition
Month and year announced	Mar. 2006	Sep. 2007	Mar. 2009	Sep. 2009	Jul. 2010	Mar. 2011	Sep. 2012	May 2014	Feb. 2014	Mar. 2016
New monographs	102	90	1	106	0	106	77	0	60	76
Amendments	272	171	1	122	2	330	176	1	173	471
Deleted monographs	8	6	0	1	0	15	4	0	1	10
Total number of monographs	1,483	1,567	1,568	1,673	1,673	1,764	1,837	1,837	1,896	1,962

- PMDA provides information such as the status of JP draft reviews or international harmonization of pharmacopoeial standards, in addition to calling for public comments on drafts (from FY 2015, only the draft of new official monographs tentatively translated in English has been posted to broadly call for opinions in Japan and from foreign countries.) on the Japanese Pharmacopoeia page of PMDA's Japanese website. In addition, the Agency provides information on international harmonization of pharmacopoeial standards to overseas users on the Japanese Pharmacopoeia page of the PMDA English website.
  (URL: http://www.pmda.go.jp/english/rs-sb-std/standards-development/jp/0009.html)



h. Implementation of the master file workshop

- A pre-application checklist (English edition) of application forms for master file registration was prepared and posted on the PMDA website so that drug substance manufacturers, in-country representatives, MAHs, etc., would become familiar with overall pharmaceutical regulations including the master file registration system. In addition, one workshop was held on content, such as how to fill out the application forms after approval, issues related to rationalizing management of registration maintenance, and recent instructions to drug substance manufacturers and in-country representatives.

(ii) Introduction of new review systems

a. Implementation of prior assessment consultations

- To initially evaluate the quality, efficacy, and safety of drugs from the pre-application stage, PMDA had offered prior assessment consultations as a pilot scheme since FY 2009. The scheme has been formally implemented since FY 2011. In FY 2015, the request forms were separately received for consultations to be conducted in the first half and the second half of the fiscal year. PMDA offered consultations upon request as much as possible, taking account of the number of SAKIGAKE designation products in the review field. Consultations provided are broken down by review category, as follows.

  Review Category 2, 1 product (number of consultation categories, 1)

b. Consideration toward the construction of the Advanced Review and Consultation with Electronic Data

- To continue making progress towards the establishment of a system for advanced review and consultation with electronic data, PMDA continued to exchange opinions with the pharmaceutical industry regarding various issues, and cooperated on the issuance of "Notification on Practical Operations of Electronic Study Data Submissions" (PFSB/ELD Notification No. 0427-1 dated April 27, 2015) and “Question and Answer Guide Regarding ‘Notification on Practical Operations of Electronic Study Data Submissions’" (PFSB/ELD Administrative Notice dated April 27, 2015), and issued “Technical Conformance Guide on Electronic Study Data Submissions” (PMDA/AREDPG Notification No. 0427001 by Director of the Advanced Review with Electronic Data Promotion Group, PMDA, dated April 27, 2015) based on discussions with relevant industries and foreign regulatory authorities.

  PMDA held briefings for industries on May 28 and June 3, 2015 in Tokyo and Osaka, respectively, in order to publicize the notifications above to persons in charge of operations in companies. In addition, PMDA held a workshop on September 28, 2015 to provide assistance for preparation of electronic data and related documents so that companies can submit product applications appropriately in accordance with specifications and standards required by PMDA.

  Further, as for issues associated with electronic data for regulatory submission, PMDA began to offer “Consultation for electronic study data submission” on May 15, 2015, to consider the details of individual products before application submission and accelerate smooth preparation and review of the application. In FY 2015, the number of applications filed and consultations conducted was 13 and 11, respectively.

- PMDA selected a developer for the Electronic Application Data System in September 2014. In FY 2015, PMDA continuously focused on building and maintaining the System, which allows companies to submit electronic data, and allows PMDA to store the data and perform statistical analysis of the data. The system pilot program began in January 2016 in cooperation with 5 pharmaceutical companies and PMDA released an operation manual for the system and an explanatory movie on its operation on the PMDA website on March 28, 2016.

  As in the previous fiscal year, upon receiving electronic clinical study data on a trial basis from pharmaceutical companies, PMDA conducted a pilot program for the use of electronic data for applications, to discuss the use of electronic data for regulatory submission and also to discuss the review process under the circumstance where actual reviews were conducted.

  Additionally, to improve the quality of reviews and consultations, PMDA began discussions on a new review process that reflected the results of the introduced pilot programs. PMDA also began developing a framework that would allow reviewers to consult what actions are to be taken in specific review and consultation cases using advanced analytical methods, such as modeling & simulation.

- Relevant PMDA staff members were encouraged to participate in both internal and external workshops about electronic data and usage of software to upgrade their skills.

(iii) Approaches to achieving "zero" review lag for drugs

- The targets for the total review time (from the application date to the approval date) for drugs for which applications were submitted on or after April 1, 2004, and approved in each fiscal year are 9 months for priority review products and 12 months for standard review products. PMDA aims to gradually increase the percentiles of products for which the targets are achieved to 80% by FY

2018. The regulatory authorities have been making efforts to achieve these targets while asking applicants for their cooperation.

- New drug applications (for drugs that are clearly different from approved drugs in terms of active ingredients, contents, administration, dosage, indications, efficacy, etc.) were reviewed by PMDA review teams consisting of experts in pharmaceutical science, veterinary medicine, medicine, biostatistics, etc.
- In order to ensure appropriate, consistent, and prompt reviews of new drugs, PMDA's review teams adhered to the "Procedures for Reviews of New Drugs" regarding reviews and related procedures, as well as the SOPs for various related operations.
- The status of reviews of new drugs (excluding applications of drug products* that are reviewed by PMDA and approved only through the administrative process at MHLW) in FY 2015 is shown below:

* Drugs that are identical to approved drugs in terms of active ingredients, administration, dosage and indications or are within the scope of approved drugs in terms of administration, dosage and indications.

a. Review times for new drugs (priority review products designated by the Minister of Health, Labour and Welfare; hereinafter referred to as "priority review products")

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	9	9	9	9	9
Percentile	60	60	70	70	80

Results

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	60
Total review time [months] (Reference, 80th percentile) [months]	6.5 (9.2)	6.1 (9.0)	7.2 (9.1)	8.8 (9.2)	8.7 (9.5)
Number of approved applications	50	53	42	44	37

Reference

Regulatory review time [months]	4.2	3.8	3.6	4.0	4.0
Applicant's time [months]	2.0	1.5	3.8	5.0	4.9

Note 1:Products covered were those for which applications were filed in or after April 2004. The number of approved applications is based on active ingredients. For details, refer to the list of approved products included in the III SUPPLEMENTARY INFORMATION

Note 2:Public knowledge-based application products related to the "Study Group on Unapproved and Off-label Drugs of High Medical Need" are included in priority review products.

Reference: When excluding public knowledge-based applications for unapproved drugs

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	60
Total review time [months] (Reference, 80th percentile) [months]	9.2 (10.7)	9.0 (10.0)	8.0 (9.9)	8.9 (9.2)	8.8 (9.8)
Regulatory review time [months]	4.1	3.4	3.4	3.8	4.0
Applicant's time [months]	5.0	4.6	4.1	5.2	5.2
Number of approved applications	18	25	31	37	33

- Priority reviews are conducted for applications for orphan drugs and other drugs that are regarded as having particularly high medical need (drugs for serious diseases and with distinctly superior efficacy or safety as compared to existing drugs or therapies). In FY 2015, 37 priority review products (including 4 public knowledge-based applications for the “Study Group on Unapproved and Off-label Drugs of High Medical Need”) were approved.
- In FY 2015, 8 applications requesting priority reviews were submitted for drugs regarded as having particularly high medical needs. In FY 2015, 6 applications were judged as “applicable” and no applications were determined to be “not applicable.”
- The total review time (60th percentile) for priority review products approved in FY 2015 was 8.7 months, achieving the target review time.

  The priority review products accounted for 32% of products approved in FY 2015, showing a decrease from 38% in FY 2014.

b. Review times for new drugs (standard review products)

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	12	12	12	12	12
Percentile	60	70	70	80	80

Results

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	70
Total review time [months] (Reference, 80th percentile) [months]	11.5 (15.7)	10.3 (11.9)	11.3 (12.3)	11.9 (12.3)	11.3 (11.7)
Number of approved applications	80	81	96	73	79

Reference

Regulatory review time [months]	6.3	5.7	6.7	6.8	7.1
Applicant’s time [months]	5.1	4.2	4.6	5.4	5.1

Note: Products covered were those for which applications were filed in or after April 2004. The number of approved applications is based on active ingredients. For details, refer to the list of approved products included in the III SUPPLEMENTARY INFORMATION

- The total review time for standard review products approved in FY 2015 was 11.3 months, achieving the target review time.

- The number of applications under review at the end of FY 2015 was 104 (including 16 applications for orphan drugs and 4 public knowledge-based applications for unapproved drugs).

Review Status of New Drugs by Fiscal Year of Application

New drugs (FY of submission)	Applications	Approved	Not approved	Withdrawn	Under review
In or before Mar. 31, 2004	140	109	0	29	2
FY 2004	87	78	0	9	0
FY 2005	57	50	0	7	0
FY 2006	102	93	0	9	0
FY 2007	92	78	0	14	0
FY 2008	81	77	0	4	0
FY 2009	106	87	1	18	0
FY 2010	116	105	0	11	0
FY 2011	130	128	0	2	0
FY 2012	140	135 (5)	0	5	0
FY 2013	123	118 (1)	0	4 (1)	1 [-2]
FY 2014	128	116 (86)	0	6 (6)	6 [-94]
FY 2015	127	29 (29)	0	3 (3)	95 [95]
Total	1,429	1,203 (116)	1	121 (10)	104 [-1]

Note 1: The figures in parentheses indicate those processed in FY 2015 (included in values to the left).
Note 2: The figures in brackets indicate difference from FY 2014.

(iv) Promotion of global clinical trials

- In order to reduce the drug lag, PMDA has promoted global clinical trials and has conducted consultations and reviews based on the following documents: "Basic Principles on Global Clinical Trials" (PFSB/ELD Notification dated September 28, 2007), “Basic Principles on Global Clinical Trials (Reference Cases)” (PFSB/ELD Administrative Notice dated September 5, 2012), and “*Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials*” (PFSB/ELD Administrative Notice dated October 27, 2014). These documents clarify basic concepts when conducting global clinical trials.

  Of 657 clinical trial notifications submitted in FY 2015, 276 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of notifications	124 [3]	138 [8]	173 [4]	181 [3]	276

Note: The previous PMDA Annual Reports showed incorrect figures for FY 2011 to FY 2014 because of miscalculation. This table indicates amended figures for these fiscal years. The figures in brackets represent increases in number after amendment.

- PMDA intends to take an active approach to global clinical trials. In FY 2015, PMDA carried out 66 consultations on global clinical trials for drugs with new active ingredients, meeting all the requests for consultations.

Number of Consultations on Global Clinical Trials with New Active Ingredients

Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of consultations	73	64	59	67	66

- PMDA participated in and supported efforts to promote global clinical trials in Asia based on the Multi Regional Clinical Trial Roadmap at APEC-LSIF-RHSC led by MHLW. Specifically, PMDA acted as Champion of the Roadmap so that the discussions held at the MRCT/GCP Inspection Pilot CoE Workshop (in Singapore in March 2016) and APEC-LSIF-RHSC (in the Philippines in August 2015 and in Peru in February 2016) could advance smoothly. In addition, PMDA has been acting as co-chair of APEC-LSIF-RHSC since FY2015 and lead discussions.

(v) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- PMDA organized the handling of priority consultations in accordance with the start of the SAKIGAKE designation system. Since FY 2015, in addition to orphan drugs, SAKIGAKE designation drugs have become the scope of priority consultations and accordingly, assessments for designation of priority consultation products were abolished.

b. Acceleration of the procedure for clinical trial consultations

- To expedite clinical trial consultations, PMDA streamlined the procedures for applicants to request consultations as well as for PMDA to receive requests. The revised procedures were implemented for requests for consultations to be provided in or after October 2010. The target duration from consultation request to consultation, about 2 months, has been firmly maintained.

c. Implementation of clinical trial consultations and improvement of the consultation service

Number of Consultations

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	447	387	354	411	371
Withdrawn	30	20	30	38	33

Number of Prior Assessment Consultations for Drugs

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	33	19	32	32	1
Withdrawn	0	0	0	0	0

Number of Consultations on Pharmacogenomics/Biomarkers

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	1	0	0	0	0
Withdrawn	0	0	0	0	0

Number of Consultations on Drug Product Eligibility for Priority Review

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	2	7	10	6	7
Withdrawn	0	0	0	0	0

Note 1: Prior assessment consultations for drugs and consultations on pharmacogenomics/biomarkers have been conducted since FY 2009, and consultations on drug product eligibility for priority review for drugs have been conducted since FY 2011. The numbers of all types of consultations were counted on the basis of delivery dates of consultation documents to PMDA.

Note 2: Prior assessment consultations for drugs were counted on the basis of number of consultation categories (quality; non-clinical, toxicity; non-clinical, pharmacology; non-clinical, pharmacokinetics; phase I study; phase II study; and phase II/III study).

- In FY 2015, PMDA conducted 371 consultations (including 33 withdrawals).
- To respond to all requests for clinical trial consultations (excluding prior assessment consultations, consultations on pharmacogenomics/biomarkers, and consultations on drug product eligibility for priority review), as a general rule, consultations are scheduled according to requests for scheduling, and when the consultation cannot be scheduled for a desired month, the consultation is scheduled within one month before or after that month. In FY 2015, PMDA provided 363 consultations (33 withdrawals), responding to all of the clinical trial consultations requested (The target was achieved).
- PMDA aimed to complete the process from conduct of clinical trial consultation to finalizing consultation records within 30 business days for 80% of products subjected to consultation. In FY 2015, the target was achieved in 356 (99.2%) of 359 consultations.
- In order to improve the quality of consultations, in January 2007, PMDA introduced a system for all clinical trial consultations in which PMDA's opinions for content to be addressed in the consultations are presented to the applicants beforehand (preliminary opinion disclosure system).

Number of Consultations for Drugs by Review Category in FY 2015

Review category	Results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs etc.)	4	3	3	2	5	4	3	4	8	5	3	3	47
Category 6-2 (Hormone drugs)	1	2	4	5	2	3	3	2	1	0	1	2	26
Category 2 (Cardiovascular drugs)	5	2	3	3	2	2	3	5	8	0	2	5	40
Category 5 (Drugs for the urogenital system etc.)	1	0	2	0	1	1	1	1	0	1	2	0	10
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	0	0	1	1
In vivo diagnostics	0	0	0	1	0	1	0	1	0	1	0	1	5
Category 3-1 (Central nervous system drugs etc.)	2	2	1	6	3	4	1	0	2	1	0	3	25
Category 3-2 (Anesthetic drugs etc.)	0	0	0	3	2	2	3	0	0	4	4	1	19
Category 4 (Antibacterial agents etc.)	2	1	2	1	2	6	3	1	1	6	1	2	28
Category 6-1 (Respiratory tract drugs etc.)	5	2	4	5	0	2	4	7	2	0	0	1	32
AIDS drugs	0	0	1	0	0	0	0	0	0	0	0	0	1
Oncology drugs	12	4	7	8	6	6	6	6	8	1	6	3	73
Bio-CMC	1	1	1	2	4	2	4	0	0	1	3	1	20
Vaccines	0	0	4	1	2	1	2	0	1	0	3	11	25
Blood products	0	1	1	0	1	0	1	0	3	0	6	4	17
Generic drugs	0	0	0	0	1	0	0	0	0	0	0	1	2
[Re-listed] Prior assessment	1	0	0	0	0	0	0	0	0	0	0	0	1
[Re-listed] Drug product eligibility for priority review	0	0	1	1	0	0	0	1	1	2	1	0	7
Pharmacogenomics/biomarkers	0	0	0	0	0	0	0	0	0	0	0	0	0
GLP/GCP/GPSP compliance inspection	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	33	18	33	37	31	34	34	27	34	20	31	39	371
Withdrawal	4	1	3	2	2	2	5	1	2	2	8	1	33
Grand Total	37	19	36	39	33	36	39	28	36	22	39	40	404

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

Note 2: Prior assessment consultations are conducted for the following categories: quality; non-clinical, toxicity; non-clinical, pharmacology; non-clinical, pharmacokinetics; phase I study; phase II study; and phase II/III study.

Note 3: The numbers of prior assessment consultations, consultations on pharmacogenomics/biomarkers, and consultations on drug product eligibility for priority review were counted on the basis of delivery dates of consultation documents to PMDA.

Note 4: Consultations on pharmacogenomics/biomarkers were conducted by the Omics Project Team.

Note 5: Consultations on GLP/GCP/GPSP compliance inspection were all conducted by Office of Conformity Audit or Office of Manufacturing/Quality and Compliance, regardless of category.

d. Reclassification of consultation categories and their uses

- PMDA exchanged opinions with MHLW and the relevant industries on clinical trial consultations. As a result, in May 2015, PMDA started new consultation services: “SAKIGAKE comprehensive evaluation consultation,” which evaluates submission data for SAKIGAKE designated products; and “Consultation on data format of submission of electronic study data,” where PMDA provides advice and instructions on scope, format, or other issues related to electronic data submission. In January 2016, PMDA also started another service, “Consultation before the start of expanded

clinical trials for drugs," which is related to clinical trials plans to be conducted for humanitarian reasons.

(vi) Promotion of evaluation of new technologies

a. Utilization of external experts

- As PMDA is required to raise the expertise in the guidance and review, particularly in the fields of the latest technologies such as biotechnology and genomics, PMDA has continued to commission external experts who have a high-level knowledge to play a role of expert advisors for PMDA, in order to seek professional opinions on scientifically important matters at Expert Discussions for reviews and post-marketing safety measures.

  (As of March 31, 2016, the number of commissioned experts is 1,385 including external experts commissioned for issues relating to safety measures)

- In FY 2015, 302 Expert Discussions were conducted (240 through document-based discussions; 62 through meetings).

- PMDA utilized external experts in Expert Discussions for regulatory reviews and clinical trial consultations for biological pharmaceuticals and regenerative medical products. PMDA also promoted exchanging information on both biological pharmaceuticals and regenerative medical products with FDA and EMA through teleconferences etc.

- PMDA cooperated with a study on a safety evaluation system for new drugs utilizing iPS cells conducted under the leadership of the National Institute of Health Sciences and collected the latest information so that PMDA can respond appropriately to the development of drugs using the latest scientific technology such as iPS cells, etc. In addition, PMDA gathered information regarding overseas studies on safety evaluation systems using iPS cells, etc. that involve organizations such as FDA and EMA, through teleconferences or participation in conferences.

b. Support for the development of national guidelines

- PMDA participated in examinations conducted as part of a research project supported by Health and Labour Sciences Research Grants (Research on global health issues), which is titled "Research on Methods for Evaluating Quality, Efficacy, etc., of Travelers' Vaccines" and led by Dr. Kazunobu Ouchi, the principal researcher. As a result of the study, PMDA supported MHLW's preparation of "Guidance for Clinical Evaluation of Vaccines for Travelers (draft)".

- PMDA cooperated with issuance of "Questions and Answers on the Guideline for the Quality, Safety, and Efficacy Assurance of Follow-on Biologics (Biosimilars)" (PFSB/ELD Administrative Notice dated December 15, 2015).

- Companion Diagnostics Working Group (WG) within Projects Across Multi-Offices for standard development cooperated with preparation of "Handling of DNA Sequencer and Other Devices Used for Genetic Testing Systems for Marketing (draft)" and "Points to Consider for Equivalence of Companion Diagnostics (draft)".

- Nanomedicine Initiative WG within Projects Across Multi-Offices for standard development cooperated with issuance of the following notifications: "Guideline for the Development of Liposome Drug Products" (PSEHB/ELD Notification No. 0328-19 by ELD, Pharmaceutical Safety and Environmental Health Bureau, MHLW, dated March 28, 2016), "Questions and Answers on the Guideline for the Development of Liposome Drug Products" (PSEHB/ELD Administrative Notice

dated March 28, 2016), and “Reflection Paper on Nanopreparations with Nucleic Acid (siRNA)” (PSEHB/ELD Administrative Notice dated March 28, 2016).

- In addition to the above, 4 notifications etc., were issued in FY 2015 with the cooperation of relevant review categories or offices in PMDA.

c. Preliminary reviews under Cartagena Act

- With regard to the use of genetically modified living organisms, preliminary reviews are conducted in relation to reviews of Type 1 Use and in confirmations of Type 2 Use under the Cartagena Act. PMDA set the target regulatory review time to be 6 months for approval of Type 1 Use and 2 months for confirmation of Type 2 Use, with the goal of achieving 50% (median) of applications for each type.

Review under the Cartagena Act (Median Regulatory Review Time)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
No. of preliminary reviews for Type 1 Use Median review time [months]	0 –	0 –	0 –	3 0.8	2 0.9
No. of preliminary reviews for Type 2 Use Median review time [months]	15 2.0	21 1.2	24 0.9	25 1.3	21 1.0

Note: "Type 1 Use" refers to cases where measures are not taken to prevent the release to the environment and "Type 2 Use" refers to cases where such measures are taken.

d. Implementation of Pharmaceutical Affairs Consultations on R&D Strategy

- PMDA has been offering Pharmaceutical Affairs Consultations on R&D Strategy since July 2011 mainly to universities, research institutions and venture companies that have promising seed-stage resources to provide guidance and advice concerning studies and clinical trials that are necessary at the initial stage of product development, in order to facilitate the development of innovative pharmaceuticals, medical devices, and regenerative medical products in Japan. The number of consultations conducted in FY 2015 is shown in the table below.
- In FY 2015, 63 on-site introductory consultation were offered in prefectures such as Fukushima, Toyama, Aichi, Hiroshima, Fukuoka, and Oita. (Of all introductory consultations conducted in FY 2015, 63 were on-site consultations.)
- Introductory consultations and pre-consultation meetings were also conducted in the Kansai branch of PMDA, which was established in October 2013.
- To promote the practical application of seed-stage resources originating in Japan, in November 2014 PMDA provided consultations, as a pilot scheme, on the development process (roadmap) to pharmaceutical companies, etc. and on investigator-initiated confirmatory clinical trial protocols.
- In October 2015, based on the “Japan Revitalization Strategy – Revised in 2015” (adopted by the Cabinet on June 30, 2015), PMDA started Pharmaceutical Affairs Consultation on R&D Strategy for Medical Devices in the Special Zones, which targets the development of innovative medical devices in core clinical trial hospitals located in the National Strategic Special Zones. This consultation service offers “Pre-consultation in special zones” and “Follow-up consultation in special zones.” Further, PMDA staff members (acting as concierges) involved in Pharmaceutical Affairs Consultation on R&D Strategy for Medical Devices in the Special Zones give advice or other information on development progress management.

Number of Pharmaceutical Affairs Consultations on R&D Strategy Conducted

Introductory consultations/ pre-consultations	FY 2011[1]	FY 2012	FY 2013	FY 2014	FY 2015	Total
Introductory consultations (Number of these consultations conducted at the Kansai branch[2])	118	302	237 (20)	271 (63)	221 (56)	1,149 (139)
Pre-consultations[3] (Number of these consultations conducted at the Kansai branch[2])	153	254	346 (26)	325 (57)	412 (60)	1,490 (143)

Face-to-face consultations on:	FY 2011[1]	FY 2012	FY 2013	FY 2014	FY 2015	Total
Drugs	20	28	66	48	58	220
Medical devices	6	5	38	16	16	81
Regenerative medical products[4]	—	—	—	2	11	13
Quality and safety of regenerative medical products[5]	5 [7]	7 [13]	19 [32]	18 [44]	29 [55]	78 [151]
Development plan[6]	—	—	—	1	0	1
Total	31 [33]	40 [46]	123 [136]	85 [111]	114 [140]	393 [466]

Note 1: Pharmaceutical Affairs Consultations on R&D strategy started on July 1, 2011.

Note 2: Consultations in Kansai branch started on October 1, 2013.

Note 3: Pre-consultations include 1 pre-consultation performed as a part of Pharmaceutical Affairs Consultation on R&D Strategy for Medical Devices in the Special Zones. (This consultation category was introduced on November 20, 2015.)

Note 4: This consultation category was introduced on November 25, 2014 (before then consultations on regenerative medical products had been included in consultations on drugs or medical devices).

Note 5: This consultation category includes Consultations on R&D Strategy for Drugs conducted until November 24, 2014. Some consultations were divided into multiple sessions over several days, to confirm the quality and safety of regenerative medical products before the submission of clinical trial notifications. The figures in brackets indicate the total number of sessions.

Note 6: This consultation category was introduced on November 25, 2014

(vii) Examination of consistency between actual manufacturing practices and the marketing approval documents of drugs

- In association with self-inspections to check the difference between actual manufacturing practices and the approval document based on “Implementation of Inspection on Consistency between Actual Manufacturing Practices and Drug Approval Documents” (PSEHB/ELD Notification No. 0119-1 dated January 19, 2016), PMDA cooperated with the issuance of two documents: a notification on the procedure for resolution of differences (“Procedure After Inspection on Consistency between Actual Manufacturing Practices and Drug Approval Documents” [PSEHB/ELD Notification No. 0212-4 dated February 12, 2016]; and related questions and answers.

Generic drugs, etc.

- PMDA implemented or considered the following measures to accelerate reviews for generic drugs, etc.

(i) Appropriate and prompt reviews

- PMDA established the Office of Generic Drugs in November 2014 and has made efforts to speed up reviews through more efficient operations.

a. Consultations and reviews based on medical care needs

- PMDA staff members have participated both Japanese and overseas academic conferences, and have also exchanged opinions with healthcare professionals to better understand their needs. The Agency has also conducted consultations and reviews, while taking into account the information obtained through these methods.

b. Development of the Japanese Pharmacopoeia draft

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

c. Implementation of master file workshop

- See 3.2.(1) **New drugs** (i)-h

d. Ensuring efficient and transparent reviews

- PMDA prepared a draft of a mock-up CTD in collaboration with various industry associations to encourage the use of the CTD/eCTD for marketing applications, with the aim of performing more efficient reviews. Where possible, Companies submitted a trial version of the CTD, for new applications filed from February 2015. The CTD application will be mandatory, in principle, from March 2017, in accordance with the notification (PSEHB/ELD dated March 11, 2016).
- PMDA further advanced discussion about the content of review reports prepared for new applications for generic drugs (trial version) based on the opinions of the parties concerned, and prepared review reports (trial version) for newly approved generic products in FY 2015.
- PMDA discussed the development of a guidance concerning bioequivalence studies for drugs that cannot be evaluated based on the existing guidelines for bioequivalence testing. PMDA also devised a basic concept regarding bioequivalence tests of the performance of aqueous eye drops and powder inhalants. As a result, a notification (PSEHB/ELD dated March 11, 2016) was issued.

(ii) Approaches to shorten review times

- PMDA established the following target regulatory review times for applications submitted on or after April 1, 2004 and that were subsequently approved, and has made efforts to achieve these targets while also asking for the cooperation of applicants.
- In order to carry out prompt and accurate reviews of generic drugs, PMDA acted in accordance with the Procedures for Review of Generic Prescription Drugs, which specify the review methods and procedures associated with reviews, and SOPs for various operations.

  Data on the achievement of the target review times were periodically collected and provided to reviewers in PMDA. Further, the Progress Management Committee for Reviews and Related Services held meetings to monitor and examine operational progress (4 meetings held in FY 2015).

- The approval status of generic drugs in FY 2015 are as follows:

a. Review time for new application for generic drugs

Target

PMDA aims to achieve the following target review time for the 50th percentile (median) of applications by FY 2018.

Type of application	Regulatory review time
New generic drugs	10 months

Results

	FY 2014	FY 2015
Approved products	1,325	635
Number of these products filed in or after April 2004	1,325	635
Median regulatory review time [months]	6.1	8.2

Note: The medians were calculated based on the applications filed in or after April 2004.

b. Review time for partial change application for generic drugs, etc. (standard review products)

Targets

PMDA aims to achieve the following target review times for the 50th percentile (median) of applications by FY 2018.

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time	15 months	14 months	13 months	12 months	10 months

Results

	FY 2014	FY 2015
Approved products	587	701
Number of these products filed in or after April 2004	586	701
Median total review time [months]	15.5	13.0

Note 1: The medians were calculated based on the applications filed in or after April 2004.

Note 2: Figures for FY 2014 were amended due to a change in the summation method.

c. Review time for partial change applications for generic drugs, etc. (excluding the products that fall under "b" above)

Targets

PMDA aims to achieve the following target review times for the 50th percentile (median) of applications by FY 2018.

Type of application	Total review time
Partial change (change of test methods etc.)	6 months
Partial change (expedited review)	3 months

Results

		FY 2014	FY 2015
Change of test methods, etc.	Approved products	1,367	1,594
	Number of these products filed in or after April 2004	1,367	1,594
	Median total review time [months]	7.3	6.9
Expedited review	Approved products	168	305
	Number of these products filed in or after April 2004	168	305
	Median total review time [months]	4.0	4.8

Note 1: The medians were calculated based on the applications filed in or after April 2004.

Note 2: Figures for FY 2014 were amended due to a change in the summation method.

Reference: Results obtained during the Second Mid-term Plan (Regulatory Review Time)

Generic drugs, etc.	FY2009	FY2010	FY2011	FY2012	FY2013
Approved products	3,271	2,633	3,091	3,421	3,504
Number of these products filed in or after April 2004	3,245	2,590	3,046	3,388	3,502
Median regulatory review time [months]	7.5	6.9	6.5	5.9	5.3

Note 1: The approved products include priority review products for which the standard regulatory review time is 6 months or less.

Note 2: The medians were calculated based on the applications filed in or after April 2004.

Reviews and Related Services Conducted for Generic Drugs, etc. by Fiscal Year

Fiscal Year	Application	Approved	Withdrawn, etc.	Under review
FY 2011	2,893	3,089	165	3,093
FY 2012	4,077	3,421	190	3,559
FY 2013	3,893	3,504	343	3,605
FY 2014	3,452	3,447	214	3,396
FY 2015	3,500	3,235	281	3,380

Note: The figures in "Withdrawn etc." do not include the number of products that were switched to other review categories during the review.

- The median regulatory review time for new generic drugs approved in FY 2015 was 8.2, achieving the target (10 months). For partial change applications of generic drugs, the median total review time for standard review products was 13.0 months, achieving the target (14 months). The median total review time for partial change applications (change of test methods etc.) was 6.9 months (target, 6 months) and that for partial change applications (expedited review) was 4.8 months (target, 3 months). PMDA aims to achieve the targets by FY 2018 by taking measures such as increasing the number of reviewers from the next fiscal year.

Document-based Compliance Assessments for Generic Drugs by Fiscal Year

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Generic drugs	1,118	1,188	1,086	1,080	1,045

- For generic drugs, PMDA conducted 1,045 assessments to examine whether application data comply with GLP, GCP, GPSP, and other standards by checking the application data against raw data such as test records, laboratory notebook, and case report forms.

(iii) Efficient conduct of clinical trial consultations

- In January 2012, PMDA started to provide pre-application consultations for generic drugs, on a trial basis, namely “Quality consultation for generic drugs” and “Consultation on the bioequivalence of generic drugs.” In FY 2015, 48 consultations were conducted. Since January 2015, PMDA has responded to all requests for consultations.

Number of Consultations for Generic Drugs

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	3	10	17	24	48
Withdrawn	0	0	1	1	8

Note: PMDA started to provide consultations for generic drugs in FY 2011.

Number of Consultations for Generic Drugs by Consultation Category in FY 2015

Consultation category	Conducted	Withdrawn
Consultations on bioequivalence of generic drugs	38	5
Quality consultations for generic drugs	10	3
Total	48	8

(iv) Examination of consistency between actual manufacturing practices and instructions given in marketing approval documents for drugs

- See **3.2.(1)** New drugs **(vii)**

Behind-the-counter (BTC) drugs, over-the-counter (OTC) drugs, and quasi-drugs

- PMDA took the following measures to promote public self-medication.

(i) Appropriate and prompt reviews

a. Reinforcement of the review system for BTC drugs and OTC drugs

- In FY 2014, staff with experience of safety or compliance operations joined Office of OTC/Quasi-drugs. In accordance with the establishment of the BTC drugs system, these staff members took a lead in improving post-marketing surveillance and handling document-based compliance assessments conducted in Office of OTC/Quasi-drugs.

  Office of OTC/Quasi-drugs performed toxicological and clinical reviews of new BTC/OCT drugs by seeking, as necessary, advice of internal experts in other Offices, in close collaboration with other Offices.

- Reviewers participated in both Japanese and overseas academic conferences, and exchanged opinions with healthcare professionals. The Agency conducted reviews and consultations, taking into account the information obtained in this manner.

- For the development of Japanese Pharmacopoeia draft, see 3.2.(1) **New drugs** (i)-g.

- PMDA made efforts to improve the quality of reviews by exchanging opinions with experts in traditional Chinese medicines/crude drugs by having reviewers participate in the Japanese Pharmacopoeia Crude Drug Committee, and, as collaborative researchers, in the research group supported by Health and Labour Sciences Research Grants, which involves the Division of Crude Drugs at the National Institute of Health Sciences (NIHS).

b. Reinforcement of the review system for quasi-drugs

- PMDA increased the number of reviewers and prepared “Checklist for application data for marketing approval of quasi-drugs, etc.” to accelerate reviews of quasi-drugs. PMDA requested manufacturers of quasi-drugs to submit the checklist together with application data to be filed in and after FY 2016, on a trial basis.

- PMDA supported the MHLW's process of the revision of Japanese Standards of Quasi-drug Ingredients and insecticide guidelines by assisting MHLW to hold meetings of the "Review Committee on Japanese Standards of Quasi-drug Ingredients" and “Review Committee on Revision of Insecticide Guidelines.”

- PMDA has made efforts to improve the quality of reviewers by having them participate in training programs, academic conferences etc., in and out of Japan and exchange opinions with specialists. PMDA conducted reviews and consultations, taking into account the information obtained in this manner.

(ii) Approaches to shorten review times

- PMDA set up the target regulatory review times for applications for BTC drugs, OTC drugs, and quasi-drugs submitted on or after April 1, 2004, and has since conducted reviews toward the achievement of these targets.

- In order to review BTC drugs, OTC drugs, and quasi-drugs promptly and accurately, PMDA executed operations in accordance with the Procedures for Review of OTC Drugs, Procedures for Review of Insecticides/Rodenticides, and Procedures for Review of Quasi-drugs, all of which specify the review methods and associated procedures, and also SOPs for various operations.

In addition, PMDA periodically collected data on the achievement of the target review time, provided the data to reviewers, and held meetings of the Progress Management Committee for Reviews and Related Services, to monitor and examine operational progress. (4 meetings held in FY 2015.)

- In monthly meetings of Review Segment Committee for Progress Management and other occasions, PMDA clarified target times for processing applications for innovative BTC/OTC drugs (i.e., target times for initial inquiries after submission, Expert Discussion, and Drug Committees) to accelerate review process. In addition, applicants delaying responding to initial inquiries from PMDA were instructed to report the reason for the delay and answer the inquiries as quickly as possible. The Drug Committee discussed and approved 4 products (identical active ingredient) with new dosage forms for OTC drugs. Then, 5 products, including the 4 products, were deliberated in the expert discussion.
- Similar to the cases of BTC and OTC drugs, PMDA clarified target times for processing applications for quasi-drugs (e.g., target time for the Cosmetics and Quasi-Drug Committees) to accelerate review process. The Cosmetics and Quasi-Drug Committee discussed and approved a new active ingredient and another ingredient that was requested to be newly listed in the positive list of cosmetic standards. Then, 4 products, including the above ingredients, were deliberated in the expert discussion.
- The approval status of BTC drugs, OTC drugs, and quasi-drugs in FY 2015 are as follows:

a. Review time for BTC drugs and OTC drugs

Target

PMDA aims to achieve the following target review time for the 50th percentile (median) of applications by FY 2018.

Type of application	Regulatory review time
BTC drugs, OTC drugs	7 months

Results

BTC drugs, OTC drugs	FY2011	FY2012	FY2013	FY2014	FY2015
Approved products	1,031	881	916	844	752
Number of these products filed in or after April 2004	1,029	881	916	844	752
Median regulatory review time [months]	3.4	4.1	4.9	6.3	5.5

Note: The median regulatory review times were calculated based on the applications filed in or after April 2004, excluding the time between completion of reviews and notification of GMP inspection results issued by prefectural governments or other authorities.

b. Review time for quasi-drugs

Target

PMDA aims to achieve the following target review time for the 50th percentile (median) of applications by FY 2018.

Type of application	Regulatory review time
Quasi-drugs	5.5 months

Results

Quasi-drugs	FY2011	FY2012	FY2013	FY2014	FY2015
Approved products	1,938	1,968	2,028	1,779	2,495
Number of these products filed in or after April 2004	1,938	1,968	2,028	1,779	2,495
Median regulatory review time [months]	5.0	4.9	4.9	4.9	4.7

Note: The median regulatory review time were calculated based on the applications filed in or after April 2004, excluding the time between completion of reviews and notification of GMP inspection results issued by prefectural governments or other authorities.

Reviews Conducted for BTC Drugs, OTC Drugs, and Quasi-drugs by Fiscal Year

Classification	Fiscal Year	Applications	Approved	Withdrawn, etc.	Under review
BTC drugs, OTC drugs	FY 2011	1,130	1,031	92	1,841
	FY 2012	1,005	881	90	1,875
	FY 2013	1,013	916	63	1,909
	FY 2014	882	844	99	1,848
	FY 2015	718	752	126	1,688
Quasi-drugs	FY 2011	2,212	1,938	97	2,190
	FY 2012	2,117	1,968	79	2,260
	FY 2013	2,298	2,028	174	2,356
	FY 2014	1,828	1,779	125	2,280
	FY 2015	2,559	2,495	155	2,189

Note: The figures in "Withdrawn etc." do not include the number of products that were switched to other review categories during the review.

- The median regulatory review time for approved products in FY 2015 was 5.5 months for BTC drugs and OTC drugs (target, 7 months) and 4.7 months for quasi-drugs (target, 5.5 months), achieving the targets for both categories.

(iii) Efficient conduct of consultations

a. Improvement of pre-application consultations for BTC drugs and OTC drugs

- PMDA began offering pre-development and pre-application consultations for OTC drugs in FY 2010 based on opinions from the industry associations. In FY 2011, PMDA started to offer consultations regarding the appropriateness of new OTC drug development activities. Also, pre-application consultations for Switch OTC drugs and consultations on key points of clinical trial protocols became fully available from May 2015. In association with a review committee on switch candidate ingredients to be held by MHLW, PMDA will exchange opinions with the industry and discuss the establishment of a consultation system for such ingredients in the future.

Consultations for OTC Drugs

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	17	4	21	21	15
Withdrawn	2	0	0	0	1

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2015

Consultation category	Conducted	Withdrawn
Pre-application consultation for switch OTC drugs	0	1
Consultation on key points of clinical trial protocols for OTC drugs	2	0
Consultation on appropriateness of development of new OTC drugs	13	0
Total	15	1

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

- PMDA continued to exchange opinions with concerned parties such as the Japan Cosmetic Industry Association to start a new pre-application consultation system for quasi-drugs. PMDA will design a specific consultation system, aiming to start a trial run of the system as soon as possible.

(iv) Examination of consistency between actual manufacturing practices and instructions given in marketing approval documents for drugs

- See **3.2.(1)** New drugs **(vii)**

Medical devices

- Various measures were implemented or investigated to accelerate reviews for new medical devices, based on the "Cooperation Plan to Accelerate Reviews of Medical Devices" (March 2014) (the successor of "Action Program to Accelerate Reviews of Medical Devices" [December 2008]), "Japan Revitalization Strategy -JAPAN is BACK-," and "Healthcare and Medical Strategy."

(i) Appropriate and prompt reviews

a. Structure for clinical trial consultations and reviews

- In order to strengthen the review system to achieve new targets, PMDA increased the number of reviewers allocated to the categories receiving a substantially greater number of new medical device applications and for which the review timeframe for such applications was likely to be prolonged.
- Reviews of new medical devices and improved medical devices were conducted by review teams consisting of experts who have academic degrees in engineering, pharmaceutical science, physical science, medicine, dentistry, veterinary medicine, statistics, etc., under the guidance of an office director and a review director.

  The review team typically comprises team leader(s) and reviewers who specialize in biological evaluations, physical and chemical property evaluations, electrical safety evaluations, and clinical evaluations.

Note: *New medical devices:*

- *Medical devices which have a clearly different structure, usage, indications, performance, etc. compared with those for which marketing approval has been granted (medical devices that have been specified as being subject to use results assessment according to the provisions of Paragraph 1, Article 23-2-9 of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics [PMD Act] at the time of approval, excluding those for which the survey period has not expired; hereinafter referred to as "approved medical devices") (as defined under the PMD Act)*
- *Medical devices subject to re-examination, which have a clearly different structure, usage, indications, performance, etc., compared to existing approved medical devices or certified medical devices (definition under the Pharmaceutical Affairs Act).*

Improved medical devices:

- *Medical devices that do not fall under "new medical devices" or "generic medical devices" (definition under the PMD Act)*
- *Medical devices that do not fall under "new medical devices" or "generic medical devices," and are not so novel as to be subject to re-examination, nor are substantially equivalent to existing medical devices in terms of structure, usage, indications, performance, etc. (definition under the Pharmaceutical Affairs Act)*

Generic medical devices:

- *Medical devices that are regarded as equivalent to existing approved medical devices in terms of structure, usage, indications, and performance; that is, medical devices that are substantially equivalent to existing approved medical devices in terms of structure, usage, indications, and performance (definition from the PMD Act)*
- *Medical devices that are regarded as substantially equivalent to existing approved medical devices in terms of structure, usage, indications, performance, etc. (definition under the Pharmaceutical Affairs Act)*

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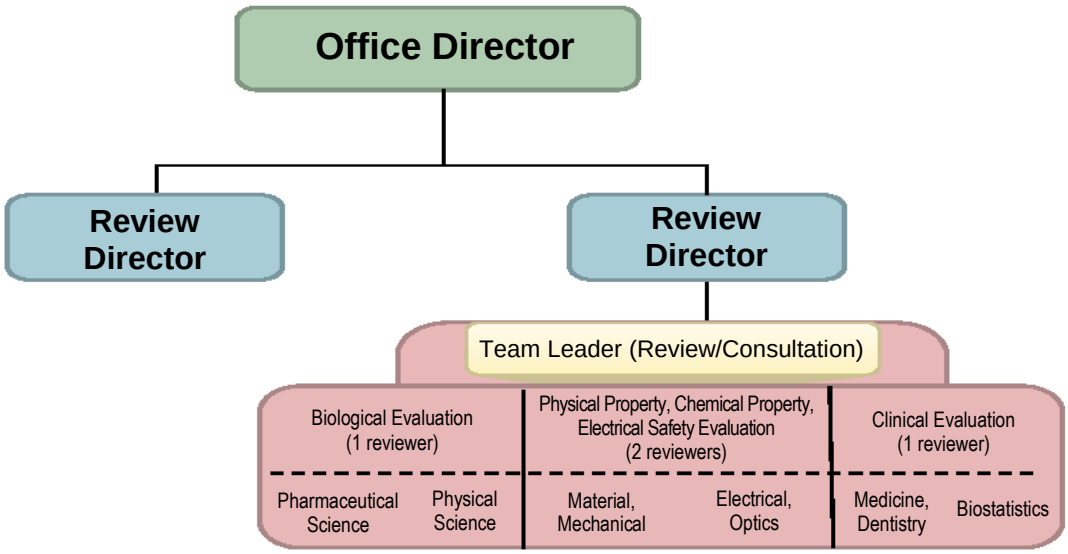
Organization for New/Improved Medical Device Reviews



- New and improved medical devices were reviewed by teams designated based on the review categories shown below. To accelerate and streamline operation and to establish more smooth and flexible review/consultation system, PMDA restructured these review categories into new review areas (see tables below) on October 1, 2015, while maintaining the 3-track system for new, improved, and generic devices. PMDA also established cross-sectional teams to deal with particular issues to promote collaboration and harmonization among departments after the restructuring.

Review Categories Covered by the Offices of New/Improved Medical Devices

<Until September 30, 2015>

Office	Review Categories	
Office of Medical Devices I	Category 3-1	Intervention devices mainly in cerebral, cardiovascular, respiratory, psychiatric, and neurological field (materials)
	Category 3-2	Non-intervention devices mainly in cerebral, cardiovascular, respiratory, psychiatric, and neurological field (materials)
	Category 4	Mainly for cerebral, cardiovascular, respiratory, psychiatric, and neurological field(appliances/machines)
	Category 8	Mainly for multicategory medical devices, advanced electronic medical devices, other uncategorized medical devices
Office of Medical Devices II (Note)	Category 1	Mainly for ophthalmology and otorhinolaryngology
	Category 2	Mainly for dentistry
	Category 5	Mainly for gastrointestinal and urinary systems, obstetrics and gynecology
	Category 6-1	Mainly for medical devices for knee/upper limb joints, hip/digital joints, etc., in orthopedic surgery area
	Category 6-2	Mainly for plates/screws, fixation materials for intramedullary nails/spines and related appliances/machines in orthopedic surgery area, and medical devices for plastic surgery and dermatology
	Category 7	Mainly for laboratory tests (*in vitro* diagnostics)

Note: Operations of Category 7 were transferred from the Office of Medical Devices II to the Office of In Vitro Diagnostics (a new office) on April 1, 2015.

<From October 1, 2015>

Offices	Review Areas	
Office of Medical Devices I	Robotic, ICT, and other devices	Mainly innovative medical devices utilizing robotics and advanced ICT technologies, multicategory medical devices, and other uncategorized medical devices
	Orthopedic and Plastic Surgery	- Medical devices mainly pertaining to hips, knees, upper extremities, hands, and digits, etc. among orthopedic devices - Medical devices such as plates, screws, intramedullary nails, spinal implants and related instruments, as well as medical devices used in plastic surgery, dermatology, etc.
Office of Medical Devices II	Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	- Materials used in the fields of brain and circulatory medicine (excluding cardiology) as well as respiratory medicine, neurology, and psychiatry - Mechanical appliances used in the fields of brain and circulatory medicine (excluding cardiology) as well as respiratory medicine, neurology, and psychiatry
	Gastroenterology, Genitourinary, and Reproductive Medicine	Mainly devices pertaining to the fields of gastroenterology, urology, and obstetrics/gynecology(OB/GYN)
	Dentistry and Oral Medicine	Mainly devices used in the field of dentistry
Office of Medical Devices III	Ophthalmology and Otorhinolaryngology	Mainly devices pertaining to the fields of ophthalmology and otorhinolaryngology
	Cardiopulmonary and cardiovascular areas	- Mainly cardiology-related materials used in medical devices pertaining to the circulatory system - Mainly cardiology-related mechanical appliances pertaining to the circulatory system
Cross-sectional teams		
(i) Clinical evaluation team (ii) Biological safety team (iii) Electrical safety (including laser) team (iv) Software (including cyber security) team (v) Generic team (including cooperation plan: clarification of substantial equivalence) (vi) International (including IMDRF) team (vii) Regulatory science team		

- To hear opinions from external experts in the course of reviews performed by review teams, expert discussions were held where necessary, and also, innovative medical devices etc., were deliberated at the Committee on Medical Devices and *In-vitro* Diagnostics of Pharmaceutical Affairs and Food Sanitation Council (PAFSC), MHLW.

Review Performance for FY 2015 (medical devices and in vitro diagnostics)

(1) Number of Expert Discussions conducted: 81 (67 document-based discussions, 14 meetings)
(2) Applications deliberated at the Committees on Medical Devices and *in vitro* Diagnostics (under PAFSC): 17
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 344 (313 medical devices, 31 *in vitro* diagnostics)

- PMDA conducted clinical trial consultations for new/improved medical devices based on the team-reviewed guidance plan drafted by three staff members consisting of a Review Director, a

consultation leader, and a deputy consultation leader. Consultation leaders and deputy consultation leaders are appointed from among review team members.

- Generic medical devices were reviewed by teams based on the review categories in association with organizational restructuring in October 2015, while maintaining the 3-track system. PMDA established cross-sectional review teams for generic medical devices and shared information to maintain the same quality of reviews across the review offices.

b. Introduction of the 3-track review system

- As one of the efforts to advance and accelerate reviews of medical devices, the 3-track review system (for new medical devices, improved medical devices, and generic medical devices) has been put in place in PMDA since FY 2011. In FY 2015, PMDA promoted the system based on the experiences in the previous fiscal year.

c. Reinforcement and transparency of the progress management of reviews

- In order to conduct reviews and related services promptly and appropriately to achieve the target review time as specified in the Mid-term Plan, PMDA held meetings of the Progress Management Committee for Reviews and Related Services once every 3 months, to ensure that the Chief Executive and other executives of PMDA can accurately grasp the progress of reviews and related services and support improvement, as needed. In this way, operational progress was monitored, while particularly relevant information for new medical devices was dealt with comprehensively and approaches for solving operational challenges were considered.
- In FY 2015, PMDA continued to hold the Review Segment Committee for Progress Management, with the Director of the Center for Product Evaluation as its head, to control the progress of reviews. In the meetings, information on the overall review status for new medical devices including QMS inspections etc., and associated issues were shared, and measures to address the issues and future approaches were examined (12 meetings held in FY 2015).

  Necessary guidance was provided on an ongoing basis by the Director of the Center for Product Evaluation and the Associate Center Director of the Review Segment Committee for Progress Management while taking into account reports from office directors of review divisions, and each review office was notified of the results of discussions and of improvement measures for products requiring prolonged review.
- In order to accelerate review times, timelines were strictly managed in accordance with the "On the Standard Review Timeline for New Medical Devices" (PFSD/ELD/OMDE Notification No. 1120-1 issued by the Director of Office of Medical Device Evaluation, ELD, PFSD, MHLW, dated November 20, 2013), "On the Standard Review Timeline for Improved Medical Devices (with Clinical Data)" (PFSD/ELD/OMDE Notification No. 0328-4 dated March 28, 2014), and "On the Standard Review Timeline for Improved Medical Devices (without Clinical Data) and Generic Medical Devices" (PFSD/ELD/OMDE Notification No. 0519-1 dated May 19, 2014).
- In accordance with the "Information Sharing about the Progress of Reviews of New Medical Devices and Improved Medical Devices" (PFSD/ELD/OMDE Notification No. 0530001 dated May 30, 2014), the progress of the PMDA review is communicated to applicants in each review stage. The relevant office directors appropriately hold meetings with applicants upon their request to explain the progress and outlook of the review to them.

d. Standardization and transparency of review

- To clarify review standards, PMDA posted on its website three documents on basic considerations for review: "Points to Consider in regard to Applications for New Medical Devices, etc.," "Points to Consider in regard to Applications for Improved Medical Devices," and "Points to Consider in regard to Applications for Generic Medical Devices." These documents were first published in FY 2008, and were later revised in conjunction with subsequent regulatory policy changes. PMDA has also explained these points to relevant reviewers and has been using them for reviews etc.
- To promote the transparency and efficiency of reviews, PMDA posted on its website the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices)," which is a revised version of the "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices (new medical devices and improved medical device)" published in FY 2009. PMDA introduced the guidelines at workshops to make them widely known. PMDA posted on its website the following guidance documents: "Points to Consider in Preparing Data for Applications of Improved Medical Devices" for improved medical devices, "Points to Consider in Preparing Data for Applications of Generic Medical Devices," "Guidelines for Preparation of Summary Technical Documentation (STED) Submitted in Applications for Medical Devices in the Category of Generic Medical Devices (without approval standards, without clinical data)," and "Confirmation of Application Documents for Generic Medical Devices" for generic medical devices. PMDA also presented these guidance documents in workshops to thoroughly disseminate them.

e. Consultations and reviews based on medical care needs

- PMDA actively exchanged opinions with healthcare professionals by participating in academic conferences in and out of Japan, town hall meetings, requested lectures, etc., to comprehend their needs. The Agency has conducted consultations and reviews, taking into account the information obtained in this manner.
- In order to encourage medical device MAHs to promote the development of medical device products that have been approved in Europe and the U.S. but are not yet approved in Japan, the Study Group on the Early Introduction of Medical Devices etc., with High Medical Need (chaired by Dr. Soichiro Kitamura, President Emeritus of National Cerebral and Cardiovascular Center) was established in the MHLW in October 2006. The study group has been actively conducting investigations. PMDA has cooperated in the operation of the study group, and provided clinical trial consultations and reviewed product applications taking into account the results of investigations by the study group. Four medical devices were approved in FY 2015 through this initiative.

f. Consistency between clinical trial consultations and reviews

- In order to ensure consistency between clinical trial consultations and reviews, review team members are involved in all clinical trial consultations for products falling under the category to which they are assigned. Consistency from consultations to reviews is maintained and teams are flexibly organized as necessary.

g. Efficient operation and implementation of the use-results evaluation system

- With the enactment of the Act for Partial Revision of the Pharmaceutical Affairs Act (Act No. 84, 2013), PMDA worked on the efficient operation and implementation of the use-results evaluation system for medical devices, which was introduced on November 25, 2014, in accordance with "Basic Principles on Products Subject to Use-results Evaluation at the Time of Approval"

deliberated and approved at the 6th meeting of the Committee on Medical Devices and In-vitro Diagnostics (MHLW) in FY 2014.

Based on this principle, 57 medical devices (including 18 medical devices selected for use-results survey) were approved in FY 2015.

- In order to implement the new system smoothly, medical devices that had been designated as products subject to re-examination before the system revision were processed with greater collaboration with the division of surveillance (Office of Non-clinical and Clinical Compliance). As a result, 14 medical devices subject to re-examination were processed in FY 2015.

(ii) Introduction of new review systems

a. Introduction of prior assessment consultation

- To preliminarily evaluate the quality, efficacy and safety of medical devices in their development stage, PMDA started to offer prior assessment consultation service as a pilot scheme in October 2010, and formally launched this consultation service in FY 2012. In FY 2015, consultations on 2 products were completed.

b. Short-term review of applications for specified partial changes

- Applications for specified partial changes were reviewed in accordance with "Regarding Acceleration of the Procedure for Specified Changes Made to Medical Devices" (PFSB/ELD/OMDE Notification No. 1110001, dated November 10, 2008). As a result, regulatory review time for 28 of 31 products approved in FY 2015 was not more than 2 months excluding the period for GCP/GLP inspections.

c. Support for the development of approval standards, certification standards, and review guidelines for medical devices

- In order to support MHLW in developing approval standards etc., for medical devices, the Committee on Medical Device Approval Standards held 5 meetings in FY 2015.

The table below shows the number of approval or certification standards reported to MHLW in FY 2015 to be established or revised. Approval standards included 3 revised standards; Certification standards included 99 revised standards for designated controlled medical devices and 7 establishment standards for designated specially controlled medical devices. (Standards for designated specially controlled medical devices were introduced in accordance with the PMD Act.) All of the standards were for medical devices of Class III risk level.

FY (for reporting)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Total
Approval standards	6	7	5	2	6	6	5	4	0	3	44
Certification standards (designated controlled medical devices)	0	14	86	64	294	84	67	82	129	99	919
Certification standards (designated specially controlled medical devices)	–	–	–	–	–	–	–	–	3	7	10
Review guidelines	0	1	2	6	0	0	0	0	0	0	9

The table below shows the number of standards established by MHLW in FY 2015 based on the reports from PMDA. Seven certification standards were established for designated controlled medical devices. All of the standards were for medical devices of Class III risk level.

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

FY (for establishment)	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Total
Approval standards	0	17	8	10	-2*	5	3	0	0	4	0	-1*	44
Certification standards (designated controlled medical devices)	363	9	24	0	17	68	274	67	2	3	109	0	936
Certification standards (designated specially controlled medical devices)	–	–	–	–	–	–	–	–	–	–	3	7	10
Review guidelines	0	0	0	0	3	1	4	0	0	0	0	0	8

** Two established approval standards in FY 2008 and one in FY 2015 were switched to certification standards, resulting in a negative number.*

List of Certification Standards for Medical Devices (FY 2015)

Established: Certification standards,7; Approval standards,0; Review guidelines, 0	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 413, dated September 30, 2015	Certification Standard for Reusable Operator-powered Resuscitators
MHLW Ministerial Announcement No. 443, dated November 18, 2015	Certification Standard for Material-Using Electric Surgical Devices, etc. (and 1 other certification standard)
MHLW Ministerial Announcement No. 478, dated October 24, 2015	Certification Standard for Non-Absorbable Sutures (and 1 other certificate standard)
MHLW Ministerial Announcement No. 118, dated March 30, 2016	Certification Standard for Blood Glucose Self-testing Device (and 1 other certification standard)

- The PMDA website concerning the information service on medical device standards provides the latest information on the certification standards and approval standards in relation to JIS, ISO/IEC, MHLW Notifications, Japanese Medical Device Nomenclature (JMDN), etc., as their components. During FY 2015, as part of system improvements to respond to the PMD Act and Medical Device International Standardization Strategy Promotion Project, PMDA upgraded the infrastructure of its English website through which information will be provided to foreign countries and substantially expanded the contents (such as purpose of use and effect on over 900 certification standards, relationship between ministerial announcements citing JIS and international specifications including ISO/IEC, and checklist to ensure conformity to basic requirements). The information on the website has been updated periodically, at least twice per month.
- PMDA provided advice on each individual product through simple consultations on the scope of changes for which partial change applications are not required, or minor change notifications are required, based on the "Procedures Associated with Partial Change for Medical Devices" (PFSB/ELD/OMDE Notification No.1023001, dated October 23, 2008).

- PMDA dealt with the procedure for changing raw materials for each individual products through simple consultations based on "Regarding the Procedure for Changing Raw Materials of Medical Devices" (PFSB/ELD/OMDE Notification No. 0329-7, dated March 29, 2013), which clarifies the principle of the procedure.
- In response to MAH inquiries concerning whether clinical study data are also necessary during consultations, PMDA provided guidance in the context of each applicable product based on notifications and similarly authoritative materials previously issued by MHLW.
- In order to clarify the scope of individual products, PMDA conducted simple consultations etc., by referring to the "Points to Consider in Preparing Application Forms for Marketing Certification of Medical Devices" (Notification No. 1120-4, issued by the Counsellor of Minister's Secretariat [for Medical Device and Regenerative Medicine Product Evaluation], MHLW, dated November 20, 2014), "Handling of Applications for Dental Implants" (PFSB/ELD/OMDE Notification No. 0713-1, dated July 13, 2012).

d. Equivalence review of generic medical devices

- PMDA conducted equivalence reviews for generic medical devices filed in FY 2015 based on the notification titled "Points to Consider in Preparing Applications for Medical Devices" (Notification No. 0120-9 by the Counsellor of Minister's Secretariat (for Medical Device and Regenerative Medicine Product Evaluation), MHLW, dated January, 20, 2015).
- In order to clarify the definition of substantial equivalence of generic medical devices based on the "Cooperation Plan to Accelerate Reviews of Medical Devices," PMDA held 5 meetings with related industry associations and strived to identify and summarize problems that needed to be resolved.

(iii) Efforts to achieve “zero” review lag for medical devices

- PMDA has made efforts with the cooperation of applicants to achieve the targets "a" through "e" presented below with respect to targets for the total time taken for reviews of medical device product applications submitted on or after April 1, 2004 that were approved each year through FY 2018 by gradually increasing its goal percentage reduction in time utilized.
- PMDA worked to improve its progress management activities for products under review in any application category (new, improved, or generic medical devices). PMDA also worked to reduce the backlog of pending applications. Specifically, to promptly complete the prolonged review of applications filed years earlier, PMDA and applicants had discussions to analyze reasons for prolonged review and resolve relevant issues for each product. In addition, reminder notices were frequently sent to applicants if their responses to PMDA's inquiries were delayed. For products for which new applications have been submitted, progress management was enhanced to accelerate reviews.
- In order to eliminate review/development lag for medical devices being developed or to be developed in the near future, PMDA encouraged medical device-related industries, medical device companies, and academic institutions to take measures such as the proactive use of clinical trial consultations prior to regulatory submission, at academic conferences or periodic opinion exchange sessions with the industries. Moreover, PMDA provided specific examples of deficiencies often seen at the time of regulatory submission, at workshops, etc., to call for improvements to be made on the applicants’ side.
- For reviews of generic medical devices, in association with organizational restructuring in October 2015 where each review office carries out a team review, PMDA organized a cross-sectional review

teams for generic medical devices and shared information to maintain the same quality of reviews across the review offices.

- In order to ensure consistency among review teams and carry out medical device review promptly and appropriately, PMDA developed SOPs relating to various operations, which describe reviews and related procedures for each type of new medical devices, improved medical devices, and generic medical devices. Relevant reviewers were given an explanation of these SOPs. PMDA also collected monthly data on the achievement level of the target review times and informed the reviewers of the achievement status.
- In order to eliminate development lag and shorten the total review time, it is also important to improve environments for the smooth conduct of global clinical trials. For this purpose, PMDA participated in the Harmonization by Doing (HBD) project, which has been undertaken by both Japan and the US, and had discussions on the conduct of global clinical trials, the development of common protocols between Japan and the US in the fields where development of medical devices is expected in the future, and the standardization of post-marketing surveillance database. In FY 2015, PMDA participated in HBD Think Tank East (held in Kyoto in September 2015) and promoted global clinical development through activities supporting the Proof of Concept (POC) project. In addition, from FY 2014, PMDA has continuously worked to accelerate reviews by exchanging information with the US FDA on review and consultation services. As part of the HBD activities, PMDA participated in scientific sessions held at academic conferences, such as the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) conference held in Fukuoka in August 2015, Harmonization By Doing (HBD) Special Session held at Kamakura Live in Yokohama in December 2015, and the Cardiovascular Research Technologies (CRT) conference held in Washington D.C. in February 2016, to discuss issues such as the challenges in the development of new medical devices and methods of utilizing a post-marketing registry with industry, governments, and academic circles. As part of its HBD-related activities, PMDA also participated in the Registry Assessment of Peripheral Interventional Devices (RAPID) meeting held in Washington D.C. in June 2015, which was planned for POC of post-marketing registry utilization so that the Japan and the US could collaborate in a discussion on ideas about registry utilization.
- PMDA worked to achieve its target total review times through these measures. The status of reviews for medical devices in FY 2015 was as follows:

a. Review times for new medical devices (priority review products)

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	10	10	10	10	10
Percentile	60	60	70	70	80

Results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	60
Total review time [months] (Reference, 80th percentile) [months]	4.3 (12.8)	9.3 (20.8)	9.0 (10.0)	8.8 (8.9)	7.9 (8.2)
Number of approved applications	6	5	14	5	8

Reference

Regulatory review time [months]	2.9	7.2	5.1	4.0	4.2
Applicant's time [months]	1.3	3.4	3.5	3.3	3.8

Note: Products covered are those for which applications were filed in or after April 2004.

- Priority reviews are conducted for applications for orphan medical devices and other devices that are regarded as having particularly high medical need (medical devices for serious diseases and with distinctly superior efficacy or safety as compared to existing medical devices or therapies). In FY 2015, 8 priority review products (all were new medical devices) were approved.

  Three medical devices regarded as having particularly high medical need were designated for priority review.

- The approval status of priority review products in FY 2015 was as follows: The total review time (60th percentile) was 7.9 months, and the achievement rate for the target total review time (10 months) was 100.0%, which was substantially higher than the target.

b. Review times for new medical devices (standard review products)

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	14	14	14	14	14
Percentile	60	60	70	70	80

Results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	60
Total review time [months] (Reference, 80th percentile) [months]	9.7 (17.8)	12.7 (15.5)	6.3 (14.8)	5.6 (10.6)	10.1 (11.9)
Number of approved applications	27	41	80	62	48

Reference

Regulatory review time [months]	5.1	5.4	4.0	3.5	5.0
Applicant's time [months]	3.4	5.0	1.6	2.2	4.3

Note: Products covered are those for which applications were filed in or after April 2004.

- The approval status of standard reviews for new medical devices in FY 2015 were as follows: The total review time (60th percentile) was 10.1 months, and the achievement rate for the target total review time (14 months) was 87.5%, which was substantially higher than the target. The number of approvals in FY 2015 was 48. The number of product applications under review at the end of FY 2015 was 23.

Review Status of New Medical Devices by Fiscal Year of Submission

New medical devices (FY of submission)	Applications	Approved	Withdrawn	Under review
In or before FY 2003 ending Mar. 31, 2004	132	54	78	0
FY 2004	56	35	21	0
FY 2005	7	7	0	0
FY 2006	23	19	4	0
FY 2007	37	31	6	0
FY 2008	32	30	2	0
FY 2009	24	20	4	0
FY 2010	28	24	2	2
FY 2011	42	40	2	0
FY 2012	64	63	0	1
FY 2013	72	72 (7)	0	0 [-7]
FY 2014	99	90 (60)	2 (1)	7 [-61]
FY 2015	30	17 (17)	0	13 [13]
Total	646	502 (84)	121 (1)	23 [-55]

Note 1:The figures in "Applications" are the number of products submitted as new medical devices.

Note 2:The number of approved products includes those approved as improved medical devices.

Note 3:The figures in parentheses in "Approved" and "Withdrawn" represent the number of applications processed in FY 2015 (included in figures to the left).

Note 4:The figures in brackets represent differences from the status reported in FY 2014.

c. Review times for improved medical devices (with clinical data)

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	10	10	10	10	10
Percentile	52	54	56	58	60

Results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	52	54
Total review time [months] (Reference, 60th percentile) [months]	13.9 (18.0)	17.3 (19.8)	11.6 (13.2)	9.9 (10.5)	11.0 (11.6)
Number of approved applications	55	44	63	35	53

Reference

Regulatory review time [months]	7.0	7.9	5.7	5.0	5.3
Applicant's time [months]	7.2	8.8	5.5	5.0	4.8

Note 1: Products covered are those for which applications were filed in or after April 2004.

Note 2: Applications filed in or before FY 2008 have been re-categorized in this table according to the new categorization implemented in FY 2009.

- As regards the approval status of improved medical devices (with clinical data) approved in FY 2015, the total review time (54th percentile) was 11.0 months, and the achievement rate for the target total review time (10 months) was 47.2%, which was lower than the target. The number of

approvals in FY 2015 was 53, showing an increase from the previous fiscal year but being nearly equal to the number of approvals in other fiscal years.

- The causes of the target not being achieved included the completion of the prolonged reviews of applications for improved medical devices (with clinical data) that were filed years earlier and 4 products which took over 150 days from the regulatory submission to the time of application for a QMS inspection for causes attributable to applicants.

Review Status of Improved Medical Devices (with Clinical Data) by Fiscal Year of Application

Improved medical devices (with clinical data) (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	34	33	1	0
FY 2010	34	33	1	0
FY 2011	26	21	5	0
FY 2012	42	39	2	1
FY 2013	46	40 (4)	3 (1)	3 [-5]
FY 2014	45	36 (28)	2 (2)	7 [-30]
FY 2015	27	8 (8)	0	19 [19]
Total	254	210 (40)	14 (3)	30 [-16]

Note 1:The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2:The number of approved products includes those approved under other application categories for medical devices.

Note 3:The figures in parentheses represent those processed in FY 2015 (included in figures to the left).

Note 4:The figures in brackets represent differences from the status reported in FY 2014.

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

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	6	6	6	6	6
Percentile	52	54	56	58	60

Results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	52	54
Total review time [months] (Reference, 60th percentile) [months]	13.3 (14.9)	9.7 (11.1)	7.5 (9.2)	6.0 (7.4)	6.0 (7.0)
Number of approved applications	218	229	231	213	233

Reference

Regulatory review time [months]	5.6	4.8	3.7	3.3	3.9
Applicant's time [months]	6.5	4.7	3.7	3.4	2.6

Note 1:Products covered are those for which applications were filed in or after April 2004.

Note 2:Applications filed in or before FY 2008 have been re-categorized in this table in accordance with the new categories implemented in FY 2009.

Note 3: The results in FY 2015 exclude standalone medical device software newly categorized as medical devices from November 25, 2014 according to the PMD Act and for which application was filed during the period of interim measures (from November 25, 2014 to February 24, 2015).

- As regards the approval status of improved medical devices (without clinical data) approved in FY 2015, the total review time (54th percentile) was 6.0 months, and the achievement rate for the target total review time (6 months) was 54.1%, achieving the target. The number of approved applications in FY 2015 was 233, showing an increase from the previous fiscal year but being nearly equal to the number of approvals in other fiscal years.

Review Status of Improved Medical Devices (without Clinical Data) by Fiscal Year of Application

Improved medical devices (without clinical data) (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	137	122	15	0
FY 2010	165	141 (1)	24	0 [-1]
FY 2011	176	160 (1)	16 (1)	0 [-2]
FY 2012	210	198	11 (1)	1 [-1]
FY 2013	190	177 (8)	11 (1)	2 [-9]
FY 2014	260 (-1)	197 (97)	3 (3)	60 [-101]
FY 2015	219	96 (96)	5 (5)	118 [118]
Total	1,357	1,091 (203)	85 (11)	181 [4]

Note 1: The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2: One changed application category was added to and 2 canceled applications were deleted from the number of applications in FY 2014.

Note 3:The number of approved products includes those approved under other application categories for medical devices.

Note 4:The figures in parentheses represent those processed in FY 2015 (included in figures to the left).

Note 5:The figures in brackets represent differences from the status reported in FY 2014.

e. Review times for generic medical devices

Targets

Fiscal Year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time [months]	4	4	4	4	4
Percentile	52	54	56	58	60

Results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	52	54
Total review time [months] (Reference, 60th percentile) [months]	5.0 (7.2)	4.0 (6.0)	3.9 (5.3)	3.9 (4.5)	4.4 (5.0)
Number of approved applications	907	1,216	958	920	868

Reference

Regulatory review time [months]	2.5	1.6	1.8	1.9	2.0
Applicant's time [months]	2.3	2.3	2.1	1.8	2.3

Note 1:Products covered are those for which applications were filed in or after April 2004.

Note 2:Applications filed in or before FY 2008 have been re-categorized in this table in accordance with the new categories implemented in FY 2009.

- As for the approval status of generic medical devices approved in FY 2015, the total review time (54th percentile) was 4.4 months, and the achievement rate for the target total review time (4 months) was 50.5%, which was lower than the target.
- A major cause was considered to be that the number of application had decreased substantially (by approximately 150) despite 868 approved applications, which was similar to the figure for the previous fiscal year. Consequently, the proportion of applications requiring prolonged review time among the number of approved applications was increased and therefore the target was unachieved.
- The reasons for the targets for products requiring prolonged reviews not being achieved included the following: 1) For causes attributable to PMDA, increased products waiting for review and inappropriate management of timelines; and 2) For causes attributable to applicants, applicants delayed responding to PMDA inquiries, and a large number of approval applications were submitted just before the enactment of the Act of Partial Revision of the Pharmaceutical Affairs Act in November 2014. Many of such applications needed more time to review due to a lack of required data.

  QMS inspections influenced the total review time for the following reasons: 1) For causes attributable to PMDA, PMDA delayed deciding whether each QMS application should be subject to a document-based inspection or an on-site inspection, and also delayed scheduling on-site inspections. This is because of a concentration of QMS applications for renewal and a substantial increase in the number of approval applications; and 2) For causes attributable to applicants, the applicants of 9 products delayed submitting QMS applications, which were filed more than 30 days after regulatory submission; the applicants of 27 products delayed submitting data required for QMS inspection or delayed responding to QMS inspection.
- In order to achieve the targets for generic medical devices, first, it is necessary that both PMDA and applicants carry out an analysis to identify the factors that led to targets not being achieved and share the results in a collaborative manner to shorten review times. Reviewers should manage the progress of each product more closely and instruct applicants to utilize pre-approval consultations proactively and give well-considered advice and instructions about matters such as compilation of application materials and adequacy of evaluation. This should lead to further improvements in shortening the application period. To improve these matters, PMDA will take a range of actions such as requesting applicants to collaborate with PMDA through the periodic opportunities to exchange opinions with industry, presenting specific cases at seminars and at other occasions. As for the delays of QMS inspection-related applications, PMDA considers that this situation is unlikely to occur in and after FY 2016, because PMDA asked for applications for QMS inspections to be submitted immediately after regulatory submission, in accordance with a MHLW notification dated July 10, 2015 (i.e., PFSB/ELD/OMDE Notification No. 0710-1 = PFSB/CND Notification No. 0710-18) issued jointly by the Counsellor of Minister's Secretariat (for Medical Device and Regenerative Medicine Product Evaluation and the Director of Compliance and Narcotics Division, PFSB, MHLW, and because a certain time has passed since the period during which many applications for renewal were filed due to revision of the Act.

Review Status of Generic Medical Devices by Fiscal Year of Application

Generic medical devices (FY of submission)	Applications	Approved	Withdrawn	Under review
FY 2009	1,126	1,038 (1)	88 (4)	0 [-5]
FY 2010	1,020	918 (2)	98 (5)	4 [-7]
FY 2011	995	931 (8)	64 (3)	0 [-11]
FY 2012	1,075	1,030 (9)	41 (6)	4 [-15]
FY 2013	921	874 (28)	23 (5)	24 [-33]
FY 2014	947 (-10)	881 (276)	39 (32)	27 [-318]
FY 2015	790	566 (566)	10 (10)	214 [214]
Total	6,874	6,238 (890)	363 (65)	273 [-175]

Note 1:The number of applications was counted based on the initial application categories for medical devices submitted and the dates the applications were received.

Note 2: A total of 8 canceled applications, 1 application for which the category was changed, and 1 case of a summation error were deleted from the number of applications in FY 2014.

Note 3:The number of approved products includes those approved under other application categories for medical devices.

Note 4:The figures in parentheses represent those processed in FY 2015 (included in figures to the left).

Note 5:The figures in brackets represent differences from the status reported in FY 2014.

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- For medical devices, there were no requests for designation for priority consultation or consultation on GLP/GCP compliance for priority consultation products.

b. Implementation of clinical trial consultations and improvement of the system

Number of Consultations

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	136	165	162	196	203
Withdrawn	4	3	11	11	4

Number of Prior Assessment Consultations for Medical Devices (Among the Numbers Listed Above)

	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	3	3	1	3
Withdrawn	0	0	0	0

Number of Consultations on Pharmacogenomics/Biomarkers (Among the Numbers Listed Above)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	0	0	0	0	0
Withdrawn	0	0	0	0	0

Note 1:Prior assessment consultations for medical devices were abolished in association with the revision of the consultation framework as of November 25, 2014.

Note 2:The numbers of prior assessment consultations for medical devices and consultations on pharmacogenomics/biomarkers were counted on the basis of delivery dates of consultation documents to PMDA.

Note 3:Prior assessment consultations for medical devices are conducted for the categories of quality, non-clinical, and clinical.

Number of Consultations for Medical Devices by Category in FY 2015

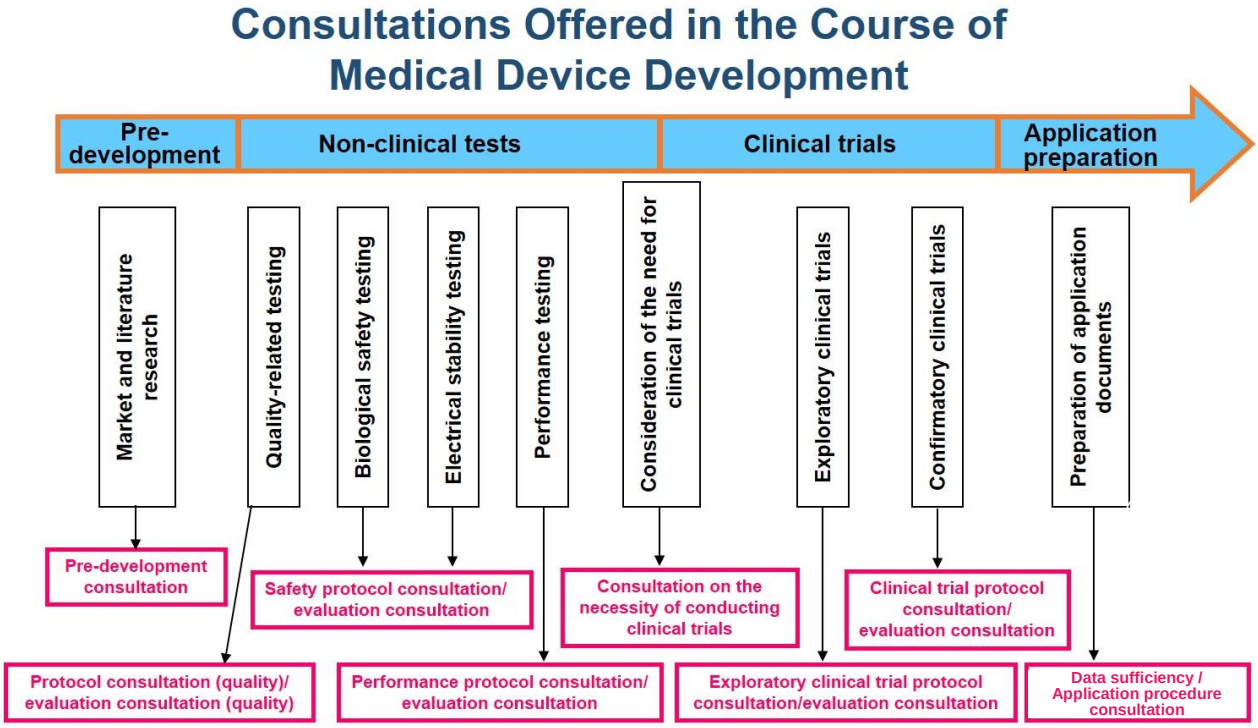
Consultation category*	Conducted	Withdrawn
Pre-development consultation for medical devices	4	1
Pre-development consultation for medical devices (preliminary consultation completed)	85	0
Consultation on necessity of clinical trials for medical devices (preliminary consultation completed)	5	0
Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.)	1	0
Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.) (preliminary consultation completed)	10	2
Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.) (additional consultation)	1	0
Protocol consultation for medical devices (safety) (1 trial) (preliminary consultation completed)	1	0
Protocol consultation for medical devices (safety) (4 or more trials)	2	0
Protocol consultation for medical devices (quality) (preliminary consultation completed)	1	0
Protocol consultation for medical devices (performance) (1 trial)	2	0
Protocol consultation for medical devices (performance) (1 trial) (preliminary consultation completed)	3	1
Protocol consultation for medical devices (performance) (1 trial) (additional consultation)	1	0
Protocol consultation for medical devices (performance) (2 trials) (preliminary consultation completed)	1	0
Protocol consultation for medical devices (performance) (3 trials) (preliminary consultation completed)	1	0
Protocol consultation for medical devices (performance) (4 or more trials) (preliminary consultation completed)	4	0
Protocol consultation for medical devices (exploratory clinical trial) (preliminary consultation completed)	3	0
Protocol consultation for medical devices (clinical trial)	3	0

Protocol consultation for medical devices (clinical trial) (preliminary consultation completed)	25	0
Protocol consultation for medical devices (clinical trial) (additional consultation)	4	0
Safety evaluation consultation for medical devices (1 trial) (protocol not evaluated) (preliminary consultation completed)	2	0
Safety evaluation consultation for medical devices (4 or more trials) (protocol not evaluated)	2	0
Safety evaluation consultation for medical devices (4 or more trials) (protocol not evaluated) (preliminary consultation completed)	3	0
Safety evaluation consultation for medical devices (4 or more trials) (additional consultation)	1	0
Quality evaluation consultation for medical devices (protocol not evaluated)	1	0
Quality evaluation consultation for medical devices (protocol not evaluated) (preliminary consultation completed)	5	0
Quality evaluation consultation for medical devices (preliminary consultation completed)	1	0
Quality evaluation consultation for medical devices (additional consultation)	1	0
Performance evaluation consultation for medical devices (1 trial) (protocol not evaluated)	2	0
Performance evaluation consultation for medical devices (1 trial) (protocol not evaluated) (preliminary consultation completed)	1	0
Performance evaluation consultation for medical devices (1 trial) (preliminary consultation completed)	1	0
Performance evaluation consultation for medical devices (2 trials) (protocol not evaluated)	1	0
Performance evaluation consultation for medical devices (2 trials) (protocol not evaluated) (preliminary consultation completed)	1	0
Performance evaluation consultation for medical devices (3 trials) (protocol not evaluated) (preliminary consultation completed)	1	0
Performance evaluation consultation for medical devices (4 or more trials) (protocol not evaluated)	2	0
Performance evaluation consultation for medical devices (4 or more trials) (protocol not evaluated) (preliminary consultation completed)	6	0
Performance evaluation consultation for medical devices (4 or more trials) (additional consultation)	1	0
Clinical trial evaluation consultation for medical devices (protocol not evaluated)	1	0
Clinical trial evaluation consultation for medical devices (protocol not evaluated) (preliminary consultation completed)	3	0
Clinical trial evaluation consultation for medical devices (preliminary consultation completed)	1	0
Data sufficiency/application category consultation for medical devices	9	0
Total	203	4

** This table shows only the categories of the consultations implemented in FY 2015.*

c. Review of consultation categories

- PMDA reviewed consultation categories and improved consultation methods (implemented on November 25, 2014) for clinical trial consultations for medical devices, to better accommodate a diverse range of needs arising during each stage of product development and to enhance the efficiency and effectiveness of consultations, taking into account the demands of industry and the Agency's previous experiences.
- In order to eliminate review/development lag for medical devices currently in development or to be developed in the near future, PMDA encouraged medical device-related industries, medical device companies, and academic institutions, etc., to take measures such as the proactive use of clinical trial consultations prior to regulatory submission, at academic conferences or through periodic exchanges of opinions with industry (reposted).



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

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

(v) Promotion of evaluation of new technologies

a. Utilization of external experts

- As PMDA is required to increase the degree of scientific sophistication of its guidance and review activities, particularly with regard to emerging technologies such as ICT and robotics, the Agency continued to commission highly knowledgeable external experts to serve as advisors to provide expert opinions on scientifically-important matters at Expert Discussions for reviews and post-marketing safety measures (reposted). (As of March 31, 2016, the number of commissioned experts is 11 including experts in safety measures.)
- The number of Expert Discussions conducted in FY 2015 was 81 (67 document-based discussions, 14 meetings).

- In order to appropriately conduct operations related to medical device products employing the latest scientific technologies, PMDA made efforts to strengthen its collaborative activities with academic and healthcare professionals and to collect relevant information at meetings of the Science Board (parent committee) and its Subcommittees on Application of Numerical Analysis to Non-clinical Evaluation and on Evaluation of Medical Devices in Pediatric Use.

b. Support for the development of national guidelines

- PMDA supported the preparation of the guidance documents for the evaluation of spinal implants for the maintenance of mobility and stability and orthopedic implants developed using three-dimensional layering technology. The prepared guidance was announced in “Publication of the Guidance Document for the Evaluation of Emerging Technology Medical Devices/Cellular and Tissue-based Products” (PFSB/ELD/OMDE Notification No. 0912-2 issued by the Counsellor of Minister's Secretariat (for Medical Device and Regenerative Medicine Product Evaluation), MHLW, dated September 12, 2014), and released on the PMDA website. In addition, PMDA cooperated with a discussion working group on “Study on How Regulations Should Be for Standalone Medical Device Software” (Research on Regulatory Harmonization and Evaluation of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics funded by the Japan Agency for Medical Research and Development in FY 2015). The outcome of the discussion was released as “Publication of Guidance on Regulatory Submission for Medical Device Software” (Administrative Notice issued by the Office of Counsellor [for Medical Device and Regenerative Medicine Product Evaluation], MHLW, dated March 31, 2016).
- The “Initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products for FY 2015” addresses various topics, including 7 medical device-related topics: orthopedics and dental area, emerging ventricular assist devices, low-invasive treatment devices, emerging endoscopic systems, emerging circulatory system treatment devices, quantitative assays, and electromagnetic/ultrasonic wave treatment devices. PMDA promoted personnel exchanges such as dispatching reviewers and other employees to research institutions such as universities, to facilitate the development of guidelines that will support the practical application of the 7 topics. In addition, PMDA participated in the initiative, discussing the development of evaluation criteria for promoting practical application and the establishment of testing methods, etc.

c. Preliminary reviews under Cartagena Act

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

d. Implementation of Pharmaceutical Affairs Consultations on R&D Strategy

- See 3.2.(1) **New drugs** (vi)-d.

e. Support project for promoting consultations/applications for innovative medical devices

- In order to prevent delays in developing innovative medical devices due to financial problems at small- and medium-sized enterprises (SMEs) and venture companies that discovered promising seed-stage technologies, PMDA implemented the “support project for promoting consultations/applications for innovative medical devices,” which provides a subsidy to SMEs and venture companies that meet certain requirements for the purpose of reducing financial burdens in consultations/applications for regulatory approval. This scheme reimburses 50% of the user fee for a consultation or a new medical device application after the user fee is paid by the relevant SME

or venture company. In FY 2014, claims for fee subsidy were filed for 2 applications and all were subsidized.

In vitro diagnostics

(i) Appropriate and prompt reviews

- PMDA's Office of In Vitro Diagnostics was established on April 1, 2015, in accordance with the "Collaborative Plan to Accelerate Reviews of *In Vitro* Diagnostics" (March 2014).
- To encourage MAHs to develop *in vitro* diagnostics that have been approved in Europe or the U.S., but have not yet been approved in Japan, the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Need was established in the MHLW in October 2006. The Study Group has held active discussions. PMDA has supported the operations of this Study Group.
- Based on "Switching of *In Vitro* Diagnostics to OTC Test Products" (PFSB/MHLW Notification No. 1225-1 dated December 25, 2014), in FY 2015, MHLW requested PMDA to evaluate "Guidelines for OTC Test Kits for Luteinizing Hormone (draft)" submitted by the pharmaceutical industry. Then, PMDA reported evaluation results to the Committee on Medical Devices and In-vitro Diagnostics. By taking actions in response to public comments and providing related information to MHLW, PMDA cooperated with the issuance of "Development of Guideline for OTC Test Kits for Luteinizing Hormone" (Notification No. 0222-1 issued by the Counsellor of Minister's Secretariat (for Evaluation and Licensing of Medical Devices, Regenerative Medicines, etc.), PSEHB, MHLW, dated February 22, 2016).

Review Status of In Vitro Diagnostics

In vitro diagnostics (FY of submission)	Applications	Approved	Withdrawn	Under review
In or before FY 2003 ending Mar. 31, 2004	327	223	76	28
FY 2004	615	596	19	0
FY 2005	69	65	4	0
FY 2006	180	173	7	0
FY 2007	197	189	8	0
FY 2008	170	160	10	0
FY 2009	183	173	10	0
FY 2010	164	157	7	0
FY 2011	177	170 (5)	7	0 [-5]
FY 2012	165	155 (2)	9 (1)	1 [-3]
FY 2013	136	119 (7)	13 (6)	4 [-13]
FY 2014	163	133 (84)	3 (1)	27 [-85]
FY 2015	196	74 (74)	2 (2)	120 [120]
Total	2,742	2,387 (172)	175 (10)	180 [14]

Note 1: The figures in parentheses indicate the number of applications processed in FY 2015 (included in left figures)

Note 2: The figures in brackets indicate increases or decreases in the number of applications processed compared with FY 2014.

Note 3: The figures are calculated based on the applications filed in or after 1994, when the equivalence review system was introduced (numerical values stored in the current application management system were used).

(ii) Expansion of consultation services

- PMDA revised consultation categories for clinical trial consultations for *in vitro* diagnostics (implemented on November 25, 2014), in order to better accommodate the diverse range of needs arising during each stage of development and to enhance the efficiency and effectiveness of consultations, taking into account requests from members of industry and the Agency's previous experience.

Number of Consultations

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	5	8	7	25	45
Withdrawn	0	0	1	0	0

Number of Prior Assessment Consultations for In Vitro Diagnostics (Among the Numbers Listed Above)

	FY 2011	FY 2012	FY 2013	FY 2014
Conducted	0	0	0	0
Withdrawn	0	0	0	0

Number of Consultations on Pharmacogenomics/Biomarkers (Among the Numbers Listed Above)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Conducted	0	0	0	0	0
Withdrawn	0	0	0	0	0

Note 1: Prior assessment consultations for in vitro diagnostics were abolished in association with the revision of the consultation framework as of November 25, 2014.

Note 2: The numbers of prior assessment consultations for in vitro diagnostics and consultations on pharmacogenomics/biomarkers were counted based on the dates of delivery of consultation documents to PMDA.

Note 3: Prior assessment consultations for in vitro diagnostics are conducted for the categories of product quality, non-clinical, and clinical.

Number of Consultations for In Vitro Diagnostics by Category in FY 2015

Consultations accepted by November 21, 2014

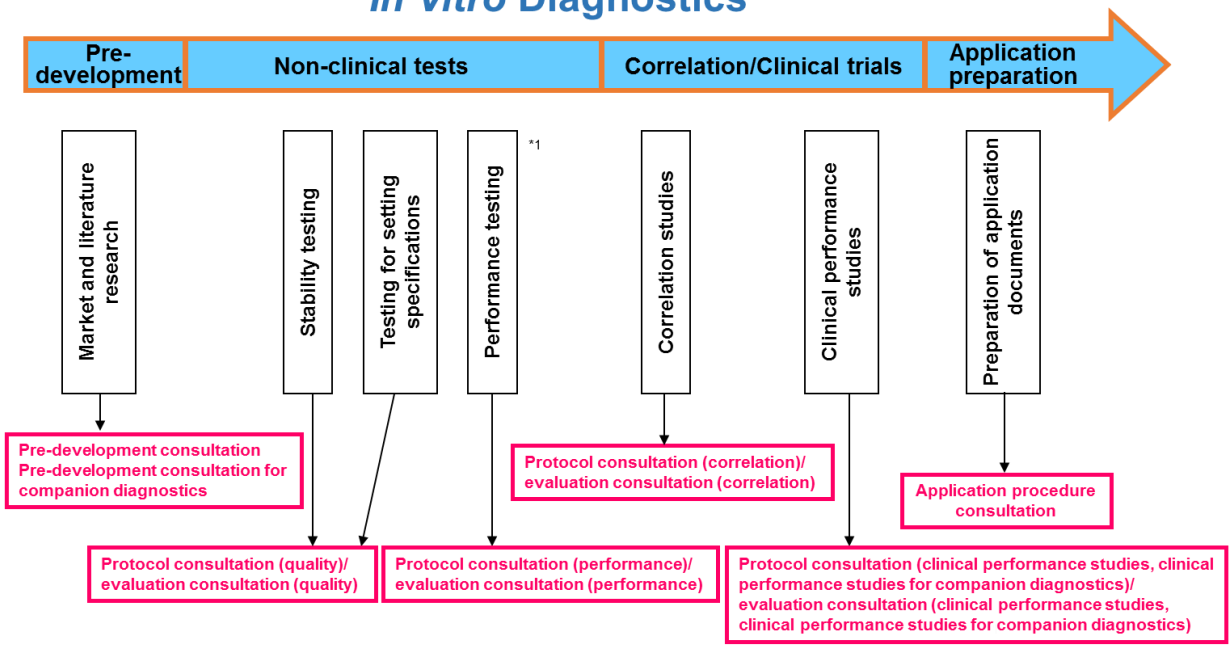
Consultation category*	Conducted	Withdrawn
Clinical performance study consultation for *in vitro* diagnostics	1	0

Consultations accepted on or after November 24, 2014

Consultation category*	Conducted	Withdrawn
Pre-development consultation for *in vitro* diagnostics	1	0
Pre-development consultation for *in vitro* diagnostics (preliminary consultation completed)	5	0
Pre-development consultation for companion diagnostics	1	0
Pre-development consultation for companion diagnostics (preliminary consultation completed)	4	0
Protocol consultation for *in vitro* diagnostics (quality) (preliminary consultation completed)	1	0
Protocol consultation for *in vitro* diagnostics (performance other than quality) (1 trial) (preliminary consultation completed)	1	0
Protocol consultation for *in vitro* diagnostics (performance other than quality) (2 trials) (preliminary consultation completed)	1	0
Protocol consultation for *in vitro* diagnostics (performance other than quality) (3 or more trials) (preliminary consultation completed)	1	0
Protocol consultation for *in vitro* diagnostics (correlation) (preliminary consultation completed)	3	0
Protocol consultation for *in vitro* diagnostics (clinical performance test)	2	0
Protocol consultation for *in vitro* diagnostics (clinical performance test) (preliminary consultation completed)	7	0
Protocol consultation for *in vitro* diagnostics, clinical performance test for companion diagnostics (preliminary consultation completed)	4	0
Quality evaluation consultation for *in vitro* diagnostics (protocol not evaluated)	1	0
Quality evaluation consultation for *in vitro* diagnostics (protocol not evaluated) (preliminary consultation completed)	2	0
Performance (other than quality) evaluation consultation for *in vitro* diagnostics (1 trial) (protocol not evaluated) (preliminary consultation completed)	1	0
Performance (other than quality) evaluation consultation for *in vitro* diagnostics (3 or more trials) (protocol not evaluated)	1	0
Correlation evaluation consultation for *in vitro* diagnostics (protocol not evaluated)	1	0
Correlation evaluation consultation for *in vitro* diagnostics (protocol not evaluated) (preliminary consultation completed)	1	0
Clinical performance evaluation consultation for *in vitro* diagnostics (protocol not evaluated)	1	0
Clinical performance evaluation consultation for *in vitro* diagnostics (protocol not evaluated) (preliminary consultation completed)	3	0
Evaluation consultation for *in vitro* diagnostics, clinical performance studies for companion diagnostics (protocol not evaluated) (preliminary consultation completed)	2	0
Total	44	0

** This table shows only the categories of consultations conducted in FY 2015.*

Consultations Offered in the Course of Development of *In Vitro* Diagnostics



*1: Refers to quality control testing and tests excluding stability testing (e.g., operation and cross-reactivity testing)

** In addition to the consultation menu in the above diagram, other categories such as additional consultations were also available.*

Regenerative medical products

(i) New review systems and appropriate and prompt reviews

- PMDA improved its review processes related to regenerative medical products in order to appropriately address the introduction of a conditional time-limited authorization for regenerative medical products in accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act. In order to ensure consistency between clinical trial consultations and reviews, PMDA flexibly organizes teams, as appropriate, while maintaining communication between consultation teams and review teams and carries out reviews/consultations appropriately and promptly.

(ii) Setting of target review time

- The target standard regulatory review time from application submission to approval for regenerative medical products approved in FY 2015 was set at 9 months, and product reviews were carried out in consideration of this target. In FY 2015, PMDA processed 2 applications filed for regenerative medical products: the total review time was 10.8 months for one application (regulatory review time, 2.2 months) and 11.9 months for the other (regulatory review time, 3.3 months). Thus, the achievement rate for the targeted regulatory review time (9 months) was 100%.
- PMDA took the following measures to achieve its target review time:
  - (i) Gathered accurate information regarding the progress of ongoing reviews and provided this information to review teams. The Progress Management Committee for Reviews and Related Services analyzed and examined operational progress to carry out progress management effectively.
  - (ii) When a problem was identified, the root cause was analyzed and feedback was provided to review teams. At briefing sessions for members of industry, applicants were urged to act vigilantly in resolving the problem.
  - (iii) Questions and answers related to applications were prepared/revised as appropriate in order to promote the transparency and efficiency of reviews.
- PMDA has been developing technical guidelines and coordinating the views of related industries and academic societies with the goal of further enhancing the transparency and efficiency of clinical trial consultations (including pharmaceutical affairs consultations on R&D strategy), clinical trial notifications, and application submissions.
- **Review times for regenerative medical products**

Targets

The following target for the standard review time should be achieved.

Type of application	Regulatory review time
Regenerative medical products	9 months

Results

	FY 2014	FY 2015
Total review time [months]	-	11.9/10.8
Regulatory review time [months]	-	3.3/2.2
Applicant's time [months]	-	8.6/8.5
Number of approved applications	0	2

Note: The figures in FY 2015 show individual review times for the 2 products approved in FY 2015.

(iii) Efficient execution of clinical trial consultations

- In order to conduct reviews more quickly and efficiently, PMDA communicated with related parties at meetings of academic societies such as the Japanese Society of Regenerative Medicine, and encouraged these parties to take advantage of consultations offered by PMDA. PMDA developed consultation services tailored to the requirements of the SAKIGAKE designation system in consideration of the particular characteristics of regenerative medical products, in addition to consultation services geared towards issues related to product quality and safety of regenerative medical products, as well as corresponding clinical trial protocols, etc. PMDA informed related parties of these consultation services and began offering the services.
- The pre-trial notification (confirmation) application scheme for gene therapy products was abolished and incorporated into the purview of Pharmaceutical Affairs Consultations on R&D Strategy for quality and safety of regenerative medical products.
- To increase the accessibility of consultation services to academic institutions and venture companies, in November 2014, PMDA implemented a pilot consultation service to provide general advice regarding matters including the development process (roadmap), as part of Pharmaceutical Affairs Consultations on R&D Strategy (Development Program Consultations on R&D Strategy). PMDA has been implementing dedicated consultations for the quality or safety of regenerative medical products, pre-consultations on regenerative medical products, with minutes recorded, and other consultations.

Number of Consultations regarding Regenerative Medical Products

	FY 2014	FY 2015
Conducted	6	18
Withdrawn	0	1

Number of Prior Assessment Consultations regarding Regenerative Medical Products (Among the Numbers Listed Above)

	FY 2014	FY 2015
Conducted	0	1
Withdrawn	0	0

Note 1: The consultation categories for regenerative medical products were established on November 25, 2014. The figure is the number of consultations conducted since then (before November 25, 2014, consultations for regenerative medical products had been included in consultations for drugs or medical devices).

Note 2: PMDA started to offer prior assessment consultations for regenerative medical products on November 25, 2014. The number of the consultations was counted on the basis of delivery dates of consultation documents to PMDA.

Note 3: For prior assessment consultations for regenerative medical products, the number of consultation categories was summed. (Set categories: safety/quality/effects, exploratory trial, verification trial)

(iv) Promotion of evaluation of new technologies

a. Utilization of external experts

- PMDA took a proactively approach to its utilization of the Science Board, in which highly knowledgeable external experts examined evaluation methods. On August 14, 2015, the CPC Subcommittee held a meeting and finalized a report entitled “Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products.”

In addition, PMDA conducted Pharmaceutical Affairs Consultations on R&D Strategy based on viewpoints presented in another report prepared by the Science Board, entitled “Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from induced Pluripotent Stem Cells (iPSCs) and iPSCs as Their Starting Materials,” dated August 20, 2013.

At international academic conferences and other similar events, PMDA exchanged opinions with members of foreign regulatory authorities such as the US FDA and the EMA about future international regulations on regenerative medical products. In March 2016, PMDA and the Japanese Society for Regenerative Medicine co-hosted an international symposium titled “International Regulatory Forum of Human Cell Therapy and Gene Therapy Products,” and invited regulatory authorities outside Japan, such as EMA and FDA to enter into a dialogue with academia and industry in and outside Japan about regulatory affairs. The symposium discussed convergence of evaluation methods and other issues related to the quality, efficacy, and safety of regenerative medical products and agreed on the necessity of promoting an integrated approach to scientific directions among international regulatory authorities.

b. Collecting knowledge

- PMDA has dispatched staff to meetings held by various societies and organizations relevant to PMDA’s activities, such as the Japanese Society for Regenerative Medicines, and also to organizations supporting the development of regenerative medical products (e.g., CiRA, Osaka University, RIKEN, Chiba University, the Institute of Medical Science of the University of Tokyo, etc.). Through these dispatch activities, PMDA is able to deepen its understanding of the needs of medical institutions engaged in the development of regenerative medical products, and is also able to gather information regarding the practical application of such products.

c. Support to the development of national guidelines

- PMDA collaborated with MHLW in developing guidelines for evaluating products developed with state-of-the-art technologies, such as regenerative medical products, and in MHLW’s initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products. The results of these activities are described below.
- In line with the initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products, PMDA supports research institutions in their research and development of seed-stage resources. PMDA also supports the development of guidelines issued by the study group for evaluating regenerative medical products (in FY 2015, guidelines on the evaluation of the following topics).
    - Cell-based products: Six topics (Hokkaido University [cerebral infarction treatment], Kyoto University [iPS platelets], Osaka University [cardiac failure, corneal epithelium disease], National Center for Child Health and Development [ES congenital hepatic disease], National Institutes of Biomedical Innovation, Health and Nutrition [quality and non-clinical evaluation], RIKEN [retinal pigment epithelium disease])
    - Gene therapy products: Two topics (The University of Tokyo [virotherapy for malignant tumor], National Center for Child Health and Development [virotherapy for WAS])
    - Other topics: One topic (Chiba University [central nervous system disorders])
- PMDA supported the development of guidance issued by working groups conducting the following studies supported by Health and Labour Sciences Research Grants while acting in the roles of observer or secretariat.

- "Study on Ensuring Quality of Specific Cell Based Products/Regenerative Medical Products" (representative researcher, Shingo Niimi)
- "Study on Least Essential and Common Technical Requirements and Standards for Evaluation of Products Derived from Stem Cells, etc. to Accelerate Practical Application of Regenerative Medicine" (representative researcher, Takao Hayakawa)

- In FY 2015, PMDA participated as an observer in group meetings regarding the regeneration of knee joint cartilage (outsourced to Shingo Niimi; chairperson, Masato Sato), a project for "Development of guidance for the approval process of brand-new medical products and regenerative medicine products." PMDA supported the development of guidance to be issued as a result of the project.

(v) Promotion of the use of Pharmaceutical Affairs Consultations on R&D Strategy

- PMDA has conducted preliminary reviews of regenerative medical products (including gene therapy products) prior to the initiation of clinical trials, to determine whether the quality and safety of the products conform to relevant guidance. The preliminary reviews were abolished in July 2011 for regenerative medical products and medical devices and in July 2013 for gene therapy products. These preliminary reviews were replaced with pharmaceutical affairs consultations on R&D strategy. PMDA has promoted the use of the Pharmaceutical Affairs Consultations on R&D strategy by doing the following activities: issuance of notifications to inform relevant parties of consultation services as well as the new consultation category of regenerative medical products established in accordance with the Act for Amendment and Partial Revision of the Pharmaceutical Affairs Act enacted in November 2014; and provision of relevant information at academic conferences. As a result, 33 clinical trials of regenerative medical products, including investigator-initiated trials by academia, were started by the end of FY 2015 with the support of PMDA [for the results of Pharmaceutical Affairs Consultations on R&D strategy, see 2. (1) (vi)-d].
- For preliminary reviews under the Cartagena Act, see 3.2.(1) **New drugs** (vi)-c.

Promotion of GLP/GCP/GPSP compliance assessments and clinical trials, etc.

- PMDA took the following measures to promote the proper execution of laboratory tests and clinical trials for drug and medical device product applications for approval and to ensure the reliability of application data.

(i) Efficient GLP/GCP/GPSP inspections and data integrity assessments for new drugs, etc.

- PMDA discussed inspection methods that take risks into consideration and a feasible method of selecting institutions for on-site inspection. In addition, PMDA exchanged ideas with the US FDA and the EMA regarding how each regulatory authority conducts compliance assessment.
- A pilot survey administered using the “GCP management sheet” (tentative name) is currently in-progress. The survey was conducted during FY 2015 with respect to 49 products made by 17 companies. In May 2015, PMDA held a meeting to exchange ideas with members of industry regarding how the pilot survey had been conducted and to answer questions. PMDA then provided information on the Q&As at a GCP/GPSP training course held in October 2015. PMDA also had a dialogue with industry about the future direction of the pilot survey in December 2015 and made efforts to improve the sample and Q&As to decrease the burden placed on companies.
- PMDA’s Office of Non-clinical and Clinical Compliance obtained information, at an early stage, on products to be filed for approval as to whether these products have already been filed for approval to regulatory authorities outside Japan, by having its staff participate in pre-review consultations for approval. In addition, Office of Conformity Audit exchanged and shared information on the planned reviews/inspections with the relevant offices in the Review Division of PMDA.
- PMDA discussed and reviewed the method for inspecting the clinical trials of 2 products for which Clinical Data Interchange Standards Consortium (CDISC) standards had already been introduced. In parallel, the current inspection process underwent a complete overhaul from the viewpoints of appropriateness and effectiveness. As a result, PMDA was able to reduce the amount of documents required to be submitted in advance and use the documents as supportive information before inspection.
- The CDISC Standards Discussion Team held periodic discussion conferences. The Team exchanged ideas with members of industry and participated in training courses as necessary to ensure adequate human resources with appropriate expertise and also to improve the compliance assessment system.

(ii) Efficient GLP/GCP/GPSP inspections and data integrity assessments for medical devices

- The Offices of Medical Devices and Office of Non-clinical and Clinical Compliance held periodic joint meetings to share information on the progress of both reviews and inspections, and conducted GLP/GCP/GPSP compliance assessments in an appropriate and timely manner. In FY 2015, GCP on-site inspections were conducted for 1 new medical device using appropriate procedures under the relevant system.
- PMDA participated in working-level meetings of “Cooperation Plan for Expediting Medical Device Reviews” and the “Task Force for Medical Device Regulations” to collect the industry’s opinions on specific requirements for inspections to facilitate expeditious reviews of medical devices.
- For a “checklist for application acceptance” for filing an application for generic medical devices that started from April 2014, PMDA opened a dialogue with members of industry regarding additional items for GLP/GCP/GPSP compliance assessments (including preparation of materials for GLP/GCP/GPSP compliance assessment).

(iii) Efficient GLP/GCP/GPSP inspections and data integrity assessments for regenerative medical products

- PMDA conducted inspections of regenerative medical products filed for approval in FY 2014 based on the inspection procedure for drugs.

(iv) Efficient GLP inspections and data integrity assessments

- Staff members in the Office of Non-clinical and Clinical Compliance participated in a training course for GLP inspectors (hosted by OECD) in India and learned about GLP inspections based on international standards. In addition, PMDA's GLP team initiated a periodic workshops on GLP-related guidance documents issued by OECD.
- To promote understanding of "Instructions for GLP Inspection in laboratories conducting tests on Drugs, Medical Devices, and Regenerative Medical Products" revised in FY 2014, PMDA prepared a Q&A sheet and posted on its website. PMDA also explained the Q&As and other activities at a GLP training course held in FY 2015 and held meetings to have a dialogue with industry.
- PMDA participated in the GLP working group of the OECD (a PMDA staff member served as a vice-chairperson) and dispatched 1 trainee to the OECD-GLP office and thereby introduced PMDA's knowledge and know-how into international GLP-related activities.

(v) Efficient GLP/GCP/GPSP inspections and data integrity assessments for re-examination (including use-results evaluation)

- PMDA increased the efficiency of inspections/assessment for re-examination of drugs by revising inspection methods, human resources, and the number of days spent on inspections. For example, when an applicant filed applications for several products around the same time, PMDA conducted inspections on the products simultaneously. PMDA thus carried out inspections promptly in FY 2015, when numerous applications for re-examination were filed. In addition, a trial inspection using a safety information management sheet was conducted. PMDA exchanged ideas with industry on the effectiveness of the inspections.
- PMDA and industry discussed methods for conducting GLP/GCP/GPSP compliance assessments in cases where electronic medical record data are used as application data for re-examination, in meetings of a working group investigating the utilization of databases of pharmacoepidemiology and electronic medical data. In addition, PMDA had a dialogue with industry on consultations services for drug re-examination inspections. Furthermore, PMDA shared problems revealed by inspections and other information at a GCP/CPSP training course in October 2015.
- PMDA's Office of Non-clinical and Clinical Compliance held a meeting with MHLW, the Office of Medical Devices (within PMDA), and industry held a meeting to exchange ideas for streamlining the operation and conduct of the use-results evaluation system newly introduced to medical devices. In the meeting, attendees discussed what data are required to be included in applications for use-results evaluation and how to conduct use-results evaluation, and PMDA gathered opinions on how to run the use-results evaluation system smoothly. In addition, PMDA issued a notification on the procedure for compliance assessment of use-results evaluation based on the opinions of MHLW and industry.

  Office of Non-clinical and Clinical Compliance shared information regarding progress of the inspection into re-examination products with Office of Medical Devices.
- PMDA exchanged ideas with industry on the operation of use-results evaluation for medical devices, and revised the notification on the procedure for GLP/GCP/GPSP compliance assessments for re-examination of medical devices. As for the re-examination inspection for medical devices, PMDA

provided information such as points to consider for GLP/GCP/GPSP compliance assessments at a GCP/GPSP training course held in October 2015 and at a lecture held by Medical Device Center in November 2015.

(vi) Proper conduct of clinical trials, etc.

- PMDA exchanged ideas with industry on the establishment of a new consultation service for individual cases related to GPSP/GPMSP compliance assessment for re-examination of drugs, and prepared the new consultation service to be launched in FY 2016.
- To further promote the proper execution of clinical trials, PMDA held GCP/GPSP workshops in Tokyo and Osaka and presented its data regarding frequently revealed findings in document-based GLP/GCP/GPSP compliance assessments, GCP on-site inspections, and GLP/GCP/GPSP compliance assessments for re-examination. Materials used for the workshops were posted on the PMDA website. In addition, PMDA representatives gave lectures regarding GLP/GCP/GPSP compliance assessments at academic conferences attended by healthcare professionals, exchanging ideas with related parties.
- In FY 2014, PMDA launched a new consultation categories concerning GCP/GLP/GPSP compliance assessments. In FY 2015, 25 consultations were conducted for drugs, 19 for medical devices, and 3 for regenerative medical products.
- PMDA responded to any invitation for lecture on GCP/GLP/GPSP, etc., in so far as it could, to facilitate the understanding of GCP/GLP/GPSP compliance assessments.

Number of Participants in GCP/GPSP Workshops

Venue	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Tokyo	1,086	1,254	1,189	1,242	1,140
Osaka	418	471	404	448	352
Total	1,504	1,725	1,593	1,690	1,492

Number of GLP/GCP/GPSP Compliance Assessments by Fiscal Year

		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Document-based assessments		2,437	2,737	2,610	2,396	2,332
	New drugs	280	286	364	370	389
	Generic drugs	1,118	1,188	1,086	1,080	1,045
	Medical devices	1,039	1,263	1,160	946	894
	Regenerative medical products	–	–	–	0	4
GCP on-site inspections		149	197	242	236	201
	New drugs	140	187	222	221	191
	Generic drugs	8	9	15	10	7
	Medical devices	1	1	5	5	1
	Regenerative medical products	–	–	–	0	2
Document-based assessments for re-examination		111	127	80	81	136
	New drugs	109	112	71	74	120
	New medical devices	2	15	9	7	16
On-site GPSP inspections for re-examination		109	112	71	74	120
	New drugs	109	112	71	74	120
	New medical devices	0	0	0	0	0
Document-based assessments for re-evaluation		0	0	0	0	19
On-site GPSP inspections for re-evaluation		0	0	0	0	19
GLP inspections		32	39	21	40	36
	Drugs	23	29	18	27	22
	Medical devices	9	10	3	13	9
	Regenerative medical products	–	–	–	0	5

Note: These figures represent the respective numbers of products for which inspection/assessment was completed. The figures for medical devices related to "document-based assessments," "GCP on-site inspections," "document-based assessments for re-examination," and "on-site GPSP inspections for re-examination" until December in 2013 represent the numbers of products for which both inspection/assessment and review/re-examination were completed.

Note: The number of document-based assessments for re-examination for medical devices in FY 2014 was amended from 5 to 7.

Promotion of GMP/GCTP/QMS inspections

(i) Efficient GMP/GCTP/QMS inspections

a. Implementation of GMP/GCTP/QMS inspections

- In accordance with the amended Pharmaceutical Affairs Act, which came into effect in FY 2005, both manufacturing and quality control procedures for drugs etc. implemented at manufacturing facilities of such products must comply with the requirements specified in the Ministerial Ordinance on GMP for Drugs and Quasi-drugs[a] and/or Ministerial Ordinance on QMS for Medical Devices and *In vitro* Diagnostics[b], in order to satisfy regulatory requirements 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 inspection by PMDA: (1) foreign manufacturing sites related to all products that require regulatory approval; and (2) Japanese manufacturing sites for new drugs, new medical devices or Class IV medical devices (high-risk medical devices such as pacemakers).

- In accordance with the Act for Partial Revision of the Pharmaceutical Affairs Act, which came into effect in November 2014, "Pharmaceutical Affairs Act" was renamed to the "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" (abbreviated to the "PMD Act"), pursuant to which the term "regenerative medical products" was defined. Before revision, a license was required to manufacture medical devices and *in vitro* diagnostics; after revision, only registration is required (change from a license-based system to a registration-based system).

- The Ordinance on QMS for Medical Devices and *In vitro* Diagnostics was also revised, and manufacturers were newly included in targets for QMS inspections. QMS inspections for medical devices with no certification standards, which had previously been conducted by prefectural governments, are now conducted by PMDA. Further, PMDA began to issue standard conformity certificates for each family of products, not for individual products. This means that a product is exempted from QMS inspection if it falls under any of "the combinations of a family of products and a manufacturing site" that have already been granted standard conformity certificates. This new system improved applicants' convenience. Approved or certified products are subject to QMS inspections every 5 years from the approval or certification date. If an approved/certified medical device or in vitro diagnostic is scheduled to undergo QMS inspection within 1 year of the enactment of the PMD Act, the MAH of the medical device or in vitro diagnostic is allowed to file an application for QMS inspection within 1 year of the enactment of the PMD Act. (This means that the previously scheduled QMS inspection can be postponed for up to 1 year.) Accordingly, a rapidly increasing number of applications for QMS inspections, especially for renewal inspections, were filed within 1 year of the enactment of the PMD Act. PMDA took actions to address such a situation by reviewing the administrative system.

- Based on information disclosed by whistleblowers, and as a result of for-cause inspections conducted by PMDA under the direction of MHLW, it was revealed that blood products marketed by a certain MAH had been manufactured using different method from the method prescribed in their corresponding approval documents over a long period of time, and the MAH separately created false manufacturing records to systematically conceal this fact (in May 2015). Due to the incident, as part of preventive measures for malpractice, GMP inspections without prior notification were initiated based on an order issued by MHLW (PSEHB/CND/ Notification No. 0115-3 dated January 15, 2016).

  In addition, PMDA conducted a study focusing the methods of GMP inspection employed by foreign regulatory authorities in order to discuss measures to prevent malpractice by drug manufacturers.

- A GCTP Ordinance[c] and Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments for regenerative medical products were established and came into effect in 2014. PMDA cooperated with the issuance of "Questions and Answers Related to Good Manufacturing Practice for Cellular and Tissue-based Products" (PFSB/CND Notification No. 0317-1 dated March 17, 2015) and "Questions and Answers Related to Good Manufacturing Practice for Cellular and Tissue-based Products (Part II)" (PFSB/CND Notification No. 0728-4 dated July 28, 2015) to promote efficient manufacturing control and quality control at manufacturing sites.

[a] *Ministerial Ordinance on Good Manufacturing Practice (GMP) for Drugs and Quasi-drugs (MHLW Ministerial Ordinance No.179 of 2004)*
[b] *Ministerial Ordinance on Quality Management System (QMS) for Medical Devices and In vitro Diagnostics (MHLW Ministerial Ordinance No.169 of 2004)*
[c] *Ministerial Ordinance on Good Gene, Cellular, and Tissue-based Products (GCTP) (MHLW Ministerial Ordinance No.93 of 2014)*

Abbreviations:
GMP: Good Manufacturing Practices
QMS: Quality Management System
GCTP: Good Gene, Cellular, and Tissue-based Products Manufacturing Practices

b. Establishment of the inspection system

- PMDA had 50 GMP/GCTP/QMS inspectors (including inspectors in the Kansai Branch) as of April 1, 2016.

  Inspectors in the Office of Manufacturing/Quality and Compliance were divided into several groups, each led by an Inspection Director, and conducted GMP/QMS, etc. on a group-by-group basis. To further improve the effectiveness of these activities, on January 1, 2016, two divisions were established within the Office: Division of Pharmaceuticals and the Division of Medical Devices. Each inspector was assigned to one of these two divisions.

  PMDA established an inspection quality assurance group in its Office of Manufacturing/Quality and Compliance to supervise quality management of drugs and quasi-drugs, in accordance with Japan’s accession, in FY 2014, to the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S: An international framework on GMP inspections, centering on European countries). PMDA also introduced another group to supervise quality management of medical devices, thereby enhancing the overall quality supervision system in PMDA.

- The processing status of GMP/GCTP/QMS inspections in FY 2015 is shown below:

GMP/GCTP/QMS Inspections Conducted under the Pharmaceuticals and Medical Devices Act

	FY 2010				FY 2011			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	1,159	1,324 (131)	120	684	1,538	1,283 (185)	31	908
In vitro diagnostics	66	81 (0)	2	19	73	85 (0)	1	6
Quasi-drugs	1	0 (0)	1	2	0	0 (0)	0	2
Medical devices	896	944 (54)	40	149	697	765 (36)	24	57
Regenerative medical products	—	—	—	—	—	—	—	—
Total	2,122	2,349 (185)	163	854	2,308	2,133 (221)	56	973

	FY 2012				FY 2013			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	1,582	1,593 (198)	40	821	1,508	1,415 (168)	75	875
In vitro diagnostics	64	48 (0)	0	16	52	67 (1)	0	7
Quasi-drugs	6	2 (0)	2	3	3	3 (1)	0	4
Medical devices	999	954 (81)	3	37	988	883 (61)	11	193
Regenerative medical products	—	—	—	—	—	—	—	—
Total	2,651	2,597 (279)	45	877	2,551	2,368 (231)	86	1,079

	FY 2014				FY 2015			
	Applications	Completed	Withdrawn	In progress	Applications	Completed	Withdrawn	In progress
Drugs*	1,877	1,672 (163)	51	1030 (0)	1,719	1,647 (165)	67	1,039
In vitro diagnostics	65	38 (1)	0	27 (0)	1 179	1 (0) 146 (33)	0 1	0 50
Quasi-drugs	5	6 (0)	0	2 (0)	2	2 (0)	0	2
Medical devices	755	512 (42)	18	225 (86)	70 2,333	178 (25) 1,854 (326)	7 38	1 436
Regenerative medical products	0	0 (0)	0	0 (0)	9	8 (3)	1	0
Total	2,702	2,228 (206)	69	1,284 (86)	4,313	3,836 (552)	114	1,528

** Excluding in vitro diagnostics.*

Note: The figures in parentheses represent the numbers of on-site inspections out of completed inspections. The columns for in vitro diagnostics and medical devices in FY 2015 include applications made under the former Act (upper) and those made under the new Act (lower). Figures cannot be simply compared between the new and former Acts or among drugs, quasi-drugs, and regenerative medical products because one application after the revised Act includes the average of three institutions.

- The processing times of GMP/GCTP/QMS inspections in FY 2015 are shown below:

Median Processing Time of GMP/GCTP/QMS Inspections

	FY 2010		FY 2011		FY 2012	
	Median total processing time (days)	Median PMDA processing time (days)	Median total processing time (days)	Median PMDA processing time (days)	Median total processing time (days)	Median PMDA processing time (days)
Drugs*	118	63	147	77	176	90
In vitro diagnostics	117	62	83	38	100	36
Quasi-drugs	–	–	–	–	219	71
Medical devices	145	69	113	21	21	44
Regenerative medical products	–	–	–	–	–	–
	FY 2013		FY 2014		FY 2015	
	Median total processing time (days)	Median PMDA processing time (days)	Median total processing time (days)	Median PMDA processing time (days)	Median Total processing time (days)	Median PMDA processing time (days)
Drugs*	118	71	172	76	172	81
In vitro diagnostics	106	66	147	102	160/120	38/72
Quasi-drugs	272	71	166	96	422	158
Medical devices	106	56	118	74	114/140	60/85
Regenerative medical products	–	–	–	–	84	54

** Excluding in vitro diagnostics.*

The figures in "In vitro diagnostics" and "Medical devices" in FY 2015 represent processing times for applications made under the former Act (left) and those made under the new Act (right).

- The table below shows the number of inspections of buildings and facilities conducted in FY 2015 at Japanese manufacturing sites licensed by the Minister of Health, Labour and Welfare, in accordance with the Regulations for Buildings and Facilities for Pharmacies, etc. No manufacturing sites for medical devices or *in vitro* diagnostics were subject to inspection because of the change from the license-based system to the registration-based system in accordance with the PMD Act.

Number of Inspections of Buildings and Facilities at Manufacturing Sites in Japan

	FY 2011		FY 2012		FY 2013		FY 2014		FY 2015	
Drugs*	25	(19)	15	(9)	9	(4)	25	(11)	26	(18)
In vitro diagnostics	3	(3)	1	(1)	3	(3)	0	(0)		–
Medical devices	0	(0)	2	(1)	0	(0)	2	(2)		–
Regenerative medical products		–		–		–	1	(1)	1	(1)
Total	28	(22)	18	(11)	12	(7)	28	(14)	27	(19)

- PMDA conducts for-cause inspections, questioning, and sampling at manufacturing facilities and other locations in Japan, at the direction of MHLW. The number of for-cause inspections conducted in FY 2015 is shown below:

Number of For-cause Inspections (Manufacturers in Japan)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs*	12	13	6	5	7
In vitro diagnostics	3	1	1	0	0
Medical devices	0	0	0	0	0
Regenerative medical products	–	–	–	0	0
Total	15	14	7	5	7

** Excluding in vitro diagnostics.*

- PMDA conducts simple consultations on GMP/GCTP/QMS inspections. The number of such consultations conducted in FY 2015 is shown below. There was an increase in number of simple consultations concerning QMS in order to comply with relevant provisions of the PMD Act.

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs*	44	38	44	32	33
In vitro diagnostics	0	0	0	0	4
Quasi-drugs	0	0	0	0	0
Medical devices	6	8	3	51	64
Regenerative medical products	–	–	–	–	3
Total	50	46	47	83	104

** Excluding in vitro diagnostics.*

c. Promotion of on-site inspections of foreign manufacturing sites

- The number of on-site inspections of foreign manufacturing sites, initiated in FY 2005, is shown below:

On-site Inspections of Foreign Drug Manufacturing Sites by Region

	Europe	North, Central and South America	Asia/Oceania	Africa	Total
FY 2005	2	8	2	0	12
FY 2006	13	20	2	1	36
FY 2007	22	22	8	0	52
FY 2008	31	19	32	0	82
FY 2009	39	20	47	0	106
FY 2010	12	24	29	0	65
FY 2011	9	7	45	0	61
FY 2012	14	14	38	0	66
FY 2013	12	10	42	0	64
FY 2014	20	3	51	0	74
FY 2015	0	2	61	0	63

Note: Breakdown of FY 2015: North, Central and South America, the United States (including Puerto Rico); Asia, Oceania, China, India, South Korea, Indonesia, Taiwan.

On-site Inspections of Foreign Medical Devices Manufacturing Sites by Region

	Europe	North, Central and South America	Asia/Oceania	Africa	Total
FY 2005	1	1	0	0	2
FY 2006	5	10	0	0	15
FY 2007	1	10	0	0	11
FY 2008	13	17	0	0	30
FY 2009	3	28	5	0	36
FY 2010	8	19	1	0	28
FY 2011	4	15	1	0	20
FY 2012	11	22	4	0	37
FY 2013	4	12	10	0	26
FY 2014	4	5	20 (2)	0	29 (2)
FY 2015	0	0	9	0	9

Note 1: Breakdown of FY 2015: Asia, Oceania, South Korea, Singapore, Taiwan, and Malaysia

Note 2: The following figures were amended due to a summation error.

FY 2014: Europe, from "5" to "4"

Asia, Oceania, from "19 (2)" to "20 (2)"

- The table below shows the number of inspections of buildings and facilities in foreign manufacturing sites conducted in FY 2015 conducted in accordance with the Regulations for Buildings and Facilities for Pharmacies, etc. No manufacturing sites of medical devices or *in vitro* diagnostics were subject to inspection because of the change from license system to registration system in accordance with the PMD Act.

Number of Inspections of Buildings and Facilities at Foreign Manufacturing Sites

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs*	579	530	383	384	356
In vitro diagnostics	60	68	79	23	–
Quasi-drugs	72	62	58	58	33
Medical devices	1,187	1,751	1,453	722	–
Regenerative medical products	–	–	–	0	0
Total	1,898	2,411	1,973	1,165	389

** Excluding in vitro diagnostics.*

Note: These figures include withdrawn applications. All inspections were done on a document basis.

- PMDA conducts for-cause inspections, questioning, and sampling at foreign manufacturers etc., at the direction of MHLW. The number of for-cause inspections conducted in FY 2015 is shown below:

Number of For-cause Inspections at Foreign Manufacturing Sites

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs*	1	4	2	1	0
In vitro diagnostics	0	0	0	0	0
Medical devices	1	1	1	0	0
Regenerative medical products	–	–	–	0	0
Total	2	5	2	1	0

** Excluding in vitro diagnostics.*

Number of On-site GMP Inspections of Foreign Drug Manufacturing Sites by Country

Region	Country	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Total
Europe	France	6	5	6	1	3	2	1	3	0	27
	Denmark	3	2	2	0	0	0	2	0	0	9
	Ireland	2	5	3	2	0	1	1	0	0	14
	UK	4	1	3	0	0	1	1	0	0	10
	Netherlands	1	1	5	0	0	2	0	0	0	9
	Spain	3	1	1	0	0	0	0	1	0	6
	Italy	2	5	3	2	0	1	2	3	0	18
	Belgium	1	2	4	3	1	0	2	3	0	16
	Austria	0	2	2	0	1	2	0	1	0	8
	Finland	0	0	2	0	0	1	0	0	0	3
	Germany	0	3	7	0	3	1	0	1	0	15
	Sweden	0	1	0	0	0	0	1	0	0	2
	Romania	0	1	0	0	0	0	1	0	0	2
	Czech	0	0	0	0	0	1	0	0	0	1
	Ukraine	0	0	0	0	0	1	0	0	0	1
	Lithuania	0	0	0	0	0	1	0	0	0	1
	Slovenia	0	2	1	0	0	0	0	0	0	3
	Portugal	0	0	0	3	0	0	0	0	0	3
	Greece	0	0	0	0	1	0	0	0	0	1
	Turkey	0	0	0	1	0	0	0	1	0	2
	Iceland	0	0	0	0	0	0	1	0	0	1
	Hungary	0	0	0	0	0	0	0	3	0	3
	Cyprus	0	0	0	0	0	0	0	1	0	1
	Latvia	0	0	0	0	0	0	0	2	0	2
	Slovakia	0	0	0	0	0	0	0	1	0	1
	Subtotal	22	31	39	12	9	14	12	20	0	159
North, Central and, South America	USA	22	14	18	23	6	14	8	3	2	110
	Canada	0	2	2	1	0	0	1	0	0	6
	Mexico	0	1	0	0	1	0	0	0	0	2
	Argentina	0	2	0	0	0	0	0	0	0	2
	Brazil	0	0	0	0	0	0	1	0	0	1
	Subtotal	22	19	20	24	7	14	10	3	2	121
Asia/Oceania	China	5	11	25	10	20	16	18	23	27	155
	India	1	12	4	7	4	4	3	4	19	58
	Singapore	2	4	0	0	0	0	2	0	0	8
	South Korea	0	3	9	10	18	14	11	13	10	88
	Indonesia	0	0	0	0	0	1	0	0	3	4
	Taiwan	0	2	6	1	1	2	6	6	2	26
	Thailand	0	0	2	0	1	0	2	1	0	6
	Vietnam	0	0	0	1	1	0	0	3	0	5
	Israel	0	0	0	0	0	1	0	0	0	1
	New Zealand	0	0	1	0	0	0	0	0	0	1
	Malaysia	0	0	0	0	0	0	0	1	0	1
	Subtotal	8	32	47	29	45	38	42	51	61	353
Grand Total		52	82	106	65	61	66	64	74	63	633

Note 1: Excluded are for-cause inspections at foreign manufacturing sites under Article 75-4 of the PMD Act.

Note 2: Puerto Rico was included in the USA.

Number of On-site QMS Inspections of Foreign Medical Device Manufacturing Sites by Country

Region	Country	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	Total
Europe	Ireland	0	6	0	4	1	3	0	1	0	15
	UK	0	1	0	0	1	0	1	2	0	5
	Italy	0	2	0	2	1	1	0	1	0	7
	Netherlands	0	1	0	1	0	0	0	0	0	2
	Switzerland	0	1	1	0	0	0	1	0	0	3
	Spain	0	1	0	0	0	1	0	0	0	2
	France	1	1	1	1	1	4	0	0	0	9
	Denmark	0	0	1	0	0	0	0	0	0	1
	Austria	0	0	0	0	0	1	0	0	0	1
	Belgium	0	0	0	0	0	1	0	0	0	1
	Turkey	0	0	0	0	0	0	1	0	0	1
	Subtotal	1	13	3	8	4	11	3	4	0	47
North, Central and South America	USA	10	16	27	19	12	21	8	4	0	117
	Mexico	0	1	0	0	1	0	0	1	0	3
	Brazil	0	0	1	0	0	0	0	0	0	1
	Canada	0	0	0	0	1	1	4	0	0	6
	Costa Rica	0	0	0	0	1	0	0	0	0	1
	Subtotal	10	17	28	19	15	22	12	5	0	128
Asia	China	0	0	3	0	0	1	1	6	0	11
	South Korea	0	0	0	1	0	0	5	8	4	18
	Thailand	0	0	0	0	0	1	0	0	0	1
	Singapore	0	0	2	0	0	0	2	1	1	6
	Philippines	0	0	0	0	0	2	0	0	0	2
	Israel	0	0	0	0	1	0	1	0	0	2
	Taiwan	0	0	0	0	0	0	1	3	3	7
	UAE	0	0	0	0	0	0	1	0	0	1
	Malaysia	0	0	0	0	0	0	0	1	1	2
	India	0	0	0	0	0	0	0	1	0	1
	Subtotal	0	0	5	1	1	4	11	20	9	51
Grand Total		11	30	36	28	20	37	26	29	9	226

Note 1: For-cause inspections at foreign manufacturing sites conducted pursuant to Article 75-4 of the PMD Act are excluded.

Note 2: Puerto Rico was included in USA.

Note 3: Only the institutions as defined under the new Act are included in the totals for FY 2015.

Note 4: The following figures were amended due to a summation error of subtotals by region for FY 2014.

Subtotal for Europe, from "5" to "4"

Subtotal for Asia, from "19" to "20"

d. Coordination between GMP/GCTP/QMS inspections and reviews

- During the review process for drugs, quasi-drugs, and regenerative medical products, the Office of Manufacturing/Quality and Compliance holds periodic meetings with the Review Division (once a month with Offices of New Drug) to exchange information on the progress of reviews and the quality of reviews related to manufacturing control and quality control, and thereby ensures that inspections are conducted at the appropriate times in the review process.
- For applications for medical devices, MHLW issued a notification so that applicants file applications for QMS inspections within 10 days after applications for marketing approval for "generic medical

devices" and "improved medical devices (without clinical data)" because review time is short for these devices. This prevents the QMS inspection from affecting approval time. In addition, Office of Manufacturing/Quality and Compliance holds periodic meetings with the Review Division (once weekly) to exchange information and be informed of the progress of reviews, in order to ensure that inspections are conducted at the appropriate times in the review process.

e. For-cause inspections of registered certification bodies

- The regulatory authority governing registered certification bodies was transferred to PMDA due to revision of the system in November 2014. Thus, in FY 2015, PMDA conducted for-cause inspections of registered certification bodies in Japan: 1 inspection at registration; 2 inspections at registration renewal; and 11 periodic inspections.

f. Inspection of MDSAP-recognized auditing organizations

- Japan declared formal participation to MDSAP[Note)] in June 2015. PMDA, therefore, started inspections of MDSAP-recognized auditing organizations. In FY 2015, PMDA conducted 2 inspections.

Note) Medical Device Single Audit Program: A single QMS inspection program with the participation of the regulatory authorities in Japan, the United States, Canada, Australia, and Brazil. Private auditing organizations conduct QMS inspections and the regulatory authorities use the inspection results.

(ii) Building of the inspection system based on the Act on Safety of Regenerative Medicine

a. Building of the inspection system

- In accordance with the Act on the Safety of Regenerative Medicine, enacted in 2013 and enforced in 2014, PMDA conducts compliance assessments to the standards for buildings and facilities specified under Article 42 of the Act of Safety of Regenerative Medicine required for obtaining license/certification of manufacturing at cell processing centers, at the request of the Health Policy Bureau in MHLW or Regional Bureau of Health and Welfare. In FY 2015, PMDA conducted on-site inspections of Japanese cell processing centers that had submitted applications, to determine whether the centers conformed to the standards.

  In addition, PMDA has to conduct for-cause inspections when requested to do so by the Health Policy Bureau of the MHLW. In FY 2015, PMDA received no request for-cause inspections from MHLW.

  To maintain a sufficient number of inspectors, PMDA started to provide training programming with regard to inspection methods to inspectors of the Office of Manufacturing/Quality and Compliance. PMDA is making efforts to obtain the number of inspectors needed in order to deal with all applications filed.

Number of Applications for License/Accreditation of Manufacturing Based on the Act on Securing of Safety of Regenerative Medicine, etc.

	FY 2014				FY 2015			
	Application	Processed	Withdrawn	Under inspection	Application	Processed	Withdrawn	Under inspection
Application for manufacturing licensure (in Japan)	19	0	0	19	43	37 (36)	2	4
Application for manufacturing licensure (outside Japan)	0	0	0	0	4	1(1)	1	2
Total	19	0	0	19	47	38 (37)	3	6

Note: The figures in parentheses represent the numbers of on-site inspections out of completed inspections.

Administrative Processing Time for Inspection for License/Accreditation of Manufacturing

	FY 2014		FY 2015	
	Median total processing time (days)	Median PMDA processing time (days)	Median total processing time (days)	Median PMDA processing time (days)
Application for manufacturing licensure (in Japan)	—	—	134	83
Application for manufacturing licensure (in foreign countries)	—	—	166	136

Number of For-cause Inspections Conducted by PMDA

Region	FY 2014	FY 2015
Japan	0	0
Outside Japan	0	0
Total	0	0

Number of On-site Inspections of Foreign Institutions by Region

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
FY 2014	-	-	-	-	-
FY 2015	0	0	2	0	2

Number of On-Site Inspections of Foreign Institutions by Region

Region	Country	FY 2014	FY 2015	Total
Europe	-	-	-	0
	Subtotal	-	0	0
North, Central, and South America	-	-	-	0
	Subtotal	-	0	0
Asia	South Korea	-	2	2
	Subtotal	-	2	2
Total		-	2	2

b. Establishment of inspection methods

With respect to standards for cell processing centers under Article 42 of the Act on the Safety of Regenerative Medicine, PMDA prepared a checklist that explains what is required to meet the standards and presents PMDA's viewpoints for inspection. The checklist is available on the PMDA website.

3.2.(2) Support for the initiative to promote the development of innovative drugs, medical devices, and regenerative medical products

(i) Establishment and revision of review standards for innovative products

- Science Board was established in May 2012, in which PMDA reviewers exchange ideas with leading researchers in Japan regarding evaluation methods, etc., for advanced science and technologies. The Science Board summarized 5 reports for the second term from April 2014 to March 2015: “Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products,” “Discussions on Evaluation of Medical Devices in Pediatric Use,” "Report on the Use of Non-clinical Studies in the Regulatory Evaluation of Oncology Drugs," “Current Status and Perspectives of Placebo-controlled Studies,” and “Report on the Use of Numerical Analysis for Strength Evaluation of Orthopedic Implants.”
- Based on the initiative to promote the development of innovative drugs, medical devices, and regenerative medical products (a project funded by MHLW), PMDA conducted personnel exchange and information sharing by accepting specially appointed experts from research institutions and dispatching PMDA staff to these research institutions, and supported not only the establishment of methods to evaluate the safety and efficacy of innovative drugs, medical devices, and regenerative medical products but also the conduct of research projects for the preparation of guidelines needed to accelerate reviews. In addition, PMDA has worked to develop human resources with expertise in innovative technologies and regulatory science both in academia and in the Agency.
- In order to ensure that reviews are conducted appropriately, safety measures, and relief services for adverse health effects and to enhance the quality of these activities, PMDA is striving to promote regulatory science research on topics including the preparation of standards, guidelines and guidance, as well as research regarding methods for conducting scientific prediction, evaluation, and judgment in PMDA’s operations. Among the regulatory science-related research activities conducted by PMDA, those designated by the Chief Executive are carried out as part of PMDA’s operations. Designation decisions are based on research purpose, how research is related to PMDA’s operations, and comments from the Regulatory Science Research Evaluation Committee. In FY 2015, 12 projects (3 new projects and 9 ongoing projects) were selected for designated research and the results of 2 of these projects were published in academic journals.
- PMDA supported the development of evaluation guidelines through the activities of 12 working groups (WG) in the Projects Across Multi-offices to Develop Standards etc. (hereinafter referred to as “Projects Across Multi-offices”). The Projects aimed to promote product development, facilitate international collaborations for review standards etc., and accelerate reviews by making clear scientific principles for reviews of drugs and medical devices. In FY 2015, PMDA cooperated with the Companion Diagnostics WG in the preparation of one notification (draft) and one administrative notice (draft) and cooperated with the Nanomedicine Initiative WG in the issue of one notification and two administrative notices.
- The Companion Diagnostics WG in Projects Across Multi-offices exchanged ideas (on a total of 8 occasions) with companies developing companion diagnostics, associated industrial groups, and associated academic societies on the development of companion diagnostic systems using next-generation DNA sequencers.
- The Pediatric Drugs WG and Orphan Drug WG in Projects Across Multi-offices held teleconferences on a regular basis with experts from regulatory authorities in the EU and the US, to share and investigate issues to be addressed. Pediatric Drugs WG participated in presentation sessions and panel discussions in workshops and international academic conferences, explaining how reviews and consultations are regarded in Japan and exchanged ideas with participants from foreign regulatory authorities toward international harmonization.

- The Companion Diagnostics WG and Omix WG in Projects Across Multi-offices examined "Methodology in Clinical Trials Using Genomic Biomarkers and Selection of Patients (draft)" prepared in a project (conducted by the Nagoya City University Graduate School of Pharmaceutical Sciences; cancer and personalized medicine) supported by the initiative to facilitate the development of innovative drugs, medical devices, and regenerative medical products.
- The Global Clinical Study WG in Projects Across Multi-offices held a workshop titled "Principles on Long-term Treatment Studies in the Global Development Strategy" co-hosted by JPMA, PhRMA, EFPIA, and PMDA on November 24, 2015, to exchange ideas among participants.

(ii) Expansion of Pharmaceutical Affairs Consultations on R&D Strategy

- Since November 2014, PMDA has provided on a trial basis general advice related to the development process (roadmap) and confirmatory clinical trial protocols to applicants including pharmaceutical companies. Further, PMDA offered on-site introductory consultations and distributed brochures to relevant academic conferences for publicity purposes. Through collaboration between relevant offices, activities were carried out promptly and appropriately.
- PMDA promoted the use of Pharmaceutical Affairs Consultations on R&D Strategy (introductory consultations and pre-application consultations) at Kansai Branch by providing relevant information at related academic societies and other opportunities. Pharmaceutical Affairs Consultations on R&D Strategy continued to be conducted with collaboration between the offices in Tokyo and the Kansai Branch.
- On August 19, 2015, PMDA concluded the "Agreement on Collaboration between Pharmaceuticals and Medical Devices Agency and Japan Agency for Medical Research and Development" with the Japan Agency for Medical Research and Development (AMED). The agreement is aimed at the creation and practical application of innovative drugs, and medical devices at an early stage. As a collaborative effort, PMDA and AMED agreed to ensure that research projects adopted by AMED that have advanced to the stage of practical application undergo, in principle, pharmaceutical affairs consultation on R&D strategy. PMDA and AMED discussed how and when these consultations should be offered in conjunction with research projects by AMED.

(iii) Implementation of approval system based on characteristics of regenerative medical products

- To address the introduction of the conditional limited-time authorization system for regenerative medical products, the relevant offices collaborated in offering Pharmaceutical Affairs Consultations on R&D Strategy, and provided relevant information at academic conferences and similar events, and thus promoted the use of the system.

(iv) Implementation of the SAKIGAKE product designation system

- In FY 2015, the "SAKIGAKE designation system" was initiated on a trial basis for drugs, medical devices, in vitro diagnostics, and regenerative medical products. PMDA improved the organizational setup for operating the system, for example, by introducing "Review Partners (concierges)" (they serve as liaison coordinators within MHLW and PMDA to manage the progress of development of SAKIGAKE designation products) and launching the "SAKIGAKE comprehensive assessment consultation" service for pre-evaluation of application documents for designated products.
- The review offices of PMDA conducted a pre-evaluation, at the request of MHLW, for products filed for SAKIGAKE designation. Based on the results of pre-evaluation, MHLW designated 6 drugs (in October 2015), 2 medical devices, and 3 regenerative medical products (in February 2016) as SAKIGAKE products. The list of SAKIGAKE designation products and their summaries were

published on the PMDA website. Review Partners started to manage progress for the designated products.

3.3 Safety Measure Services

(i) Proper assessment of adverse drug reaction and medical device malfunction reports

- In order to improve the safety of marketed drugs, medical devices, and regenerative medical products and to enable patients and healthcare professionals to use them properly, PMDA works to efficiently collect and examine product safety information, rapidly process such information, devise appropriate preventative and remedial measures, and promptly provides easy-to-understand safety information, to ensure that reviews and safety measures function in an integrated manner.
- In FY 2015, PMDA received approximately 400,000 reports on serious adverse reactions and infections attributable to drugs, approximately 46,000 reports on medical device malfunctions and infections attributable to medical devices, and 49 reports on regenerative medical product malfunctions and infections attributable to such products, from companies both in and outside Japan. PMDA inputs the collected information into a database and shares such information with MHLW. In addition, PMDA monitors information regarding new measures implemented by foreign regulatory agencies such as FDA and EMA with respect to drugs, medical devices, and other products. The purpose of these monitoring activities is to help PMDA to conduct daily assessment of its responses to issues concerning products marketed in Japan. PMDA also reviews academic literature in conjunction with these activities for the purpose of analyzing and sharing information on adverse drug reactions and device malfunctions. In addition, PMDA is working to implement comprehensive safety measures for drugs, medical devices, and regenerative medical products in the post-marketing stage by enhancing cooperation between review offices and safety offices, and between the relief office and safety offices.
- Based on daily reviews conducted by the product safety teams, PMDA assesses and reviews such reports on adverse drug reactions, medical device malfunctions etc., with MHLW every week, seeks opinions from external experts and companies, and proposes necessary safety measures, such as revision of precautions in package inserts, to MHLW. Particularly urgent issues are responded to immediately in cooperation with MHLW.
- The following table displays the numbers of reports (in terms of the number of active ingredients for the drugs, and the number of term names for medical devices) submitted to MHLW for products for which safety measures such as revisions to package inserts were determined to be necessary. PMDA analyzes near-incident case reports collected by the Japan Council for Quality Health Care while seeking opinions from experts. The number of near-incident case reports submitted to MHLW was categorized under "Medical Safety."

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs	185	198	160	100	87[*2]
Medical devices	17	15	14	4	28
Regenerative medical products	-	-	-	0[*1]	0
Medical safety	6	6	6	6	6

**1 Number of reports after enactment of the PMD Act on November 25, 2014*

**2 Total of 84 reports concerning drug products and 3 reports concerning in vitro diagnostics.*

- Actions taken by MHLW based on reports from PMDA, such as revisions of Precautions, were as follows (includes duplicated measures).

		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs	Directions for revision to precautions in package insert	185	198	160	100	87*1
	Posting articles and cases on PMDSI	41	36	40	29	28*2
Medical devices	Directions for revision to precautions in package insert or issuance of notifications on self-check*3	23 (5)	16 (4)	11 (3)	4 (2)	28 (3)
	Posting articles on PMDSI	4	1	4	1	1
Regenerative medical products*4	Directions for revision to precautions in package inserts or issuance of notifications on self-check	-	-	-	0	0
	Posting articles on PMDSI	-	-	-	0	0

**1 Total of 84 reports concerning drug products and 3 reports concerning in vitro diagnostics.*

**2 Total of 27 reports concerning drug products and 1 report concerning in vitro diagnostics.*

**3 Figures in parentheses indicate the number of notifications, etc.*

**4 Number of reports after enactment of the PMD Act on November 25, 2014*

- As collaborative activities with the review offices, Offices of Safety I and II evaluate adverse drug reactions reported in accordance with early post-marketing phase vigilance (EPPV) requirements in collaboration with the review staff. Office of Safety staff also participate in the review process (in clinical trial consultations, assessments of post-marketing surveillance plans, reviews of draft package inserts, Expert Discussions, etc.) for new drugs, new medical devices, and new regenerative medical products. As for collaboration with Office of the Relief Fund, in accordance with the PMD Act, PMDA has organized information and conducted a survey of applications for relief benefits. In addition, information, such as the names of drugs and adverse drug reactions in claims for payment/non-payment of relief benefits that have received judgment, is provided to the safety offices and is reflected in safety measures implemented.
- In FY 2015, PMDA made the following efforts to collect, organize, and examine reports concerning adverse drug reactions, medical device malfunctions, and similar reports, that have been submitted by manufacturing/marketing authorization holders (MAHs) and medical institutions:
  a. Upgraded systems related to adverse drug reactions information management and support of safety measures
  b. Updated master files in terms of names of drug products, adverse drug reactions, and MAHs
  c. Encouraged staff members to attend academic conferences to gather information
  d. Held weekly liaison meetings concerning drugs, medical devices, and regenerative medical products with MHLW
- PMDA's systems related to adverse drug reactions information management and support of safety measures are needed to comply with the ICH-E2B (R3) guideline, which is the next-generation international data exchange standard for adverse drug reaction reporting which will become effective in FY 2016. In FY 2015, PMDA conducted a large-scale test in cooperation with MAHs and development vendors and entered the results back into these systems in order to prepare for the implementation of ICH-E2B (R3) from April 2016.

○ Collection of adverse reaction reports etc.

1-1) Number of reports relating to drugs

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Reports from MAHs	260,473	306,410	308,383	352,908	399,852
(adverse drug reactions, in Japan)	(36,641)	(41,254)	(38,329)	(49,198)	(50,977)
(infections caused by drugs, in Japan)	(100)	(159)	(98)	(78)	(88)
(adverse drug reactions, outside Japan)	(220,410)	(261,823)	(266,506)	(300,191)	(345,161)
(infections caused by drugs, outside Japan)	(45)	(39)	(33)	(25)	(32)
(research reports)	(841)	(884)	(962)	(1,099)	(1,219)
(foreign safety measure reports)	(1,347)	(1,134)	(1,317)	(1,219)	(1,273)
(periodic infection reports)	(1,089)	(1,117)	(1,138)	(1,098)	(1,102)
Reports from healthcare professionals	5,231	4,147	5,420	6,180	6,129
([1]Safety information reporting system)	(3,388)	(3,304)	(4,067)	(4,782)	(4,891)
([2]Vaccines*)	(1,843)	(843)	(1,353)	(1,398)	(1,238)
Total	265,704	310,557	313,803	359,088	405,981

** For FY 2010 through 2012, the figures indicate the total numbers of reports on adverse reactions following vaccination with cervical cancer vaccine, Hib vaccine, pediatric pneumococcal conjugate vaccine, and influenza vaccines. From FY 2013 onward, the figures indicate the total numbers of reports on adverse reactions following vaccination with all vaccines.*

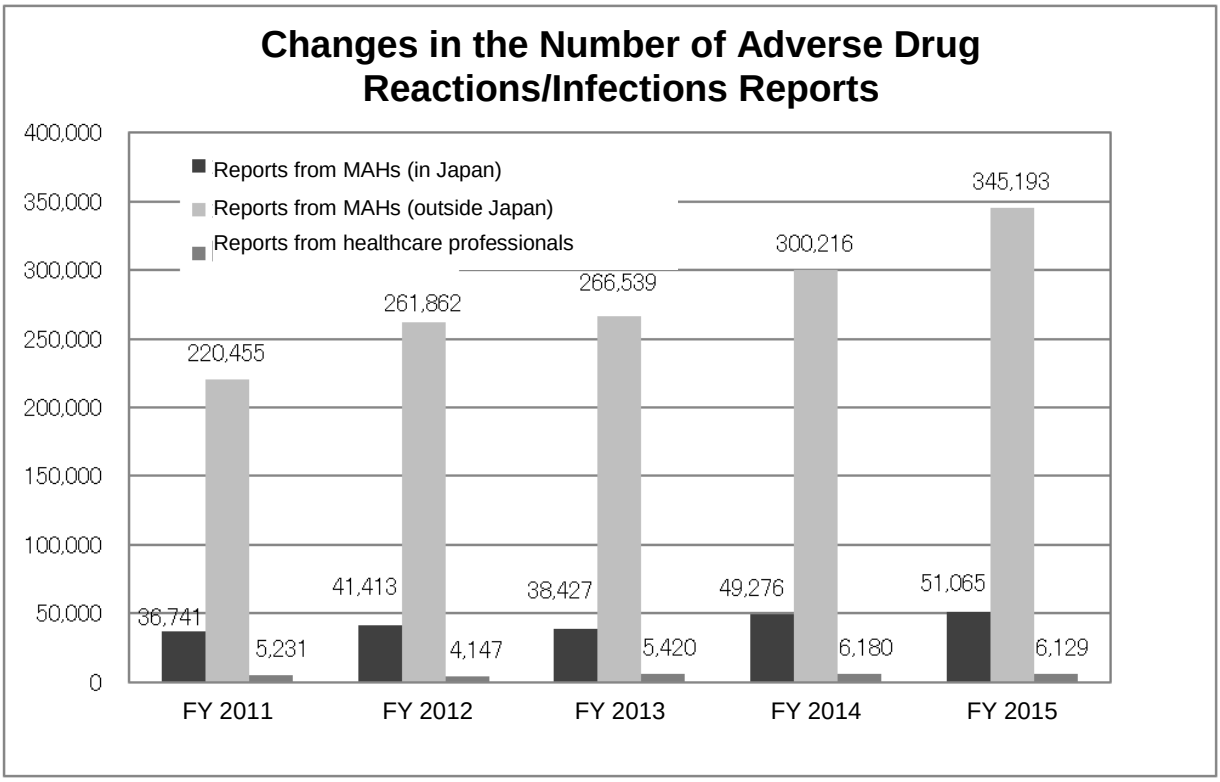
- After the enactment of the PMD Act, there were no case reports on suspected malfunctions of mechanical part of combination drugs through FY 2014; however, in FY 2015, there were 38 reports in Japan and 60 reports out of Japan.

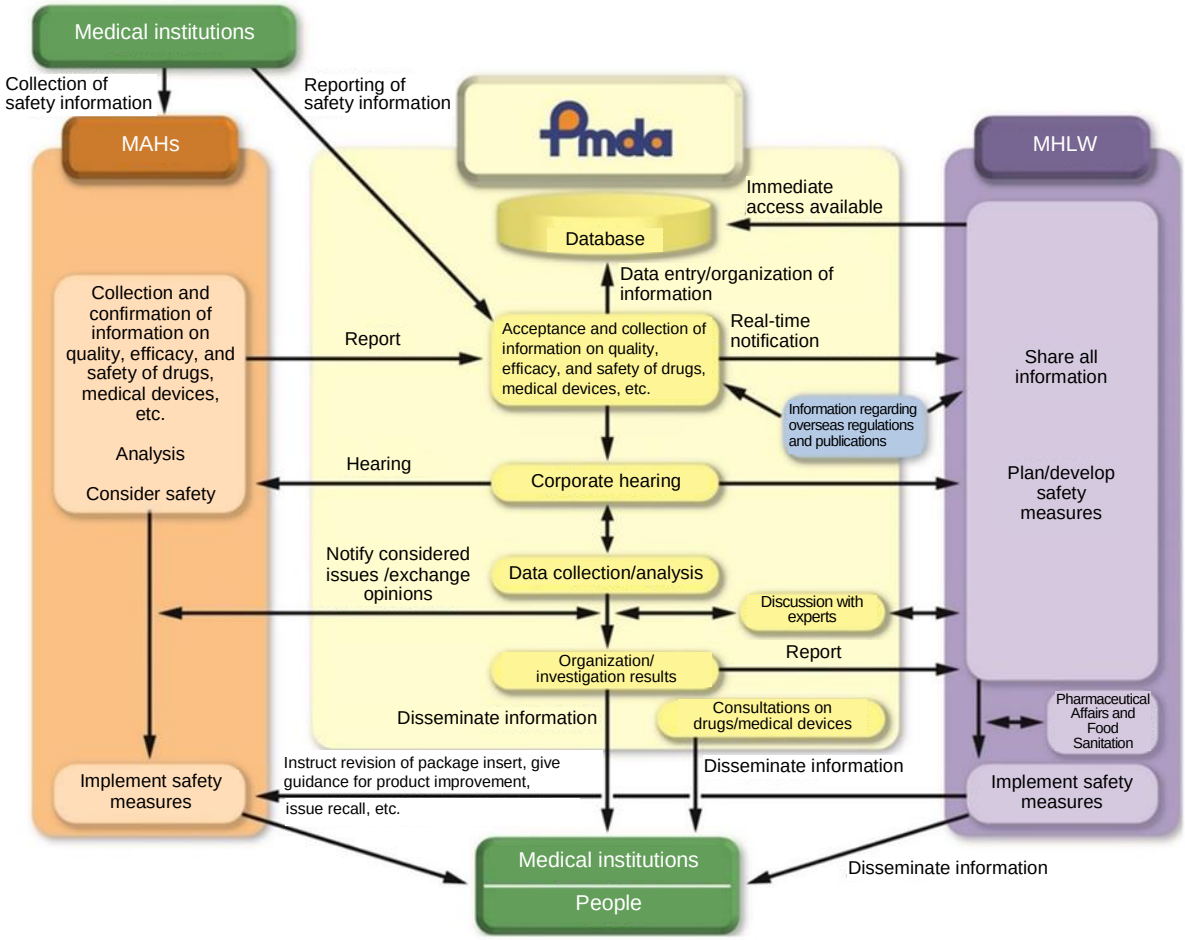
	FY 2014*	FY 2015
Cases of malfunctions of combination drugs (in Japan)	0	38
Cases of malfunctions of combination drugs (outside Japan)	0	60

** Number of cases after the enactment of the PMD Act on November 25, 2014.*

- PMDA began receiving individual case reports on adverse reactions attributable to quasi-drugs/cosmetics from April 1, 2014.

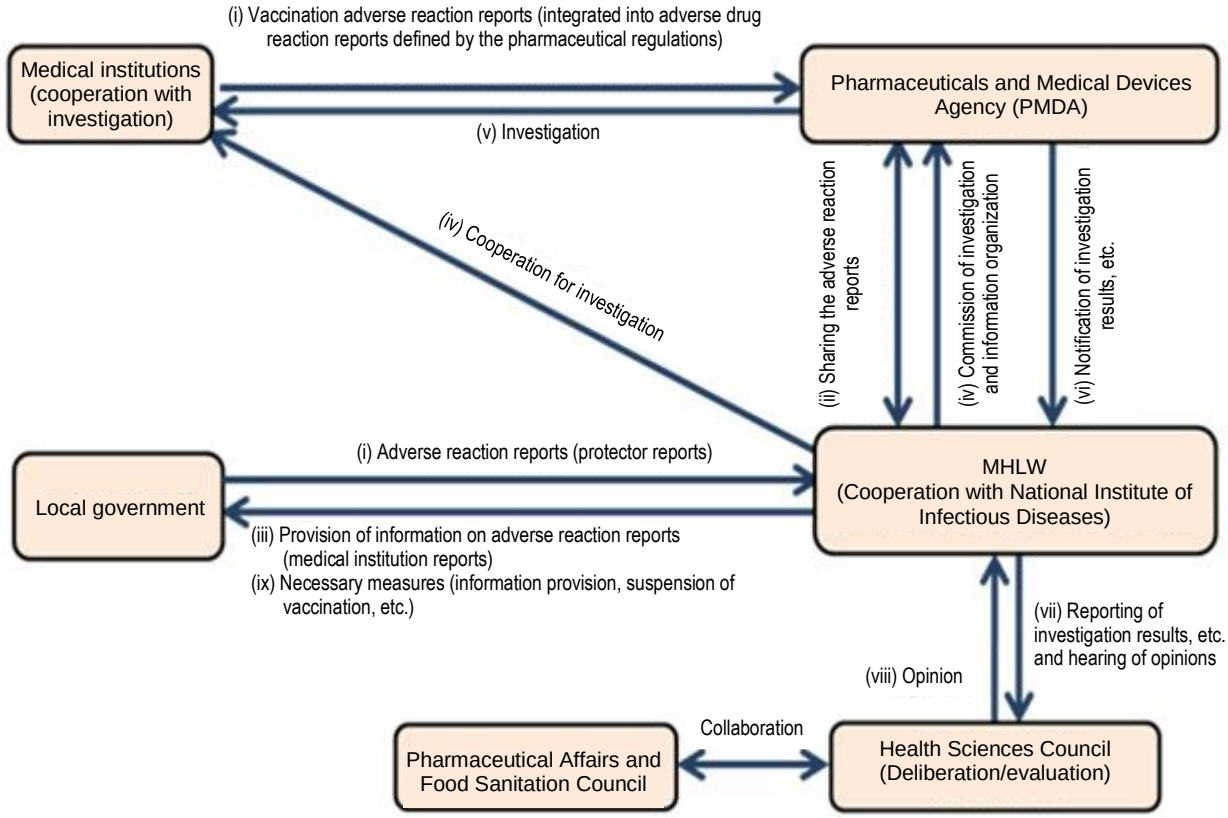
	FY 2014	FY 2015
Quasi-drugs	561	323
Cosmetics	116	114


Changes in the Number of Adverse Drug Reactions/Infections Reports
400,000
350,000
300,000
250,000
200,000
150,000
100,000
50,000
0
Reports from MAHs (in Japan)
Reports from MAHs (outside Japan)
Reports from healthcare professionals
36,741
220,455
5,231
41,413
261,862
4,147
38,427
266,539
5,420
49,276
300,216
6,180
51,065
345,193
6,129
FY 2011
FY 2012
FY 2013
FY 2014
FY 2015


Medical institutions
Collection of safety information
Reporting of safety information
MAHs
PMDA
MHLW
Immediate access available
Database
Data entry/organization of information
Collection and confirmation of information on quality, efficacy, and safety of drugs, medical devices, etc.
Analysis
Consider safety
Report
Acceptance and collection of information on quality, efficacy, and safety of drugs, medical devices, etc.
Real-time notification
Information regarding overseas regulations and publications
Share all information
Hearing
Corporate hearing
Plan/develop safety measures
Notify considered issues /exchange opinions
Data collection/analysis
Discussion with experts
Organization/ investigation results
Report
Disseminate information
Consultations on drugs/medical devices
Pharmaceutical Affairs and Food Sanitation
Instruct revision of package insert, give guidance for product improvement, issue recall, etc.
Disseminate information
Implement safety measures
Implement safety measures
Medical institutions
People
Disseminate information

1-2) Reports on adverse reactions following vaccination based on the Preventive Vaccination Act

Pursuant to Article 14 of the Preventive Vaccination Act (Act No. 68 of 1948), PMDA has been conducting projects for investigating and organizing vaccination adverse reaction reports. As of November 25, 2014, vaccination adverse reaction reports must be submitted to PMDA in accordance with the revisions to the Preventive Vaccination Act and the Ministerial Ordinance for Enactment of the Preventive Vaccination Act (see diagram below). In FY 2015, PMDA received 1,238 vaccination adverse reactions reports. Upon receiving vaccination adverse reaction reports, PMDA provides information to MAHs on suspect vaccines, and also issues directions on how to properly deal with such events under the PMD Act. With regard to reported cases of vaccination adverse reactions, PMDA conducted interviews as needed with doctors who diagnosed the adverse reactions and those who administered vaccinations. In the cases of deaths and particular serious adverse reactions (e.g., anaphylactic reaction), PMDA sought opinions from experts regarding matters such as the appropriateness of diagnosis for the adverse reactions and causal relationship between the adverse reactions and vaccines, thereby contributing to safety assessment of vaccines at MHLW.



1-3) Adverse drug reaction reports from patients

The final recommendations by the Committee for Investigation of Drug-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings at MHLW (April 2010; hereinafter referred to as “Committee Recommendations for Drug-induced Hepatitis Cases”) highlighted the need to establish a system that utilizes information from patients for safety measures. Also in the report submitted by the Investigational Sub-committee on Revision of Pharmaceutical Regulatory Systems of the Health Science Council at MHLW (January 2012), it was suggested that information on adverse drug reactions reported by patients themselves should be utilized.

Based on these recommendations, PMDA set up the Direct Patient Reporting System for Adverse Drug Reactions on March 26, 2012 with reference to the outcomes of a study supported by the Health and Labour Sciences Research Grants from FY 2009 to FY 2011 ("Research on System for Receiving Adverse Drug Reaction Reports from Patients"), and has been conducting a project for receiving adverse drug reaction reports from patients on a trial basis via the Internet. In this project, adverse drug reaction reports are to be collected from patients who experienced drug-induced adverse reactions or their family. The purpose of those reports is to improve safety measures for drugs through such means as identifying trends in occurrence of adverse reactions to drugs. PMDA intends to improve the system, through measures such as developing a standard operating procedure for a detailed investigation method, which accounts for the protection of personal information, so that a trial of the procedure can be carried out, and then formally start receiving reports by FY 2018.

The number of adverse drug reaction reports from patients collected by FY 2015 is shown in the following table. PMDA has been disclosing the reported cases as they come to hand.

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Adverse drug reaction reports from patients (total number)*	30	154	122	91	186

** The figures indicate the numbers of reports at the end of each fiscal year. Reports may be withdrawn at the request of reporters. Reports on items not classified as adverse drug reaction reports from patients (including quasi-drugs, cosmetics, and health foods) are excluded.*

1-4) PMDA's detailed investigation on reports from medical institutions

The Committee Recommendations for Drug-induced Hepatitis Cases recommended that PMDA develop a system to conduct necessary investigations, such as direct inquiries to healthcare professionals, for death/serious cases among adverse drug reactions etc., reported from medical institutions. Based on the above, PMDA has been conducting detailed investigations of the reports submitted by medical institutions.

Cases of suspected serious adverse drug reactions that meet either of the following criteria are subject to investigation by PMDA: (1) No information was provided by a medical institution to a MAH; or (2) Whether information has been provided by a medical institution to a MAH is unknown. PMDA thus conducted detailed investigations into these cases as necessary. Cases not subject to investigation by PMDA were investigated in detail by MAHs as necessary.

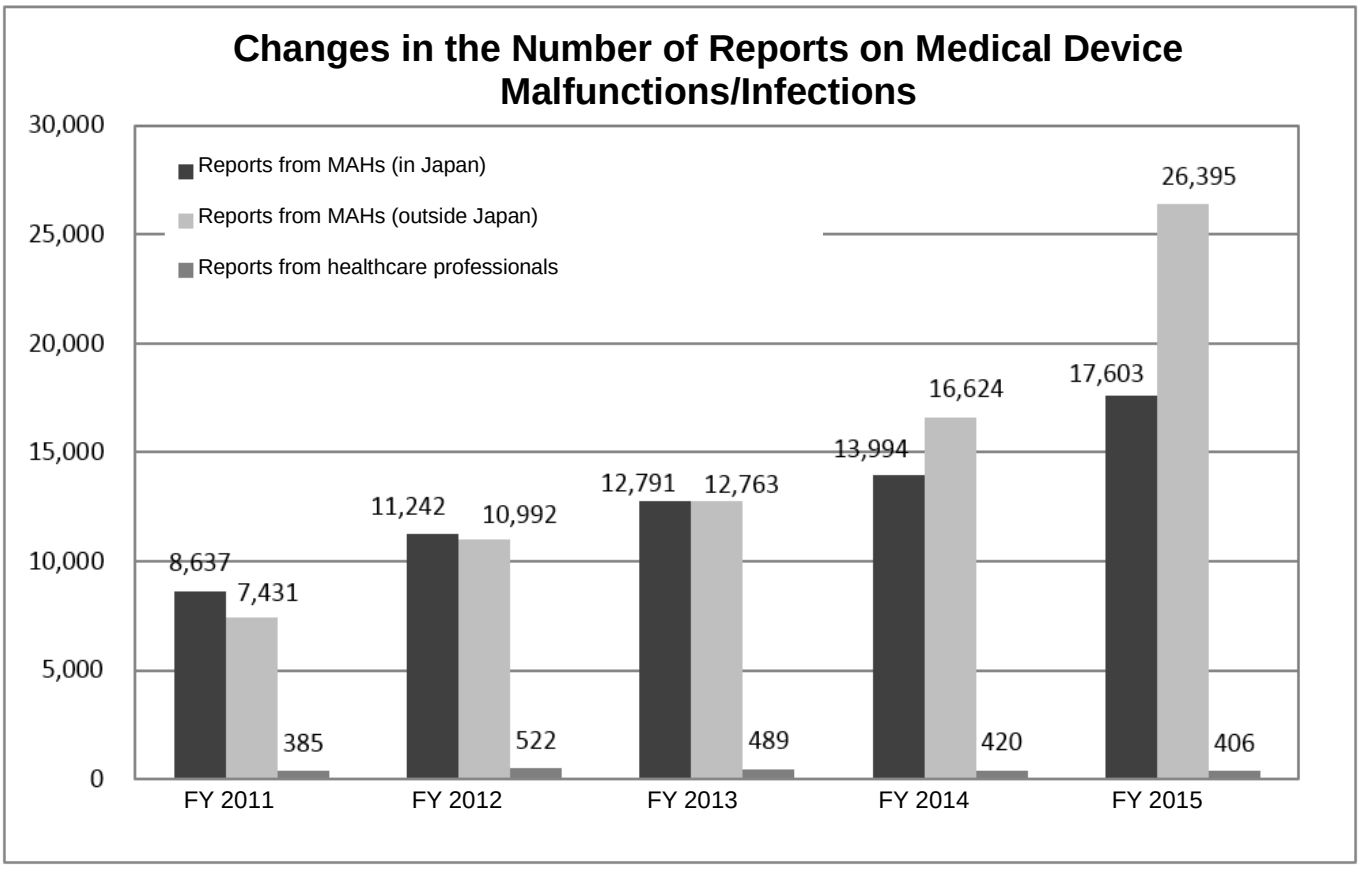
The number of cases investigated by PMDA as of the end of FY 2015 is shown in the following table.

	FY 2012	FY 2013	FY 2014	FY 2015
Number of cases investigated by PMDA	663	862	1,067	1,100

PMDA provides MAHs of primary suspect drugs with information on cases subject to investigation by PMDA that were reported from medical institutions, via the internet (using a dedicated server).

2) Number of reports relating to medical devices

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Reports from MAHs	17,192	23,643	27,303	32,490	46,406
(medical device malfunctions, in Japan)	(8,637)	(11,242)	(12,791)	(13,994)	(17,603)
(medical device malfunctions, outside Japan)	(7,431)	(10,992)	(12,763)	(16,624)	(26,394)
(infections caused by medical devices, in Japan)	(0)	(0)	(0)	(0)	(0)
(infections caused by medical devices, outside Japan)	(0)	(0)	(0)	(0)	(1)
(research reports)	(2)	(3)	(5)	(20)	(598)
(foreign safety measure reports)	(1,060)	(1,337)	(1,669)	(1,779)	(1,742)
(periodic infection reports)	(62)	(69)	(75)	(73)	(68)
Reports from healthcare professionals	385	522	489	420	406
Total	17,577	24,165	27,792	32,910	46,812



3) Number of reports relating to regenerative medical products

	FY 2014	FY 2015
Reports from MAHs	17	49
(product malfunctions, in Japan)	12	35
(product malfunctions, outside Japan)	0	0
(infections caused by products, in Japan)	0	0
(infections caused by products, outside Japan)	0	0
(research reports)	0	0
(foreign safety measure reports)	0	0
(periodic infection reports)	5	14
Reports from healthcare professionals	0	0
Total	17	49

** Reporting in respect of regenerative medical products was initiated on November 25, 2014, the date of enactment of the PMD Act. The figures for FY 2014 indicate the number of reports submitted between November 25, 2014 and the end of March 2015.*

(ii) Sophistication of safety measures

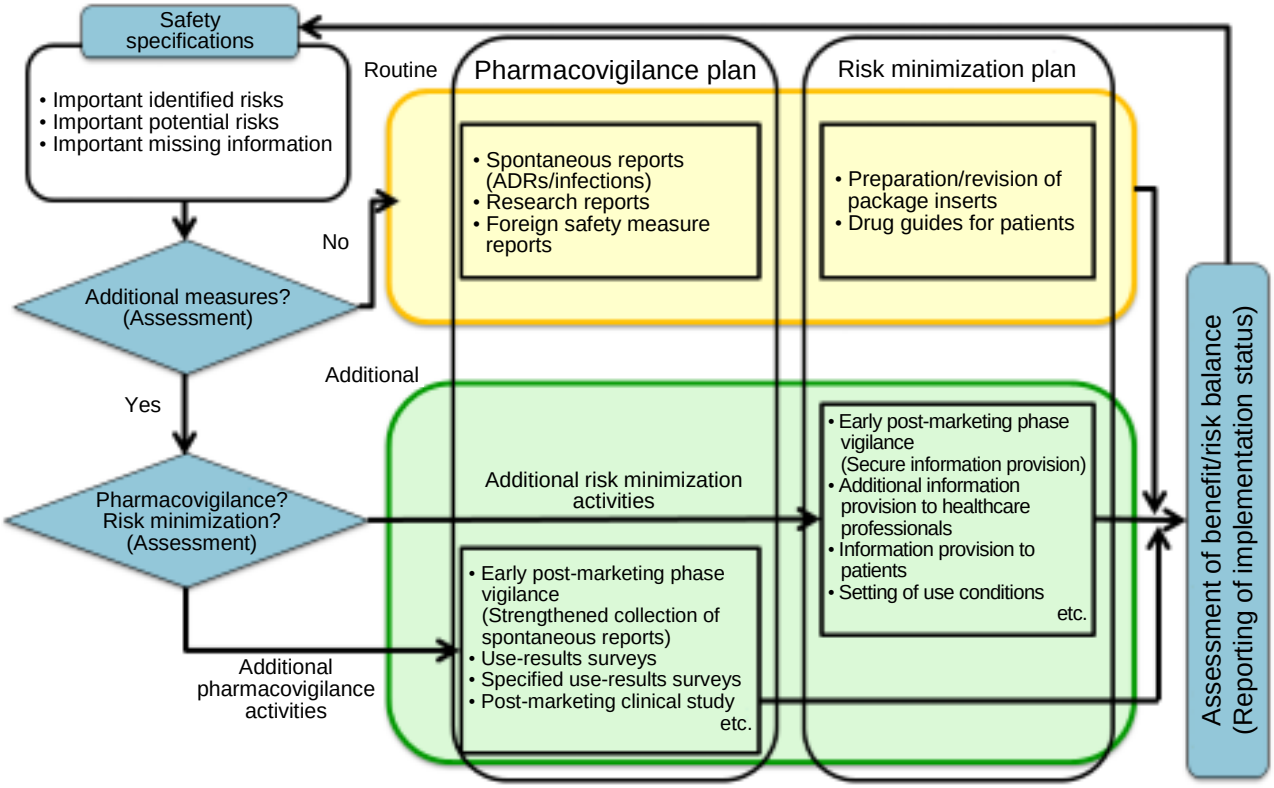
a. Introduction of the risk management system and implementation of appropriate safety measures based on the risk management plan for drugs

PMDA launched a full-scale risk management system in FY 2011, and has been improving the system to consistently manage drug safety from the development phase to post-marketing phase by having Risk Managers also work in Offices of New Drugs. The number of Risk Managers has gradually been increased. As of March 2016, 14 Risk Managers were assigned to each team in Offices of New Drugs.

In April 2013, Risk Management Plan (RMP) was introduced, in order to evaluate benefits and risks throughout the period from the development phase to the post-marketing phase and to implement necessary safety measures based on the evaluation. In October 2013, submitting a RMP together with submission dossier was made mandatory for applicants who seek regulatory approval for their products. Under the leadership of Risk Managers, the safety and review offices cooperate in the evaluation of proposed RMPs for products under review, by identifying safety specifications and assessing the appropriateness of pharmacovigilance and risk minimization activities. Inquiries regarding RMPs are sent from PMDA to applicants during the review process. The evaluation of RMPs is completed by the end of the review process.

In FY 2015, new RMPs for 65 products and revised RMPs for 111 products (total) were disclosed on the PMDA website. As of the end of March 2016, RMPs for 185 products had been disclosed.

Overall image of RMP

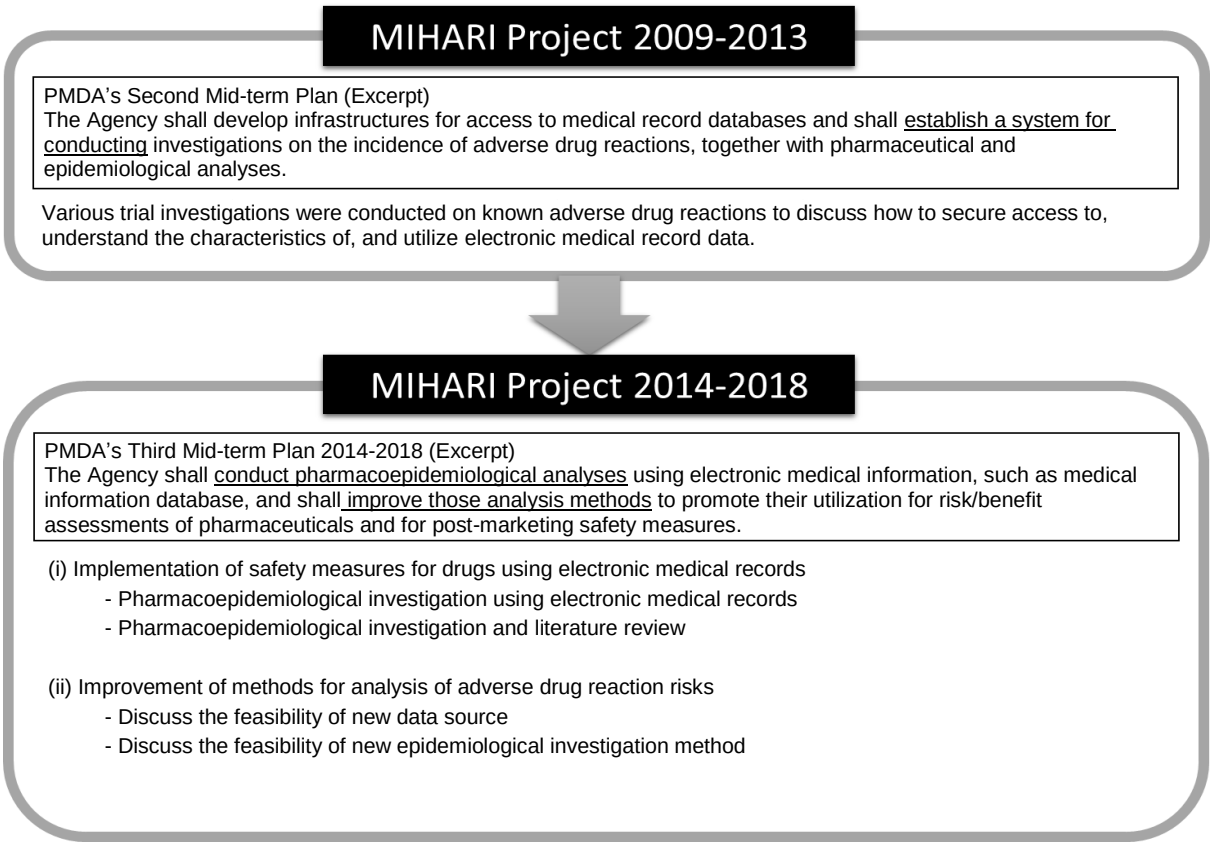


b. Use of electronic medical records etc.

- In accordance with the Third Mid-term Plan, PMDA intends to perform pharmacoepidemiological analysis using digitized medical information, such as medical information database, and advance the analytical method, in order to utilize digitized information for risk-benefit assessment or safety measures for drugs.

  Accordingly, based on results obtained during the period of the Second Mid-term Plan, PMDA is promoting the following activities through MIHARI Project (starting in FY 2009) during the term of the Third Mid-term Plan: (1) implementation of safety measures for drugs using electronic medical records; and (2) improvement of methods for analysis of adverse drug reaction risk. The purpose of these activities is to proactively utilize investigation and analytical methods that use electronic medical records, including claims data and hospital information system data, for post-marketing drug safety evaluation (see figure below).

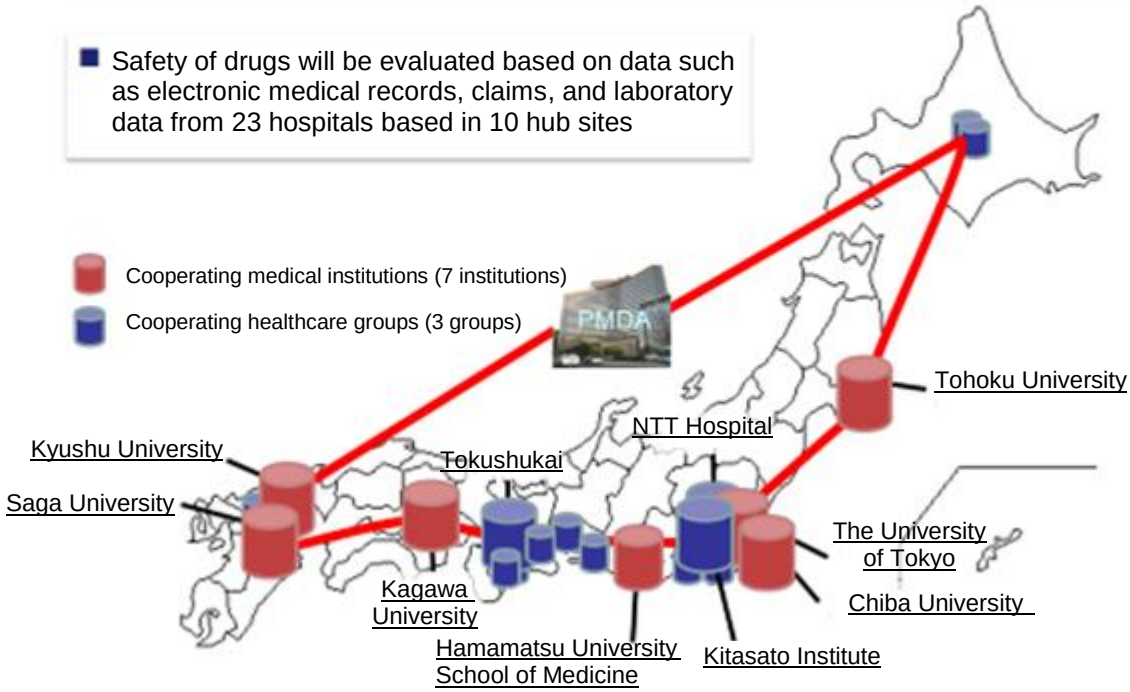
Direction of the MIHARI Project in the Third Mid-term Plan



In FY 2015, in cooperation with the new drug review offices, the safety offices reviewed pharmacoepidemiological literature submitted by pharmaceutical companies, investigated how drugs are actually prescribed, and, at the request of MHLW, also investigated how products that had had their Precautions (in package inserts) revised were actually being prescribed. In addition, To examine the pharmacoepidemiological methods applied, the safety offices used claims data from health insurance associations to conduct surveys to assess the following studies: "Comparison of cardiovascular risk by antidiabetic drug classes," "Prescription of nonsteroidal anti-inflammatory drugs and risk of acute asthmatic attack using self-controlled case series," and "Prescription of antipsychotic drugs and risk of drug-induced parkinsonism based on Sequence Symmetry Analysis and Nested Case Control design." The safety offices then summarized the various characteristics of these approaches and made a presentation to related academic societies. Further, the safety offices planned a trial survey of "Comparison of cardiovascular risk by antidiabetic drug classes" using the National Claim Data managed by the Health Insurance Bureau of MHLW as a new data source. The survey results underwent a crude analysis and will be further analyzed in detail to be evaluated in the future.

- As an important data source for the MIHARI Project, PMDA has been advancing the establishment of the medical information database network (MID-NET) system in the "Project for developing the medical information database infrastructure" of MHLW since FY 2011. Specifically, PMDA is establishing a system to collect electronic medical information stored in 23 hospital at 10 hubs including university hospitals nationwide (cooperating medical institutions) selected by MHLW through open recruitment and is also developing its analytical system to enable the database to be used for safety measures (see below diagram).

Medical Institutions Cooperating in the Medical Information Database Development Project



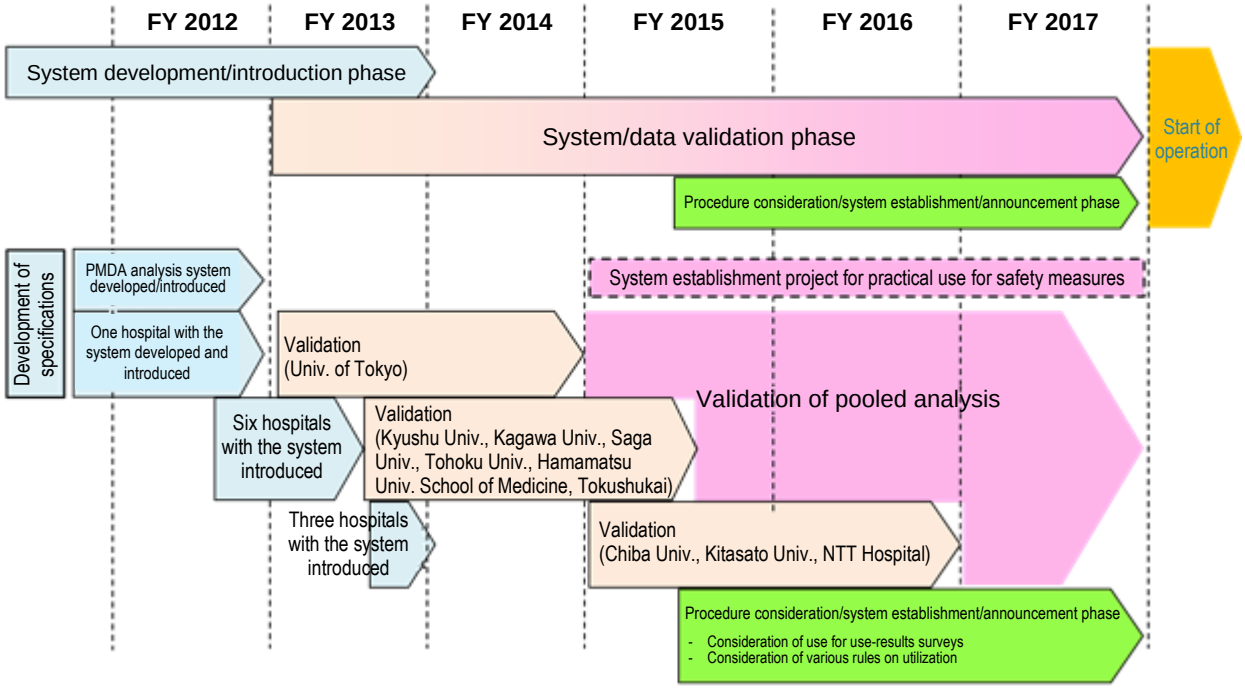
- Development of the medical information database system was initiated in FY 2011 and had been completed at 10 cooperating medical institutions by the beginning of April 2014.

  In FY 2015, continuing on from FY 2014, PMDA has taken the lead in conducting verification to control and improve the quality of stored data in the database and has made the improvements necessary for its utilization. PMDA will promote trial utilization of medical information stored in the database for practical application in safety measures.

- The purpose of trial utilization of the database is as follows: (1) integrate the results of analyses, performed by a number of medical intuitions, of issues relating to drug safety measures, and validate the processes for integrating the analysis results; (2) gain knowledge that would contribute to practical database use (e.g., findings from characteristics evaluation of the database, matters to be considered when analyzing data from the database). In FY 2015, PMDA selected several tasks related to drug safety measures and conducted preliminary research on the feasibility of the tasks. Based on research results obtained in FY 2015, PMDA will select the tasks to be analyzed in detail from FY 2016 onward and conduct such analysis.

- PMDA participates in discussions through participation in the “Workshop on Medical Information Database Operation” activity established by MHLW in January 2016. Since starting its participation, PMDA has been making progress in its preparations in advance of the start of full-scale operation of the medical information database, including opening use to pharmaceutical companies and other third-parties from FY 2018.

Progress and Plan for Development of the Medical Information Database Infrastructure



c. Collection of data on medical devices (implantable ventricular-assist devices [IVADs])

- As part of its objectives under the Third Mid-term Plan related to the Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS) Project, PMDA intends to make improvements to its system for the collection of post-marketing product information by incorporating (in collaboration with relevant academic societies, companies, etc.) a patient registration system (registry) for confirming long-term safety. Case accumulation was originally initiated in FY 2010 as a registry modeling project as part of an industry-government-academia collaboration. Subsequently, in FY 2015, PMDA advanced discussions with relevant academic societies, companies, etc. on how the new system will operate going forward. As of February 2, 2016, a total 591 patients (479 for IVAD, 112 for extracorporeal VAD) had been enrolled in J-MACS at 38 medical institutions nationwide. The number of enrolled patients, survival rates, and other data have been progressively updated on the PMDA website.

d. Building the patient registration system (registry) for regenerative medical products

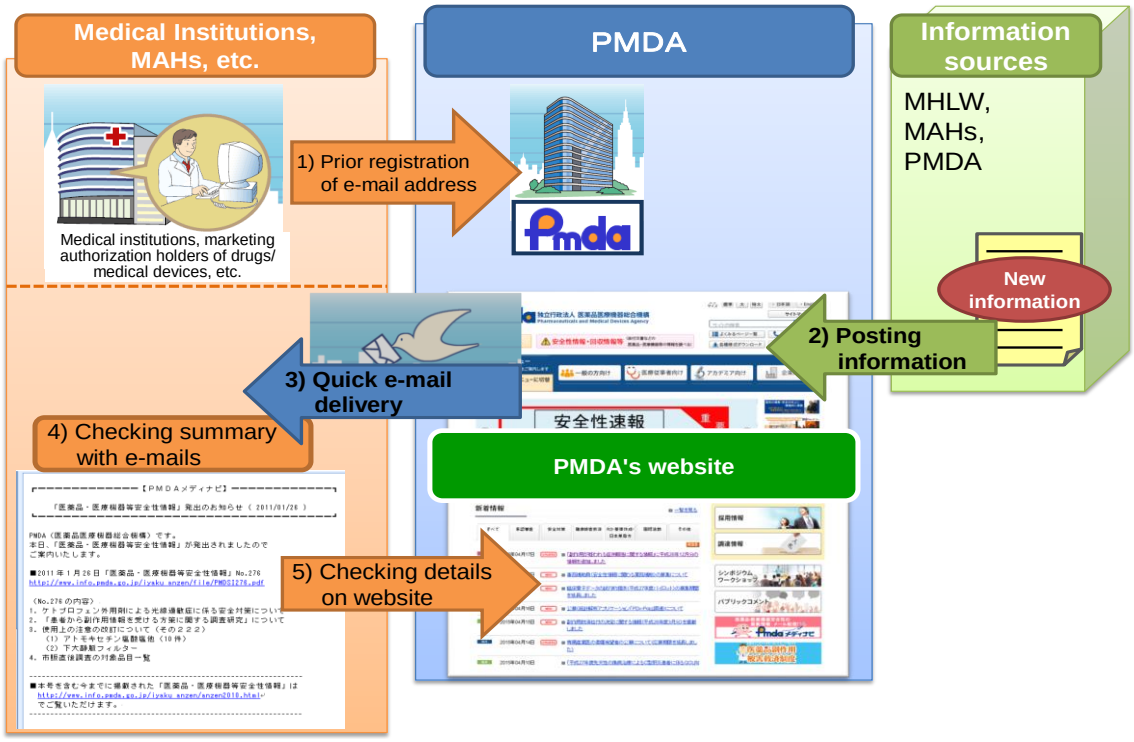
- In the "Workshop on the Proper Composition of a Project for a Patient Registration System for Cellular and Tissue-based Products" at MHLW, a plan for building the "patient registration system" for registering information on patients using regenerative medical products was prepared in order to enhance post-marketing safety measures for regenerative medical products. To this end, under the Third Mid-term Plan, PMDA will build the patient registration system (registry) for verifying long-term safety in collaboration with relevant academic societies, companies, etc.
- In FY 2015, PMDA established a patient registration system (database) and prepared procedure manuals for its operation. PMDA also advanced preparations for the start of its operation, for example, by establishing a workshop and providing operational guidance on the patient registration system for regenerative medical products.

(iii) Establishment of a post-marketing safety system through information feedback

a. Provision of information via website content and e-mail distribution (use of the pharmaceuticals and medical devices information e-mail service (PMDA medi-navi))

- PMDA promptly posts important safety information including revisions to precautions in package inserts on its website on a daily basis, and distributes such information to healthcare professionals and relevant persons at companies by e-mail (PMDA medi-navi) upon issuance thereof. PMDA has also been taking steps to enhance the scale of its information provision activities by posting various safety information, including package inserts, on its website.
- The PMDA medi-navi service provides immediate notification of important safety information, such as “Yellow Letters” (Dear Healthcare Professional Letters of Emergent Safety Communications), “Blue Letters” (Dear Healthcare Professional Letters of Rapid Safety Communications), mandated revisions to Precautions information in product package inserts, and Class I recalls. Use of this information by healthcare professionals is both necessary and critical. During FY 2015, PMDA amended the system: for example, PMDA added a mail address change function, distributed e-mails in HTML format, began distribution of Class II recall information, and enhanced capabilities such as by adding the My Drug List function (distributing designated e-mails to notify that the information in the package inserts of registered drugs had been revised and an additional function for comparing new package inserts with earlier ones). To enhance public awareness of the medi-navi service and to increase the number of subscribers, PMDA also broadened its PR activities related to the service. Registration for the PMDA medi-navi service has become an essential component of the factors used to calculate additional dispensing fees in pharmacies due to the FY 2016 revisions to the health insurance medical fee structure.
- As a result, there were 135,487 subscribers to the PMDA medi-navi at the end of FY 2015, an increase of 131.8% over FY 2013, exceeding the targeted increase of 120% (123,348 subscribers) (representing an increase of 23,408 subscribers). Subscriber institutions included approximately 41,200 hospitals or clinics, 46,800 pharmacies, 8,800 dental clinics or other medical facilities, and 17,700 MAHs or distributors.
- In addition, at the end of FY 2015, there were 9,992 subscribers to the "My Drug List for Safety Update" (in operation from June 2011), an additional service offered by the PMDA medi-navi., was 9,992 at the end of FY 2015.

Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)



Breakdown of Content Distributed through the PMDA medi-navi during FY 2015

Content of e-mails*1	Number of e-mails	Content of e-mails*1	Number of e-mails
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)	0	Approval information (medical devices)	10
Product Recalls (Class I)	21	Approval information (prescription drugs)	25
Product Recalls (Class II)*2	7	Approval information (regenerative medical products)	2
Pharmaceuticals and Medical Devices Safety Information	10	Notifications on drugs, Notifications on medical devices	37
Drug Safety Update (DSU)	10	Information on proper use of drugs	9
Revision of PRECAUTIONS of drugs	12	Information on drug risk under evaluation	10
Revision of PRECAUTIONS of medical devices	3	Information on products submitted for public knowledge-based applications that are covered by insurance	2
Revision of PRECAUTIONS of quasi-drugs and cosmetics	0	Notice of decision on payment/non-payment of adverse reaction relief benefits	12
Revision of PRECAUTIONS of regenerative medical products	0	Risk Management Plan (RMP)	39
Notification on self-check (medical devices)	0	Information on generic drugs	5
PMDA Medical Safety Information	5	Others	18

**1 According to the items distributed on and after March 22, 2016 (after system improvement).*

**2 Distribution was started on March 24, 2016.*

*Number of Information Documents Released on the PMDA's Website as of the End of FY 2015[*1]*

		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Package insert information[*2]						
	Prescription drugs	12,064	12,435	12,921	14,912	14,843
	Medical devices	15,584	17,539	19,309	20,504	22,001
	Regenerative medical products	-	-	-	2	3
	OTC drugs	10,136	10,158	10,234	11,127	11,360
	BTC drugs	-	-	-	20	15
	In vitro diagnostics	3,994	4,054	4,076	4,247	4,238
Drug Guide for Patients[*3]		1,307 (1,951 products)	1,748 (2,453 products)	2,155 (3,409 products)	2,701 (4,482 products)	3,213 (5,911 products)
Guidance for persons receiving vaccination[*3]		-	-	-	72 (74 products)	73 (75 products)
Safety information issued by MHLW						
	Directions for revision of package inserts (drugs)	-[*2]	-[*2]	257	272	284
	Notification of safety measures (drugs)	-[*2]	-[*2]	-[*2]	-[*2]	40
	Directions for revision of package inserts (medical devices)	41	45	48	50	53
	Notification of safety measures (medical devices)	-[*2]	-[*2]	-[*2]	-[*2]	83
	Notification on self-check	50	51	51	52	52
	Pharmaceuticals and Medical Devices Safety Information	-[*2]	-[*2]	168	178	188
	MHLW Press release	-[*2]	-[*2]	69	69	73[*4]
Dear Healthcare Professional Letters of Emergent Safety Communications (Yellow Letters)		24	25	27	30	24
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)						15[*5]
Risk Management Plan (RMP)		-	-	6[*6]	117[*6]	180
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])		81	91	101	111	121
Information about case reports						
	Information about case reports on suspected ADR	210,412	254,392	292,720	338,224	387,162
	Information about case reports on suspected malfunction	62,898	73,012	84,766	98,407	116,182
	Information about case reports on suspected malfunction of regenerative medical products	-	-	-	-	35
	Information about case reports on suspected malfunction in the mechanical part of combination drugs	–	–	–	–	6
Notification related to medical safety measures		77	87	96	108	119
PMDA Medical Safety Information		29	36	43	45	48
Manuals for management of individual serious adverse drug reactions		75	75	75	75	75
Information on approved new drugs • Review reports, summaries of product applications		592 active ingredients (1,189 products)	666 active ingredients (1,314 products)	700 active ingredients (1,416 products)	834 active ingredients (1,652 products)	[*7]
Information on recalls[*8]						
	Drugs (including *in vitro* diagnostics)	2,299	1,907	1,913	1,817	375
	Quasi-drugs					49
	Cosmetics					229
	Medical Devices					1,223
Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)						
	E-mails issued[*9]	259	207	215	234	223
	Subscribers	55,372	84,146	102,790	112,079	135,487

*[1] *Because of the change in the number of pages posted due to the renewal of the PMDA website in March 2015, some figures do not represent the additional posted pages as the difference between the total pages until FY 2014 and those posted during and after FY 2015.*

*[2] *Not totaled.*

*[3] *The numbers of package inserts and products are indicated. These figures may decrease due to discontinuation of products.*

*[4] *The total number of "MHLW press release (drug-related)," "MHLW press release (medical devices)," and "MHLW press release (quasi-drugs and cosmetics)" pages posted.*

*[5] *The number of Yellow and Blue Letter pages posted. (This figure also includes documents released as the same position of the Letters of Rapid Safety Communications in and before September 2011.)*

*[6] *The number of files posted, including the number of revised files.*

*[7] *See 3.4.(4) Promoting provision of information such as review reports.*

*[8] *Added as necessary; and deleted after two years, in principle*

*[9] *These figures represent the total number of e-mails sent during each fiscal year. A single e-mail may related to several subjects; therefore, when the number of e-mails is tabulated based on the number of subjects addressed, the number of e-mails will differ from the figures in the table columns.*

b. Provision of information on package inserts

- PMDA began to accept package insert notifications for pharmacy drugs (except for *in vitro* diagnostics, drugs requiring no approval, and pharmacy-compounded drugs), behind-the-counter (BTC) drugs, class IV medical devices, and regenerative medical products, in accordance with enactment of the PMD Act on November 25, 2014 and has continuously worked to ensure smooth implementation in FY 2015. (Note: The term "pharmacy drugs" refer to prescription drugs and pharmacy-compounded drugs.) For drugs and medical devices, PMDA accepts notifications delivered through the website, and for BTC drugs and regenerative medical products, PMDA accepts notifications delivered by hand or sent by post.
- At the end of FY 2015, PMDA had posted 14,843 package inserts for prescription drugs on its website. Upon issuance of notifications from MHLW directing revisions of package inserts, PMDA posts such notifications requiring revisions on its website and provides links to the corresponding package inserts.
- Although only submission of instructions for use of Class IV medical devices is required under the PMD Act, instructions for the use of Class I, II, and III medical devices have also been made available on the PMDA website. By the end of FY 2015, instructions for 22,001 devices were posted on the PMDA website. PMDA has also posted notifications mandating revisions of instructions for use in conjunction with the issuance of such information, and has been providing links to the corresponding instructions for use.
- For regenerative medical products, three package inserts were accessible on the website as of the end of FY 2015, following enactment of the PMD Act on November 25, 2014.
- For OTC drugs, 11,360 package inserts were accessible on the website as of the end of FY 2015.
- For BTC drugs, PMDA started providing information on package insert upon enactment of the revised Pharmaceutical Affairs Act in June 2014. A total of 15 package inserts were accessible on the website as of the end of FY 2015.
- For *in vitro* diagnostics, 4,238 package inserts could be accessed from the website as of the end of FY 2015.

c. Public release of adverse drug reaction reports and device malfunction reports

1) Public release of adverse drug reaction reports

- The following types of data obtained from adverse drug reaction reports submitted by MAHs in Japan were disclosed within approximately 4 months of receipt: fiscal year and quarter of the year reported, reporting category, type, job category of reporter, investigation status, gender, age, primary disease, body height, body weight, suspected drug/brand name, reason for use, route of administration, single-dose, start date of administration, end date of administration, action against suspected drug, adverse events (onset date), presence/absence of recurrence due to re-administration, outcome, suspected concomitant drug, and other concomitant drug.
- Reports received from medical institutions that are investigated by PMDA are also published. At the end of FY 2015, PMDA had posted 387,162 reports that were submitted by November 2015.
- Since April 2012, PMDA has also provided datasets pertaining to adverse drug reaction cases (contained in the Japanese Adverse Drug Event Report database [JADER]) which are released to the public after being exported into CSV format. These datasets become available for public investigation and research purposes approximately four months after their submission.

2) Public release of information concerning medical device malfunction reports

- The following types of data obtained from medical device malfunction reports submitted by MAHs in Japan have been disclosed: fiscal year reported, gender, age, outcome, term name, condition of the medical device, and adverse events experienced by patient. As of November 2015, the time needed to release these reports was shortened from six months to four months.

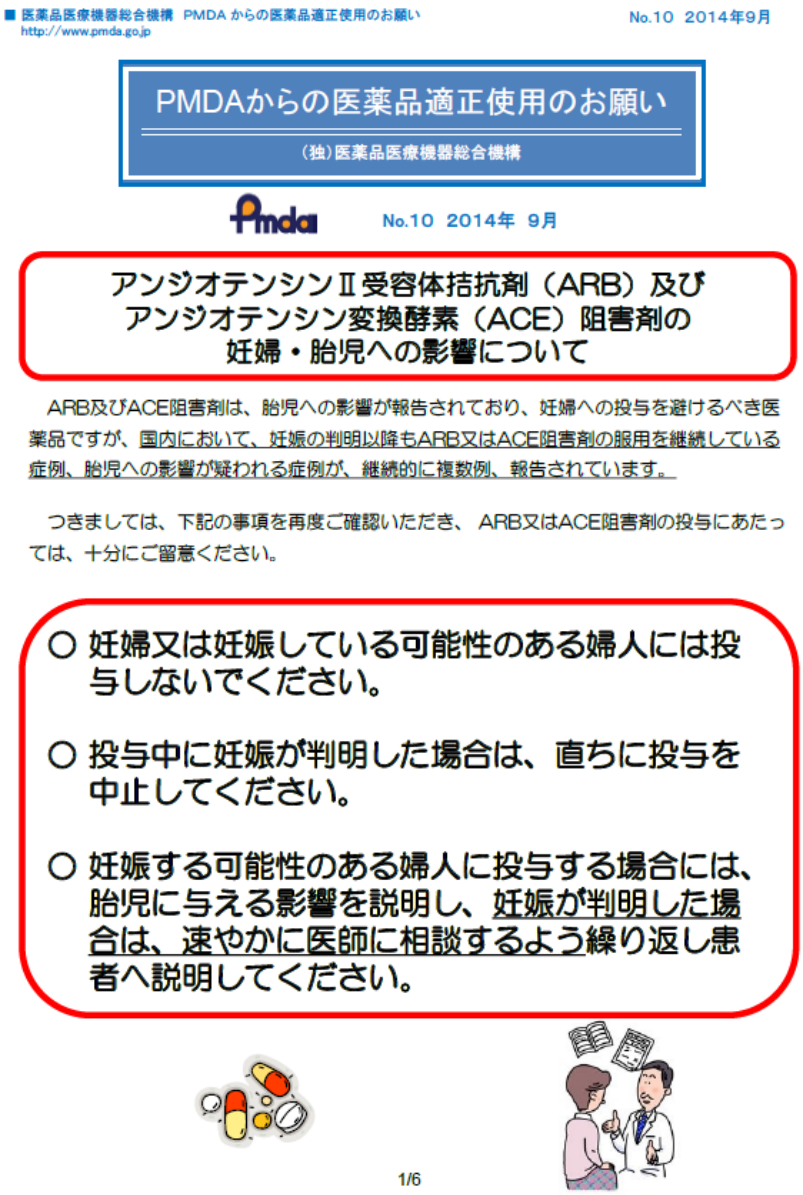
  In total, 116,182 reports (submitted by November 2015) had been posted by the end of FY 2015.

3) Public release of information on malfunction reports of regenerative medical products and combination drugs

- PMDA began releasing reports concerning malfunction of regenerative medical products and of the mechanical part of combination drugs submitted by MAHs in July and October 2015, respectively. In total, 35 reports on regenerative medical products (submitted by November 2015) and 6 reports on combination drugs (submitted by November 2015) had been posted by the end of FY 2015.

d. Provision of the Request for Proper Use of Drugs

If specific measures concerning the proper use (including dose and frequency as well as frequency of testing for adverse reactions) of a drug have already been recommended in its package insert or other materials prepared by the applicable MAH, but it is determined that improper use persists or testing is not properly conducted, patients' claims for relief benefits for adverse reactions caused by such drugs may be rejected. In order to avoid such cases, PMDA prepares "PMDA Request for Proper Use of Drugs" publications and provides the relevant information to healthcare professionals and related academic societies. This activity helps to ensure the proper use of drugs that have been associated with adverse drug reactions due to improper use despite repeated precautions having been issued.



■ 医薬品医療機器総合機構 PMDA からの医薬品適正使用のお願い
http://www.pmda.go.jp
No.10 2014年9月

PMDAからの医薬品適正使用のお願い

(独)医薬品医療機器総合機構

No.10 2014年 9月

アンジオテンシンⅡ受容体拮抗剤（ARB）及び
アンジオテンシン変換酵素（ACE）阻害剤の
妊婦・胎児への影響について

ARB及びACE阻害剤は、胎児への影響が報告されており、妊婦への投与を避けるべき医薬品ですが、国内において、妊娠の判明以降もARB又はACE阻害剤の服用を継続している症例、胎児への影響が疑われる症例が、継続的に複数例、報告されています。

つきましては、下記の事項を再度ご確認いただき、ARB又はACE阻害剤の投与にあたっては、十分にご留意ください。

○ 妊婦又は妊娠している可能性のある婦人には投与しないでください。

○ 投与中に妊娠が判明した場合は、直ちに投与を中止してください。

○ 妊娠する可能性のある婦人に投与する場合には、胎児に与える影響を説明し、妊娠が判明した場合は、速やかに医師に相談するよう繰り返し患者へ説明してください。

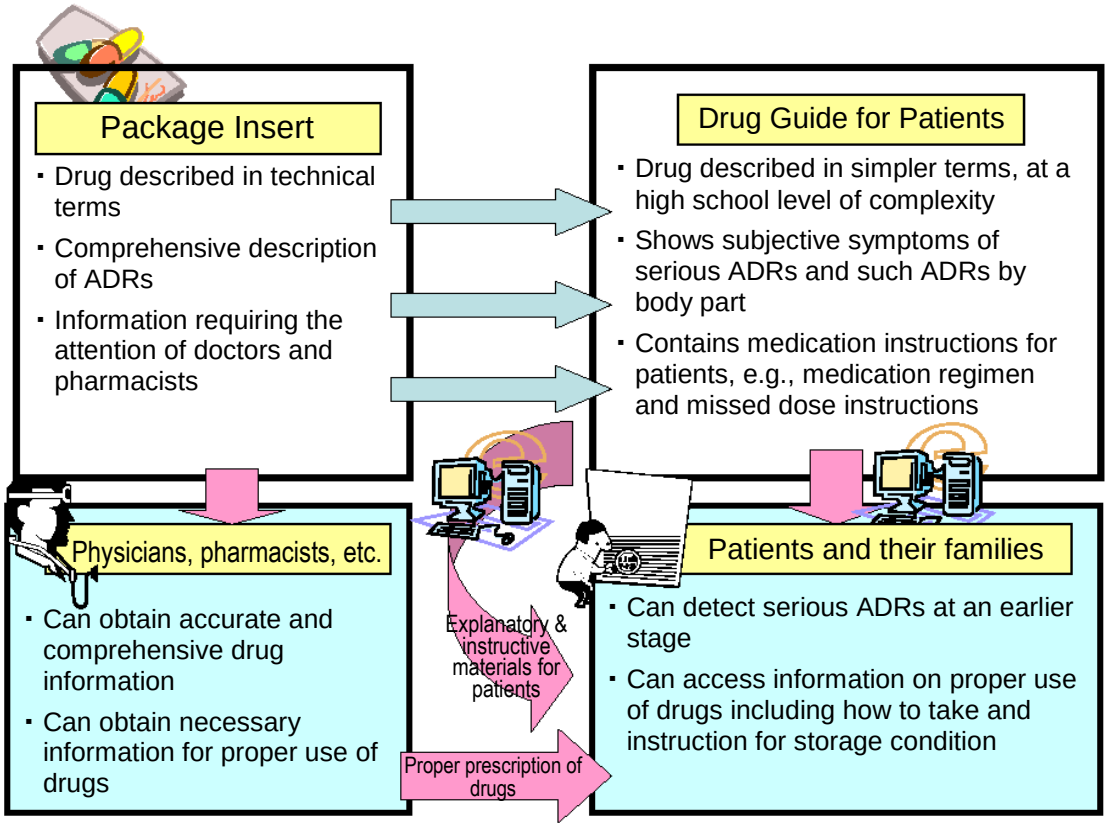
1/6

e. Provision of information such as Drug Guide for Patients and manuals for management of individual serious adverse drug reactions

1) Provision of Drug Guides for Patients

- To promote proper understanding of prescription drugs among patients and to facilitate earlier detection of serious adverse drug reactions, Drug Guides for Patients have been discussed and revised according to “Guidelines for Developing the Drug Guide for Patients” (PFSB Notification No. 0630001 dated June 30, 2005) and has been available on the PMDA website since January 2006. In FY 2015, 91 Drug Guides for Patients (including 18 for generic drugs) were prepared for products newly marketed or products for which the Precautions had been revised. A total of 3,213 Drug Guides for Patients (5,911 products) had been posted by the end of FY 2015.

Package Inserts for Prescription Drugs and Drug Guide for Patients



2) Provision of Guides for patients receiving vaccinations

- The "Guide for Patients Receiving Vaccinations" has been available on the PMDA website since June 2014, to promote proper understanding of vaccines among persons receiving vaccinations and their families and to enable detection of serious adverse reactions at an earlier stage. This was done after consideration of several documents, such as “Guidelines for Developing the Guide for Persons Receiving Vaccinations” (PFSB Notification No. 0331-7 dated March 31 2014). In FY 2015, 1 Guide for Persons Receiving Vaccinations was prepared for the newly marketed Pneumococcal 10-valent conjugate vaccine adsorbed (Non-Typeable *Haemophilus influenzae* (NTHi) protein D, diphtheria or tetanus toxoid conjugates) A total of 73 Guides for Persons Receiving Vaccinations (75 products) had been posted by the end of FY 2015.

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

- The manuals for the management of individual serious adverse drug reactions prepared by MHLW in its initiative of comprehensive actions for serious adverse drug reactions have been made available on the PMDA website since November 2006. As of the end of FY 2011, manuals for a total of 75 adverse drug reactions were posted on the website.

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

- The MHLW’s initiative of comprehensive actions for serious adverse drug reactions was terminated in FY 2010, and consequently, no information was added to the manual in FY 2015, but the manuals are being reviewed for a future revision.

f. Provision of medical safety information

- PMDA extracts, evaluates, and examines near-incident cases associated with drugs, medical devices, and regenerative medical products from the "Project Report on Collection of Medical Incident Information," "Annual Report of the Project to Collect and Analyze Near-incident Cases from Pharmacies," etc. published by the Japan Council for Quality Health Care. In FY 2015, 1,972 cases associated with drugs and 350 cases associated with medical devices were evaluated and the results were reported to MHLW. These 2,322 cases were posted on the PMDA website and are also shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 2,322	1,972	350
1) Cases for which safety measures for the use of drugs, medical devices, or regenerative medical products taken by MAHs, etc. were considered necessary or possible.	2	0
2) Cases for which measures have already been taken, or are currently under consideration, by the MAHs, etc.	22	21
3) Cases for which the available information is insufficient for the MAHs to consider safety measures, or cases that were likely to have resulted from human errors or human factors.	1,948	329

- Since November 2007, PMDA has issued PMDA Medical Safety Information publications, which are prepared in reference to input provided by healthcare professionals such as physicians, pharmacists, nurses, and clinical engineers, in addition to non-medical specialists in fields such as ergonomics. These publications provide precautions through not only text, but also easy-to-understand charts to help healthcare professionals use medical products more safely. The information provided addresses events that were reported repeatedly or that led to issuance of revisions to package inserts, among near-incident cases, adverse drug reaction reports, and malfunction reports. In FY 2015, the following 3 issues were posted on the web page.

No.	Posted on	PMDA Medical Safety Information titles
No.46	May 2015	Precautions When Handling the Blood Purification Devices
No.47	September 2015	Handling of Lines for Drug Solution Administration
No.48	January 2016	Precautions in Handling Three-way Stopcocks

g. Release of information on drug risks under evaluation

- In order to further enhance safety measures for drugs, PMDA releases (1) risk information that PMDA monitors closely because it could lead to revisions to Precautions in package inserts and (2) risk information that has attracted attention from foreign regulatory authorities, academic societies, etc. and is under evaluation by MHLW/PMDA. These types of information have been posted on the PMDA website, as appropriate, since July 2011, as risk information under evaluation in order to provide the information earlier, before the determination of safety measures.

h. Information provision in English

- To promote dissemination of information on safety measures to foreign countries, PMDA translated into English information on revision of Precautions of medical devices (including self-inspection), and two safety documents issued by MHLW in relation to the early post-marketing phase vigilance

and posted the information on the PMDA's English website. In addition, the Agency translated into English the PMDA Risk Communications, information on revision of Precautions of drugs, the PMDA Medical Safety Information, and the Pharmaceuticals, and Medical Devices Safety Information, which is issued by MHLW. These documents are available on the PMDA English website.

i. Responses to consultation requests from MAHs

- In order to contribute to improvement of post-marketing safety measures by MAHs, PMDA provided various consultations (on post-marketing safety measures for drugs, medical devices, regenerative medical products, and medical safety) requested by MAHs. These medical safety consultations were in particular related to revisions to package inserts, post-marketing risk management plans, consultation on 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 provided consultations by category for FY 2015 is shown below:

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs	670	704	776	869	991
Medical devices	163	179	95	325	772
Medical safety	59	80	31	72	116
Regenerative medical products*	-	-	-	0	4

** The figure indicates the number of consultations following enactment of the PMD Act on November 25, 2014.*

- Consultations for medical safety conducted in FY 2015 were mainly in respect of names of new drugs, packaging/labeling, and near-incident cases for drugs, medical devices, and regenerative medical products. PMDA provided all consultations in an appropriate and prompt manner.

j. Provision of consultations on drugs/medical devices to general consumers and patients

- PMDA offers a telephone consultation service to support safe and secure use of drugs and household medical devices by both patients and general consumers.
- In FY 2015, the number of persons receiving consultations was 12,551 (15,311 calls) for drugs and 406 (451 calls) for medical devices.
- PMDA has identified and compiled a list of consultations related to generic drug products from a larger listing of drug product consultations, and provided this data to the Secretariat of the Generic Drug Quality Information Review Group (a review group consisting of experts established at the National Institute of Health Sciences [NIHS]).

Number of Persons Receiving Consultations on Drugs/Medical Devices

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Persons receiving consultations on drugs [persons/day]	8,945 [36.7]	9,679 [39.5]	10,244 [42.0]	11,556 [47.4]	12,551 [51.7]
(of which consultations on generic drugs)	(453)	(493)	(626)	(543)	(600)
Persons receiving consultations on medical devices [persons/day]	660 [2.7]	700 [2.9]	547 [2.2]	370 [1.5]	406 [1.7]

k. Status of communication and use of transmitted safety information within medical institutions

- To promote the proper use of drugs and medical devices, it is important that necessary safety information, such as safety measures to be taken, is appropriately communicated to and used by healthcare professionals in clinical settings. Accordingly, since FY 2010, PMDA has been conducting a survey to ascertain the status of procurement, communication, and use of safety information in medical institutions and pharmacies, and to discuss the use of safety information in clinical settings. The survey results to date are available on the PMDA website.
- The results of a survey (conducted in 8,481 hospitals nationwide) to ascertain the status of procurement, communication, and use of safety information on drugs in hospitals conducted in FY 2014 was released on the PMDA website in June 2015. Methods for raising awareness of the appropriate management of drug safety information in hospitals based on these results were discussed at various workshops that were held in collaboration with Japanese Society of Hospital Pharmacists and other groups. In addition, the survey (in 500 randomly-sampled general clinics) to ascertain the status of procurement, communication, and use of safety information on medical devices in hospitals was released on the PMDA website in March 2016. Its results will be fed back to those involved in clinical practice in collaboration with Japan Association for Clinical Engineers and other groups.

Summary of survey results (excerpt)
Survey to ascertain the status of procurement, communication, and use of safety information on drugs in hospitals

1. Obtaining appropriate information based on the characteristics of the information media
2. Utilization of appropriate information at time drugs are adopted
3. Secure and effective communication of safety information
4. Promotion of utilization of risk communication tools in clinical settings
5. Promotion of collaboration between hospitals and pharmacies

Summary of survey results (excerpt)
Survey to ascertain the status of procurement, communication, and use of safety information on medical devices in hospitals

1. Improving the information management system and use of information in line with the actual circumstances prevailing at institutions

(1) Reliable access to information

(2) Communication of accurate information

(3) Addressing information management at an organizational level

(4) Utilization of electronic information including the PMDA website and the PMDA medi-navi

2. Issues related to information provision by companies and governmental organizations

**See PMDA website for details.*

- In FY 2015, PMDA conducted the following two surveys and released their results on the PMDA website: 1) a survey (in 10% of general clinics providing healthcare services as stipulated by health insurance [8,737 institutions]) on the status of procurement, communication, and use of drug safety information in clinics, and 2) a survey (in 10% of health insurance pharmacies [5,664 institutions])

on the status of procurement, communication, and use of medical device safety information in pharmacies. PMDA will feed back and promote proper procurement, communication, and use of information in the clinical setting in collaboration with professional organizations.

Outline of surveys conducted to date

FY	Title	Target	Period	Remarks
2010	Survey on the status of communication and use of drug safety information	Hospitals nationwide (8,679 institutions)	January 13, 2011 to February 10, 2011	Questionnaire survey (response rate, 41.2%)
2011	Survey on the status of communication and use of drug safety information	Hospitals nationwide (8,640 institutions)	January 20, 2012 to February 10, 2012	Questionnaire survey (response rate, 25.9%)
2012	Survey on the status of procurement, communication, and use of drug safety information	Hospitals nationwide (8,541 institutions)	January 7, 2013 to February 28, 2013	Questionnaire survey (response rate, 53.4%)
		Half of all pharmacies nationwide (26,915 institutions)	January 7, 2013 to February 28, 2013	Questionnaire survey (response rate, 64.6%)
2013	Survey on the status of procurement, communication, and use of good practices on drug safety information	14 hospitals and clinics/pharmacies near the hospitals in Japan	October 2013 to February 2014	Door-to-door survey
	Basic survey on the status of procurement, communication, and use of medical device safety information	9 hospitals/clinics in Japan	October 2013 to February 2014	Door-to-door survey
2014	Survey on the status of procurement, communication, and use of drug safety information	Hospitals nationwide (8,481 institutions)	December 15, 2014 to March 13, 2015	Questionnaire survey (response rate, 57.8%)
	Survey on the status of procurement, communication, and use of medical device safety information	500 general hospitals (sampled randomly)	February 9, 2015 to March 13, 2015	Questionnaire survey (response rate, 40.0%)
2015	Survey on the status of procurement, communication, and use of drug safety information	10% of general clinics *limited to institutions providing healthcare services as stipulated by health insurance (8,737 institutions)	October 6, 2015 to December 14, 2015	Questionnaire survey (response rate, 53.1%)
		10% of health insurance pharmacies (5,664 institutions)	October 6, 2015 to December 14, 2015	Questionnaire survey (response rate, 68.2%)

I. Workshops related to post-marketing safety measures

- PMDA gave presentations on its approaches to improving and strengthening safety measures, revisions to precautions in package inserts, the effective use of the PMDA's web page, and PMDA's consultation services, at various workshops and academic conferences.

3.4. Promotion of Regulatory Science, Internationalization, etc.

3.4.(1) Promotion of regulatory science

(i) Use of the Science Board

- The Science Board was established in May 2012 as an external body tasked with the deliberation of the scientific aspects of drug, medical device, and regenerative medical product reviews to more appropriately review products that utilize advanced science and technologies. The Science Board also works to advance regulatory science and reinforce collaboration and communication with academia and medical professionals to promote future innovation in healthcare. Materials relating to individual products may be used for discussion; therefore, meetings are closed to the public. Members are external experts in such areas as medicine, dentistry, pharmacy, and engineering.
- The following five reports summarizing discussions were prepared and released on the PMDA website in the Second Term (from April 2014 to March 2015) (reposted).
  1) Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products
  2) Discussions on Evaluation of Medical Devices in Pediatric Use
  3) Report on the use of non-clinical studies in the regulatory evaluation of oncology drugs
  4) Current Status and Perspectives of Placebo-controlled Studies
  5) Report on the Use of Numerical Analysis for Strength Evaluation of Orthopedic Implants
- The No. 3) report in the Second Term was posted on the website and also published in an academic journal (*Cancer Science*) and underwent scientific evaluation.

(ii) Enhancement of regulatory science research

- With respect to electronic submission of clinical trial data for new drugs, see 3. 2. (1) New Drugs (ii)-b.
- In order to properly conduct reviews, safety measures, and relief services for adverse health effects and to enhance the quality of these activities, PMDA is striving to promote regulatory science research on topics including the preparation of standards, guidelines, and guidance and how to conduct scientific forecasting, evaluation, and judgment. Some regulatory science research activities conducted by PMDA are designated by the Chief Executive as within the scope of PMDA's official operations. This designation is dependent on research purpose, how the research is related to PMDA's operations, and on comments from the Regulatory Science Research Evaluation Committee. In FY 2015, 12 projects (3 new projects and 9 ongoing projects) were selected as designated research and the results of 2 of these projects were published in academic journals (reposted).
- For innovative products, see 3.2. (2) (i).
- PMDA conducted regulatory science research in collaboration with external organizations such as academic institutions. (27 projects used public research funds, such as AMED and Health and Labour Science Research Grants.) In addition, 2 joint studies are presently being conducted in conjunction with the National Institute of Health Sciences.
- In order to conduct the designated research appropriately, PMDA held a meeting of the Regulatory Science Research Evaluation Committee and other meetings and selected new designated research projects for FY 2016 based on the relevant rules. For the first time, PMDA also held a meeting where the final report on designated research was presented. Three projects that were

concluded in FY 2014 were highly evaluated because they provided information that was published in academic papers and were followed by new studies, which was a favorable outcome.

- PMDA developed rules, formats, etc. for regulatory science research to match actual situations and conducted expedited review for application issues (4 products) based on “Rules for Handling Ethical Reviews at the Pharmaceuticals and Medical Devices Agency” to improve the environment and systems for such research activities.
- PMDA held an exhibition on the topic of regulatory science studies to present the outcomes of such studies conducted by PMDA employees so that regulatory science researchers could exchange information. Another purpose was to enhance the motivation of employees to conduct their own studies.
- In order to appropriately evaluate the performance of employees conducting designated research projects, PMDA has made it possible to describe such engagement in a personnel evaluation sheet since FY 2015 and made efforts to improve the motivation of employees to conduct their own studies.
- PMDA developed and reinforced the collaborative graduate school program, established the framework for a comprehensive partnership system to support joint research activities with academia, etc., and concluded comprehensive partnership agreements with the National Cancer Center Japan, Hiroshima University, Keio University, and University of Tsukuba.
- In the working groups (WGs) within Projects Across Multi-Offices for standard development (hereinafter referred to as “Projects Across Multi-Offices”), PMDA shared review and consultation cases and related information, collected information on the regulatory situation overseas, and exchanged opinions with external experts and regulatory authorities overseas where appropriate.
- PMDA made presentations at academic conferences on the discussions held as part of the Projects Across Multi-Offices and performed PR activities (Companion Diagnostics WG [14 academic presentations/lectures and 1 paper], Pediatric Drugs WG [9 academic presentations and 1 paper], Orphan Drugs WG [3 academic presentations and 1 explanatory meeting], and Cardiovascular Risk Evaluation WG [6 academic presentations/lectures and 1 paper]).
- The Projects Across Multi-Offices exchanged opinions about evaluation policy and other issues with development companies, and related industrial groups and academic societies (Companion Diagnostics WG exchanged ideas with development companies and related industrial groups [7 occasions] and with related academic societies [one occasion], and conducted other activities [See 3.4.(2).(v)]).
- The Global Clinical Study WG in Projects Across Multi-offices held a workshop titled “Principles on Long-term Treatment Studies in the Global Development Strategy” co-hosted by JPMA, PhRMA, EFPIA, and PMDA on November 24, 2015 to exchange opinions.

(iii) Enhancement of staff training

a. Lectures and guidance given by experts

- In order to improve the skills of its staff, PMDA provided its employees with the following training opportunities: special training programs including lectures on product development activities at companies, given by external experts invited from Japan and other countries; training in respective review parts with the cooperation of the National Institute of Health Sciences (NIHS) (14 sessions); training programs in laws and regulations such as the PMD Act, to learn about the regulatory system etc. (1 session); training programs in clinical study design, to learn biostatistics (12

sessions); and training programs in pharmacoepidemiology to learn features of pharmacoepidemiological study design (5 sessions).

- A total 13 employees were dispatched to technical training programs conducted by external institutions (e.g., the Pharmaceuticals Promotion Association's General Course, National Institute of Public Health, and Union of Japanese Scientists and Engineers). For acquisition of basic knowledge concerning medical devices, Class I and Class II medical engineering (ME) technical training courses were also provided (16 employees).

b. Overseas dispatch

- To provide opportunities to learn about actual situations regarding review and safety measures provided by overseas authorities, PMDA dispatched employees for a fixed term (2 employees).

c. On-site training

- PMDA conducted on-site training programs, including visits to drug and medical device manufacturing facilities (4 facilities), IRBs of medical institutions, etc.
- Product hands-on training using medical devices was provided (3 facilities).
- PMDA provided radioactivity technology training, including hands-on training in radioactivity measurement, to offer opportunities for learning about technical knowledge and skills in radioactivity (12 employees).
- Seven employees were dispatched to two hospitals for practical training under hospital pharmacists and two employees to two hospitals for practical training under hospital engineers, to ensure that PMDA employees do their work in line with the reality of clinical practice. In addition, 11 employees were dispatched to 2 medical institutions to observe testing procedures, treatments, etc. using medical devices.

(iv) Promotion of interaction with outside researchers and collaboration on investigative research

a. Promotion of initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products

- PMDA works to develop personnel who are familiar with regulatory science through personnel exchanges with research institutions, including universities, based on the initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products (a project funded by MHLW), and also promotes cooperation on research projects concerning methods for evaluating the efficacy and safety of products developed using advanced technologies. In FY 2015, PMDA conducted personnel exchanges with 24 universities, etc., accepted 21 researchers as specially appointed experts (including non-regular staff), and dispatched a total 54 employees (including non-regular staff).

b. Promotion of collaboration and cooperative relationships through comprehensive partnership agreements, etc.

- In FY 2015, PMDA reinforced the existing collaborative graduate school program by concluding comprehensive partnership agreement with graduate schools, to reinforce collaboration with academia. PMDA advanced discussions with academia to promote cooperation and collaboration across a broad range of fields with medical and research institutions within a partnership framework, including the National Center for Global Health and Medicine. In FY 2015, PMDA concluded

comprehensive partnership agreements with the National Cancer Center Japan, Hiroshima University, Keio University, and University of Tsukuba.

- PMDA accepted 1 graduate student from a graduate school with which PMDA had concluded a comprehensive graduate school agreement (Gifu Pharmaceutical University Graduate School) to provide research education and guidance
- As a part of its initiatives to increase recognition of regulatory science, PMDA responded supportively and cooperatively to university requests for PMDA staff members to give lectures (FY 2015: 27 universities, 49 lectures).

3.4.(2) Actions taken for internationalization

- PMDA has received high international praise as a result of resolving the review lag for drugs and medical devices in the First and Second Mid-term Plan and has been asked to make additional international contributions. Under such circumstances, PMDA formulated and released the “PMDA International Strategic Plan 2015” in June 2015 as its new international strategy, based on expectations expressed in and outside Japan.

  The Strategy stipulates the international activities to be undertaken by PMDA through the periods covered by the Third and Fourth Mid-term Plan until 2023, based on the recent changes in the circumstances surrounding regulatory authorities and also based on the International Pharmaceutical Regulatory Harmonization Strategy of MHLW (released in June 2015).

(i) Strengthening of cooperation with the U.S., the EU, Asian countries, and relevant international organizations

Information exchanges with regulatory authorities in Europe and the United States, etc.

- PMDA exchanged information regarding consultations held with companies on clinical studies and regarding review and safety measures with FDA in the United States, EMA in Europe, and other organizations, based on a non-disclosure agreement and made use of such information to ensure that review and safety measures were correctly implemented based on the latest scientific knowledge available to PMDA.
- Further, PMDA held meetings with regulatory authorities in countries/regions such as Brazil, Taiwan, and Thailand and endeavored to establish cooperative relationships with these countries/regions. As a result of negotiations, PMDA and the regulatory agencies in Taiwan and Thailand agreed that products approved in Japan would be covered by brief reviews in Taiwan and Thailand.
- In addition, PMDA exchanged GMP inspection reports with the United States (FDA), Canada (Health Canada), Ireland (HPRA), and other countries to improve inspection efficiency. Furthermore, PMDA reinforced practical collaboration between Japan and Taiwan by conducting joint GCP inspections and exchanging information on QMS inspections.

Japanese Pharmacopoeia

- PMDA held training sessions on the Japanese Pharmacopoeia for staff of the Thailand FDA and promoted understanding of Japanese Pharmacopoeia, to encourage foreign regulatory authorities to approve the use of the Japanese Pharmacopoeia as a reference pharmacopoeia. PMDA also further collaborated with Brazil, where the Japanese Pharmacopoeia had already been adopted as a reference pharmacopoeia. For example, PMDA raised the pharmacopoeia as a topic at a meeting with Brazilian regulatory authorities.

Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

- To promote better understanding of Japan's regulatory systems for drugs and medical devices among Asian countries, PMDA has taken steps to preparations to establish an educational organization for the personnel employed by the regulatory authorities of Asian countries. The organization's name is "Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs" (established as of April 1, 2016) within PMDA.

Dispatching liaison officers

- PMDA continued to dispatch liaison officers to the United States and Europe to collect information and reinforce collaboration. PMDA dispatched liaison officers to the US FDA in particular, focusing on placements related to specialized fields such as medical devices, clinical pharmacology, GMP, and CDISC. In addition, PMDA dispatched liaison officers to the U.S. Pharmacopeial Convention to advance harmonization efforts between the US and Japan, and also to gather information on trends in CMC (Chemistry, Manufacturing and Control) practices in the US.
- PMDA conducted overseas GCP inspections, accompanied where possible by representatives of the regulatory authorities of the investigated countries, which had been contacted by PMDA in advance. PMDA exchanged information with US FDA and EMA, focusing on product issues in global clinical trials. PMDA discussed collaboration and improvement of circumstances regarding GCP, by dispatching employees in Office of Non-clinical and Clinical Compliance to the FDA and EMA. The employees participated in training programs offered by FDA and EMA and exchanged information with the agencies on compliance assessment methods for GLP/GCP/GPSP.
- PMDA participated in the Sixth International Meetings of World Pharmacopoeias, which was held by WHO in September 2015, and cooperated in the preparation of Good Pharmacopoeia Practice as a member of the draft formulation group.
- In September 2015, PMDA held a meeting with the pharmacological regulatory authority of Brazil (Agência Nacional de Vigilância Sanitária [ANVISA]). Both parties concluded a memorandum on cooperation on pharmacopoeia.

(ii) Strengthening of activities for international harmonization, etc.

Major actions taken for drugs

- International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) held conferences in Japan (Fukuoka) and the United States (Jacksonville) in June and December 2015, respectively. Japan has proposed the introduction of 2 new topics (E17, Multi-Regional Clinical Trials; E1, Genomic Sampling and Management of Genomic Data). Japan acts as rapporteur for the topics and promotes the development of related guidelines under Japan's leadership.
- PMDA also addressed the issue of the organizational improvement of ICH by improving ICH organizational rules and reviewing the rules on discussions so that discussions at ICH can be conducted smoothly under the leadership of Japan.

Major actions taken for medical devices

- International Medical Device Regulators Forum (IMDRF) held conferences in Japan (Kyoto) and Brazil (Brasília) in September 2015 and March 2016, respectively. Japan has been serving as the chair since 2015 to develop the next 5-year plan of IMDRF and finalize IMDRF guidance documents (including documents on the application of a quality control system to the medical device program).
- Events such as the special program of Harmonization by Doing (HBD) were held in Kyoto and Yokohama (both Japan) in September and December 2015, respectively. PMDA continuously

promoted HBD activities to accelerate information communication by taking such actions as broad diffusion of the outcomes obtained through HBD activities.

- In addition, PMDA also attended ISO working groups on the revision of ISO 14155 (GCP for medical devices) so that it can be accepted in Japan.

Major actions taken in other fields

- As a leading country in capacity building activities, in International Coalition of Medicines Regulatory Authorities (ICMRA), PMDA investigated the implementation status of capacity building in participating countries and presented a summary of the suggestions on what the future direction should be. In addition, PMDA played a major role in establishing ICMRA's official website to raise public awareness of the coalition's activities.
- PMDA participated in the Pharmacopoeial Discussion Group PDG (PDG) meetings held in July and November 2015, at which 1 excipient and 1 general test were revised and harmonized. In addition, PMDA sought public comments in Japan for 2 general tests that will be harmonized by PDG.
- PMDA held a total 5 Expert Discussion meetings on drug names and reported 60 Japanese accepted names (JAN) to MHLW. Three consultations on applications for international non-proprietary names (INN) were also conducted. PMDA participated in the WHO-hosted conferences on INN in April and October 2015.
- PMDA participated in the International Generic Drug Regulators Programme (IGDRP) meeting held in May and November 2015 and exchanged opinions on, in particular, the master file, handling of bioequivalence with the regulatory authorities. In addition, PMDA discussed the likelihood of harmonization of regulations on bioequivalence evaluation between Japan and overseas in a research project supported by Health and Labour Science Research Grants.
- PMDA participated in the 9th International Cooperation on Cosmetics Regulation meeting (ICCR-9) held in Belgium in November 2015 and exchanged information on regulations of cosmetics with regulators from the U.S., Europe, Canada, Brazil, and China.

  PMDA also participated in the 2nd meeting of the Self-Medication Collaborative ASIAN Regulator Expert Roundtable (Self-CARER) held in Thailand in September 2015 and exchanged information with regulators from Asian countries.
- For details regarding PMDA's contributions to enhancing international recognition of the Japanese Pharmacopoeia through cooperation in WHO-organized international pharmacopoeial activities, see 4. (2) (i).
- PMDA cooperated with the Project on Promotion of an International Standardization Strategy for Medical Devices conducted by MHLW. Based on the road map prepared in the project's inaugural year of FY 2014, PMDA conducted the following activities to support Japan's efforts to become a leader in international standardization of specifications and standards that originate in Japan or that reflect Japanese ideas: promotion of proactive participation in events such as ISO/IEC international conferences, improvement of framework for collaboration with organizations such as Japanese review groups, and activities to promote the establishment of trust relationships and reinforcement of collaboration with regulatory authorities in Asian, Western, and other countries. Specifically, PMDA selected 7 themes in important fields for which international standardization should be promoted in a strategic manner, participated in 172 conferences of the ISO/IEC specification review committee (25 international conferences, 101 meetings of the Japanese committee, and 46 teleconferences), which included one of the themes above, i.e., medical robots and additive manufacturing, and took part in standardization activities, including proposals from Japan. In addition, PMDA started a project to support the participation of academia in international

conferences. In FY 2015, 3 experts were dispatched to international conferences to participate in deliberations on specifications and gathered information. Furthermore, PMDA proposed to related groups the importance of establishing a framework so that information, issues, etc. obtained through the activities referred to above can be shared among Japanese review groups, resulting in the establishment of "Liaison Conference of Specification Review Groups" in the Japan Federation of Medical Devices Associations. As part of its collaboration with Asian countries and so that Japan will be able to take the lead in international standardization (ISO/IEC and other standards), PMDA visited Taiwan, Singapore (co-chair country of AMDC [ASEAN Medical Device Committee]), and Thailand, one of the major countries, to exchange ideas with regulatory authorities on the utilization of specifications and standards. In these countries, PMDA also held seminars involving industry, disseminated information and raised awareness regarding the utilization of Japanese specifications and standards, in order to promote ongoing cooperation and collaboration among the regulatory authorities in Japan and Taiwan, Singapore, and Thailand.

- In addition to assuming the position of vice chair of the Working Group on GLP of OECD, PMDA dispatched an employee to the OECD as the person in charge of GLP, and thereby introduced PMDA's knowledge and know-how into international GLP-related activities (acting as chairperson from April 2016).
- PMDA has conducted mutual acceptance of GLP investigation results based on the OECD's mutual data acceptance system.
- PMDA exchanged opinions with representatives from relevant industries on expanding the scope of English-language data acceptable in product approval applications.

(iii) Promotion of personnel exchanges

Personnel exchange with FDA

- PMDA negotiated with U.S. FDA about the new dispatch of personnel and secured the opportunity to dispatch its staff to the fields PMDA had been targeting, including medical devices, clinical pharmacology, and CDISC.

Hosting of training seminars and symposiums

- PMDA held the PMDA Training Seminar (for drugs in October 2015 and for medical devices in February 2016) and took proactive steps to accept trainees from regulatory authorities and other organizations in Thailand and Malaysia, and provided trainees with necessary information on how the regulatory infrastructure could be improved, a topic that trainees were eager to learn about.
- PMDA held symposiums co-hosted by Brazil (September 2015) and Taiwan (November 2015) to promote understanding of Japanese pharmaceutical regulations among Asian countries.

(iv) Development of internationally-oriented human resources with excellent communication skills

Presentation in English and other events

- PMDA capitalized on opportunities to hold lectures and workshops at Drug Information Association (DIA), Regulatory Affairs Professionals Society (RAPS), and other events and made arrangements for presentations in English on the services provided by PMDA's departments.
- PMDA made efforts to foster internationally active persons by dispatching several employees to attend an educational program on inspections organized by EMA, and another program regarding drug regulations sponsored by the Maureen and Mike Mansfield Foundation.

Enrichment of English-language training

- PMDA improved English training courses in FY 2015 based on the evaluation of the courses offered in FY 2014. Specifically, PMDA changed eligibility criteria for participation and how much of training fee is covered by PMDA for individual training courses, depending on how much individual employees need English language skills for their work. Further, PMDA enhanced the quality and content of training programs.

(v) Improvement and strengthening of international publicity and provision of information

Providing information to foreign countries

- PMDA distributed monthly “PMDA Updates” to stakeholders concerned with the current status of the efforts being made by PMDA regarding international conferences or bilateral relationships, and posted this information on the PMDA website so that it could be broadcast widely and continuously to the general public including persons involved in foreign regulatory authorities.
- In FY 2015, PMDA received 417 inquiries (by email) from foreign countries and gave 397 responses. PMDA responded to inquiries from foreign countries by explaining its policies and activities.
- In addition, PMDA created content for its English website throughout the year to make information available.
- Further, PMDA set up a booths at the DIA Annual Meetings in Europe and the United States, as well as the DIA New Drug Development Conference (Japan), the DIA Japan Annual Meeting, and the RAPS Annual Meeting to publicize its activities.

Translation of review reports into English

- PMDA translated product review reports into English including drugs approved in Japan that may have an impact on foreign countries, posted them on its website, and announced the level of review for approval in Japan (40 products in FY 2015).
- PMDA posted English-language summaries of these reports by the Science Board on its English website. (These reports were (i) Proposal on Basic Principle to Quality Assurance of Cell Therapy [CT] Products, (ii) Discussions on Evaluation of Medical Devices in Pediatric Use, (iii) Report on the use of non-clinical studies in the regulatory evaluation of oncology drugs, (iv) Current Status and Perspectives of Placebo-controlled Studies, and (v) Report on the Use of Numerical Analysis for Strength Evaluation of Orthopedic Implants.) Report of above (iii) was submitted to and published in *Cancer Science*.
- Information on Projects Across Multi-offices for standards development is posted on the English website.
- The concept underlying regulations governing companion diagnostics in Japan was summarized by Companion Diagnostics WG, and submitted to and published in *Nature Biotechnology*.

3.4.(3) Measures for intractable diseases and orphan diseases, etc.

- In the Orphan Drug Working Group in Projects Across Multi-offices in PMDA, the Agency has been discussing methods for promoting orphan drug development by collaborating with MHLW and by exchanging information with EMA. In addition, PMDA invited the person in charge of orphan drugs in EMA in September to exchange information and opinions on how discussions should be advanced in the future.

- In Pediatric Drugs WG in Projects Across Multi-offices in PMDA, PMDA participated and gathered information in the working group on orphan drugs for pediatrics from five countries/regions: Japan, the United States, Europe, Canada, and Australia.

3.4.(4) Promoting provision of information such as review reports

a. Improving provision of information

- To encourage the proper use of drugs, medical devices, etc. and to ensure transparency of product reviews, PMDA releases information on reviews of product approval applications (e.g., review reports) on the PMDA website, in collaboration with MHLW and with the cooperation and understanding of relevant companies. In FY 2015, PMDA released new review reports and a summary of product applications for regenerative medical products, and review reports on designation for the use-results evaluation of medical devices.

b. Releasing information related to review reports

Review reports on new drugs

- New drugs fall into 1 of 2 categories, based on information submitted: those to be deliberated on by the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (referred to as "deliberation products"); and those to be reported to the Drug Committees of PAFSC (hereinafter referred to as "report products"). For "deliberation products," both "review reports" that describe details and results of reviews and "summaries of product applications" that summarize submitted data are subject to public release. For "report products," "review reports" are subject to public release. These documents are published on the PMDA website after conferring with the relevant companies regarding the content to be released for each product, based on a Notification Issued by the Evaluation and Licensing Division (ELD) of the Pharmaceutical and Food Safety Bureau (PFSB) at MHLW.
- In FY 2015, PMDA released 118 review reports, 79 summaries of product applications, and 53 re-examination reports.

  The percentage of review reports released within 1 month after approval was 100% (70% in FY 2014) and the percentage of summaries of product applications released within 3 months after approval was 100% (94% in FY 2014).

  Note: The median times from approval (for re-examination reports, from notification of results) to release were 1 day for review reports, 32 days for summary of product applications, and 6 days for re-examination reports.

Review reports on new medical devices

- In FY 2015, PMDA released 16 review reports, 17 summaries of product applications and 15 re-examination reports for new medical devices.

  The percentage of review reports released within one month after approval was 93% (44% in FY 2014) and the percentage of summaries of product applications released within 3 months after approval was 94% (38% in FY 2014).

  Note: The median times from approval (for re-examination reports, from notification of results) to release were 17 days for review reports, 72 days for summary of product applications, and 7 days for re-examination reports.

Review reports on new regenerative medical products

- In FY 2015, PMDA released 2 review reports and 2 summaries of product applications for new regenerative medical products.

Review reports on BTC drugs and quasi-drugs

- In FY 2015, PMDA released 2 review reports and 2 summaries of product applications for BTC drugs, and 3 review reports and 2 summaries of a product application for quasi-drugs.

Number of review reports released

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
New drugs	132	121	120	130	118
New medical devices	12	11	19	9	16
New regenerative medical products	-	-	-	-	2
BTC and OTC drugs	5	5	5	3	2
Quasi-drugs	0	0	0	1	3

3.4.(5) Ensuring the impartiality of judgments by external experts

- It is necessary to take steps to ensure impartiality and transparency in the judgments made by external experts commissioned by PMDA. The “Rules for Convening Expert Discussions etc., by the Pharmaceuticals and Medical Devices Agency” (December 25, 2008; revised on February 16, 2016) was set forth to ensure transparency of PMDA's services by releasing review reports and information on conflicts of interest among commissioned external experts, thereby allowing outside parties to verify the decision-making process. In accordance with the rules, PMDA discloses cash contributions and contract payments received by external experts commissioned by PMDA for Expert Discussions on reviews and safety measures. The disclosure is made immediately after confirmation of approval of new product applications, the development of safety measures, or the development of approval standards or review guidelines for drugs, etc. Disclosed information is reported to the Advisory Council and the Committee on Review and Safety Operations.

3.4.(6) Provision of training in specially-controlled medical device certification standards

- In conjunction with the establishment of specially controlled medical device certification standards (3 standards), reviewers at the registered certification bodies were trained by PMDA to conduct product certification review and compliance assessments based on the standards.

3.4.(7) Improvement of quality of reviews/safety operations through enhancement of information systems

- Since August 25, 2014, PMDA has been operating an application/review computer system that was designed based on the Optimization Plan for Operations and Systems and improved the system by fixing the order of priority necessary for its operation. For example, data in the system was updated. (Specifically, the name of a MHLW department was updated from “Pharmaceutical and Food Safety Bureau” to “Pharmaceutical Safety and Environmental Health Bureau” in accordance with organizational change in MHLW.) In January 2016, PMDA began the pilot test associated with development of an electronic data system for applications. In addition, on March 31, 2016, PMDA issued "Points to Consider for Reports on Post-marketing Adverse Drug Reactions and Reports on Clinical Trial Adverse Drug Reactions," for implementation of E2B/R3 and took actions for operation of the system.

- Final decision documents for regulatory approval of drugs, etc., clinical trial notifications for agents and devices, etc., were converted into digital image data to reduce storage space and enable long-term storage. Review process was streamlined and accelerated by using the search function for digital image data.
- Based on requests from Osaka prefecture, the Osaka Pharmaceutical Manufacturers Association, the Osaka Chamber of Commerce and Industry, and the Kansai Economic Federation, PMDA started a teleconference consultation system at its Kansai Branch and improved the quality and availability of consultation services for applicants based in the Kansai area. After making arrangements with Osaka prefecture and other organizations, PMDA prepared for the start of operations in FY 2016, including relocating the Kansai Branch in order to add additional conference rooms and to seek bids for the provision and installation of a teleconferencing system.
- PMDA modified the application/review and the new eCTD viewer systems for managing interactions between the systems and the electronic application data system. For the start of acceptance of application data via the gateway from autumn 2016, the systems began to operate under the environment for verification and started the pilot test involving applicant companies from January 2016.
- PMDA created eCTD ver. 4.0 following progress in relevant discussions at ICH, and offered a free release in FY 2014. PMDA also offered without charge a revised tool to simplify the viewing of electronic application data.

III. SUPPLEMENTARY INFORMATION

Reviews and Safety Measure Services

1. New drug application review services

Number of approved products

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Prescription drugs	3,592	3,898	4,003	3,944	3,664
BTC and OTC drugs	1,031	881	916	844	752
In vitro diagnostics	173	147	166	109	172
Quasi-drugs	1,938	1,968	2,028	1,779	2,495
Cosmetics	0	0	0	0	0
Total	6,734	6,894	7,113	6,676	7,083

Number of approved new drug applications

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of approved new drug applications	130	134	138	118	116
Priority review products among these new drugs	50	53	42	44	37

Reference 1 Approved new drug applications (FY 2015)

	FY 2015	
		Filed in or after FY 2004 (included in left figures)
Overall		
Number of approved applications	116	116
Total review time (months)	10.8	10.8
60th percentile	11.2	11.2
70th percentile		
Regulatory review time (months)	5.5	5.5
60th percentile	6.7	6.7
70th percentile		
Applicant's time (months)	5.0	5.0
60th percentile	5.5	5.5
70th percentile		

Note: The above table includes applications filed in or before March 2004, which are excluded from targets in the Third Mid-term Plan.

Reference 2 Approved new drug applications (only those with new active ingredients)

Total review time for new drugs (priority review products)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	60
Total review time (months)	9.7	9.0	9.1	*9.1*	*9.5*
Number of approved applications	11	17	15	24	17

Reference

Regulatory review time (months)	3.6	3.3	3.4	3.8	3.8
Applicant's time (months)	5.3	4.6	5.3	5.4	6.0

Note: Figures are calculated based on the products (drugs with new active ingredients) for which applications were filed in or after FY 2004.

Total review time for new drugs (standard review products)

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Percentile	50	50	50	60	70
Total review time (months)	12.2	11.2	11.9	*12.1*	*11.2*
Number of approved applications	30	27	24	28	25

Reference

Regulatory review time (months)	5.8	5.5	6.2	*6.5*	*5.9*
Applicant's time (months)	6.7	5.6	5.4	6.5	6.7

Note: Figures are calculated based on the products (drugs with new active ingredients) for which applications were filed in or after FY 2004.

Reference 3 Review Time Targets of Third Mid-term Plan

Priority review products

Fiscal year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time (months)	9	9	9	9	9
Percentile	60	60	70	70	80

Standard review products

Fiscal year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time (months)	12	12	12	12	12
Percentile	60	70	70	80	80

Application and approval status of BTC and OTC drugs and quasi-drugs by category

BTC and OTC drugs

New application categories	1	2	3-1	3-2	3-3	4	5-1	5-2	5-3	5-4	6	7-1	7-2	8	Total
Products filed in FY 2015	0	0	0	1	0	8	0	3	0	4	6	34	8	637	701
Products approved in FY 2015	0	0	0	0	0	11	0	0	2	3	6	68	17	596	703

Former application categories	1	2	3	4-1	4-2	OTC test agents	Total
Products approved in FY 2015	0	0	0	0	3	0	3

Note 1: Application categories for BTC and OTC drugs were revised on January 1, 2009. In the table above, the numbers 1, 2, 3, 4-1, and 4-2 are the "former category" before the revision.

Note 2: Application categories for BTC and OTC drugs:

<Former categories> 1: Drugs with new active ingredients (Direct OTC drugs)
2: Drugs with new active ingredients for OTC (Switch OTC drugs)
3: Relatively innovative drugs excluding the above "1" and "2"
4-1: Other drugs (Relatively less innovative drugs)
4-2: Other drugs (Drugs that are not innovative)

<New categories> 1: Drugs with 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 a new dosage
4: BTC (OTC) drugs with new active ingredients (Switch OTC drugs)
5-1: BTC (OTC) drugs with new routes of administration
5-2: BTC (OTC) drugs with new indications
5-3: OTC (BTC) drugs in new dosage forms
5-4: OTC (BTC) drugs with a new dosage
6: New OTC (BTC) 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)

Application category	Pest control agents	Total
Products filed in FY 2015	17	17
Products approved in FY 2015	46	46

Note 3: The product category containing pest control agents was revised on November 25, 2014; however, this category is similar to the former category containing insecticides/antimicrobial agents. Accordingly, the above figures cover both product categories.

Quasi-drugs

New application categories	1	2-1	2-2	2-3	2-4	2-5	3	4	5-1	5-2	5-3	Total
Products filed in FY 2015	2	1	1	27	6	3	14	475	1,808	57	51	2,445
Products approved in FY 2015	0	0	0	0	2	4	4	431	1,512	24	20	1,997

Former application categories	1 and 3	2	Total
Products approved in FY 2015	49	364	413

Note 4: The application categories for quasi-drugs were revised on November 25, 2014. The figures for "1," "2," and "3" in the above table represent the number of products approved under the former categories before the revision.

Note 5: Application categories for quasi-drugs:

<Former categories> 1: Products that contain a new active ingredient
2: Products that are not innovative
3: Innovative products excluding the above "1"

<New categories> 1: Quasi-drugs with new active ingredients
2-1: Quasi-drugs with new indications
2-2: Quasi-drugs in new dosage forms
2-3: Quasi-drugs with new strengths
2-4: New combination quasi-drugs
2-5: Quasi-drugs with new routes of administration
3: Quasi-drugs containing new excipients
4: Similar quasi-drugs
5-1: Identical quasi-drugs
5-2: Newly designated quasi-drugs
5-3: Newly categorized quasi-drugs

Note 6: The numbers of "Products filed in FY 2015" were calculated by category at the time of filing.

Note 7: The numbers of "Products approved in FY 2015" were calculated by category at the time of approval.

Note 8: The numbers of quasi-drugs in former application categories include pest control agents.

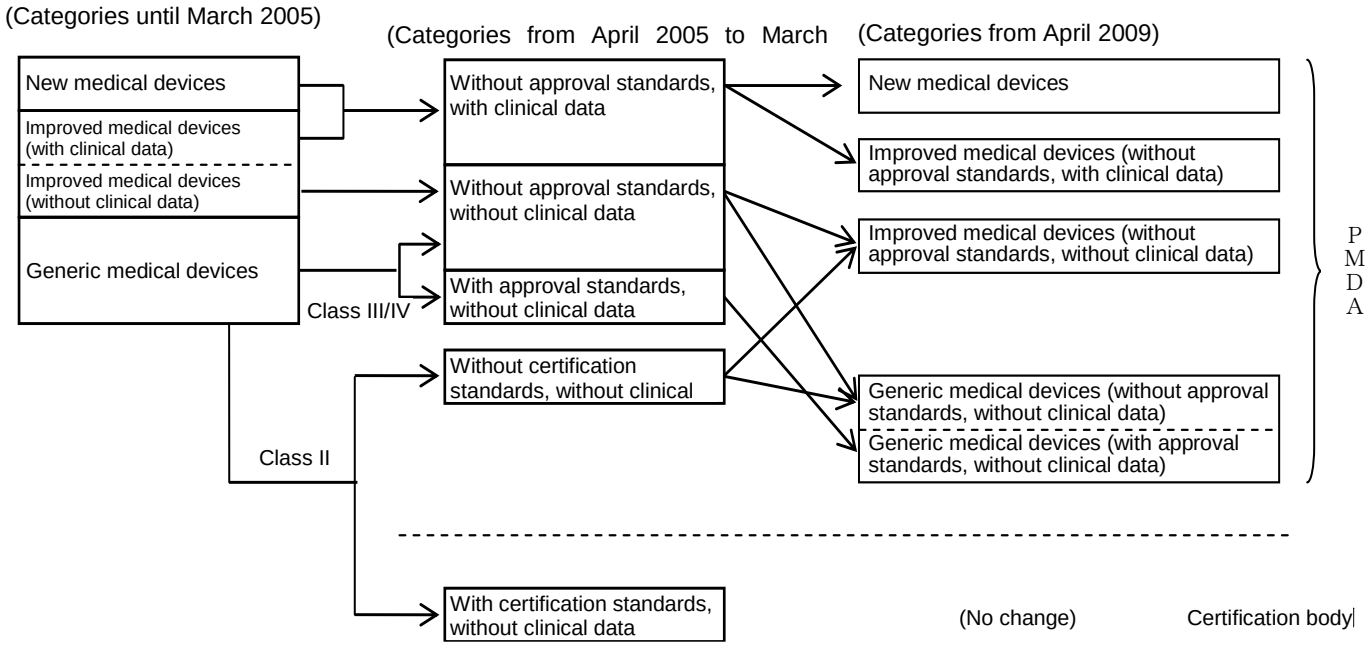
Application category	Quasi-drugs for pest control	Total
Products filed in FY 2015	114	114
Products approved in FY 2015	85	85

Note 9: The category for quasi-drugs and pest control agents was established on November 25, 2014.

2. Medical device and *in vitro* diagnostic review services

2.(1) Changes in application categories

In accordance with the enactment of the revised Pharmaceutical Affairs Act in April 2005, the former application categories were revised based on the clinical data or approval standards available. With regard to medical devices certified according to the certification standards established by the Minister of Health, Labour and Welfare, the entity that certifies such medical devices was changed from the Minister of Health, Labour and Welfare to third-party certification bodies.



Note: Roman numerals II, III, and IV indicate the classification of medical devices based on risk. If a malfunction occurs, class II medical devices have relatively low risk to the human body; class III medical devices have relatively high risk to the human body; and malfunctions of class IV medical devices may directly lead to life-threatening conditions.

Since the enactment of the Pharmaceutical Affairs Act in April 2005, Class II medical devices have been classified as controlled medical devices and class III/IV medical devices as specially controlled medical devices.

Number of approved medical devices

		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Medical devices		1,227	1,535	1,347	1,235	1,217
Priority review products (included in above figures)		6	5	14	5	8*
Re-listed	New medical devices	33	46	94	67	56
	Improved medical devices (with clinical data) (From FY 2009 onward)	44	37	60	35	53
	Improved medical devices (without clinical data) (From FY 2009 onward)	186	218	227	213	240
	Generic medical devices (From FY 2009 onward)	874	1,191	943	917	868
	Without approval standards, with clinical data	11	7	1	0	0
	Without approval standards, without clinical data	42	30	17	3	0
	With approval standards, without clinical data	0	0	1	0	0
	Controlled medical devices (without approval and certification standards, without clinical data)	21	4	1	0	0
	Improved medical devices (until FY 2004)	14	1	3	0	0
	Generic medical devices (until FY 2004)	2	1	0	0	0

**A total of 8 new medical devices are included.*

Reference 1 Approved new medical device applications (FY 2015)

	FY 2015	
		Filed in or after FY 2004 (included in left figures)
Overall		
Number of approved applications	56	56
Total review time (months) (60th percentile)	9.7	9.7
Regulatory review time (months) (60th percentile)	4.8	4.8
Applicant's time (months) (60th percentile)	4.3	4.3

Note: Reviews of all medical device applications filed in or before March 2004 (i.e., before the beginning of the term of the Third Mid-term Plan) had been completed before FY 2015. Therefore, the right and left figures are the same.

Reference 2 Approved new medical device applications and their review times

	FY 2012			FY 2013		
	Total	New	Partial change	Total	New	Partial change
New medical devices (Priority and standard review products)	46	27	19	94	51	43
Number of approved applications	12.5	14.9	3.5	6.7	13.5	3.3
Median total review time (months)	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Achievement rate	5.4	7.8	1.7	4.8	6.1	2.0
Median regulatory review time (months)	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Achievement rate						
Priority review products						
Number of approved applications	5	2	3	14	11	3
Median total review time (months)	9.3	33.4	8.8	9.0	9.6	5.2
Achievement rate	(80%)	(50%)	(100%)	(86%)	(82%)	(100%)
Median regulatory review time (months)	7.2	10.1	5.4	5.1	5.5	4.6
Achievement rate	(40%)	(0%)	(67%)	(71%)	(64%)	(100%)
Standard review products						
Number of approved applications	41	25	16	80	40	40
Median total review time (months)	12.7	14.9	3.4	6.3	13.8	3.2
Achievement rate	(90%)	(84%)	(100%)	(79%)	(58%)	(100%)
Median regulatory review time (months)	5.4	7.7	1.7	4.0	6.4	2.0
Achievement rate	(68%)	(48%)	(100%)	(74%)	(53%)	(95%)

	FY 2014			FY 2015		
	Total	New	Partial change	Total	New	Partial change
New medical devices (Priority and standard review products)	67	24	43	56	22	34
Number of approved applications	5.6	8.9	4.3	9.7	10.5	6.9
Total review time (months) (60th percentile)	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Achievement rate	3.5	4.8	2.9	4.8	4.8	4.8
Regulatory review time (months) (60th percentile)	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Achievement rate						
Priority review products						
Number of approved applications	5	2	3	8	6	2
Total review time (months) (60th percentile)	8.8	8.9	5.4	7.9	8.1	7.2
Achievement rate	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)
Regulatory review time (months) (60th percentile)	4.0	5.6	2.8	4.2	4.1	4.2
Achievement rate	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)
Standard review products						
Number of approved applications	62	22	40	48	16	32
Total review time (months) (60th percentile)	5.6	9.1	4.2	10.1	11.9	6.9
Achievement rate	(98%)	(96%)	(100%)	(88%)	(75%)	(94%)
Regulatory review time (months) (60th percentile)	3.5	4.8	2.9	5.0	5.4	4.9
Achievement rate	(94%)	(96%)	(93%)	(85%)	(75%)	(91%)

Note 1: Applications filed in or after April 2004 are covered.

Note 2: Review time targets of the First Mid-term Plan

Priority review products

Review process for 70% of applications should be completed within 9 months.

Overall and standard review products

Review process should be completed within 12 months for the following percentages of applications: FY 2004, 70%; FYs 2005 and 2006, 80%; and FYs 2007 and 2008, 90%

Target Review Times of the Second Mid-term Plan

The review times shown in the following table should be achieved for 50% (median) of products.

Priority review products

Fiscal year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time (months)	16	16	15	13	10
Regulatory review time (months)	8	8	7	7	6
Applicant's time (months)	9	9	8	6	4

Standard review products

Fiscal year	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total review time (months)	21	21	20	17	14
Regulatory review time (months)	8	8	8	7	7
Applicant's time (months)	14	14	12	10	7

Reference 3 Review Time Targets of Third Mid-term Plan

Priority review products

Fiscal year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time (months)	10	10	10	10	10
Percentile	60	60	70	70	80

Standard review products

Fiscal year	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Total review time (months)	14	14	14	14	14
Percentile	60	60	70	70	80

Reference 4 Medical devices approved based on clinical trial results

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of medical devices with foreign clinical trial results	43 (5)	26 (3)	42 (8)	30 (2)	34 (11)
Number of medical devices with Japanese clinical trial results	14	23	24	11	24

Note 1: The figures in parentheses indicate the number of medical devices with both Japanese and foreign clinical trial results (included in left figures).

Note 2: In FY 2015, 21 medical devices were approved based on clinical evaluation reports, in addition to the 58 medical devices presented in this table.

2.(2) Review service for *in vitro* diagnostic products

(i) Approved *in vitro* diagnostic products and their review times

PMDA reviews and approves applications of *in vitro* diagnostics (drugs exclusively used to diagnose diseases). Approximately 71% (122 of 172 products) of *in vitro* diagnostics applications approved in FY 2015 were processed within the standard administrative processing period (6 months).

Approved *in vitro* diagnostics applications and their review times

	FY 2011	Filed in or after FY 2004 (included in left figures)	FY 2012	Filed in or after FY 2004 (included in left figures)	FY 2013	Filed in or after FY 2004 (included in left figures)
Number of approved applications	173	173	147	147	166	166
Median total review time (months)	7.4	7.4	6.0	6.0	5.4	5.4
Median regulatory review time (months)	4.1	4.1	3.4	3.4	2.7	2.7
Achievement rate	(76%)	(76%)	(69%)	(69%)	(81%)	(81%)

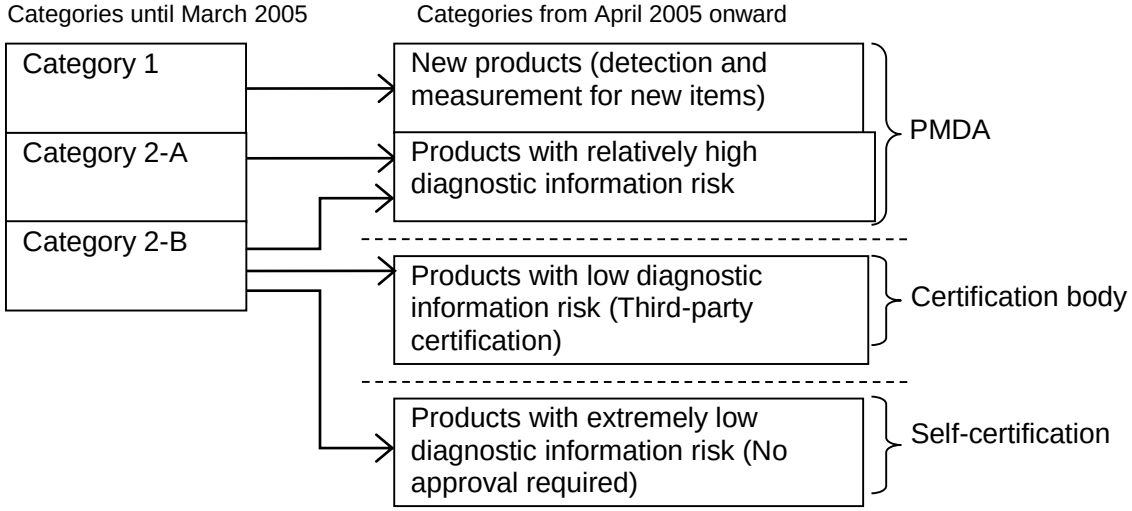
	FY 2014	Filed in or after FY 2004 (included in left figures)	FY 2015	Filed in or after FY 2004 (included in left figures)
Number of approved applications	109	109	172	172
Median total review time (months)	5.3	5.3	7.2	7.2
Median regulatory review time (months)	2.6	2.6	3.9	3.9
Achievement rate	(80%)	(80%)	(71%)	(71%)

Note 1: Percentages in parentheses indicate achievement rates of regulatory target review time (i.e., the percentage of applications for which the review was completed within 6 months.)

Note 2: The numbers of approved applications are calculated based on the products filed on or after April 1, 2002.

(ii) Changes in application categories

After the revision of the Pharmaceutical Affairs Act which came into effect in April 2005, the former application categories were changed to new ones defined according to the level of diagnostic information risk. *In vitro* diagnostics with an extremely low diagnostic information risk were transferred from the Minister's approval system to a self-certification system. Formerly, the Minister of Health, Labour and Welfare approved *in vitro* diagnostics with low diagnostic information risk for which the certification standards have been developed; this approval system was changed to a third-party certification system.



3 Other review-related services

3.(1) Survey services related to clinical trial notifications

PMDA has been conducting surveys on clinical trial notifications for new active ingredients (APIs categorized as new drugs), new medical devices, and new regenerative medical products in order to ensure subject safety. Surveys on clinical trial notifications for new medical devices started in April 2005 and for new regenerative medical products in November 2014.

(i) The status of initial clinical trial notifications for drugs in FY 2015 is as follows: 127 notifications submitted, surveys on 132 notifications completed, and 6 notifications withdrawn.

(ii) In FY 2015, the clinical trial notifications for drugs (i.e., notifications other than initial clinical trial notification) consisted of 530 nth clinical trial notifications, 4,566 protocol change notifications, 507 trial completion notifications, 70 trial discontinuation notifications, and 102 development discontinuation notifications.

Number of clinical trial notifications for drugs

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Initial clinical trial notification	165 (3)	132 (13)	127 (6)	151 (20)	127 (10)
n-th clinical trial notification	524 (56)	424 (19)	474 (25)	450 (33)	530 (45)
Protocol change notification	3,997	4,568	4,356	4,321	4,566
Trial completion notification	497	495	446	498	507
Trial discontinuation notification	46	57	61	67	70
Development discontinuation notification	80	70	78	117	102
Total	5,309	5,746	5,542	5,604	5,902

Note 1: The figures in parentheses indicate the number of notifications of "investigator-initiated clinical trials."

Note 2: Miscalculations were identified for the following figures, which have been corrected.

Change notification

FY 2011 4,011 to 3,997
FY 2012 4,571 to 4,568
FY 2013 4,357 to 4,356
FY 2014 4,322 to 4,321

Completion notification

FY 2011 483 to 497
FY 2012 492 to 495
FY 2013 445 to 446
FY 2014 497 to 498

(iii) The status of initial clinical trial notifications for equipment/devices in FY 2015 is a follows: 31 notifications submitted, surveys on 29 notifications completed, and 1 notification withdrawn.

(iv) In FY 2015, clinical trial notifications for equipment/devices consisted of 10 nth clinical trial notifications, 283 protocol change notifications, 22 trial completion notifications, 5 trial discontinuation notifications, and 2 development discontinuation notifications.

Number of clinical trial notifications for equipment/devices

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Initial clinical trial notification	25 (3)	32 (2)	31 (4)	31 (7)	31 (8)
nth clinical trial notification	4 (0)	11 (1)	14 (0)	6 (2)	10 (0)
Protocol change notification	173	227	253	240	283
Trial completion notification	31	21	30	33	22
Trial discontinuation notification	3	0	6	6	5
Development discontinuation notification	3	0	6	2	2
Total	239	291	340	318	353

Note: The figures in parentheses indicate the number of notifications of "investigator-initiated clinical trials."

(v) The status of initial clinical trial notifications for processed cells in FY 2015 is as follows: 10 notifications submitted, surveys on 5 notifications completed, and 3 notifications withdrawn.
(vi) In FY 2015, the clinical trial notifications for processed cells consisted of 3 n-th clinical trial notifications and 19 protocol change notifications, with no trial completion notifications, trial discontinuation notifications, or development discontinuation notifications.

Number of clinical trial notifications for processed cells, etc.

	FY 2014	FY 2015
Initial clinical trial notification	3 (1)	10 (2)
N-th clinical trial notification	1 (1)	3 (2)
Protocol change notification	2	19
Trial completion notification	0	0
Trial discontinuation notification	0	0
Development discontinuation notification	0	0
Total	6	32

Note: The figures in parentheses indicate the number of notifications of "investigator-initiated clinical trials."

3.(2) Survey service for adverse reaction reports from clinical trials

PMDA examines information regarding reported adverse reactions to drugs, devices, and processed cells, and can request the sponsors, etc. via MHLW to consider taking such actions as discontinuation of clinical trials if deemed necessary. In FY 2015, 86,039 reports on adverse drug reactions were reported during clinical trials. Of these reports, 1,339 were reported during Japanese clinical trials.

Adverse drug reaction reports during clinical trials

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of ADR reports during clinical trials	38,465	55,534	58,275	71,689	86,039
(In Japan)	657	891	780	910	1,339
(Outside Japan)	37,808	54,643	57,495	70,779	84,700

Note 1: The figures represent the initial reports of case reports, research reports, safety measure reports, and other reports.

Note 2: Electronic report submission started on October 27, 2003. According to the change of the reporting method, the first follow-up reports submitted on or after October 27, 2003 are classified as initial reports" even though actual initial reports had already been filed before the date. On or after the date, one report for co-development product should be submitted by each company.

In FY 2015, the number of malfunction reports on devices during clinical trials was 2,966.

Device malfunction reports from clinical trials

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Number of malfunction reports from clinical trials	861	1,055	1,518	2,119	2,966

Note 1: The figures represent the initial reports of case reports, research reports, action reports, and other reports.
Note 2: Electronic report submission has been required since July 1, 2014. According to the change of the reporting method, the first follow-up reports submitted on or after July 1, 2014 are classified as initial reports" even though actual initial reports had had already been filed before the date.

In FY 2015, 50 malfunction reports related to processed cells were submitted during clinical trials.

Number of malfunction reports on processed cells during clinical trials

	FY 2014	FY 2015
Number of malfunction reports during clinical trials	0	50

Note: The figures represent the initial reports of case reports, research reports, action reports, and other reports.

3.(3) Registration service for the drug master file

The Drug Master File (DMF) contains information regarding the manufacturing of drug substances for which DMF registration applications were filed by the manufactures of the drugs substances (since April 2005).

In FY 2015, 2,019 applications for DMF registration were filed (i.e., applications for registration, applications for a change of registration, minor change notifications, applications for renewal/issue of registration certificate, notifications of succession of registration, and applications for re-issue of registration), and 502 applications were registered in the DMF.

Number of DMF registration applications filed and registered

	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Applications filed	1,474	1,562	1,918	2,017	2,019
Applications registered	273	341	387	443	502

Note: "Applications registered" consists of applications for DMF registrations and change registrations, including carry-over applications from the previous fiscal year.

Table 1. Number of Drugs, etc. Filed and Approved (FY2011 – FY 2015)

Category			Number of products filed					Number of products approved				
		Fiscal Year	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
Drugs, etc.	New drugs	New	125	157	142	115	162	115	128	160	142	109
		Partial change	366	402	326	364	350	408	377	344	362	320
		Total	491	559	468	479	512	523	505	504	504	429
	Generic drugs	New	1,154	1,764	1,467	1,166	905	1,185	1,539	1,438	1,325	635
		Partial change	1,738	2,313	2,424	2,286	2,595	1,906	1,882	2,066	2,122	2,600
		Total	2,892	4,077	3,891	3,452	3,500	3,091	3,421	3,504	3,447	3,235
	BTC/OTC drugs	New	748	784	747	671	523	725	619	657	638	589
		Partial change	382	221	266	211	195	306	262	259	206	163
		Total	1,130	1,005	1,013	882	718	1,031	881	916	844	752
	In vitro diagnostics	New	96	70	51	89	83	87	71	69	40	80
		Partial change	81	95	85	74	113	86	76	97	69	92
		Total	177	165	136	163	196	173	147	166	109	172
	Quasi-drugs	New	1,981	1,923	2,002	1,666	2,329	1,678	1,784	1,763	1,631	2,322
		Partial change	231	194	296	162	230	260	184	265	148	173
		Total	2,212	2,117	2,298	1,828	2,559	1,938	1,968	2,028	1,779	2,495
	Cosmetics	New	0	0	0	0	0	0	0	0	0	0
		Partial change	0	0	0	0	0	0	0	0	0	0
		Total	0	0	0	0	0	0	0	0	0	0
Total		New	4,104	4,698	4,409	3,707	4,002	3,790	4,141	4,087	3,776	3,735
		Partial change	2,798	3,225	3,397	3,097	3,483	2,966	2,781	3,031	2,907	3,348
		Total	6,902	7,923	7,806	6,804	7,485	6,756	6,922	7,118	6,683	7,083

Note 1: The number of product applications filed in FY 2015 and their application categories are as of April 7, 2016. The number of product applications and their application categories may be changed if the categories are revised after filing of application.

Note 2: The number of products filed was calculated based on the date of application.

Note 3: The figures in "New drugs" represent the number of products, including products classified into "administrative review category." The same applies to the other categories.

Table 2. Number of Medical Devices Filed and Approved (FY 2011 – FY 2015)

Year \ Fiscal		Number of products filed					Number of products approved				
		FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015
New medical devices	New	26	36	28	37	14	14	27	51	24	22
	Partial change	16	28	44	63	16	19	19	43	43	34
	Total	42	64	72	100	30	33	46	94	67	56
Improved medical devices (with clinical data) (in or after FY 2009)	New	26	37	36	36	23	32	32	54	27	43
	Partial change	0	5	10	9	4	12	5	6	8	10
	Total	26	42	46	45	27	44	37	60	35	53
Improved medical devices (without clinical data) (in or after FY 2009)	New	131	172	137	194	144	129	159	172	156	151
	Partial change	47	40	50	68	74	57	59	55	57	89
	Total	178	212	187	262	218	186	218	227	213	240
Generic medical devices (in or after FY 2009)	New	405	341	375	418	319	368	402	355	396	351
	Partial change	591	737	544	544	469	506	789	588	521	517
	Total	996	1,078	919	962	788	874	1,191	943	917	868
Medical devices (with clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	9	7	1	0	0
	Partial change	-	-	-	-	-	2	0	0	0	0
	Total	-	-	-	-	-	11	7	1	0	0
Medical devices (without approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	30	15	6	0	0
	Partial change	-	-	-	-	-	12	15	11	3	0
	Total	-	-	-	-	-	42	30	17	3	0
Medical devices (with approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	0	0	1	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	0	0	1	0	0
Controlled medical device (without approval standards and certification standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	11	4	1	0	0
	Partial change	-	-	-	-	-	10	0	0	0	0
	Total	-	-	-	-	-	21	4	1	0	0
Improved medical devices (in or before FY 2004)	New	-	-	-	-	-	4	1	2	0	0
	Partial change	-	-	-	-	-	0	0	1	0	0
	Total	-	-	-	-	-	4	1	3	0	0
Improved medical devices (humans, animals, etc.) (in or before FY 2004)	New	-	-	-	-	-	0	0	0	0	0
	Partial change	-	-	-	-	-	10	0	0	0	0
	Total	-	-	-	-	-	10	0	0	0	0
Generic medical devices (in or before FY 2004)	New	-	-	-	-	-	2	1	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	2	1	0	0	0
Total	New	588	586	576	685	500	599	648	643	603	567
	Partial change	654	810	648	684	563	628	887	704	632	650
	Total	1,242	1,396	1,224	1,369	1,063	1,227	1,535	1,347	1,235	1,217

Note 1: The number of product applications filed in FY 2015 and their application categories are as of April 7, 2016. The number of product applications and their application categories may be changed if the categories are revised after filing of application.

Note 2: The number of products filed was calculated based on the date of application.

Note 3: The number of products approved was calculated according to the categories at the time of approval based on fiscal year of application.

Table 3. Number of Regenerative Medical Products Filed and Approved (FY 2014 – FY 2015)

Category \ Fiscal year		Number of products filed		Number of products approved	
		FY 2014	FY 2015	FY 2014	FY 2015
Cellular and Tissue-based Products	New	2	0	0	2
	Partial change	0	3	0	2
	Total	2	3	0	4

Note 1: The number of products filed was calculated based on the date of application.

Note 2: The figures in the table represent the number of products, including products classified into "administrative review category."

Table 4. Products Approved in FY 2015: New Drugs

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	May 26, 2015	1	Irribow Tablets 2.5 μg Irribow Tablets 5 μg Irribow OD Tablets 2.5 μg Irribow OD Tablets 5 μg (Astellas Pharma Inc.)	Change Change Change Change	Ramosetron hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of diarrhea-predominant irritable bowel syndrome in women.
1	Jul. 3, 2015	2	Xiaflex Inj. (Asahi Kasei Pharma Corporation)	Approval	Collagenase *(Clostridium histolyticum)*	A drug with a new active ingredient indicated for the treatment of Dupuytren's contracture.
1	Sep. 28, 2015	3	P-Tol Chewable Tab. 250 mg P-Tol Chewable Tab. 500 mg (Kissei Pharmaceutical Co., Ltd.)	Approval Approval	Sucroferric oxyhydroxide	Drugs with a new active ingredient indicated for the improvement of hyperphosphatemia in patients with chronic kidney disease who are receiving dialysis.
1	Sep. 28, 2015	4	Zagallo Capsules 0.1 mg Zagallo Capsules 0.5 mg (GlaxoSmithKline K.K.)	Approval Approval	Dutasteride	A drug with a new indication and a new dosage in an additional dosage form, and a drug with a new indication and a new dosage, indicated for the treatment of the male pattern hair loss (androgenetic alopecia) in men.
1	Nov. 20, 2015	5	kenketu Glovenin-I for I.V. Injection 500 mg kenketu Glovenin-I for I.V. Injection 2500 mg kenketu Glovenin-I for I.V. Injection 5000 mg (Nihon Pharmaceutical Co., Ltd.)	Change Change Change	Freeze-dried polyethylene glycol treated human normal immunoglobulin	Drugs with a new additional indication for the treatment of bullous pemphigoid (for use when steroid drugs are not sufficiently effective).
1	Feb. 29, 2016	6	Rituxan Injection 10 mg/mL (Zenyaku Kogyo Co., Ltd.)	Change	Rituximab (genetical recombination)	A drug with a new additional indication and a new dosage for prophylaxis of antibody-mediated rejection in patients who underwent ABO-incompatible kidney or liver transplantation. [Orphan drug]
1	Feb. 29, 2016	7	Kiklin Capsules 250 mg (Astellas Pharma Inc.)	Change	Bixalomer	A drug with a new expanded indication for the improvement of hyperphosphatemia in patients with chronic kidney disease.
1	Mar. 18, 2016	8	Proemend for Intravenous Infusion 150 mg (Ono Pharmaceutical Co., Ltd.)	Change	Fosaprepitant meglumine	A drug with new additional pediatric dosages indicated for the treatment of gastrointestinal symptoms (nausea and vomiting, including delayed phase) associated with administration of antineoplastic drugs (cisplatin, etc.).
1	Mar. 28, 2016	9	Marduox Ointment (Chugai Pharmaceutical Co., Ltd.)	Approval	Maxacalcitol / Betamethasone butyrate propionate	A new combination drug indicated for the treatment of psoriasis vulgaris.
2	Jun. 26, 2015	10	Livalo Tablets 1 mg Livalo Tablets 2 mg Livalo OD Tablets 1 mg Livalo OD Tablets 2 mg (Kowa Company, Ltd.)	Change Change Change Change	Pitavastatin calcium	Drugs with a new additional pediatric dosage indicated for the treatment of familial hypercholesterolemia.
2	Aug. 24, 2015	11	Tracleer Tablets 62.5 mg (Actelion Pharmaceuticals Japan Ltd.)	Change	Bosentan hydrate	A drug with a new additional indication for inhibiting development of digital ulcer in patients with systemic scleroderma (only for patients who currently have digital ulcers or have a history of digital ulcer.) [Orphan drug]
2	Aug. 24, 2015	12	INOflo for Inhalation 800 ppm (INO Therapeutics LLC)	Change	Nitric oxide	A drug with a new additional indication and a new dosage for the improvement of pulmonary hypertension in the perioperative period of cardiac surgery. [Orphan drug]
2	Aug. 24, 2015	13	Artist Tablets 2.5 mg Artist Tablets 10 mg Artist Tablets 20 mg (Daiichi Sankyo Company, Limited)	Change Change Change	Carvedilol	Drugs with a new additional indication and a new dosage for the treatment of tachycardiac atrial fibrillation.
2	Aug. 24, 2015	14	Exelon Patch 4.5 mg Exelon Patch 9 mg Exelon Patch 13.5 mg Exelon Patch 18 mg (Novartis Pharma K.K.) Rivastach Patch 4.5 mg Rivastach Patch 9 mg Rivastach Patch 13.5 mg Rivastach Patch 18 mg (Ono Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change Change	Rivastigmine	Drugs with a new dosage indicated for inhibiting progression of symptoms of dementia in mild and moderate Alzheimer's dementia.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	Sep. 24, 2015	15	Xarelto Tablets 10 mg Xarelto Tablets 15 mg (Bayer Yakuhin, Ltd.)	Change Change	Rivaroxaban	Drugs with a new additional indication and a new dosage for the treatment and prevention of recurrence of deep vein thrombosis and pulmonary thromboembolism.
2	Sep. 28, 2015	16	Mulpleta Tablets 3 mg (Shionogi & Co., Ltd.)	Approval	Lusutrombopag	A drug with a new active ingredient indicated for the improvement of thrombocytopenia in patients with chronic liver disease for whom an elective invasive procedure is planned.
2	Sep. 28, 2015	17	Ventavis inhalation solution 10 μg (Bayer Yakuhin, Ltd.)	Approval	Iloprost	A drug with a new active ingredient indicated for the treatment of pulmonary arterial hypertension.
2	Sep. 28, 2015	18	Tracleer pediatric dispersible tablets 32 mg (Actelion Pharmaceuticals Japan Ltd.)	Approval	Bosentan hydrate	A drug with a new indication and a new dosage in a new additional dosage form indicated for the treatment of pulmonary arterial hypertension. [Orphan drug]
2	Dec. 21, 2015	19	Eliquis Tablets 2.5 mg Eliquis Tablets 5 mg (Bristol-Myers K.K.)	Change Change	Apixaban	Drugs with a new additional indication and a new dosage for the treatment and prevention of the recurrence of venous thromboembolism (deep vein thrombosis and pulmonary thromboembolism).
2	Dec. 21, 2015	20	FP-OD Tablet 2.5 (FP Pharmaceutical Corporation)	Change	Selegiline hydrochloride	A drug with a revised indication and a new dosage for the treatment of Parkinson's disease (When used in combination with levodopa-containing products; patients are classified as Stage I to IV on the Hoehn and Yahr scale, and when not used in combination with levodopa-containing products; patients are classified as Stage I to III on the Hoehn and Yahr scale).
2	Jan. 22, 2016	21	Repatha·SC Injection 140 mg Syringe Repatha·SC Injection 140 mg Pen (Amgen Astellas BioPharma K.K.)	Approval Approval	Evolocumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of familial hypercholesterolemia and hypercholesterolemia (for use only in patients who are at higher risk of developing cardiovascular event and have not responded sufficiently to HMG-CoA reductase inhibitors).
3-1	May 26, 2015	22	Cymbalta Capsules 20 mg Cymbalta Capsules 30 mg (Shionogi & Co., Ltd.)	Change Change	Duloxetine hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of pain associated with fibromyalgia.
3-1	Jun. 26, 2015	23	Botox for injection 50 Units Botox for Injection 100 Units (GlaxoSmithKline K.K.)	Change Change	Botulinum toxin type A	Drugs with a new additional indication and a new dosage for the treatment of strabismus.
3-1	Jun. 26, 2015	24	Radicut Inj. 30 mg Radicut Bag for I.V. Infusion 30 mg (Mitsubishi Tanabe Pharma Corporation)	Change Change	Edaravone	Drugs with a new additional indication and a new dosage for delaying the functional disorder in patients with amyotrophic lateral sclerosis (ALS). [Orphan drug]
3-1	Sep. 24, 2015	25	Lamictal Tablets 2 mg for Children Lamictal Tablets 5 mg for Children Lamictal Tablets 25 mg Lamictal Tablets 100 mg (GlaxoSmithKline K.K.)	Change Change Change Change	Lamotrigine	Drugs with a new additional indication and a new dosage for use in the monotherapy for the treatment of typical absence seizures in patients with epilepsy.
3-1	Sep. 28, 2015	26	Effexor SR Capsules 37.5 mg Effexor SR Capsules 75 mg (Pfizer Japan Inc.)	Approval Approval	Venlafaxine hydrochloride	Drugs with a new active ingredient indicated for the treatment of depression.
3-1	Sep. 28, 2015	27	Copaxone S.C. Injection 20 mg Syringe (Takeda Pharmaceutical Company Limited)	Approval	Glatiramer acetate	A drug with a new active ingredient indicated for the prevention of relapse in multiple sclerosis. [Orphan drug]
3-1	Nov. 20, 2015	28	Lexapro Tablets 10 mg (Mochida Pharmaceutical Co., Ltd.)	Change	Escitalopram oxalate	A drug with a new additional indication for the treatment of social anxiety disorder.
3-1	Feb. 29, 2016	29	E Keppra Tablets 250 mg E Keppra Tablets 500 mg E Keppra Dry Syrup 50% E Keppra for I.V. Infusion 500 mg (UCB Japan Co., Ltd.)	Change Change Change Change	Levetiracetam	Drugs with a new additional indication for use as an adjunctive therapy with other antiepileptic drugs to treat tonic-clonic seizures in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Feb. 29, 2016	30	Risperdal Tablets 1 mg Risperdal Tablets 2 mg Risperdal Fine Granules 1% Risperdal OD Tablets 0.5 mg Risperdal OD Tablets 1 mg Risperdal OD Tablets 2 mg Risperdal Oral Solution 1 mg/mL (Janssen Pharmaceutical K.K.)	Change Change Change Change Change Change Change	Risperidone	Drugs with a new additional indication and a new dosage for the treatment of irritability associated with autism spectrum disorder in children and adolescents.
3-1	Feb. 29, 2016	31	Tryptanol Tablets 10 Tryptanol Tablets 25 (Nichi-Iko Pharmaceutical Co., Ltd.) Amitriptyline Hydrochloride Tablets 10 mg "Sawai" Amitriptyline Hydrochloride Tablets 25 mg "Sawai" (Sawai Pharmaceutical Co., Ltd.)	Change Change Change Change	Amitriptyline hydrochloride	Drugs with a new additional indication and a new dosage for the treatment of peripheral neuropathic pain. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
3-1	Mar. 18, 2016	32	Cymbalta Capsules 20 mg Cymbalta Capsules 30 mg (Shionogi & Co., Ltd.)	Change Change	Duloxetine hydrochloride	Drugs with a new additional indication for the treatment of pain associated with chronic low back pain.
3-1	Mar. 28, 2016	33	Sabril Granule Sachets 500 mg (Sanofi K.K.)	Approval	Vigabatrin	A drug with a new active ingredient indicated for the treatment of infantile spasms. [Orphan drug]
3-1	Mar. 28, 2016	34	Sycrest Sublingual Tablets 5 mg Sycrest Sublingual Tablets 10 mg (Meiji Seika Pharma Co., Ltd.)	Approval Approval	Asenapine maleate	Drugs with a new active ingredient indicated for the treatment of schizophrenia.
3-1	Mar. 28, 2016	35	Fycompa Tablets 2 mg Fycompa Tablets 4 mg (Eisai Co., Ltd.)	Approval Approval	Perampanel hydrate	Drugs with a new active ingredient indicated for use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) and tonic-clonic seizures in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-2	Jun. 26, 2015	36	Emla Cream (Sato Pharmaceutical Co., Ltd.)	Change	Lidocaine/Propitocaine	A drug with a new additional indication and a new dosage for adults indicated for the relief of pain during pricking with injection needles and intravenous indwelling needles, and with a new pediatric dosage indicated for the relief of pain during skin laser radiation therapy and pricking with injection needles and intravenous indwelling needles.
3-2	Jun. 26, 2015	37	Eylea Intravitreal Injection 40 mg/mL Eylea Intravitreal Injection Kit 40 mg/mL (Bayer Yakuhin, Ltd.)	Change Change	Aflibercept (genetical recombination)	Drugs with a revised indication for the treatment of macular edema following retinal vein occlusion.
3-2	Dec. 21, 2015	38	(1) Xylocaine Injection Polyamp 0.5% (AstraZeneca K.K.) (2) Lidocaine Hydrochloride Injection 0.5% [Pfizer] (Mylan Seiyaku Ltd.)	Change Change	(1) Lidocaine hydrochloride monohydrate (2) Lidocaine hydrochloride	Drugs with a new additional indication and a new dosage for the intravenous regional anesthesia in upper extremity surgery. [Public knowledge-based application after PAFSC's preliminary assessment]
4	May 26, 2015	39	Diflucan Capsules 50 mg Diflucan Capsules 100 mg (Pfizer Japan Inc.)	Change Change	Fluconazole	Drugs with new additional indications and a new dosage for the treatment of vaginitis and vulvovaginitis caused by *Candida* .
4	May 26, 2015	40	Clavamox combination Dry Syrup for pediatric (GlaxoSmithKline K.K.)	Change	Clavulanate potassium/Amoxicillin hydrate	A drug with a new additional indication for the treatment of sinusitis.
4	Jun. 26, 2015	41	Zosyn for Intravenous Injection 2.25 Zosyn for Intravenous Injection 4.5 Zosyn for I.V. Infusion bag 4.5 (Taiho Pharmaceutical Co., Ltd.)	Change Change Change	Tazobactam/ Piperacillin hydrate	Drugs with a new additional indication and a new dosage for the treatment of febrile neutropenia.
4	Jul. 3, 2015	42	Harvoni Combination Tablets (Gilead Sciences, Inc.)	Approval	Ledipasvir acetonate/Sofosbuvir	A new combination drug with new active ingredients indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1). [Priority review]
4	Jul. 3, 2015	43	Olanedine Antiseptic Solution 1.5% Olanedine Solution 1.5% Antiseptic Applicator 10 mL Olanedine Solution 1.5% Antiseptic Applicator 25 mL (Otsuka Pharmaceutical Factory, Inc.)	Approval Approval Approval	Olanexidine gluconate	Drugs with a new active ingredient indicated for skin antisepsis at surgical sites (in surgical fields).

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Aug. 24, 2015	44	Vfend Tablets 50 mg Vfend Tablets 200 mg Vfend for Intravenous Use 200 mg Vfend Dry Syrup 2800 mg (Pfizer Japan Inc.)	Change Change Change Change	Voriconazole	Drugs with a new additional indication and new dosages for the prophylaxis of deep mycosis in patients after hematopoietic stem cell transplantation.
4	Aug. 24, 2015	45	(1) Cravit Tablets 250 mg (2) Cravit Tablets 500 mg (3) Cravit Fine Granules 10% (Daiichi Sankyo Company, Limited) (4) Levofloxacin Tablets 250 mg "DSEP" (5) Levofloxacin Tablets 500 mg "DSEP" (6) Levofloxacin Fine Granules 10% "DSEP" (Daiichi Sankyo Espha Co., Ltd.)	Change Change Change Change Change Change	Levofloxacin hydrate	Drugs with new additional indications and a new dosage for the treatment of pulmonary tuberculosis and other tuberculosis.
4	Sep. 24, 2015	46	Ciproxan-I.V. 200 (Bayer Yakuhin, Ltd.)	Change	Ciprofloxacin	A drug with a new increased dose for adults indicated for the treatment of sepsis, pneumonia, etc., and also with new indications and new dosages for children for both the treatment of complicated cystitis, pyelonephritis and anthrax, and the improvement of symptoms associated with respiratory infection caused by *Pseudomonas aeruginosa* in cystic fibrosis.
4	Sep. 24, 2015	47	Cravit Intravenous Drip Infusion 500 mg/100 mL Cravit Intravenous Drip Infusion 500 mg/20 mL (Daiichi Sankyo Company, Limited)	Change Change	Levofloxacin hydrate	Drugs with new additional indications for the treatment of cystitis, pyelonephritis, secondary infection of trauma, burns or surgical wounds, and others.
4	Sep. 28, 2015	48	Zebiax Lotion 2% (Maruho Co., Ltd.)	Approval	Ozenoxacin	A drug with a new active ingredient indicated for the treatment of superficial skin infections and acne (accompanied by purulent inflammation).
4	Sep. 28, 2015	49	Viekirax Combination Tablets (AbbVie G.K.)	Approval	Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir	A new combination drug with new active ingredients indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1). [Priority review]
4	Jan. 22, 2016	50	Luconac Solution 5% (Sato Pharmaceutical Co., Ltd.)	Approval	Luliconazole	A drug with a new indication in a new dosage form indicated for the treatment of tinea unguium.
4	Mar. 28, 2016	51	Malarone Combination Tablets Malarone Pediatric Combination Tablets (GlaxoSmithKline K.K.)	Change Approval	Atovaquone / Proguanil hydrochloride	A drug with a revised pediatric dosage and an additional dosage form indicated for the treatment and prevention of malaria.
4	Mar. 28, 2016	52	Primaquine Tablets 15 mg "Sanofi" (Sanofi K.K.)	Approval	Primaquine phosphate	A drug with a new active ingredient indicated for the treatment of malaria caused by *Plasmodium vivax* and *Plasmodium oval* .
5	Jan. 22, 2016	53	Utrogestan Vaginal Capsules 200 mg (Fuji Pharma Co., Ltd.)	Approval	Progesterone	A drug with a new route of administration indicated for luteal support as part of assisted reproductive technology for infertile women.
5	Mar. 28, 2016	54	Luteum Vaginal Suppository 400 mg (Aska Pharmaceutical Co., Ltd.)	Approval	Progesterone	A drug with a new route of administration indicated for luteal support as part of assisted reproductive technology for infertile women.
6-1	May 26, 2015	55	Talion Tablets 5 mg Talion Tablets 10 mg Talion OD Tablets 5 mg Talion OD Tablets 10 mg (Mitsubishi Tanabe Pharma Corporation)	Change Change Change Change	Bepotastine besilate	Drugs with a new additional pediatric dosage indicated for the treatment of allergic rhinitis, urticaria, and itching associated with skin diseases (eczema/dermatitis, cutaneous pruritus).
6-1	May 26, 2015	56	Cimzia 200 mg Syringe for S.C. Injection (UCB Japan Co. Ltd.)	Change	Certolizumab pegol (genetical recombination)	A drug with a revised indication for the treatment of rheumatoid arthritis (including prevention of structural joint damage).
6-1	May 26, 2015	57	Solu-Cortef Injection 100 mg Solu-Cortef for Intravenous Use 250 mg Solu-Cortef for Intravenous Use 500 mg (Pfizer Japan Inc.)	Change Change Change	Hydrocortisone sodium succinate	Drugs with a new additional indication and a new dosage for the treatment of bronchial asthma. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Jul. 3, 2015	58	Plaquenil Tablets 200 mg (Sanofi K.K.)	Approval	Hydroxychloroquine sulfate	A drug with a new active ingredient indicated for the treatment of cutaneous lupus erythematosus and systemic lupus erythematosus.
6-1	Jul. 3, 2015	59	Ofev Capsules 100 mg Ofev Capsules 150 mg (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval	Nintedanib ethanesulfonate	Drugs with a new active ingredient indicated for the treatment of idiopathic pulmonary fibrosis. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Aug. 24, 2015	60	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with new additional indications and a new dosage for the treatment of entero-Behcet's disease, neuro-Behcet's disease, and vasculo-Behcet's disease in patients who have not responded sufficiently to conventional therapies. [Orphan drug]
6-1	Sep. 28, 2015	61	Spiolto Respimat 28 puffs Spiolto Respimat 60 puffs (Nippon Boehringer Ingelheim Co., Ltd.)	Approval Approval	Tiotropium bromide hydrate/Olodaterol hydrochloride	New combination drugs with a new active ingredient indicated for the relief of symptoms secondary to airway obstructive disorder in chronic obstructive pulmonary disease (chronic bronchitis, emphysema) (when a combination treatment of an inhaled long-acting anticholinergic and a long-acting beta-2 agonist is needed).
6-1	Sep. 28, 2015	62	Loqoa Tape (Taisho Pharmaceutical Co., Ltd.)	Approval	Esflurbiprofen/Mentha oil	A new combination drug with a new active ingredient indicated for the relief of inflammation and pain associated with osteoarthritis.
6-1	Sep. 28, 2015	63	Miticure House Dust Mite Sublingual Tablets 3,300 JAU Miticure House Dust Mite Sublingual Tablets 10,000 JAU (Torii Pharmaceutical Co., Ltd.)	Approval Approval	*Dermatophagoides farinae* extract, *Dermatophagoides pteronyssinus* extract	Drugs with new active ingredients indicated for the allergen immunotherapy for house dust mite antigen-induced allergic rhinitis.
6-1	Dec. 21, 2015	64	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of acute-phase Kawasaki's disease in patients who have not responded sufficiently to conventional therapies. [Orphan drug]
6-1	Dec. 21, 2015	65	Cosentyx for S.C. Injection 150 mg Syringe Cosentyx for S.C. Injection 150 mg (Novartis Pharma K.K.)	Change Change	Secukinumab (genetical recombination)	Drugs with a new additional indication for the treatment of pustular psoriasis in patients who have not responded sufficiently to conventional therapies.
6-1	Mar. 28, 2016	66	Nucala for s.c. Injection 100 mg (GlaxoSmithKline K.K.)	Approval	Mepolizumab (genetical recombination)	A drug with 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).
6-2	Jul. 3, 2015	67	Lantus XR Inj. SoloStar (Sanofi K.K.)	Approval	Insulin glargine (genetical recombination)	A drug in a new dosage form indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
6-2	Jul. 3, 2015	68	Trulicity Subcutaneous Injection 0.75 mg Ateos (Eli Lilly Japan K.K.)	Approval	Dulaglutide (genetical recombination)	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Jul. 3, 2015	69	Strensiq Subcutaneous Injection 12 mg/0.3 mL Strensiq Subcutaneous Injection 18 mg/0.45 mL Strensiq Subcutaneous Injection 28 mg/0.7 mL Strensiq Subcutaneous Injection 40 mg/1 mL Strensiq Subcutaneous Injection 80 mg/0.8 mL (Alexion Pharma G.K.)	Approval Approval Approval Approval Approval	Asfotase alfa (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of hypophosphatasia. [Orphan drug]
6-2	Aug. 24, 2015	70	Tresiba Flex Touch Tresiba Penfill (Novo Nordisk Pharma Ltd.)	Change Change	Insulin degludec (genetical recombination)	Drugs with a new additional pediatric dosage indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
6-2	Sep. 28, 2015	71	Marizev Tablets 25 mg Marizev Tablets 12.5 mg (MSD K.K.)	Approval Approval	Omarigliptin	Drugs with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Sep. 28, 2015	72	EquMet Combination Tablets LD EquMet Combination Tablets HD (Novartis Pharma K.K.)	Approval Approval	Vildagliptin/Metformin hydrochloride	New combination drugs indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of vildagliptin with metformin hydrochloride is deemed appropriate).
6-2	Dec. 21, 2015	73	Suiny Tab. 100 mg (Sanwa Kagaku Kenkyusho Co., Ltd.)	Change	Anagliptin	A drug with a revised indication for the treatment of type 2 diabetes mellitus.
6-2	Jan. 22, 2016	74	Bonviva Tablet 100 mg (Chugai Pharmaceutical Co., Ltd.)	Approval	Ibandronate sodium hydrate	A drug with a new route of administration indicated for the treatment of osteoporosis.
6-2	Mar. 28, 2016	75	Kanuma Intravenous Infusion 20 mg (Alexion Pharma G.K.)	Approval	Sebelipase alfa (genetical recombination)	A drug with a new active ingredient indicated for the treatment of lysosomal acid lipase deficiency. [Orphan drug]
In vivo diagnostics	Sep. 28, 2015	76	Allergen Scratch Extract Positive control "TORII" Histamine dihydrochloride (Japan Tobacco Inc.)	Approval	Histamine dihydrochloride	A drug with a new indication and a new dosage in a newly-added dosage form indicated for positive control in skin tests when diagnosing allergy.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
In vivo diagnostics	Jan. 22, 2016	77	Provocholine Powder for Inhalation Solution 100 mg (Sanwa Kagaku Kenkyusho Co., Ltd.) Kenbran Powder for Inhalation Solution 100 mg (Santen Pharmaceutical Co., Ltd.)	Approval Approval	Methacholine chloride	Drugs with a new active ingredient indicated for tests in the diagnosis of bronchial airway hyperresponsiveness.
In vivo diagnostics	Mar. 28, 2016	78	ColomforT Oral Suspension 25% (Fushimi Pharmaceutical Co.,Ltd.)	Approval	Barium sulfate	A drug with a new indication and a new dosage in an additional dosage form indicated for the support of computed tomographic colonography with labelling of bowel contents.
Radio-pharmaceuticals	Sep. 28, 2015	79	Octreoscan Injection (Fujifilm RI Pharma Co.,Ltd.)	Approval	Indium pentetoreotide (^{111}In)	A drug with a new active ingredient indicated for the diagnosis of neuroendocrine tumor by using somatostatin receptor scintigraphy.
Oncology drugs	May 26, 2015	80	Laserphyrin 100 mg for Injection (Meiji Seika Pharma Co., Ltd)	Change	Talaporfin sodium	A drug with a new additional indication for the treatment of recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy. [Orphan drug]
Oncology drugs	May 26, 2015	81	Pegintron Powder for Injection 50 μg/0.5 mL Pegintron Powder for Injection 100 μg/0.5 mL Pegintron Powder for Injection 150 μg/0.5 mL (MSD K.K.)	Change Change Change	Peginterferon alfa-2b (genetical recombination)	Drugs with a new additional indication and a new dosage for the adjuvant treatment of melanoma. [Orphan drug]
Oncology drugs	May 26, 2015	82	Rituxan Injection 10 mg/mL (Zenyaku Kogyo Co., Ltd.)	Change	Rituximab (genetical recombination)	A drug with a new dosage for the treatment of CD20-positive, B-cell non-Hodgkin's lymphoma. [Orphan drug]
Oncology drugs	Jun. 26, 2015	83	Velcade Injection 3 mg (Janssen Pharmaceutical K.K.)	Change	Bortezomib	A drug with a new additional indication and a new dosage for the treatment of patients with mantle cell lymphoma. [Orphan drug]
Oncology drugs	Jun. 26, 2015	84	Endoxan for Injection 100 mg Endoxan for Injection 500 mg (Shionogi & Co., Ltd.)	Change Change	Cyclophosphamide hydrate	Drugs with a revised indication and a new dosage for the relief of symptoms of malignant lymphoma. [Expedited review]
Oncology drugs	Jun. 26, 2015	85	Prednisolone Tablets 5 mg "Takeda" Prednisolone Powder 1% "Takeda" (Takeda Pharmaceutical Company Limited) Predonine Tablets 5 mg (Shionogi & Co., Ltd.)	Change Change Change	Prednisolone	Drugs with revised indications and a new dosage for the treatment of malignant lymphoma and similar diseases (closely-related diseases). [Expedited review]
Oncology drugs	Jul. 3, 2015	86	Yervoy Injection 50 mg (Bristol-Myers K.K.)	Approval	Ipilimumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of unresectable melanoma. [Orphan drug]
Oncology drugs	Jul. 3, 2015	87	Farydak Capsules 10 mg Farydak Capsules 15 mg (Novartis Pharma K.K.)	Approval Approval	Panobinostat lactate	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Sep. 24, 2015	88	Jakavi Tablets 5 mg (Novartis Pharma K.K.)	Change	Ruxolitinib phosphate	A drug with a new additional indication and a new dosage for the treatment of polycythemia vera (use only when conventional therapies are not sufficiently effective or inappropriate).
Oncology drugs	Sep. 24, 2015	89	Taxol Injection 30 mg Taxol Injection 100 mg (Bristol-Myers K.K.) Paclitaxel Inj. 30 mg/5 mL "NK" Paclitaxel Inj. 100 mg/16.7 mL "NK" (Nippon Kayaku Co., Ltd.) Paclitaxel I.V. Infusion 30 mg/5 mL "Hospira" Paclitaxel I.V. Infusion 100 mg/16.7 mL "Hospira" (Hospira Japan Co., Ltd.) Paclitaxel Injection 30 mg "Sawai" Paclitaxel Injection 100 mg "Sawai" Paclitaxel Injection 150 mg "Sawai" (Sawai Pharmaceutical Co., Ltd.) Paclitaxel Intravenous Infusion 30 mg "Sandoz" Paclitaxel Intravenous Infusion 100 mg "Sandoz" (Sandoz K.K.) Paclitaxel Injection 30 mg "NP" Paclitaxel Injection 100 mg "NP" (Nipro Corporation) Paclitaxel Injection 30 mg "Pfizer" Paclitaxel Injection 100 mg "Pfizer" (Mylan Seiyaku Ltd.)	Change Change Change Change Change Change Change Change Change Change Change Change Change	Paclitaxel	Drugs with a new dosage indicated for the treatment of gastric cancer. [Public knowledge-based application after PAFSC's preliminary assessment]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Sep. 28, 2015	90	Caprelsa Tablets 100 mg (AstraZeneca K.K.)	Approval	Vandetanib	A drug with a new active ingredient indicated for the treatment of unresectable medullary thyroid cancer. [Orphan drug]
Oncology drugs	Sep. 28, 2015	91	Leuplin Pro for Injection Kit 22.5 mg (Takeda Pharmaceutical Company Limited)	Approval	Leuprorelin acetate	A drug in a new dosage form indicated for the treatment of prostate cancer and premenopausal breast cancer.
Oncology drugs	Sep. 28, 2015	92	Yondelis I.V. infusion 0.25 mg Yondelis I.V. infusion 1 mg (Taiho Pharmaceutical Co., Ltd.)	Approval Approval	Trabectedin	Drugs with a new active ingredient indicated for the treatment of patients with soft tissue sarcoma. [Orphan drug]
Oncology drugs	Nov. 20, 2015	93	(1) Xeloda Tablet 300 (Chugai Pharmaceutical Co., Ltd.) (2) Elplat I.V. Infusion Solution 50 mg (3) Elplat I.V. Infusion Solution 100 mg (4) Elplat I.V. Infusion Solution 200 mg (Yakult Honsha Co., Ltd.)	Change Change Change Change	(1) Capecitabine (2) - (4) Oxaliplatin	Drugs with a revised indication for the treatment of gastric cancer.
Oncology drugs	Nov. 20, 2015	94	Hycamtin for Injection 1.1 mg (Nippon Kayaku Co., Ltd.)	Change	Nogitecan hydrochloride	A drug with a new additional indication and a new dosage for the treatment of advanced or recurrent cervical cancer.
Oncology drugs	Nov. 20, 2015	95	Tykerb Tablets 250 mg (GlaxoSmithKline K.K.)	Change	Lapatinib tosilate hydrate	A drug with new dosages indicated for the treatment of inoperable or recurrent breast cancer with HER2 overexpression.
Oncology drugs	Dec. 17, 2015	96	Opdivo Intravenous Infusion 20 mg Opdivo Intravenous Infusion 100 mg (Ono Pharmaceutical Co., Ltd.)	Change Change	Nivolumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of unresectable advanced/relapsed non-small-cell lung cancer. [Priority review]
Oncology drugs	Dec. 21, 2015	97	Revlimid Capsules 2.5 mg Revlimid Capsules 5 mg (Celgene K.K.)	Change Change	Lenalidomide hydrate	Drugs with a revised indication for the treatment of multiple myeloma.
Oncology drugs	Jan. 22, 2016	98	Targretin Capsules 75 mg (Minophagen Pharmaceutical Co., Ltd.)	Approval	Bexarotene	A drug with a new active ingredient indicated for the treatment of cutaneous T-cell lymphoma. [Orphan drug]
Oncology drugs	Feb. 29, 2016	99	Halaven Injection 1 mg (Eisai Co., Ltd.)	Change	Eribulin mesylate	A drug with a new additional indication for the treatment of soft tissue sarcoma. [Orphan drug]
Oncology drugs	Feb. 29, 2016	100	Nexavar Tablets 200 mg (Bayer Yakuhin, Ltd.)	Change	Sorafenib tosilate	A drug with a revised indication for the treatment of unresectable thyroid cancer. [Orphan drug]
Oncology drugs	Feb. 29, 2016	101	Opdivo Intravenous Infusion 20 mg Opdivo Intravenous Infusion 100 mg (Ono Pharmaceutical Co., Ltd.)	Change Change	Nivolumab (genetical recombination)	Drugs with a new dosage indicated for the treatment of unresectable melanoma. [Orphan drug]
Oncology drugs	Mar. 28, 2016	102	Tafinlar Capsules 50 mg Tafinlar Capsules 75 mg (Novartis Pharma K.K.)	Approval Approval	Dabrafenib mesilate	Drugs with a new active ingredient indicated for the treatment of unresectable melanoma with BRAF mutation. [Orphan drug]
Oncology drugs	Mar. 28, 2016	103	Mekinist Tablets 0.5 mg Mekinist Tablets 2 mg (Novartis Pharma K.K.)	Approval Approval	Trametinib dimethyl sulfoxide	Drugs with a new active ingredient indicated for the treatment of unresectable melanoma with BRAF mutation. [Orphan drug]
Oncology drugs	Mar. 28, 2016	104	Xofigo Injection (Bayer Yakuhin, Ltd.)	Approval	Radium (^{223}Ra) dichloride	A drug with a new active ingredient indicated for the treatment of castration-resistant prostate cancer with bone metastases.
Oncology drugs	Mar. 28, 2016	105	Zykadia Capsules 150 mg (Novartis Pharma K.K.)	Approval	Ceritinib	A drug with a new active ingredient indicated for the treatment of unresectable advanced/relapsed anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer with resistance or intolerance to crizotinib.
Oncology drugs	Mar. 28, 2016	106	Tagrisso Tablets 40 mg Tagrisso Tablets 80 mg (AstraZeneca K.K.)	Approval Approval	Osimertinib mesilate	Drugs with a new active ingredient indicated for the treatment of inoperable or recurrent epidermal growth factor receptor (EGFR) T790M mutation-positive non-small-cell lung cancer with resistance to EGFR tyrosine kinase inhibitors.
Oncology drugs	Mar. 28, 2016	107	Imbruvica Capsules 140 mg (Janssen Pharmaceutical K.K.)	Approval	Ibrutinib	A drug with a new active ingredient indicated for the treatment of relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Vaccines	Jan. 22, 2016	108	Vaxem Hib Suspension Liquid for Injection (Takeda Pharmaceutical Company Limited)	Approval	*Haemophilus influenzae* type b vaccine absorbed (mutated diphtheria CRM_{197} conjugate)	A drug with a new active ingredient indicated for the prophylaxis of *Haemophilus influenzae* type b infections.
Vaccines	Feb. 29, 2016	109	Tribik (The Research Foundation for Microbial Diseases of Osaka University)	Change	Adsorbed diphtheria-purified pertussis-tetanus combined vaccine	A drug with a new dosage indicated for the prevention of pertussis, diphtheria, and tetanus.
Vaccines	Mar. 18, 2016	110	Freeze-dried Live Attenuated Varicella Vaccine "Biken" (The Research Foundation for Microbial Diseases of Osaka University)	Change	Freeze-dried live attenuated varicella vaccine	A drug with a new additional indication for the prevention of herpes zoster in individuals 50 years of age and older.
Vaccines	Mar. 18, 2016	111	Adsorbed Cell Culture-derived Influenza Vaccine H5N1 for Intramuscular Injection 30μg/mL "Kitasato Daiichi Sankyo" (Kitasato Daiichi Sankyo Vaccine Co., Ltd.)	Change	Adsorbed cell culture-derived influenza vaccine (H5N1)	A drug with a new additional pediatric dosage indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]
Blood products	Jul. 3, 2015	112	Acoalan Injection 600 (Kyowa Hakko Kirin Co., Ltd.)	Approval	Antithrombin gamma (genetical recombination)	A drug with a new active ingredient indicated for the treatment of thrombophilia due to congenital antithrombin (AT) deficiency (CAD) and disseminated intravascular coagulation (DIC) accompanied by a decrease in AT.
Blood products	Mar. 28, 2016	113	Adynovate Intravenous 250 Adynovate Intravenous 500 Adynovate Intravenous 1000 Adynovate Intravenous 2000 (Baxter Limited)	Approval Approval Approval Approval	Rurioctocog alfa pegol (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Blood products	Mar. 28, 2016	114	Kovaltry for iv injection 250 Kovaltry for iv injection 500 Kovaltry for iv injection 1000 Kovaltry for iv injection 2000 Kovaltry for iv injection 3000 Kovaltry for iv injection Kit 250 Kovaltry for iv injection Kit 500 Kovaltry for iv injection Kit 1000 Kovaltry for iv injection Kit 2000 Kovaltry for iv injection Kit 3000 (Bayer Yakuhin, Ltd.)	Approval Approval Approval Approval Approval Approval Approval Approval Approval Approval	Octocog beta (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Bio-CMC	Mar. 28, 2016	115	Insulin Glargine BS Injection Kit "FFP" Insulin Glargine BS Injection 100 Unit/mL "FFP" (Fujifilm Pharma Co., Ltd.)	Approval Approval	Insulin glargine (genetical recombination) [insulin glargine biosimilar 2]	Follow-on biologics indicated for the treatment of diabetes mellitus where insulin therapy is indicated.

Table 5. Products Approved in FY 2015: New Medical Devices

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Ophthalmology and Otorhinolaryngology	Feb. 15, 2016 Total review time: 228 days Regulatory review time: 112 days	– Domestic clinical study results	1	Suncon Kyoto-CS (Sun Contact Lens Co., Ltd.)	Approval	Instrument & apparatus 72 Limbal-supported contact lens for abnormal corneal shape	A limbal-supported, rigid contact lens for patients with ocular sequelae of Stevens-Johnson syndrome or toxic epidermal necrolysis, to alleviate symptoms associated with severe dry eye, etc. as well as to correct visual acuity. An investigator-initiated clinical trial was conducted in Japan to evaluate the efficacy and safety of the product in patients with ocular sequelae for whom the product is indicated. [Orphan device]
Ophthalmology and Otorhinolaryngology	Mar. 25, 2016 Total review time: 564 days Regulatory review time: 203 days	Jun. 25, 2012 Foreign clinical study results	2	iStent Trabecular Micro-Bypass Stent System (Glaukos Corporation)	Approval	Medical products 4 Heparin using intraocular drain	A device consisting of the iStent, a titanium-alloy glaucoma implant designed to maintain patency of an outflow canal passing through the trabecular meshwork so that aqueous humor drains from the anterior chamber into Schlemm's canal and is directed naturally to the normal outflow canal, and its inserter. The surface of the iStent is coated with porcine-derived heparin. Results from foreign clinical studies were submitted to evaluate the efficacy and safety of the device in patients with mild-to-moderate glaucoma requiring cataract surgery, for whom the device is indicated.
3-1	Apr. 17, 2015 Total review time: 219 days Regulatory review time: 123 days	Jan. 26, 2015 Foreign and domestic clinical study results	3	Pipeline Flex Flow Diverter System (Covidien Japan, Inc.)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A flow diverter system used for endovascular therapy for large or giant wide-neck intracranial aneurysm in internal carotid artery from petrous through superior hypophyseal, except for the acute phase of aneurysm that are at risk of rupture. Results from foreign clinical studies conducted to evaluate the efficacy and safety of this product in the treatment of intracranial aneurysm and domestic clinical studies conducted to confirm the compatibility of this product with the domestic medical environment were submitted. [Priority review product]
3-1	Apr. 21, 2015 Total review time: 63 days Regulatory review time: 60 days	Sep. 3, 2014 Domestic clinical study results	4	XIENCE Alpine Drug Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A stent system consisting of a drug-eluting stent used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion (a lesion length of 32 mm or less) with a reference vessel diameter of 2.25-3.75 mm and a delivery catheter used to implant a stent to the site of stenosis. This application is for a partial change of approval application for medical device to add a stent size of 2.25 mm diameter. The added drug-eluting stent of this product is identical to the company's existing approved product "XIENCE PRIME SV Drug Eluting Stent" (Approval No. 22500BZX00070000) and "XIENCE Xpedition Drug Eluting Stent" (Approval No. 22500BZX00309000). The stent delivery system is identical to that of this product of 2.5 mm diameter except for the balloon size. Results from clinical studies on "XIENCE PRIME SV Drug Eluting Stent," the stent part of which is identical to this product, were submitted to evaluate the efficacy and safety of this product. (The original product is in a reexamination period)
3-1	Jul. 23, 2015 Total review time: 56 days Regulatory review time: 42 days	– No clinical study results	5	Promus Premier Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting stent system used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion of 34 mm or less in length with a reference vessel diameter of 2.25-3.50 mm. The application was submitted for an extension of expiration period from the previously approved 18 months to 24 months. (A "partial change" application submitted during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-1	Aug. 28, 2015 Total review time: 113 days Regulatory review time: 99 days	Feb. 17, 2012 No clinical study results	6	Resolute Integrity SV Coronary Stent System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A stent system for percutaneous coronary stent placement consisting of a zotarolimus-eluting stent to be inserted and placed at the site of a lesion to maintain the vascular lumen and a delivery catheter used to deliver the stent to the site of the lesion. The application was submitted to change the specified test method related to the drug that was previously approved. (A "partial change" application submitted during the reexamination period)
3-1	Sep. 17, 2015 Total review time: 353 days Regulatory review time: 268 days	– Domestic clinical study results	7	SeQuent Please Drug Eluting Balloon Catheter (Nipro Corporation)	Change	Instrument & apparatus 51 Balloon-dilating catheter for coronary angioplasty	A balloon-dilating catheter for coronary angioplasty with a paclitaxel-coated balloon. The drug can be delivered to the vascular intima by dilating this catheter at the lesion site after predilation by a regular balloon used for percutaneous coronary intervention. The application was submitted for an additional indication of new coronary lesions with a reference vessel diameter of less than 3.0 mm. (A "partial change" application). Results from domestic clinical studies were submitted for the evaluation of the efficacy and safety of this product in patients with the additional indication compared to the intervention with balloon angioplasty.
3-2	Apr. 17, 2015 Total review time: 359 days Regulatory review time: 201 days	Jan. 13, 2012, Sep. 10, 2013 Foreign clinical study results	8	GORE CTAG Thoracic Endoprosthesis (W.L. GORE & Associates, Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	The product consists of a stent graft used for treatment of thoracic aorta and delivery system used to deliver and implant the stent graft in the target site. The application is for a partial change to add the indications of traumatic thoracic aortic injury and acute complicated Stanford B aortic dissection in the item of intended use or indications. Results from clinical studies conducted to verify the efficacy and safety for traumatic thoracic aortic injury and acute complicated Stanford B aortic dissection were submitted.
3-2	Apr. 17, 2015 Total review time: 361 days Regulatory review time: 283 days	Jul. 15, 2014 (LVIS and LVIS Jr.3.5) Oct. 14, 2014 (LVIS Jr. 2.5) Domestic clinical study results	9	LVIS Stent (Terumo Corporation)	Approval	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthetic material for embolization in vessels of the central circulation system to prevent the protrusion and/or dislodgement of embolic coils into/from the parent artery during coil embolization in patients who have a wide-neck cerebral aneurysm (defined as that with a neck part of 4 mm or greater, or dome/neck ratio of less than 2) in the parent artery with a diameter of 2.0 to 4.5 mm, among the patients who have an unruptured aneurysm (with a maximum diameter of 5 mm or greater) which is difficult to treat surgically (including surgical clipping) or by coil embolization using an embolization coil alone. This product is a stent formed with woven nitinol wire, which is expected to improve the tracking of vessel shape and is a closed-cell stent with characteristic of no cell opening or no protrusion into cerebral aneurysm. Results from domestic clinical studies conducted to evaluate the efficacy and safety of this product in treatment of aneurysm were submitted. (The original product is in a reexamination period)
3-2	Jun. 8, 2015 Total review time: 94 days Regulatory review time: 78 days	Nov. 30, 2012 No clinical study results	10	Solitaire FR Revascularization Device (Covidien Japan, Inc.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	An emboli-removal catheter in the central circulatory system to restore blood flow in patients in the acute phase of cerebral infarction (in principle, within 8 hours from the onset) who are ineligible for intravenous tissue plasminogen activator (t-PA) or who failed to restore blood flow with intravenous t-PA therapy. The application is for a partial change to add a new type catheter with a modified junction between push wire and multi-cell retriever in order to make the structure less liable to crack. (A partial change during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
3-2	Aug. 28, 2015 Total review time: 70 days Regulatory review time: 35 days	- No clinical study results	11	GORE CTAG Thoracic Endoprosthesis (W.L. GORE & Associates, Co.,Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft system consisting of a polytetrafluoroethylene (PTFE) graft and a self-expanding nitinol stent to keep the graft extended, and a delivery catheter to deliver and implant the stent graft in the target site. The application was submitted for addition of raw materials used for the soft tip at the end of delivery catheter due to termination of raw material supply which was previously approved. (A "partial change" application submitted during the post-market performance review period)
3-2	Sep. 18, 2015 Total review time: 357 days Regulatory review time: 160 days	Dec. 16, 2002 Domestic clinical study results	12	DC Bead (Eisai Co., Ltd.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A hydrophilic microbead used for vascular embolization, composed of cross-linked polyvinyl alcohol polymer (Approval No. 22500BZX00182000). The application was submitted for an additional indication of vascular embolization therapy for hypervascular tumors and arteriovenous malformations to the approved indication of transcatheter arterial embolization therapy for patients with hepatocellular carcinoma. Results from a domestic clinical study were submitted for the evaluation of the efficacy and safety of this device for patients with the additional indication. (A "partial change" application submitted during the reexamination period)
3-2	Sep. 18, 2015 Total review time: 779 days Regulatory review time: 264 days	Feb. 20, 2007 Clinical evaluation report	13	Cook Spectrum M/R Impregnated Central Venous Catheter Kit (Cook Japan Inc.)	Approval	Instrument & apparatus 51 Antimicrobial central venous catheter introducer kit	This product is a central venous catheter impregnated with minocycline and rifampin to reduce catheter-related bloodstream infections (CRBSIs). A clinical evaluation report was submitted to evaluate the effectiveness in reducing CRBSI and the safety of the device.
4	Apr. 6, 2015 Total review time: 206 days Regulatory review time: 151 days	- No clinical study results	14	Activa SC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa SC is an implantable electrical stimulation device used for deep brain stimulation to improve various symptoms associated with movement disorders by delivering an electrical stimulus to the deep brain (thalamus, subthalamic nucleus, or internal globus pallidus). The application is for a partial change to enable MRI tests to be performed only when the patient's condition meets imaging criteria. Results from nonclinical studies evaluating the safety under MRI conditions were submitted. (A partial change during the reexamination period)
4	Apr. 6, 2015 Total review time: 206 days Regulatory review time: 151 days	- No clinical study results	15	Activa RC (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	Activa RC is a rechargeable and implantable electrical stimulation device used for deep brain stimulation to improve various symptoms associated with movement disorders by delivering an electrical stimulus to the deep brain (thalamus, subthalamic nucleus, or internal globus pallidus). The application is for a partial change to enable MRI tests to be performed only when the patient's condition meets imaging criteria. Results from nonclinical studies evaluating the safety under MRI conditions were submitted. (A partial change during the reexamination period)
4	Apr. 17, 2015 Total review time: 322 days Regulatory review time: 117 days	Sep. 28, 2012 Foreign clinical study results	16	S-ICD Lead (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable defibrillator /pacemaker lead	The device is a subcutaneous implantable cardioverter-defibrillator (S-ICD) lead used in patients at high risk of sudden cardiac death caused by ventricular tachycardia. Foreign clinical study reports were submitted to evaluate the efficacy and safety of the device for treatment of lethal arrhythmia.
4	Apr. 17, 2015 Total review time: 322 days Regulatory review time: 134 days	Sep. 28, 2012 Foreign clinical study results	17	S-ICD Pulse Generator (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 12 Automatic implantable defibrillator	The device is a subcutaneous implantable cardioverter-defibrillator (S-ICD) used in patients at high risk of sudden cardiac death caused by ventricular tachycardia. Foreign clinical study reports were submitted to evaluate the efficacy and safety of the device for treatment of lethal arrhythmia.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
4	May 26, 2015 Total review time: 158 days Regulatory review time: 48 days	- No clinical study results	18	PD Laser BT (Panasonic Healthcare Co., Ltd.)	Change	Instrument & apparatus 31 PDT semiconductor laser	A laser irradiation device designed for photodynamic therapy. This device is to be used in combination with "Laserphyrin 100 mg for Injection" (Approval No. 21500AMZ00509000) as an oncotropic photo-sensitizer, targeting primary malignant brain tumor as an additional treatment to the surgical resection. The application is for a partial change to change the site of manufacture. (A partial change during the reexamination period)
4	Jun. 15, 2015 Total review time: 175 days Regulatory review time: 148 days	Oct. 12, 2010 No clinical study results	19	Thermogard System (ZOLL Circulation, Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A temperature management device to regulate the body temperature by heat exchange with the blood within a blood vessel through a central venous catheter balloon in which a perfusion fluid (physiological saline) circulates in patients who need fever control. The application is for a partial change to correct the error in the approved product information. (A partial change during the reexamination period)
4	Jun. 18, 2015 Total review time: 212 days Regulatory review time: 52 days	Dec. 16, 2011 Domestic and foreign clinical study results	20	EXCOR Pediatric Ventricular Assist Device (Cardio Incorporated)	Approval	Instrument & apparatus 7 Single-use external ventricular assist system	The device is an external ventricular assist system used for improving circulation of pediatric severe heart failure patients. Foreign clinical study reports to evaluate the survival rate, survival period, adverse events, etc. in pediatric patients using the device and a Japanese clinical study report to confirm the compatibility of the device with the domestic medical environment were submitted. [Orphan device]
4	Sep. 9, 2015 Total review time: 292 days Regulatory review time: 197 days	Apr. 17, 2003 Clinical evaluation report	21	Freezor Cryoablation Catheter Series (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A catheter used in cryoablation of cardiac tissue for treatment of atrioventricular nodal reentry tachycardia (AVNRT). A clinical evaluation report summarizing results of foreign clinical studies and published literatures was submitted for evaluation of the efficacy and safety in treatment of AVNRT. (The original product is in a reexamination period)
4	Sep. 9, 2015 Total review time: 292 days Regulatory review time: 197 days	Dec. 10, 2010 Clinical evaluation report	22	Medtronic CryoConsole (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 31 Versatile cryosurgical unit	A cryosurgical unit to be used for treatment of arrhythmia. The device is for the exclusive use with cryoablation catheters. The application was submitted for addition of a function "the cryomapping mode", which is available when used in combination with the “Freezor Cryoablation Catheter Series” (Approval No. 22700BZX00252000) . (A "partial change" application submitted during the reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Oct. 22, 2015 Total review time: 160 days Regulatory review time: 94 days	Oct. 15, 2014 No clinical study results	23	Libra Single 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Electrical brain stimulation device for tremor	An implantable stimulator for tremor used for deep brain stimulation (DBS), with the purpose of relieving various symptoms associated with Parkinson's disease, dystonia symptoms, or symptoms of essential tremor, by stimulating the deep brain. The application was submitted for an additional pocket adapter model used for connecting this device and the company's own approved DBS stimulator to other manufacturer's extension/lead. (A "partial change" application submitted during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Nov. 24, 2015 Total review time: 137 days Regulatory review time: 107 days	- No clinical study results	24	LVIS Stent (Terumo Corporation)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A prosthetic material for embolization in vessels of the central circulation system to prevent the protrusion and/or dislodgement of embolic coils into/from the parent artery during coil embolization in patients who have a wide-neck cerebral aneurysm (defined as that with a neck of 4 mm or greater, or dome/neck ratio of less than 2) in the parent artery with a diameter of 2.0 to 4.5 mm, among the patients who have an unruptured aneurysm (with a maximum diameter of 5 mm or greater) which is difficult to treat surgically (including surgical clipping) or by coil embolization using an embolization coil alone. The application was submitted to add a LVIS stent (type 2) in which the stent weave density was changed to realize easier operability at the curvature of the vessels and in which the flare shape was changed for improved manufacturing efficiency. (A "partial change" application) (The original product is in a reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 2, 2015 Total review time: 341 days Regulatory review time: 200 days	Jan. 22, 2014 Foreign clinical study results	25	VALIANT Thoracic Stent Graft System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft system consisting of a stent graft for treatment of the thoracic aorta and a delivery catheter used to deliver and implant the stent graft in the target site. The application was submitted for an additional indication of acute complicated Stanford type B aortic dissection (A "partial change" application). Results from clinical studies conducted in the United States to verify the efficacy and safety of the product for acute complicated Stanford type B aortic dissection were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 2, 2015 Total review time: 56 days Regulatory review time: 29 days	- No clinical study results	26	DC Bead (Eisai Co., Ltd.)	Change	Instrument & apparatus 51 Prosthetic material for embolization in vessels of the central circulation system	A hydrophilic microsphere (spherical particulate) composed of cross-linked polyvinyl alcohol polymer. This product is used for vascular embolization in patients with hypervascular tumors or arteriovenous malformations. The application was submitted to change the manufacturing site. (A "partial change" application submitted during the post-market performance review period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 4, 2015 Total review time: 94 days Regulatory review time: 12 days	- No clinical study results	27	PD Laser BT (Panasonic Healthcare Co., Ltd.)	Change	Instrument & apparatus 31 PDT semiconductor laser	A laser irradiation device designed for photodynamic therapy. This device is to be used in combination with "Laserphyrin 100 mg for Injection" (Approval No. 21500AMZ0050900) as an oncotropic photo-sensitizer, targeting primary malignant brain tumor as an additional treatment to surgical resection. The application was submitted to change the manufacturing site. (A "partial change" application submitted during the reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 18, 2015 Total review time: 266 days Regulatory review time: 138 days	- No clinical study results	28	Kawasumi Najuta Thoracic Stent Graft System (Kawasumi Laboratories, Incorporated)	Change	Instrument & apparatus 7 Aortic stent graft	A device consisting of a stent graft for treatment of thoracic aortic aneurysm and a delivery system used to deliver and implant the stent graft in the target site. The application was submitted for an additional type of delivery catheter with an effective sheath length of 950 mm and a compatible guidewire diameter of 0.035 inch. (A "partial change" application submitted during the reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Jan. 5, 2016 Total review time: 292 days Regulatory review time: 155 days	- Domestic clinical study results	29	Revive SE Thrombectomy device (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	An emboli-removal catheter in the central circulatory system to restore blood flow by removing clots from blood vessels in the brain in patients in the acute phase of cerebral infarction (in principle, within 8 hours from the onset) who are ineligible for intravenous tissue plasminogen activator (t-PA) or who failed to restore blood flow with intravenous t-PA therapy. Results from a single-arm clinical study conducted in Japan to confirm that the efficacy and safety of the device is practically equivalent to those of the approved medical device "Merci Retriever (Approval No. 22200BZX00596000) were submitted. (The original product is in a reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Jan. 29, 2016 Total review time: 304 days Regulatory review time: 176 days	Jan. 13, 2014 No clinical study results	30	Trevo Pro Clot Retriever (Stryker Japan K.K.)	Change	Instrument & apparatus 51 Emboli-removal catheter in the central circulatory system	An emboli-removal catheter in the central circulatory system intended to restore blood flow by removing thrombus for patients with acute-phase cerebral infarction (generally, within 8 hours of symptom onset) who are ineligible for intravenous tissue plasminogen activator (t-PA) or who failed to restore blood flow with intravenous t-PA therapy. The application was submitted for an additional model (Type 3) with the tip structure at end of the retriever being removed and for additional size variations in effective length and diameter of the stent that are within the range of other approved devices. (A "partial change" application submitted during the reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 15, 2016 Total review time: 152 days Regulatory review time: 113 days	Jan. 22, 2007 No clinical study results	31	Thermogard System (ZOLL Circulation, Inc.)	Change	Instrument & apparatus 12 Central venous placement temperature management system	A system for heat exchange with the blood using a central venous catheter accompanying a heat exchange balloon placed inside a blood vessel intended for the use in patients requiring body temperature management. Temperature-controlled physiological saline circulates within the balloon of the central venous catheter, which allows heat exchange between the balloon surface and the blood in contact with the surface, thereby controlling the temperature of the whole body. The application was submitted for an additional component, Quattro・ICY IVTM Catheter, and an additional indication of body temperature management (temperature management therapy) in patients under cardiac arrest or after return of (spontaneous) circulation. (A "partial change" application)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 15, 2016 Total review time: 257 days Regulatory review time: 144 days	Jun. 14, 2005 Clinical evaluation report Domestic clinical study results	32	Gore Viabahn Stent Graft (W. L. Gore & Associates, Co., Ltd.)	Approval	Instrument & apparatus 7 Heparin using stent graft in the central circulation	A stent graft system consisting of a stent graft and delivery catheter, used for the treatment for arterial injury in the chest, abdomen, or pelvis, or for maintenance of arterial patency of the superficial femoral artery. A clinical evaluation report and results of the domestic clinical study were submitted to evaluate the efficacy and safety of the device in vascular injury treatment, and vascular patency treatment, respectively. [Priority review product]
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 15, 2016 Total review time: 452 days Regulatory review time: 225 days	ICY Catheter: Oct. 23, 2003 Quattro Catheter: Feb. 15, 2007 Domestic clinical study results	33	Quattro・ICY IVTM Catheter (ZOLL Circulation, Inc.)	Approval	Instrument & apparatus 12 Central venous placement temperature management system	A central venous catheter with a balloon for heat exchange used for body temperature management (temperature management therapy) in patients under cardiac arrest or after return of (spontaneous) circulation. The catheter is designed to be connected to the console of the approved "Thermogard System" (Approval No. 22400BZI00010000). Temperature-controlled physiological saline circulates within the balloon of the central venous catheter, which allows heat exchange between the balloon surface and the blood in contact with the surface, thereby controlling the temperature of the whole body. A clinical study was conducted in Japan in patients who are under cardiac arrest suspected to be caused by intrinsic cardiac dysfunction or who are after return of (spontaneous) circulation, to evaluate whether body temperature of these patients can be managed appropriately enabling therapeutic hypothermia, and to evaluate the safety.
Cardiopulmonary Circulation	Nov. 18, 2015 Total review time: 357 days Regulatory review time: 215 days	－ Domestic clinical study results	34	SATAKE・HotBalloon Catheter (Toray Industries, Inc.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A balloon ablation catheter utilizing a high-frequency current to treat drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. Results from domestic clinical studies using the previous product as an investigational device were submitted to verify the efficacy and safety in patients with drug-resistant symptomatic paroxysmal atrial fibrillation in comparison with control groups receiving antiarrhythmic drugs.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Cardiopulmonary Circulation	Dec. 18, 2015 Total review time: 232 days Regulatory review time: 177 days	Sep. 28, 2012 No clinical study results	35	S-ICD Pulse Generator (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	The device is a subcutaneous implantable cardioverter-defibrillator (S-ICD) used in patients at high risk of sudden cardiac death caused by ventricular tachycardia. The application was submitted for addition of a device which is thinner than the existing one. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Dec. 24, 2015 Total review time: 182 days Regulatory review time: 114 days	- No clinical study results	36	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	A ventricular assist device used to improve circulation until heart transplantation in patients showing continuous decompensation in spite of drug therapy or circulation assist techniques such as an external ventricular assist system, and for whom it is considered difficult to survive without a heart transplant. The application was submitted for addition of surgical accessories and nonsterile supply of the existing surgical accessories. (A "partial change" application) [Orphan device]
Cardiopulmonary Circulation	Mar. 11, 2016 Total review time: 301 days Regulatory review time: 146 days	Jun. 17, 2015 Foreign clinical study results	37	Edwards Sapien 3 (Edwards Lifesciences Limited)	Approval	Instrument & apparatus 7 Transcatheter bovine pericardial valve	A prosthetic heart valve system used for transcatheter valve implantation for patients with severe symptomatic aortic valve stenosis and for whom surgical aortic valve replacement cannot be performed due to their general condition and comorbidities. Foreign clinical study results were submitted to demonstrate that the efficacy and safety of the new device are equivalent to those of the existing approved model, Sapien XT. (The original product is in a reexamination period)
5	May 26, 2015 Total review time: 244 days Regulatory review time: 140 days	- Domestic clinical study results	38	EC-PDT Probe (Panasonic Healthcare Co., Ltd.)	Approval	Instrument & apparatus 31 Single-use probe for PDT semiconductor laser	A probe for laser irradiation used for photodynamic therapy using talaporfin sodium for recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy. This probe is connected to PD Laser to irradiate the target lesion from the esophageal lumen with laser light oscillated from PD Laser. Results from a domestic phase II study (an investigator-initiated clinical trial) conducted to evaluate the efficacy and safety of photodynamic therapy using talaporfin sodium, PD Laser, and this product for recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy were submitted. [Orphan device]
5	May 26, 2015 Total review time: 237 days Regulatory review time: 133 days	- Domestic clinical study results	39	PD Laser (Panasonic Healthcare Co., Ltd.)	Change	Instrument & apparatus 31 PDT semiconductor laser	A laser irradiation device used for photodynamic therapy using talaporfin sodium. The application is for a partial change to add recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy to the target diseases. This device irradiates the target lesion with laser light from the esophageal lumen when an exclusive EC-PDT probe for the device is connected. Results from a domestic phase II study (an investigator-initiated clinical trial) conducted to evaluate the efficacy and safety of photodynamic therapy using talaporfin sodium, this device, and the EC-PDT probe for recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy were submitted. [Orphan device]
Gastroenterology, Genitourinary, and Reproductive Medicine	Mar. 9, 2016 Total review time: 82 days Regulatory review time: 9 days	- No clinical study results	40	EC-PDT Probe (Panasonic Healthcare Co., Ltd.)	Change	Instrument & apparatus 31 Single-use probe for PDT semiconductor laser	A probe for laser irradiation used for photodynamic therapy using talaporfin sodium for recurrent esophageal cancer associated with local persistence after chemoradiotherapy or radiotherapy. This probe is connected to PD Laser to irradiate the target lesion from the esophageal lumen with laser light oscillated from PD Laser. The application was submitted to change the manufacturing site. (A "partial change" application submitted during the post-market performance review period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
6-1	Aug. 13, 2015 Total review time: 360 days Regulatory review time: 98 days	Jul. 9, 2008 Clinical evaluation report	41	Comprehensive Reverse Shoulder System (Biomet Japan, LLC)	Approval	Medical products 4 Total shoulder prosthesis	A reverse shoulder prosthesis used in cases of rotator cuff dysfunction such as rotator cuff tear arthropathy or massive rotator cuff tear. The device consists of humeral and glenoid components, and is used in combination with the approved humeral stem. A clinical evaluation report summarizing clinical data on foreign clinical literatures and foreign post-marketing surveillance was submitted to show the clinical equivalence of the product to overall reverse shoulder prostheses used in foreign countries. (The original product is in a reexamination period)
6-1	Aug. 13, 2015 Total review time: 104 days Regulatory review time: 55 days	May. 12, 2014 No clinical study results	42	Trabecular Metal Reverse Shoulder System Vivacit-E Polyethylene Liner (Zimmer K.K.)	Approval	Medical products 4 Humeral component for shoulder prosthesis	An insert consisting of humeral components of a reverse shoulder prosthesis used in cases of rotator cuff dysfunction such as rotator cuff tear arthropathy or massive rotator cuff tear. The insert adopts vitamin E blended highly crosslinked polyethylene as the raw material, which has already been used for the approved device. The device is used in combination with the humeral stem or other components of the company's own approved products, "Trabecular Metal Reverse Shoulder System" (Approval No. 22500BZX00475000). (The original product is in a reexamination period)
6-1	Aug. 28, 2015 Total review time: 147 days Regulatory review time: 47 days	Dec. 19, 2005 No clinical study results	43	Trabecular Metal Reverse Shoulder System (Zimmer K.K.)	Change	Medical products 4 Total shoulder prosthesis	A reverse shoulder prosthesis used in cases of rotator cuff dysfunction such as rotator cuff tear arthropathy or massive rotator cuff tear. The application was submitted for addition of manufacturing conditions of a component, "TM Reverse Base Plate", and addition and deletion of the sterile manufacturing facilities. (A "partial change" application submitted during the reexamination period)
6-1	Sep. 2, 2015 Total review time: 306 days Regulatory review time: 104 days	Feb. 2, 2007 Clinical evaluation report	44	DELTA XTEND Reverse Shoulder System (Modular) (Johnson & Johnson K.K.)	Approval	Medical products 4 Total shoulder prosthesis	A reverse total shoulder prosthesis used in cases of rotator cuff dysfunction to replace the shoulder joint function. The part of the components to be implanted within bones is applied with surface roughening by grit blasting and plasma spray coating of hydroxyapatite, allowing cementless fixation. A clinical evaluation report summarizing clinical data on foreign clinical literatures and foreign post-marketing surveillance was submitted to show the clinical equivalence of the product to overall reverse shoulder prostheses used in foreign countries. (The original product is in a reexamination period)
6-1	Sep. 2, 2015 Total review time: 306 days Regulatory review time: 108 days	Feb. 2, 2007 Clinical evaluation report	45	DELTA XTEND Reverse Shoulder System (Monobloc) (Johnson & Johnson K.K.)	Approval	Medical products 4 Humeral component for shoulder prosthesis	The humeral stem of a reverse shoulder prosthesis used in cases of rotator cuff dysfunction, to replace shoulder joint function. The devise is used in combination with the components of the "DELTA XTEND Reverse Shoulder System (Modular)" which have been filed simultaneously, and is fixed to bone with cement. A clinical evaluation report summarizing clinical data on foreign clinical literatures and foreign post-marketing surveillance was submitted to show the clinical equivalence of the product to overall reversed shoulder prostheses used in foreign countries. (The original product is in a reexamination period)
6-1	Sep. 14, 2015 Total review time: 297 days Regulatory review time: 89 days	Jun. 5, 2010 No clinical study results	46	Aequalis Reversed Cementless (Tornier S.A.S.)	Approval	Medical products 4 Humeral component for shoulder prosthesis	The humeral component of a reverse shoulder prosthesis used in cases of rotator cuff dysfunction such as rotator cuff tear arthropathy or massive rotator cuff tear. The component includes a stem and a metaphysis of which surfaces are treated of grit blasting and plasma spraying of hydroxylapatite, allowing cementless fixation. The device is used in combination with the components of the company's own approved product, "Aequalis Reversed Shoulder Prosthesis" (Approval No. 22500BZI00021000). (The original product is in a reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
8	May 19, 2015 Total review time: 425 days Regulatory review time: 239 days	- Domestic and foreign clinical study results	47	Radioactive Pharmaceutical Synthesizer FASTlab (GE Healthcare Japan Corporation)	Change	Instrument & apparatus 10 Radiopharmaceutical synthesizer	A radioactive pharmaceutical synthesizer used for the automated preparation of a radioisotope labeled compound, flutemetamol (^{18}F) injection by remote control system indicated for the visualization of beta-amyloid plaque in the brain in patients with cognitive impairment who are suspected of having Alzheimer's disease. Results from domestic and foreign clinical studies were submitted as evaluation data on the efficacy and safety of this product and flutemetamol (^{18}F) injection.
8	Sep. 28, 2015 Total review time: 546 days Regulatory review time: 161 days	－ Domestic and foreign clinical study results	48	Radiopharmaceutical Synthesis Device MPS200Aβ (Sumitomo Heavy Industries, Ltd.)	Approval	Instrument & apparatus 10 Radiopharmaceutical synthesizer	Radiopharmaceutical Synthesis Device used for the semi-automated preparation of a radioisotope labeled compound, florbetapir (^{18}F) injection, by a remote control system indicated for the visualization of beta-amyloid plaque in the brains in patients with cognitive impairment who are suspected of having Alzheimer's disease. Results from non-clinical studies, and domestic and foreign clinical studies were submitted as evaluation data on the efficacy and safety of this product and florbetapir (^{18}F) injection.
Robotic, ICT, and other devices (not classified as other categories)	Nov. 25, 2015 Total review time: 245 days Regulatory review time: 107 days	－ Domestic clinical study results	49	HAL For Medical Use (Lower Limb Type) (CYBERDYNE Inc.)	Approval	Instrument & apparatus 58 Biosignal-responsive motor function improvement device	The device is composed of components that are to be attached to a patient, including a base component, battery pack, upper and lower leg cuff, and sensor shoes, and is used to improve walking function in patients with impaired ambulation caused by slowly progressive neurologic or muscular disease (spinal muscular atrophy, spinobulbar muscular atrophy, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, distal myopathy, sporadic inclusion body myositis, congenital myopathy, muscular dystrophy). Results from a domestic clinical trial (an investigator-initiated clinical trial) conducted to confirm the safety and effect in the improvement of walking function were submitted. [Orphan device]
Robotic, ICT, and other devices (not classified as other categories)	Dec. 22, 2015 Total review time: 777 days Regulatory review time: 193 days	Feb. 18, 2009 Foreign and domestic clinical study results	50	da Vinci Si Surgical System (Intuitive Surgical G.K.)	Change	Instrument & apparatus 12 Surgical robot, operation unit	A device to assist surgeon's manipulation in endoscopic surgery in areas of general digestive surgery, thoracic surgery, cardiac surgery (limited to intracardiac surgical operations under cardiac arrest), urology, and gynecology. The application was submitted for an additional indication for cardiac surgery (limited to intracardiac surgical operations under cardiac arrest) (A "partial change" application). In the United States and Japan, studies on mitral valve repair and atrial septal defect closure were conducted using the similar approved device “da Vinci Surgical System” (approval No. 22100BZX01049000). By extrapolating these results, the success rate of surgery and safety of this device were demonstrated.
Robotic, ICT, and other devices (not classified as other categories)	Dec. 22, 2015 Total review time: 804 days Regulatory review time: 222 days	Mar. 19, 2008 Foreign and domestic clinical study results	51	da Vinci Surgical System (Intuitive Surgical G.K.)	Change	Instrument & apparatus 12 Surgical robot, operation unit	A device to assist surgeon's manipulation in endoscopic surgery in areas of general digestive surgery, thoracic surgery, cardiac surgery (limited to intracardiac surgical operations under cardiac arrest), urology, and gynecology. The application was submitted for an additional indication for cardiac surgery (limited to intracardiac surgical operations under cardiac arrest) (A "partial change" application). In the United States and Japan, studies on mitral valve repair and atrial septal defect closure were conducted, and the success rate of surgery and safety of this device were demonstrated.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval /Partial Change	Classification Generic Name	Notes
Specified partial change	Sep. 2, 2015 Total review time: 29 days Regulatory review time: 19 days	- No clinical study results	52	Promus Premier Stent System (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Coronary stent	A drug-eluting stent system used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion of 34 mm or less in length, with a reference vessel diameter of 2.25-3.50 mm. The application was submitted for addition of the colorant raw material used for the tip of the monorail delivery catheter, falling under a "specified partial change" based on "Acceleration of Procedure for Specified Change for Medical Devices" (PFSB/ELD/OMDE Notification No.1110001 dated on November 10, 2008). (A "partial change" application submitted during the reexamination period)
Specified partial change	Mar. 22, 2016 Total review time: 92 days Regulatory review time: 65 days	- No clinical study results	53	COOK Zenith Dissection Endovascular System (Cook Japan Inc.)	Change	Instrument & apparatus 7 Aortic stent graft	A stent graft system used for the treatment of acute complicated Stanford type B aortic dissection. The application was submitted to add a graft material as a "specified partial change" based on "Acceleration of Procedure for Specified Change for Medical Devices" (PFSB/ELD/OMDE Notification No. 1110001 dated on November 10, 2008). (A "partial change" application submitted during the reexamination period)
Cellular and tissue-based products	Apr. 28, 2015 Total review time: 224 days Regulatory review time: 144 days	- No clinical study results	54	Jace (Japan Tissue Engineering Co.,Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	An autologous cultured epidermis manufactured with epidermal cells indicated for use in patients with severe and extensive burn when sufficient donor sites for autologous skin grafts are not available and the total area of deep dermal and full-thickness burns is 30% or more of the total body surface area. This application is for a partial change in the manufacturing process to add the available culture media in each cell culture process. Results of comparing characteristics of product before and after the change in the manufacturing process were submitted.
Cellular and tissue-based products	May 22, 2015 Total review time: 196 days Regulatory review time: 96 days	- No clinical study results	55	Jacc (Japan Tissue Engineering Co.,Ltd.)	Change	Instrument & apparatus 7 Human autologous cells and tissue	An autologous cultured cartilage indicated for use in patients with a cartilage deficiency area of 4 cm^2 or more without other standard surgical treatment options, in order to improve clinical symptoms of traumatic cartilage deficiency and osteochondritis dissecans. This application is for a partial change related to the addition of a sub-component, which is to measure the shape and size of cartilage deficiency site in knee joints, for the final product. Results of evaluation based on the sterilization and biological safety testing of sub-component were submitted.
Bio-derived Device (Quality)	Aug. 13, 2015 Total review time: 97 days Regulatory review time: 41 days	Jan. 17, 2014 No clinical study results	56	CoreValve (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Transcatheter porcine pericardial valve	A self-expanding biological percutaneous aortic valve (porcine pericardial valve) system used for transcatheter valve implantation in the native aortic valve for patients with symptomatic severe aortic stenosis attributed to sclerosis and degeneration of the cusp of the native aortic valve, for whom surgery cannot be performed. The application was submitted to change the manufacturing process of this device (viral inactivation process). (A "partial change" application submitted during the post-market performance review period)

Table 6. Products Approved in FY 2015: Improved Medical Devices (with Clinical Data)

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
1	Jun. 3, 2015 Total review time: 239 days Regulatory review time: 96 days	Dec. 17, 2014 Foreign clinical study results	1	Tecnis Multifocal 1-Piece (AMO Japan K.K.)	Change	Instrument & apparatus 72 Multifocal posterior chamber lens	A multifocal posterior chamber lens to be inserted as a substitute for a crystalline lens to correct near and/or far vision in patients with aphakia. This application is for a partial change to mainly add a low ADD model to the current models. Results of comparative studies using an existing approved monofocal posterior chamber lens as controls to evaluate clinical efficacy and fundamental safety, including visual function of the additional model as a multifocal posterior chamber lens, were submitted.
1	Jul. 8, 2015 Total review time: 265 days Regulatory review time: 104 days	Dec. 21, 2011 Foreign clinical study results	2	Catalys Precision Laser (AMO Japan K.K.)	Approval	Instrument & apparatus 31 Ophthalmic pulsed laser surgical instrument	An ophthalmic pulsed laser surgical instrument used for the anterior capsulotomy, the lens fragmentation, and creation of corneal incisions in cataract surgery. A foreign clinical study was conducted to confirm that this device has no particular issues as compared with the conventional standard technique used in cataract surgery.
1	Aug. 28, 2015 Total review time: 423 days Regulatory review time: 203 days	Jun. 27, 2003 Domestic clinical study results	3	MED-EL Middle Ear Implant VSB (MED-EL Elektro-Medizinische Ger äte GmbH)	Approval	Medical products 4 Middle Ear Implant	A middle ear implant system that processes signals incorporated from a microphone and vibrates a floating mass transducer implanted in the middle ear. Domestic clinical studies were conducted to confirm improved hearing in patients with conductive hearing loss or with mixed conductive-sensorineural hearing loss.
1	Sep. 16, 2015 Total review time: 266 days Regulatory review time: 143 days	Jan. 29, 2014 Foreign clinical study results	4	Air Optix Colors (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Daily wear, two-week replacement, reusable colored contact lenses with vision correction, and reusable colored contact lenses without vision correction. These contact lenses have additional feature of colored ring-shaped regions to the previously approved two-week replacement, silicone hydrogel contact lenses, “Air Optix (22000BZX00109000)”. Novelty was recognized in clear coat which directly contacts with the cornea. Results from multicenter, randomized, open clinical studies conducted in the United States were submitted to confirm efficacy and safety in wearing the lenses to correct visual acuity.
1	Sep. 16, 2015 Total review time: 266 days Regulatory review time: 143 days	Jan. 29, 2014 Foreign clinical study results	5	Air Optix Bright (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Daily wear, two-week replacement, reusable colored contact lenses with vision correction, and reusable colored contact lenses without vision correction. These contact lenses have additional feature of colored ring-shaped regions to the previously approved two-week replacement, silicone hydrogel contact lens “Air Optix (22000BZX00109000)”. The application was submitted for obtaining multiple brand names for “Air Optix Colors.”
Ophthalmology and Otorhinolaryngology	Oct. 19, 2015 Total review time: 263 days Regulatory review time: 159 days	- Domestic clinical study results	6	1 Day Menicon PremiO (Menicon Co., Ltd.)	Approval	Instrument & apparatus 72 Single-use colored contact lenses for correcting visual acuity	Daily wear, single-use, colored contact lenses for correction of visual acuity. The lens is composed of silicone hydrogel with a water content of 56% and an oxygen permeability (Dk) of 64, and is wholly colored in pale blue, containing ultraviolet absorber. Plasma treatment on the surface of the lens improves the wetness of the lens surface at the time of wearing. Novelty was recognized in the raw material. Results from single-arm, open-label, clinical studies conducted in Japan were submitted to confirm efficacy and safety in wearing the lenses to correct visual acuity.
Ophthalmology and Otorhinolaryngology	Oct. 28, 2015 Total review time: 188 days Regulatory review time: 91 days	Aug. 30, 2013 Domestic clinical study results	7	MyDay (CooperVision Japan, Inc.)	Approval	Instrument & apparatus 72 Single-use colored contact lenses for correcting visual acuity	Daily wear, single-use, colored contact lenses for correction of visual acuity. The lens is composed of stenfilcon A, a silicone hydrogel material with a water content of 54% and an oxygen permeability (Dk) of 80, and is wholly colored in pale blue, containing ultraviolet absorber. Novelty was recognized in the raw material. Results from single-arm, open-label, clinical studies conducted in Japan were submitted to confirm efficacy and safety in wearing the lenses to correct visual acuity.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
2	Jul. 17, 2015 Total review time: 263 days Regulatory review time: 82 days	Aug. 20, 2014 Foreign clinical study results	8	Straumann Implant (Roxolid SLActive) BLT (Straumann Japan K.K.)	Approval	Medical products 4 Dental implant body	A bone level dental implant, which is to be placed into the jawbone and has an apically tapered root apex. Similar to the approved device “Straumann Implant (SLActive) BL” (Approval No. 22600BZX00257000), this device is supplied in a sealed vial filled with normal saline to keep hydrophilic nature of titanium until just before use, which accelerates the osseointegration and enables the early loading. This device has the identical shape and roughened surface treatment to the previously approved device “Straumann Implant (Ti SLA) BLT” (Approval No. 22700BZX00167000). However, this device adopts a titanium alloy with zirconium as a raw material to improve strength as compared with the approved device made of pure titanium. Results from multicenter, randomized, comparative studies conducted in foreign countries were submitted to demonstrate that the device has a bone bonding ability equivalent to that of the approved device made of pure titanium.
2	Aug. 26, 2015 Total review time: 413 days Regulatory review time: 189 days	Feb. 26, 2009 Foreign clinical study results	9	Straumann Implant (Roxolid SLActive) BL (Straumann Japan K.K.)	Approval	Medical products 4 Dental implant body	A bone level dental implant, which is placed into the jawbone and has a straight root apex. Similar to the approved device “Straumann Implant (SLActive) BL” (Approval No. 22600BZX00257000), this device is supplied in a sealed vial filled with normal saline to keep hydrophilic nature of titanium until just before use, which accelerates the osseointegration and enables the early loading. This device adopts a titanium alloy with zirconium as a raw material to improve strength as compared with the approved device made of pure titanium. Results from multicenter, randomized, comparative studies conducted in foreign countries were submitted to demonstrate that the device has a bone bonding ability equivalent to that of the approved device made of pure titanium.
Dentistry and Oral Medicine	Dec. 25, 2015 Total review time: 540 days Regulatory review time: 315 days	Feb. 26, 2009 Foreign clinical study results	10	Straumann Implant (Roxolid SLActive) TL (Straumann Japan K.K.)	Approval	Medical products 4 Dental implant body	A tissue level dental implant, which is partially or wholly placed into the jawbone. The device has the identical shape and surface treatment to the previously approved device “Straumann Implant (SLActive) TL” (Approval No. 22600BZX00016000). The point of improvement is that the device adopts a titanium alloy with zirconium as a raw material to improve strength. Results from foreign clinical studies were submitted for the evaluation of the efficacy and safety of this raw material.
3-1	Jul. 31, 2015 Total review time: 189 days Regulatory review time: 92 days	Sep. 3, 2014 Foreign clinical study results	11	XIENCE Alpine Drug Eluting Stent (Abbott Vascular Japan Co., Ltd.)	Change	Instrument & apparatus 7 Coronary stent	A stent system consisting of a drug-eluting stent used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion (a lesion length of 32 mm or less) with a reference vessel diameter of 2.25-4.25 mm and a delivery catheter used to implant a stent to the site of stenosis. The application was submitted for an additional stent size of 4.0 mm diameter. The added stent of 4.0 mm diameter is identical to the approved stent of 3.5 mm diameter. The stent delivery system is identical to the approved product except for the balloon size. (A "partial change" application) Results from clinical studies conducted using the company's own approved product with a stent identical to this product were submitted for evaluation of the efficacy and safety of this added size in clinical use.
3-1	Aug. 7, 2015 Total review time: 346 days Regulatory review time: 135 days	− Global clinical trial results	12	Ultimaster (Terumo Corporation)	Approval	Instrument & apparatus 7 Coronary stent	A coronary stent system consisting of a sirolimus-eluting stent used for the treatment of patients with symptomatic ischemic heart disease and a delivery catheter used to implant the stent at stenotic lesions. The coating layer of the stent is composed of sirolimus and bioabsorbable polymer only, so that the stent behaves as a bare-metal stent in the late phase after the stent implantation. Results from the global clinical trials conducted to evaluate the efficacy and safety of this device for patients with symptomatic ischemic heart disease were submitted.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 9, 2015 Total review time: 412 days Regulatory review time: 234 days	May 6, 2011 Foreign clinical study results	13	AFX Stent Graft System (Cosmotec Co., Ltd.)	Approval	Instrument & apparatus 7 Aortic stent graft	AFX Stent Graft System consists of a stent graft and delivery system for the endovascular treatment of infrarenal abdominal aortic aneurysms. The device has the basic structure of the company's own approved product “Powerlink Stent Graft System” (Approval No. 22000BZX00110000) (hereinafter referred to as “Powerlink”) with thinner outer diameter of the delivery catheter achieved by thinning the graft material. The indications for this device are the same as those for the Powerlink. In addition, a suprarenal cuff extension, which was not included in the Powerlink, was added as a component. Results from foreign clinical studies were submitted for the evaluation of the efficacy and safety of the cuff extension.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Oct. 22, 2015 Total review time: 269 days Regulatory review time: 156 days	– Domestic clinical study results	14	LSO1470 Laser (Medico's Hirata Inc.)	Approval	Instrument & apparatus 31 Diode laser	A laser surgical device for treatment of varicose veins of lower extremities by guiding the laser light oscillated from semiconductor laser element into a fiber and irradiating a vein of lower extremities to occlude the saphenous vein. The wavelength of the laser is 1470 nm. In order to verify the efficacy and safety of the product, a single-arm clinical study was conducted to compare the clinical study results of the approved product of 980 nm “ELVeS Laser” (Approval No. 22200BZX00660000).
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 8, 2016 Total review time: 326 days Regulatory review time: 158 days	Jul. 21, 2015 Global clinical trial results	15	Innova Vascular Stent (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Stent for blood vessel	A self-expanding vascular stent used for the treatment of symptomatic vascular disease in superficial femoral artery or proximal popliteal artery, with reference vessel diameters from 4 mm to 7 mm, lesion lengths up to 150 mm on each limb, and for treatment of acute or impending occlusion in the aforementioned sites following the failure of interventional treatment. Results from global clinical trial were submitted to evaluate the efficacy and safety of the device in the treatment of symptomatic vascular diseases.
3-2	Jul. 6, 2015 Total review time: 684 days Regulatory review time: 483 days	Dec. 3, 2001 Domestic clinical study results Foreign clinical study results	16	Bioglue Surgical Adhesive (Century Medical, Inc.)	Change	Medical products 4 Albumin-use adhesive	A surgical adhesive consisting of two solutions: glutaraldehyde and bovine serum albumin. The product has already been approved (approval No. 22200BZY00003000) for the use for adhesion and hemostasis at the suture site of an artificial blood vessel associated with closure of aortic dissection and a false lumen (including dissecting aneurysm of the aorta) as its intended use. The application was submitted to expand the indications to “assistance in adhesion and hemostasis at the resection/suture site of the aorta and at the suture site of the heart.” (A "partial change" application) Results from domestic and foreign clinical studies on cardiovascular surgeries, etc. were submitted for evaluation of the efficacy and safety of this product.
3-2	Jul. 23, 2015 Total review time: 266 days Regulatory review time: 169 days	– Foreign clinical study results Domestic clinical study results	17	Cook Zenith AAA-LP Endovascular Graft (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	A stent graft system for abdominal aortic aneurysms which has the basic structure of the company's own approved product “Cook Zenith AAA Endovascular Graft” (Approval No. 21800BZY10175000) with the smaller outer diameter of the delivery catheter achieved by thinning the graft material. Results from domestic and foreign clinical studies were submitted for the evaluation of the efficacy and safety of this device for patients with abdominal aortic aneurysm.
3-2	Aug. 28, 2015 Total review time: 184 days Regulatory review time: 104 days	– Clinical evaluation report	18	Inoue Balloon for Aortic Valve (Toray Industries, Inc.)	Approval	Instrument & apparatus 51 Balloon-dilating catheter for valvuloplasty	A balloon catheter used for percutaneous transluminal aortic valvuloplasty (PTAV) for aortic valve stenosis. The device has identical shape and structure to those of the approved product, Inoue Balloon for mitral valve (Approval No. 16300BZZ01718000). A clinical evaluation report was submitted to demonstrate the safety and efficacy on use of this product in PTAV.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
Cardiopulmonary Circulation	Oct. 19, 2015 Total review time: 174 days Regulatory review time: 104 days	Jun. 24, 2014 Foreign clinical study results	19	Solo Stentless Biological Valve (Sorin Group Italia S.r.l.)	Approval	Instrument & apparatus 7 Bovine pericardial valve	A stentless biological valve made of bovine pericardial membrane to replace the malfunctioning aortic valve due to disease or injury. The device is designed to be implanted in the supra annular position with a single suture line, which was impossible with conventional stentless biological valves. Results from foreign clinical studies conducted based on ISO 5840 were submitted for the evaluation of the efficacy and safety of this product.
Cardiopulmonary Circulation	Nov. 6, 2015 Total review time: 329 days Regulatory review time: 214 days	－ Foreign clinical study results	20	Accolade MRI (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	An implantable cardiac pacemaker used to treat bradycardia. Patients implanted with the device can have an MRI scan only when the condition meets imaging criteria. A clinical evaluation report was submitted to demonstrate the safety of this device in MRI scans. In addition, results from foreign clinical studies were submitted for evaluation of the efficacy and safety of a function that automatically regulates the pulse amplitude in atrial pacing.
Cardiopulmonary Circulation	Nov. 6, 2015 Total review time: 329 days Regulatory review time: 214 days	－ Clinical evaluation report	21	Ingevity AFx (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker lead	A pacemaker lead used when connected to an implantable cardiac pacemaker, etc. Patients implanted with the device can have an MRI scan only when the condition meets imaging criteria. A clinical evaluation report summarizing the clinical data on the product in foreign countries was submitted for the evaluation of the safety of this device in MRI scans.
Cardiopulmonary Circulation	Nov. 6, 2015 Total review time: 329 days Regulatory review time: 214 days	－ Clinical evaluation report	22	Ingevity (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Endocardial implantable pacemaker lead	A pacemaker lead used when connected to an implantable cardiac pacemaker, etc. Patients implanted with the device can have an MRI scan only when the condition meets imaging criteria. A clinical evaluation report summarizing the clinical data on the product in foreign countries was submitted for the evaluation of the safety of this device in MRI scans.
Cardiopulmonary Circulation	Nov. 18, 2015 Total review time: 357 days Regulatory review time: 279 days	－ Domestic clinical study results	23	SATAKE・HotBalloon Generator (Toray Industries, Inc.)	Approval	Instrument & apparatus 29 Electronic surgical unit for percutaneous ablation	A high-frequency generator used for percutaneous catheter ablation to treat tachyarrhythmia. The device was developed as a high-frequency generator used exclusively with the “SATAKE HotBalloon Catheter” (Approval No. 22700BZX00355000). Results from domestic clinical studies using the previous product as an investigational device were submitted to verify the efficacy and safety in patients with drug-resistant symptomatic paroxysmal atrial fibrillation in comparison with control groups receiving antiarrhythmic drugs.
Cardiopulmonary Circulation	Nov. 27, 2015 Total review time: 245 days Regulatory review time: 153 days	Oct. 2, 2015 Domestic and foreign clinical study results	24	Synergy Stent System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system consisting of an everolimus-eluting stent used for the treatment of patients with symptomatic ischemic heart disease who have a new coronary lesion (a lesion length of 34 mm or less) with a reference vessel diameter of 2.25-4.00 mm and a delivery catheter used to implant a stent at the site of stenosis. Results from domestic and foreign clinical studies with the use of previous products were attached to demonstrate that this device has efficacy and safety equivalent to those of the approved coronary stents.
Cardiopulmonary Circulation	Dec. 9, 2015 Total review time: 230 days Regulatory review time: 130 days	- Domestic clinical study results	25	Kaneka Bare Metal Stent CO-R1 (Kaneka Corporation)	Approval	Instrument & apparatus 7 Coronary stent	A coronary stent used for the treatment (including treatment of acute or impending occlusion associated with failure of intervention therapy) of patients with symptomatic ischemic heart disease who have a new or recurrent coronary lesion (a lesion length of 28 mm or less) with a reference vessel diameter of 3.0-4.0 mm. Results from domestic clinical studies were submitted for evaluation of the efficacy and safety of this device.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
Cardiopulmonary Circulation	Jan. 12, 2016 Total review time: 817 days Regulatory review time: 179 days	Jun. 10, 2010 Foreign clinical study results	26	AtriCure Left Atrial Appendage Clip (Century Medical, Inc.)	Approval	Instrument & apparatus 30 Clip for cardiac tissue	A device used to occlude the left atrial appendage in patients with a risk of thromboembolism including atrial fibrillation and other conditions during an open-heart cardiovascular surgery. Results from foreign clinical studies conducted to evaluate the efficacy and safety of the device were submitted.
Cardiopulmonary Circulation	Feb. 2, 2016 Total review time: 347 days Regulatory review time: 276 days	- Clinical evaluation report	27	Durata ICD Screw-in Lead (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device consists of an implantable defibrillator/pacemaker lead and accessories that are connected to a pulse generator for use in the treatment of tachyarrhythmia. A clinical evaluation report was submitted to evaluate the safety of the device under MRI scans. The application was submitted to allow patients with a certain model of the device to undergo an MRI scan under predefined conditions. (A "partial change" application)
Cardiopulmonary Circulation	Feb. 2, 2016 Total review time: 347 days Regulatory review time: 276 days	- Clinical evaluation report	28	Durata ICD Lead Single Coil (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device consists of an implantable defibrillator/pacemaker lead and accessories that are connected to a pulse generator for use in the treatment of tachyarrhythmia. A clinical evaluation report was submitted to evaluate the safety of the device under MRI scans. The application was submitted to allow patients with a certain model of the device to undergo an MRI scan under predefined conditions. (A "partial change" application)
Cardiopulmonary Circulation	Feb. 2, 2016 Total review time: 347 days Regulatory review time: 276 days	- Clinical evaluation report	29	Ellipse ICD (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	The device consists of an implantable defibrillator and accessories. It is intended to be used for patients at high risk of sudden death due to ventricular tachyarrhythmia. A clinical evaluation report was submitted to evaluate the safety of the device under MRI scans. The application was submitted to allow patients with a certain model of the device to undergo an MRI scan under predefined conditions. (A "partial change" application)
Cardiopulmonary Circulation	Feb. 2, 2016 Total review time: 347 days Regulatory review time: 276 days	- Clinical evaluation report	30	Ellipse Limited ICD (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	The device consists of an implantable defibrillator and accessories. It is intended to be used for patients at high risk of sudden death due to ventricular tachyarrhythmia. A clinical evaluation report was submitted to evaluate the safety of the device under MRI scans. The application was submitted to allow patients with a certain model of the device to undergo an MRI scan under predefined conditions. (A "partial change" application)
4	Jun. 22, 2015 Total review time: 214 days Regulatory review time: 108 days	- Clinical evaluation report	31	Assurity MRI (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker to regulate the heart rhythm by delivering the electrical stimulus to myocardium for a long period. The patients implanted with the device can have an MRI scan under specific conditions. A clinical evaluation report summarizing the results of the foreign clinical studies related to the device was submitted to evaluate the safety of the device on MRI scan.
4	Jun. 22, 2015 Total review time: 214 days Regulatory review time: 118 days	- Clinical evaluation report	32	Endurity MRI (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable cardiac pacemaker	The device is an implantable cardiac pacemaker to regulate the heart rhythm by delivering the electrical stimulus to myocardium for a long period. The patients implanted with the device can have an MRI scan under specific conditions. A clinical evaluation report summarizing the results of the foreign clinical studies related to the device was submitted to evaluate the safety of the device on MRI scan.
4	Jun. 22, 2015 Total review time: 214 days Regulatory review time: 120 days	- Clinical evaluation report	33	Tendril STS (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable cardiac pacemaker lead. The patients implanted with the specific model of the leads can have an MRI scan under specific conditions. The application is for a partial change for the leads that can be labeled as MR conditional. A clinical evaluation report summarizing the results of the foreign clinical studies related to the device was submitted to evaluate the safety of the device on MRI scan.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
4	Jun. 22, 2015 Total review time: 214 days Regulatory review time: 120 days	- Clinical evaluation report	34	Tendril STS J (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable cardiac pacemaker lead. The patients implanted with the specific model of the leads can have an MRI scan under specific conditions. This application is submitted in relation to the partial change application for "Tendril STS" (Approval No. 22200BZX00085000), which is identical to this device and has obtained the approval for multiple trade names.
5	Jun. 24, 2015 Total review time: 1470 days Regulatory review time: 215 days	Sep. 4, 2007 Clinical evaluation report	35	ERBE JET2 (AMCO Inc.)	Approval	Instrument & apparatus 12 Hydraulic knife	A hydraulic knife used for incision, ablation, or resection of liver tissue. This knife incises, ablates, or resects the liver tissue using the hydraulic pressure energy of a high pressure water jetting from the tip of hand-held applicator. A clinical evaluation report was provided in order to evaluate that the safety of the technique using this product was not inferior to the conventional technique.
5	Aug. 5, 2015 Total review time: 390 days Regulatory review time: 185 days	Mar. 26, 2007 Clinical evaluation report	36	Revolix 120 (Takai Hospital Supply Co,. Ltd.)	Approval	Instrument & apparatus 31 Thulium YAG laser	A thulium YAG laser used for incision, hemostasis, coagulation and vaporization of soft biological tissue under direct vision or endoscopy. This device is also used for treatment of prostatic hyperplasia. Laser light irradiated from this device (wavelength of 2.0 μm, continuous wave) has a similar wavelength of the approved product, the holmium YAG laser (wavelength of 2.1 μm, pulse wave). However, this device irradiates a continuous wave and has increased maximum output as compared with that of the approved device. A clinical evaluation report was submitted to compare and evaluate the treatment outcomes between this device and existing therapies for transurethral prostate treatment, in which the high output is utilized.
5	Aug. 13, 2015 Total review time: 371 days Regulatory review time: 166 days	− Domestic clinical study results	37	Surefilter (Nipro Corporation)	Approval	Instrument & apparatus 7 Slow continuous hemofilter	A slow continuous hemofilter used for elimination of unnecessary metabolites and excess fluid in the blood of patients with renal failure complicated by cardiovascular diseases such as multiple organ failure, severe complications, and edema. This device has novelty in that the material of the hollow fiber membrane is polyether sulfone. Clinical studies were conducted to evaluate the usefulness of this device in patients with acute renal failure, etc., for whom slow continuous hemofiltration is indicated.
Gastroenterology, Genitourinary, and Reproductive Medicine	Nov. 24, 2015 Total review time: 378 days Regulatory review time: 235 days	- Clinical evaluation report	38	Electrohydraulic Lithotripter Lithotron EL 27 (Century Medical, Inc.)	Approval	Instrument & apparatus 12 Intracorporeal electrohydraulic shock wave lithotripter	An intracorporeal electrohydraulic shock wave lithotripter that crushes gallstones using shock waves generated by a high-voltage discharge between electrodes exposed at the tip of probe. Test results on electrical safety, electromagnetic compatibility, biological safety, stability, durability, and performance of this device were submitted. In addition, clinical results on electrohydraulic shock wave lithotripsy (hereinafter referred to as “EHL”) of this device for gallstones were evaluated. A clinical evaluation report was submitted to compare the treatment outcomes of EHL for gallstones between by this device and by other devices employing the same principle as this device (including the approved devices).
Gastroenterology, Genitourinary, and Reproductive Medicine	Dec. 21, 2015 Total review time: 360 days Regulatory review time: 235 days	- Clinical evaluation report	39	Modulith (Sumire Medical Corporation)	Change	Instrument & apparatus 12 Extracorporeal lithotripter	An extracorporeal lithotripter used to generate shock waves and irradiate from outside the body to fragment and crush calculi formed in the body. The application was submitted to add the treatment of pancreatolithiasis to the previously approved intended use or indications. (A "partial change" application) In order to add the treatment of pancreatolithiasis, the efficacy equivalent to that of the approved device used for the treatment of pancreatolithiasis was assessed based on a clinical evaluation report. Since the safety of treatment of pancreatolithiasis by focal pressure exceeding that of the approved device was difficult to evaluate with the clinical evaluation report, the safety was guaranteed through restrictions with the contraindications and prohibitions listed in the package insert.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
Gastroenterology, Genitourinary, and Reproductive Medicine	Feb. 24, 2016 Total review time: 462 days Regulatory review time: 232 days	Sep. 15, 2010 Domestic clinical study results	40	Ceralas HPD Laser (Integral Corporation)	Approval	Instrument & apparatus 31 Diode laser	A diode laser with a central wavelength of 980 nm (continuous wave) used in laser vaporization for benign prostatic hyperplasia. The device differs from existing approved medical devices indicated for benign prostatic hyperplasia in that the use of continuous wave laser with a wavelength of 980 nm and the maximum output power 300 W emitted from the oscillator. Domestic clinical study results were submitted to evaluate the efficacy and safety of the device in the treatment of benign prostatic hyperplasia.
Gastroenterology, Genitourinary, and Reproductive Medicine	Mar. 11, 2016 Total review time: 268 days Regulatory review time: 128 days	- Domestic clinical study results	41	P (LA/CL) Suture (Kono Seisakusho Co., Ltd.)	Approval	Medical products 2 Synthetic absorbable suture	Synthetic monofilament absorbable sutures prepared from lactide-caprolactone copolymer fibers. New raw materials were used to improve the suture workability. Therefore, domestic clinical study results were attached to evaluate the efficacy and safety of the device in procedures such as suturing, anastomosis, and ligation in general surgery.
6-1	Sep. 17, 2015 Total review time: 269 days Regulatory review time: 161 days	- Domestic clinical study results	42	AG-PROTEX HIP System (KYOCERA Medical Corporation)	Approval	Medical products 4 Total hip prosthesis	A product containing a small amount of silver in the hydroxyapatite coating of the company's own approved acetabular cup, "SQRUM HA Shell" (Approval No. 22500BZX00152000) and femur stem " KYOCERA PerFix HA Stem Fullcoat" (Approval No. 22100BZX01118000), in anticipation of an antibacterial effect. Results from a domestic clinical study were submitted to confirm that the device has equivalent efficacy to the approved hip prosthesis and that no serious malfunction occurs.
6-2	Apr. 21, 2015 Total review time: 299 days Regulatory review time: 110 days	Jan. 7, 2010 Foreign clinical study results	43	Juvederm Vista Ultra XC (Allergan Japan KK)	Approval	Medical Products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft-tissue using hyaluronic acid used to correct facial wrinkles and folds. The product is "Juvederm Vista Ultra" (22600BZX00108000), an existing approved product of Allergan Japan KK, with added lidocaine hydrochloride to relieve pain at the time of treatment. Results from randomized, within-subject controlled studies conducted in the United States were submitted to verify the effect of pain relief compared to that of the existing approved product.
6-2	Apr. 21, 2015 Total review time: 299 days Regulatory review time: 110 days	Jan. 7, 2010 Foreign clinical study results	44	Juvederm Vista Ultra Plus XC (Allergan Japan KK)	Approval	Medical Products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft-tissue using hyaluronic acid used to correct facial wrinkles and folds. The product is "Juvederm Vista Ultra Plus" (22600BZX00109000), an existing approved product of Allergan Japan KK, with added lidocaine hydrochloride to relieve pain at the time of treatment. Results from randomized, within-subject controlled studies conducted in the United States were submitted to verify the effect of pain relief compared to that of the existing approved product.
6-2	Jun. 9, 2015 Total review time: 473 days Regulatory review time: 64 days	Jan. 29, 2010 Foreign clinical study results	45	Restylane Lido (Galderma KK)	Approval	Medical Products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft-tissue made of hyaluronic acid designed to improve appearance of facial wrinkles and folds, which is indicated for injection into the mid to deep dermis. Lidocaine hydrochloride is added to relieve pain at the time of injection. A report on prospective, randomized, within-subject controlled study conducted in the United States, and 3 additional clinical study reports were submitted in order to verify the effects on correction of nasolabial fold and pain relief.
6-2	Jun. 9, 2015 Total review time: 473 days Regulatory review time: 64 days	Jan. 29, 2010 Foreign clinical study results	46	Restylane Perlane Lido (Galderma KK)	Approval	Medical Products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material into soft-tissue made of hyaluronic acid designed to improve appearance of facial wrinkles and folds, which is indicated for injection into the deep dermis to superficial subcutis. Lidocaine hydrochloride is added to relieve pain at the time of injection. A report on prospective, randomized, within-subject controlled study conducted in Europe, and 5 additional clinical study reports were submitted in order to verify the effects on correction of nasolabial fold and pain relief.

Review Category	Approval Date	Date Approved in US Clinical Study Results: Domestic/Foreign	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Generic Name	Notes
Orthopedic and Plastic Surgery	Dec. 2, 2015 Total review time: 383 days Regulatory review time: 173 days	- Domestic clinical study results	47	Biohesive Ag Light (Alcare Co., Ltd.)	Approval	Medical products 4 Antibacterial wound dressing and protecting material	A hydrocolloid dressing containing silver sulfadiazine in anticipation of an antibacterial effect. The device is intended to be used for wounds reaching into dermis, which is the limited-use purpose of the company's own approved antibacterial wound dressing and protecting material “Biohesive Ag” (Approval No. 22300BZX00001000). Results from clinical studies previously submitted for application of the above approved product and data on those results with new analyzation using a stratified analysis were submitted to confirm the efficacy and safety of this product in wounds reaching into dermis.
Orthopedic and Plastic Surgery	Mar. 9, 2016 Total review time: 217 days Regulatory review time: 111 days	- Clinical evaluation report	48	Lima Delta Ceramic Liners (Lima Japan K.K.)	Approval	Medical products 4 Artificial hip joint, acetabular component	The device is an acetabular component for a hip prosthesis made of the material "Biolox delta" (manufactured by CeramTec) and is used in combination with the approved Lima's device, "Lima Delta Ceramic Head" (Approval No. 22500BZX00311000), which is made of the same material as the new device. Given that this is the Lima's first liner made of Biolox delta and the novelty exists in the combination of raw materials, a clinical evaluation report based on the post-market performance outside Japan was submitted to confirm the equivalent efficacy and safety of the new combination to those of the conventional combination using different materials.
Orthopedic and Plastic Surgery	Mar. 28, 2016 Total review time: 396 days Regulatory review time: 123 days	Aug. 11, 2014 Foreign clinical study results	49	enLIGHTen (Cutera K.K.)	Approval	Instrument & apparatus 31 Neodymium:YAG laser	Q-switched neodymium (Nd): YAG laser used for the vaporization and removal of benign pigmented lesions on the body surface. The pulse width can be set at 750 psec or 2 nsec, allowing the treatment with high peak powers. Foreign clinical study results were submitted to evaluate the risk of complications or adverse events associated with an increase in peak power.
Orthopedic and Plastic Surgery	Mar. 30, 2016 Total review time: 496 days Regulatory review time: 148 days	Feb. 5, 2004 Clinical evaluation report	50	SmartSet GMV Endurance Gentamicin Bone Cement (Johnson & Johnson K.K.)	Approval	Medical products 4 Orthopedic Bone Cement	This product is orthopedic bone cement containing gentamicin sulfate as antibiotic, and is indicated for use in the second stage of a two-stage revision for total joint arthroplasty after the initial infection has been cleared. A clinical evaluation report was submitted to demonstrate that a necessary fixation can be obtained, and the safety of the device is equivalent to that of bone cements without antibiotics.
Robotic, ICT, and other devices (not classified as other categories)	Mar. 30, 2016 Total review time: 581 days Regulatory review time: 271 days	- Domestic clinical study results	51	Chest Tomosynthesis CAD: Cadviser TS （Shimadzu Corporation）	Approval	Instrument & apparatus 9 Diagnostic x-ray imaging system workstation	An X-ray diagnostic imaging workstation intended to provide imaging information for diagnosis, which is the computer-processed image data of the lung field from thoracic tomosynthesis images produced using an X-ray fluoroscopy system or an X-ray diagnostic system. The device has the computer-aided detection (CAD) functions, in which potential pulmonary nodules are extracted and the information is provided to prevent misdiagnosis that the nodules are overlooked by radiologists. This CAD function is intended to assist in reading images by radiologists, but not to perform screening or definitive diagnosis of lung cancer based only on the results provided by the device. Domestic clinical study results were submitted to evaluate the clinical diagnostic ability of the CAD function.

Table 7. Products Approved in FY 2015: Regenerative Medical Products

Review Category	Approval Date	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification	Non-proprietary Name	Notes
Regenerative Medical Products	Sep. 18, 2015	TEMCELL HS Inj. (JCR Pharmaceuticals Co., Ltd.)	Approval	Human somatic stem cell-processed products	Human (allogeneic) bone marrow-derived mesenchymal stem cell	A human (allogeneic) bone marrow-derived mesenchymal stem cell that can be obtained by expanding and culturing the nucleated cell isolated from the bone marrow aspirate of healthy adult donor. The product is administered via intravenous infusion to treat acute graft-versus-host disease (acute GVHD) after allogeneic hematopoietic stem cell transplantation. [Orphan regenerative medical products]
Regenerative Medical Products	Sep. 18, 2015	HeartSheet (Terumo Corporation)	Conditional/Time -limited Approval	Human somatic stem cell-processed products	Human (autologous) skeletal myoblast-derived cell sheet	A human (autologous) skeletal myoblast-derived cell product consisting of the patient's skeletal myoblast that has been cultured, proliferated, and cryopreserved as a main component, and the instruments, etc. for shaping the cell sheets in medical institutions as sub-components. The product is used for treating serious heart failure caused by ischemic heart disease by applying the sheet-shaped cells to the surface of the heart during the open chest surgery when standard therapies are not sufficiently effective.

Table 8. Changes in the Number of Reports of Adverse Reactions/Malfunctions

(1) Drugs

Fiscal Year	Reports from MAH (Japan)	Reports from MAH (outside Japan)	Reports from healthcare professionals		Total	Research reports
			Safety information reporting system	Vaccines*		
FY 2011	36,741	220,455	3,388	1,843	262,427	841
FY 2012	41,413	261,862	3,304	843	307,422	884
FY 2013	38,427	266,539	4,067	1,353	310,386	962
FY 2014	49,276	300,216	4,782	1,398	355,672	1,009
FY 2015+	51,103	345,253	4,891	1,238	402,485	1,219

* *The figures from FY 2010 to FY 2012 represent the total number of reports of adverse reactions to cervical cancer vaccine, Hib vaccine, pediatric pneumococcal vaccine, and influenza vaccine. The figures from FY 2013 onward represent the total number of reports of adverse reactions to all vaccines.*

\+ *The reports in FY 2015 include case reports of suspected malfunction of device parts in combination products.*

(2) Medical Devices

Fiscal Year	Reports from MAH (Japan)	Reports from MAH (outside Japan)	Reports from healthcare professionals	Total	Research reports
FY 2011	8,637	7,431	385	16,453	2
FY 2012	11,242	10,992	522	22,756	3
FY 2013	12,791	12,763	489	26,043	5
FY 2014	13,994	16,624	420	31,038	20
FY 2015	17,603	26,395	406	44,404	598

(3) Regenerative Medical Products

Fiscal Year	Reports from MAH (Japan)	Reports from MAH (outside Japan)	Reports from healthcare professionals	Total	Research reports
FY 2014*	12	0	0	12	0
FY 2015	35	0	0	35	0

* *The number of reports after the Pharmaceutical and Medical Devices Act came into effect on November 25, 2014.*

Table 9. Revisions to PRECAUTIONS for Drugs, etc. and Other Information as Directed by MHLW during FY 2015

○ Revisions to PRECAUTIONS for drugs, etc. and other information implemented by MHLW based on PMDA reports in FY 2015

	Drugs	Medical devices
Directions concerning revisions to PRECAUTIONS in product package insert*1	87*2	28
Information published as Pharmaceuticals and Medical Devices Safety Information	28*3	1

** Note 1: Including the issuance of notifications concerning self-checks for medical devices, etc.*

** Note 2: Total of 84 for drugs and 3 for in vitro diagnostics.*

** Note 3: Total of 27 for drugs and 1 for in vitro diagnostics.*

○ Revisions to PRECAUTIONS for Drugs, as Directed by MHLW during FY 2015

Date	Drug name
Apr. 1, 2015	01. Cetuximab (genetical recombination) 02. Panitumumab (genetical recombination)
Apr. 23, 2015	01. Duloxetine hydrochloride 02. Azilsartan 03. Clopidogrel sulfate 04. Clopidogrel sulfate/Aspirin 05. Cefotaxime sodium 06. Asunaprevir Daclatasvir hydrochloride
Jun 2, 2015	01. Crizotinib 02. Technetium (^{99m}Tc) hydroxymethylene-diphosphonate injection Kit for the preparation of technetium (^{99m}Tc) hydroxymethylene-diphosphonate injection
Jul 7, 2015	01. Tramadol hydrochloride (OD tablets, capsules, and injection) Tramadol hydrochloride/Acetaminophen 02. Indapamide 03. Anagliptin 04. Abiraterone acetate 05. Asunaprevir Daclatasvir hydrochloride 06. Adefovir pivoxil 07. Influenza HA vaccine 08. Interferon beta-1a (genetical recombination)
Aug. 6, 2015	01. Hydroxyzine hydrochloride Hydroxyzine pamoate 02. Memantine hydrochloride 03. Deferasirox 04. Sterile talc 05. Panitumumab (genetical recombination) 06. Pomalidomide 07. Laninamivir octanoate hydrate Zanamivir hydrate
Sep. 15, 2015	01. Amantadine hydrochloride 02. Ipragliflozin L-proline Luseogliflozin hydrate Tofogliflozin hydrate 03. Canagliflozin hydrate Dapagliflozin propylene glycolate hydrate 04. Fingolimod hydrochloride 05. Nivolumab (genetical recombination)

Date	Drug name
	06. Azithromycin hydrate 07. Asunaprevir Daclatasvir hydrochloride
Oct. 20, 2015	01. Galantamine hydrobromide 02. Magnesium oxide 03. Dutasteride 04. Ceftriaxone sodium hydrate 05. Roxithromycin 06. Asunaprevir Daclatasvir hydrochloride 07. Laxative drug containing magnesium oxide (OTC drugs)
Nov. 24, 2015	01. Fomepizole 02. Nivolumab (genetical recombination) 03. Lenvatinib mesilate 04. Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Nov. 26, 2015	01. Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir
Jan. 12, 2016	01. Azilsartan 02. Azilsartan/Amlodipine besilate Amlodipine besilate 03. Aliskiren fumarate/Amlodipine besilate 04. Irbesartan/Amlodipine besilate 05. Candesartan cilexetil/Amlodipine besilate
	06. Telmisartan/Amlodipine besilate 07. Valsartan/Amlodipine besilate 08. Amlodipine besilate/Atorvastatin calcium hydrate 09. Nintedanib ethanesulfonate 10. Tazobactam/Piperacillin hydrate 11. Piperacillin sodium 12. Atovaquone 13. Itraconazole 14. Atovaquone/Proguanil hydrochloride
Feb. 16, 2016	01. Methylphenidate hydrochloride 02. Esomeprazole magnesium hydrate 03. Eribulin mesilate 04. Entecavir hydrate
Mar. 22, 2016	01. Flunitrazepam (injections) 02. Loxoprofen sodium hydrate (for oral use) 03. Paliperidone palmitate 04. Risperidone (injections) 05. Verteporfin 06. Furosemide 07. Mirabegron

Date	Drug name
	08. Products containing loxoprofen sodium hydrate (OTC drugs for oral use)
Mar. 23, 2016	01. Mycophenolate mofetil

**Note: More detailed information is available on the PMDA website (3 in vitro diagnostics were not included in the above list).*

Table 10. Revisions to PRECAUTIONS for Medical Devices and Other Information, as Directed by MHLW Based on Reports from PMDA during FY 2015

Date	Title
Jul. 21, 2015	Revision of the Precautions in the package insert of Medical Devices and *In Vitro* Diagnostics for Blood Glucose Measurements Using Enzymatic Electrodes (8 term names)
Jul. 29, 2015	Partial modifications to instructions on revisions of the precautions associated with amendments to the notes on compilation for medical device package inserts (6 term names)
Aug. 31, 2015	Sample wording for the package insert of medical devices (14 term names)

**Note: More detailed information is available on the PMDA website.*

Table 11. FY 2015 Pharmaceuticals and Medical Devices Safety Information (No.322-331)

Date	No.	Table of Contents
Apr. 28, 2015	322	1. Adherence to the Cleaning and Disinfection Method to Prevent Transmission of Multidrug-resistant Bacteria by Duodenoscope 2. Important Safety Information (1) Cyclophosphamide hydrate (2) Sitagliptin phosphate hydrate (3) Triamcinolone acetonide (for intramuscular, intra-articular, and intradermal injections) (4) Pazopanib hydrochloride (5) Panitumumab (genetical recombination) 3. Revision of Precautions (No. 264) Rebamipide (ophthalmic suspension) (and 2 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Precautions Concerning Recurrence and Similar Incidents of Medical Accidents
May 26, 2015	323	1. Utilization of New Bar Code Labeling and Termination of JAN/ITF Code Labeling on Prescription Drugs 2. Important Safety Information (1) Asunaprevir and daclatasvir hydrochloride 3. Revision of Precautions (No. 265) Duloxetine hydrochloride (and 4 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Jul 7, 2015	324	1. Risk Management Plan 2. Important Safety Information (1) Crizotinib (2) Technetium (^{99m}Tc) hydroxymethylene-diphosphonate injection, Kit for the preparation of technetium (^{99m}Tc) hydroxymethylene-diphosphonate injection 3. List of Products Subject to Early Post-marketing Phase Vigilance
Aug. 6, 2015	325	1. Surveillance on Access to, Dissemination, and Utilization of Drug Safety Information in Medical Institutions 2. Important Safety Information (1) Asunaprevir and daclatasvir hydrochloride (2) Abiraterone acetate (3) Indapamide (4) Influenza HA vaccine (5) Interferon beta-1a (genetical recombination) 3. Revision of Precautions (No. 266) Tramadol hydrochloride (OD tablets, capsules, and injections) and tramadol hydrochloride/acetaminophen (and 2 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
Sep. 15, 2015	326	1. Epidemiological Survey on Vaccination and Sudden Death of Infants 2. Important Safety Information (1) Sterile talc (2) Panitumumab (genetical recombination) 3. Revision of Precautions (No. 267) (1) Hydroxyzine hydrochloride (2) Hydroxyzine pamoate (and 4 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
Oct. 27, 2015	327	1. Utilization of Blood Glucose Meters, etc. that Use Enzymatic Electrodes 2. Precautions Concerning Recurrent and Similar Incidents of Medical Accidents 3. Important Safety Information (1) Asunaprevir and daclatasvir hydrochloride (2) Amantadine hydrochloride (3) Nivolumab (genetical recombination) (4) Sodium-glucose co-transporter 2 (SGLT2) inhibitors 4. Revision of Precautions (No. 268) Fingolimod hydrochloride and azithromycin hydrate 5. List of Products Subject to Early Post-marketing Phase Vigilance
Dec. 1, 2015	328	1. Hypermagnesaemia Caused by Magnesium Oxide 2. Summary of the Relief System for Adverse Drug Reaction and Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs 3. Project of the Japan Drug Information Institute in Pregnancy 4. Important Safety Information (1) Asunaprevir and daclatasvir hydrochloride 5. Revision of Precautions (No. 269) Galantamine hydrobromide (and 4 others) 6. List of Products Subject to Early Post-marketing Phase Vigilance
Jan. 7, 2016	329	1. Adverse Reaction to Influenza Vaccines in the 2014 Season 2. Safety of Influenza Antiviral Drugs 3. Important Safety Information (1) Lenvatinib mesilate 4. Revision of Precautions (No. 270) Fomepizole (and 3 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Precautions Regarding Handling of Fire during Long-term Oxygen Therapy (LOT)
Feb, 9, 2016	330	1. Preventative Measures for Accidental Ingestion of Pharmaceuticals by Children 2. Important Safety Information (1) Amlodipine besilate (2) Itraconazole 3. Revision of Precautions (No. 271) Azilsartan (and 12 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
Mar. 15, 2016	331	1. “Children and Pharmaceuticals” Data Collecting Network Development Project 2. Important Safety Information (1) Eribulin mesilate 3. Revision of Precautions (No. 272) Methylphenidate hydrochloride (and 2 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

**Note: More detailed information is available on the PMDA website.*

Table 12. FY 2015 PMDA Medical Safety Information

No.	Month and year published	Title
46	May 2015	Precautions When Handling the Blood Purification Device
47	September 2015	Handling of Lines for Drug Solution Administration
48	January 2016	Precautions in Handling of Three-way Stopcocks

**Note: Detailed information is available on the PMDA's website.*

Table 13. List of User Fees

13-1. List of user fees (since November 25, 2014) for reviews etc. of pharmaceuticals, quasi-drugs, and cosmetics based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145, 1960)

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of drugs					
	New license	On-site		152,300	152,300
				Article 31, Paragraph 1, Item 1 (a)	
		Document		114,700	114,700
				Article 31, Paragraph 1, Item 1 (b)	
	Renewal of existing license	On-site		100,200	100,200
				Article 31, Paragraph 1, Item 2 (a)	
		Document		56,900	56,900
				Article 31, Paragraph 1, Item 2 (b)	
	Change/addition of classification	On-site		100,200	100,200
				Article 31, Paragraph 1, Item 3 (a)	
		Document		56,900	56,900
				Article 31, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers' accreditation of drugs					
	New accreditation	On-site		137,100 + overseas travel expenses	137,100 + overseas travel expenses
				Article 31, Paragraph 2, Item 1 (a)	
		Document		59,700	59,700
				Article 31, Paragraph 2, Item 1 (b)	
	Renewal of existing license	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 31, Paragraph 2, Item 2 (a)	
		Document		40,900	40,900
				Article 31, Paragraph 2, Item 2 (b)	
	Change/addition of classification	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 31, Paragraph 2, Item 3 (a)	
		Document		40,900	40,900
				Article 31, Paragraph 2, Item 3 (b)	

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of drugs (new approval)						
New drugs (No. 1) (non-orphan drugs)			First application products	23,788,100 Article 32, Paragraph 1, Item 1 (a)-(1)	6,747,000 + overseas travel expenses Article 32, Paragraph 2, Item 1 (a) and Paragraph 3	30,535,100 + overseas travel expenses
			Line extension products	2,464,000 Article 32, Paragraph 1, Item 1 (a)-(3)	1,686,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (c) and Paragraph 3	4,150,600 + overseas travel expenses
New drugs (No. 1) (orphan drugs)			First application products	19,934,100 Article 32, Paragraph 1, Item 1 (a)-(2)	3,379,900 + overseas travel expenses Article 32, Paragraph 2, Item 1 (b) and Paragraph 3	23,314,000 + overseas travel expenses
			Line extension products	2,061,500 Article 32, Paragraph 1, Item 1 (a)-(4)	841,500 + overseas travel expenses Article 32, Paragraph 2, Item 1 (d) and Paragraph 3	2,903,000 + overseas travel expenses
New drugs (No. 2) (non-orphan drugs)			First application products	11,353,100 Article 32, Paragraph 1, Item 1 (a)-(5)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (e) and Paragraph 3	13,886,700 + overseas travel expenses
			Line extension products	1,174,300 Article 32, Paragraph 1, Item 1 (a)-(7)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 1 (g) and Paragraph 3	1,807,900 + overseas travel expenses
New drugs (No. 2) (orphan drugs)			First application products	9,345,700 Article 32, Paragraph 1, Item 1 (a)-(6)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 1 (f) and Paragraph 3	10,613,400 + overseas travel expenses
			Line extension products	1,004,100 Article 32, Paragraph 1, Item 1 (a)-(8)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 1 (h) and Paragraph 3	1,323,100 + overseas travel expenses
Generic prescription drugs		with inspections		618,200 Article 32, Paragraph 1, Item 1 (a)-(9)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	948,400 + overseas travel expenses
		without inspection		618,200 Article 32, Paragraph 1, Item 1 (a)-(9)		618,200
BTC/OTC drugs	Switch to OTC status, etc.	First application products	with inspections	1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	1,621,800 + overseas travel expenses
			without inspection	1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)		1,291,600
		Line extension products	with inspections	1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	1,621,800 + overseas travel expenses
			without inspection	1,291,600 Article 32, Paragraph 1, Item 1 (a)-(10)		1,291,600
	Others		with inspections	110,300 Article 32, Paragraph 1, Item 1 (a)-(11)	330,200 + overseas travel expenses Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	440,500 + overseas travel expenses
			without inspection	110,300 Article 32, Paragraph 1, Item 1 (a)-(11)		110,300
Quasi-drugs			New active ingredients	2,981,100 Article 32, Paragraph 1, Item 1 (b)-(1)		2,981,100
			New dosage, etc.	246,600 Article 32, Paragraph 1, Item 1 (b)-(2)		246,600
			Others	63,500 Article 32, Paragraph 1, Item 1 (b)-(6)		63,500
Review for approval of drugs (new approval)						
Pest control agents			New active ingredients	4,987,900 Article 32, Paragraph 1, Item 1 (a)-(12) and (b)-(3)		4,987,900
			New dosage, etc.	392,200 Article 32, Paragraph 1, Item 1 (a)-(13) and (b)-(4)		392,200
			Others	95,500 Article 32, Paragraph 1, Item 1 (a)-(14) and (b)-(5)		95,500
Cosmetics				63,500 Article 32, Paragraph 1, Item 1 (c)		63,500
New application for change or replacement of brand name				35,600 Article 32, Paragraph 1, Item 1 (d)		35,600

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification						User fees		
						Review	Inspection	Total
Review for approval of drugs (approval for partial changes to approved matters)								
	New drugs (No. 1) (non-orphan drugs)	Changes in indications, etc.	First application products			10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
			Line extension products			1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
		Others				205,100 Article 32, Paragraph 1, Item 2 (a)-(3)	124,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	329,300 + overseas travel expenses
	New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products			8,434,300 Article 32, Paragraph 1, Item 2 (a)-(4)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	9,702,000 + overseas travel expenses
			Line extension products			875,600 Article 32, Paragraph 1, Item 2 (a)-(5)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	1,194,600 + overseas travel expenses
		Others				132,700 Article 32, Paragraph 1, Item 2 (a)-(6)	112,900 + overseas travel expenses Article 32, Paragraph 2, Item 2 (f) and Paragraph 3	245,600 + overseas travel expenses
	New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products			10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
			Line extension products			1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
		Others				205,100 Article 32, Paragraph 1, Item 2 (a)-(3)	124,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	329,300 + overseas travel expenses
	New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products			8,434,300 Article 32, Paragraph 1, Item 2 (a)-(4)	1,267,700 + overseas travel expenses Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	9,702,000 + overseas travel expenses
			Line extension products			875,600 Article 32, Paragraph 1, Item 2 (a)-(5)	319,000 + overseas travel expenses Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	1,194,600 + overseas travel expenses
		Others				132,700 Article 32, Paragraph 1, Item 2 (a)-(6)	112,900 + overseas travel expenses Article 32, Paragraph 2, Item 2 (f) and Paragraph 3	245,600 + overseas travel expenses
	Generic prescription drugs	Changes in indications, etc.	First application products			10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	2,533,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	12,724,100 + overseas travel expenses
			Line extension products			1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	633,600 + overseas travel expenses Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	1,691,000 + overseas travel expenses
		Changes based on guidelines, etc.				53,400 Article 32, Paragraph 1, Item 2 (a)-(7)		53,400
		Others				307,700 Article 32, Paragraph 1, Item 2 (a)-(8)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	493,900 + overseas travel expenses
	BTC/OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	with inspections	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	10,376,700 + overseas travel expenses
					without inspection	10,190,500 Article 32, Paragraph 1, Item 2 (a)-(1)		10,190,500
				Line extension products	with inspections	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	1,243,600 + overseas travel expenses
					without inspection	1,057,400 Article 32, Paragraph 1, Item 2 (a)-(2)		1,057,400
			Others		with inspections	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	242,600 + overseas travel expenses
					without inspections	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)		56,400
		Changes based on guidelines, etc.			with inspections	35,600 Article 32, Paragraph 1, Item 2 (a)-(10)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	221,800 + overseas travel expenses
					without inspection	35,600 Article 32, Paragraph 1, Item 2 (a)-(10)		35,600
		Others			with inspections	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)	186,200 + overseas travel expenses Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	242,600 + overseas travel expenses
					without inspection	56,400 Article 32, Paragraph 1, Item 2 (a)-(9)		56,400
	Quasi-drugs/cosmetics					35,600 Article 32, Paragraph 1, Item 2 (b)-(1) and (c)		35,600
	Pest control agents					48,400 Article 32, Paragraph 1, Item 2 (a)-(11) and (b)-(2)		48,400

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification					User fees		
					Review	Inspection	Total
GMP inspection of drugs							
Approval, partial change and manufacture for export		New drugs		In Japan		760,900 Article 32, Paragraph 5, Item 1 (b)-(1)	760,900
				Overseas		960,200 + overseas travel expenses Article 32, Paragraph 5, Item 1 (b)-(2) and Paragraph 7	960,200 + overseas travel expenses
		Biological drugs/Radiopharmaceuticals, etc.		In Japan		685,100 Article 32, Paragraph 5, Item 1 (a)-(1)	685,100
				Overseas		868,600 + overseas travel expenses Article 32, Paragraph 5, Item 1 (a)-(2) and Paragraph 7	868,600 + overseas travel expenses
		Sterile drugs/Sterile quasi-drugs		In Japan		522,600 Article 32, Paragraph 5, Item 1 (c)-(1)	522,600
				Overseas		658,300 + overseas travel expenses Article 32, Paragraph 5, Item 1 (c)-(2) and Paragraph 7	658,300 + overseas travel expenses
		Other Drugs/quasi-drugs		In Japan		379,500 Article 32, Paragraph 5, Item 1 (d)-(1)	379,500
				Overseas		478,000 + overseas travel expenses Article 32, Paragraph 5, Item 1 (d)-(2) and Paragraph 7	478,000 + overseas travel expenses
		Packaging, labeling, storage, external testing, etc.		In Japan		65,600 Article 32, Paragraph 5, Item 2 (a) and Paragraph 6, Item 1 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 32, Paragraph 5, Item 2 (b) and Paragraph 6, Item 1 (b) and Paragraph 7	87,200 + overseas travel expenses
Renewal of approval/Renewal of manufacture for export		Biological drugs/ Radiopharmaceuticals, etc.	Basic	In Japan		448,500 Article 32, Paragraph 5, Item 3 (a)-(1)	448,500
				Overseas		570,100 + overseas travel expenses Article 32, Paragraph 5, Item 3 (a)-(2) and Paragraph 7	570,100 + overseas travel expenses
			Addition of products	In Japan		31,400 Article 32, Paragraph 5, Item 3 (a)-(1)	31,400
				Overseas		31,400 Article 32, Paragraph 5, Item 3 (a)-(2)	31,400
		Sterile drugs/ Sterile quasi-drugs	Basic	In Japan		390,900 Article 32, Paragraph 5, Item 3 (b)-(1)	390,900
				Overseas		493,800 + overseas travel expenses Article 32, Paragraph 5, Item 3 (b)-(2) and Paragraph 7	493,800 + overseas travel expenses
			Addition of products	In Japan		12,800 Article 32, Paragraph 5, Item 3 (b)-(1)	12,800
				Overseas		12,800 Article 32, Paragraph 5, Item 3 (b)-(2)	12,800
GMP inspection of drugs							
Renewal of approval/Renewal of manufacture for export		Other Drugs/quasi-drugs	Basic	In Japan		346,100 Article 32, Paragraph 5, Item 3 (c)-(1)	346,100
				Overseas		421,100 + overseas travel expenses Article 32, Paragraph 5, Item 3 (c)-(2) and Paragraph 7	421,100 + overseas travel expenses
			Addition of products	In Japan		9,900 Article 32, Paragraph 5, Item 3 (c)-(1)	9,900
				Overseas		9,900 Article 32, Paragraph 5, Item 3 (c)-(2)	9,900
		Packaging, labeling, storage, external testing, etc.	Basic	In Japan		265,900 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	265,900
				Overseas		347,800 + overseas travel expenses Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b) and Paragraph 7	347,800 + overseas travel expenses
			Addition of products	In Japan		6,900 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	6,900
				Overseas		6,900 Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b)	6,900
GLP inspection of drugs							
	GLP		In Japan			2,121,400 Article 32, Paragraph 4, Item 1 (a) and Paragraph 10, Item 2 (a)-(1)	2,121,400
			Overseas			2,347,900 + overseas travel expenses Article 32, Paragraph 4, Item 1 (b) and Paragraph 10, Item 2 (a)-(2) and Paragraph 11	2,347,900 + overseas travel expenses

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification				User fees		
				Review	Inspection	Total
GCP inspection of drugs						
New GCP		First application products	In Japan		2,801,000	2,801,000
					Article 32, Paragraph 4, Item 2 (a)-(1) and (b)-(1)	
			Overseas		3,098,000 + overseas travel expenses	3,098,000 + overseas travel expenses
					Article 32, Paragraph 4, Item 2 (a)-(2) and (b)-(2)	
		Line extension products	In Japan		741,400	741,400
					Article 32, Paragraph 4, Item 2 (a)-(3) and (b)-(3)	
			Overseas		773,300 + overseas travel expenses	773,300 + overseas travel expenses
					Article 32, Paragraph 4, Item 2 (a)-(4) and (b)-(4)	
	GCP inspection of generic drugs		In Japan		663,600	663,600
					Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	
			Overseas		977,400 + overseas travel expenses	977,400 + overseas travel expenses
					Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	
	GCP inspection of BTC /OTC drugs		In Japan		663,600	663,600
					Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	
			Overseas		977,400 + overseas travel expenses	977,400 + overseas travel expenses
					Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	
Re-examination of drugs						
Re-examination		First application products		806,600	2,750,100 + overseas travel expenses	3,556,700 + overseas travel expenses
				Article 32, Paragraph 9, Item 1	Article 32, Paragraph 10, Item 1 (a) and Paragraph 11	
		Line extension products		271,500	917,600 + overseas travel expenses	1,189,100 + overseas travel expenses
				Article 32, Paragraph 9, Item 2	Article 32, Paragraph 10, Item 1 (b) and Paragraph 11	
GPSP		First application products	In Japan		2,256,000	2,256,000
					Article 32, Paragraph 10, Item 2 (b)-(1)	
			Overseas		2,478,500 + overseas travel expenses	2,478,500 + overseas travel expenses
					Article 32, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	
		Line extension products	In Japan		774,100	774,100
					Article 32, Paragraph 10, Item 2 (b)-(3)	
			Overseas		794,400 + overseas travel expenses	794,400 + overseas travel expenses
					Article 32, Paragraph 10, Item 2 (b)-(4) and Paragraph 11	

13-2. List of user fees (since November 25, 2014) for reviews etc. of medical devices and in vitro diagnostics under the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145, 1960)

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
Review for approval of medical devices and in vitro diagnostics (new approval)					
New medical devices (Class Ⅳ)			10,881,700	854,300 + overseas travel expenses	11,736,000 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(1)	Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	
New medical devices (Class Ⅱ/Ⅲ)			7,766,200	854,300 + overseas travel expenses	8,620,500 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(3)	Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	
Improved medical devices with clinical data (Class Ⅳ)			6,213,000	683,500 + overseas travel expenses	6,896,500 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(2)	Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	
Improved medical devices with clinical data (Class Ⅱ/Ⅲ)			3,721,200	683,500 + overseas travel expenses	4,404,700 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(4)	Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	
Improved medical devices without clinical data, without approval standards (Class Ⅳ)			2,355,400	70,500 + overseas travel expenses	2,425,900 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(7)	Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	
Generic medical devices without clinical data, without approval standards (Class Ⅳ)			1,767,700	70,500 + overseas travel expenses	1,838,200 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(8)	Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	
Improved/generic medical devices without clinical data, without approval standards (Class Ⅱ/Ⅲ)			1,409,900	70,500 + overseas travel expenses	1,480,400 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(9)	Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	
Generic medical devices with approval standards (Class Ⅳ)			429,200	70,500 + overseas travel expenses	499,700 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(5)	Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	
Generic medical devices with approval standards (Class Ⅱ/Ⅲ)			344,100	70,500 + overseas travel expenses	414,600 + overseas travel expenses
			Article 33, Paragraph 1, Item 1 (a)-(6)	Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	
In vitro diagnostics	New products		2,147,500		2,147,500
			Article 33, Paragraph 1, Item 1 (b)-(2)		
	Out of scope of approval standards		2,147,500		2,147,500
			Article 33, Paragraph 1, Item 1 (b)-(2)		
	Nonconformity with approval standards	With clinical data	2,147,500		2,147,500
			Article 33, Paragraph 1, Item 1 (b)-(2)		
		Without clinical data	996,900		996,900
			Article 33, Paragraph 1, Item 1 (b)-(4)		
	Conformity with approval standards	Without clinical data	362,000		362,000
			Article 33, Paragraph 1, Item 1 (b)-(3)		
	Addition of series		60,300		60,300
			Article 33, Paragraph 1, Item 1 (b)-(1)		
Change of brand name			35,600		35,600
			Article 33, Paragraph 1, Item 1 (c)		

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification				User fees		
				Review	Inspection	Total
Review for approval of medical devices and in vitro diagnostics (approval of partial changes to approved matters)						
	New medical devices (Class Ⅳ)			5,446,600	854,300 + overseas travel expenses	6,300,900 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(1)	Article 33, Paragraph 2, Item 2 (a) and Paragraph 3	
	New medical devices (Class Ⅱ/Ⅲ)			3,887,300	854,300 + overseas travel expenses	4,741,600 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(3)	Article 33, Paragraph 2, Item 2 (a) and Paragraph 3	
	Improved medical devices with clinical data (Class Ⅳ)			3,109,900	683,500 + overseas travel expenses	3,793,400 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(2)	Article 33, Paragraph 2, Item 2 (b) and Paragraph 3	
	Improved medical devices with clinical data (Class Ⅱ/Ⅲ)			1,872,400	683,500 + overseas travel expenses	2,555,900 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(4)	Article 33, Paragraph 2, Item 2 (b) and Paragraph 3	
	Improved medical devices without clinical data, without approval standards (Class Ⅳ)			1,181,200	38,200 + overseas travel expenses	1,219,400 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(7)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	Generic medical devices without clinical data, without approval standards (Class Ⅳ)			884,200	38,200 + overseas travel expenses	922,400 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(8)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	Improved/generic medical devices without clinical data, without approval standards (Class Ⅱ/Ⅲ)			709,500	38,200 + overseas travel expenses	747,700 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(9)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	Generic medical devices with approval standards (Class Ⅳ)			217,600	38,200 + overseas travel expenses	255,800 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(5)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	Generic medical devices with approval standards (Class Ⅱ/Ⅲ)			173,600	38,200 + overseas travel expenses	211,800 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(6)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	Others (medical devices)			143,500	38,200 + overseas travel expenses	181,700 + overseas travel expenses
				Article 33, Paragraph 1, Item 2 (a)-(10)	Article 33, Paragraph 2, Item 2 (c) and Paragraph 3	
	In vitro diagnostics	Out of scope of approval standards	With clinical data	998,300		998,300
				Article 33, Paragraph 1, Item 2 (b)-(2)		
			Without clinical data	503,600		503,600
				Article 33, Paragraph 1, Item 2 (b)-(3)		
		Nonconformity with approval standards	With clinical data	998,300		998,300
				Article 33, Paragraph 1, Item 2 (b)-(2)		
			Without clinical data	503,600		503,600
				Article 33, Paragraph 1, Item 2 (b)-(3)		
		Conformity with approval standards	Without clinical data	206,200		206,200
				Article 33, Paragraph 1, Item 2 (b)-(4)		
		Addition of series		31,900		31,900
				Article 33, Paragraph 1, Item 2 (b)-(1)		
	Others (in vitro diagnostics)			143,500		143,500
				Article 33, Paragraph 1, Item 2 (b)-(5)		

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification				User fees		
				Review	Inspection	Total
QMS inspection of medical devices and in vitro diagnostics						
	Issuance fee for certification of conformity with approval standards				50,400	50,400
					Article 33, Paragraph 5, Item 1 (a) and Item 2 (a) and Item 3 (a)	
	Fee paid by MAH	New	New medical devices		386,600	386,600
					Article 33, Paragraph 5, Item 1 (a)-(2)	
			Class Ⅳ		374,500	374,500
					Article 33, Paragraph 5, Item 1 (a)-(3)	
			Biological products		398,500	398,500
					Article 33, Paragraph 5, Item 1 (a)-(1)	
			Other medical devices		374,500	374,500
					Article 33, Paragraph 5, Item 1 (a)-(4)	
			In vitro diagnostics		272,900	272,900
					Article 33, Paragraph 5, Item 1 (a)-(5)	
		Partial change	Class Ⅳ		134,000	134,000
					Article 33, Paragraph 5, Item 2 (a)-(2)	
			Biological products		145,600	145,600
					Article 33, Paragraph 5, Item 2 (a)-(1)	
			Other medical devices		127,800	127,800
					Article 33, Paragraph 5, Item 2 (a)-(3)	
			In vitro diagnostics		93,200	93,200
					Article 33, Paragraph 5, Item 2 (a)-(4)	
		Renewal	Class Ⅳ		167,600	167,600
					Article 33, Paragraph 5, Item 3 (a)-(2)	
			Biological products		176,900	176,900
					Article 33, Paragraph 5, Item 3 (a)-(1)	
			Other medical devices		149,200	149,200
					Article 33, Paragraph 5, Item 3 (a)-(3)	
			In vitro diagnostics		129,700	129,700
					Article 33, Paragraph 5, Item 3 (a)-(4)	

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification				User fees		
				Review	Inspection	Total
QMS inspection of medical devices and in vitro diagnostics						
	New	Design			86,100	86,100
					Article 33, Paragraph 5, Item 1 (b)-(1) and Paragraph 9, Item 1 (a)	
		Sterilization			91,200	91,200
					Article 33, Paragraph 5, Item 1 (b)-(3) and Paragraph 9, Item 1 (c)	
		Assembly, etc.			104,100	104,100
					Article 33, Paragraph 5, Item 1 (b)-(2) and Paragraph 9, Item 1 (b)	
		Others			90,500	90,500
					Article 33, Paragraph 5, Item 1 (b)-(4) and Paragraph 9, Item 1 (d)	
		Unregistered			87,500	87,500
					Article 33, Paragraph 5, Item 1 (b)-(5) and Paragraph 9, Item 1 (e) and Paragraph 10, Item 1	
	Partial change	Design			64,400	64,400
					Article 33, Paragraph 5, Item 2 (b)-(1)	
		Sterilization			75,900	75,900
					Article 33, Paragraph 5, Item 2 (b)-(3)	
		Assembly, etc.			87,700	87,700
					Article 33, Paragraph 5, Item 2 (b)-(2)	
		Others			75,800	75,800
					Article 33, Paragraph 5, Item 2 (b)-(4)	
		Unregistered			75,900	75,900
					Article 33, Paragraph 5, Item 2 (b)-(3)	
	Renewal	Design			68,800	68,800
					Article 33, Paragraph 5, Item 3 (b)-(1) and Paragraph 9, Item 2 (a)	
		Sterilization			80,100	80,100
					Article 33, Paragraph 5, Item 3 (b)-(3) and Paragraph 9, Item 2 (c)	
		Assembly, etc.			97,400	97,400
					Article 33, Paragraph 5, Item 3 (b)-(2) and Paragraph 9, Item 2 (b)	
		Others			79,600	79,600
					Article 33, Paragraph 5, Item 3 (b)-(4) and Paragraph 9, Item 2 (d)	
		Unregistered			76,100	76,100
					Article 33, Paragraph 5, Item 3 (b)-(5) and Paragraph 9, Item 2 (e) and Paragraph 10, Item 2	
	Options	Micro machine			47,500	47,500
					Article 33, Paragraph 6, Item 1	
		Nano materials			47,500	47,500
					Article 33, Paragraph 6, Item 2	
		Others			47,500	47,500
					Article 33, Paragraph 6, Item 3	
	Travel expenses for on-site inspection (per day)		In Japan		212,400	212,400
					Article 33, Paragraph 7, Item 1 and Paragraph 11	
			Overseas		179,500 + overseas travel expenses	179,500 + overseas travel expenses
					Article 33, Paragraph 7, Item 2 (a) and (b)	
	Re-issue/renewal of compliance certification				11,000	11,000
					Article 33, Paragraph 15	
GLP inspection of medical devices						
	GLP		In Japan		2,121,400	2,121,400
					Article 33, Paragraph 4, Item 1 (a) and Paragraph 13, Item 2 (a)-(1)	
			Overseas		2,347,900 + overseas travel expenses	2,347,900 + overseas travel expenses
					Article 33, Paragraph 4, Item 1 (b) and Paragraph 13, Item 2 (a)-(2) and Paragraph 14	
GCP inspection of medical devices						
	GCP		In Japan		653,400	653,400
					Article 33, Paragraph 4, Item 2 (a)	
			Overseas		944,700 + overseas travel expenses	944,700 + overseas travel expenses
					Article 33, Paragraph 4, Item 2 (b)	

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
Use-results evaluation of medical devices and in vitro diagnostics					
	Target medical devices and in vitro diagnostics		502,600 Article 33, Paragraph 12, Item 1 (a) and Item 2	642,400 + overseas travel expenses Article 33, Paragraph 13, Item 1 and Paragraph 14	1,145,000 + overseas travel expenses
	Child items with multiple brand names of the target medical device		35,600 Article 33, Paragraph 12, Item 1 (b)		35,600
	GPSP	In Japan		628,200 Article 33, Paragraph 13, Item 2 (b)-(1)	628,200
		Overseas		976,100 + overseas travel expenses Article 33, Paragraph 13, Item 2 (b)-(2) and Paragraph 14	976,100 + overseas travel expenses

13-3. List of user fees (since November 25, 2014) for reviews etc. of regenerative medical products based on the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (Act No. 145, 1960)

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification			User fees		
			Review	Inspection	Total
Assessment for manufacturing license of regenerative medical products					
	New license	On-site		152,300	152,300
				Article 34, Paragraph 1, Item 1 (a)	
		Document		114,700	114,700
				Article 34, Paragraph 1, Item 1 (b)	
	Renewal of existing license	On-site		100,200	100,200
				Article 34, Paragraph 1, Item 2 (a)	
		Document		56,900	56,900
				Article 34, Paragraph 1, Item 2 (b)	
	Change/addition of classification	On-site		100,200	100,200
				Article 34, Paragraph 1, Item 3 (a)	
		Document		56,900	56,900
				Article 34, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers accreditation of regenerative medical products					
	New accreditation	On-site		137,100 + overseas travel expenses	137,100 + overseas travel expenses
				Article 34, Paragraph 2, Item 1 (a)	
		Document		59,700	59,700
				Article 34, Paragraph 2, Item 1 (b)	
	Renewal of existing license	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 34, Paragraph 2, Item 2 (a)	
		Document		40,900	40,900
				Article 34, Paragraph 2, Item 2 (b)	
	Change/addition of classification	On-site		66,400 + overseas travel expenses	66,400 + overseas travel expenses
				Article 34, Paragraph 2, Item 3 (a)	
		Document		40,900	40,900
				Article 34, Paragraph 2, Item 3 (b)	
Review for approval of regenerative medical products (new approval)					
	New regenerative medical products		10,881,700	854,300 + overseas travel expenses	11,736,000 + overseas travel expenses
			Article 35, Paragraph 1, Item 1 (a)	Article 35, Paragraph 2, Item 1 and Paragraph 3	
	Regenerative medical products in case of new application for approval after the conditional time-limited authorization		5,446,600	854,300 + overseas travel expenses	6,300,900 + overseas travel expenses
			Article 35, Paragraph 1, Item 1 (b)	Article 35, Paragraph 2, Item 1 and Paragraph 3	
	Application for change of brand name		35,600		35,600
			Article 35, Paragraph 1, Item 1 (c)		
Review for approval of regenerative medical products (approval of partial changes to approved matters)					
	Regenerative medical products (change of indications, etc.)		5,446,600	854,300 + overseas travel expenses	6,300,900 + overseas travel expenses
			Article 35, Paragraph 1, Item 2 (a)	Article 35, Paragraph 2, Item 2 (a) and Paragraph 3	
	Regenerative medical products (other changes)		1,181,300	38,200 + overseas travel expenses	1,219,500 + overseas travel expenses
			Article 35, Paragraph 1, Item 2 (b)	Article 35, Paragraph 2, Item 2 (b) and Paragraph 3	

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

(Yen)

Classification					User fees		
					Review	Inspection	Total
GCTP inspection of regenerative medical products							
	Approval/partial change	Manufacturing sites other than those conducting only packaging, labelling, or storage		In Japan		760,900 Article 35, Paragraph 5, Item 1 (a)	760,900
				Overseas		960,200 + overseas travel expenses Article 35, Paragraph 5, Item 1 (b) and Paragraph 7	960,200 + overseas travel expenses
		Packaging, labelling, or storage		In Japan		65,600 Article 35, Paragraph 5, Item 2 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 35, Paragraph 5, Item 2 (b) and Paragraph 7	87,200 + overseas travel expenses
		Testing institutions		In Japan		65,600 Article 35, Paragraph 6, Item 1 (a)	65,600
				Overseas		87,200 + overseas travel expenses Article 35, Paragraph 6, Item 1 (b) and Paragraph 7	87,200 + overseas travel expenses
	Renewal	Manufacturing sites other than those conducting only packaging, labelling, or storage	Basic	In Japan		448,500 Article 35, Paragraph 5, Item 3 (a)-(1)	448,500
				Overseas		570,100 + overseas travel expenses Article 35, Paragraph 5, Item 3 (a)-(2) and Paragraph 7	570,100 + overseas travel expenses
			Addition of products	In Japan		31,400 Article 35, Paragraph 5, Item 3 (a)-(1)	31,400
				Overseas		31,400 Article 35, Paragraph 5, Item 3 (a)-(2)	31,400
		Packaging, labelling, or storage	Basic	In Japan		265,900 Article 35, Paragraph 5, Item 3 (b)-(1)	265,900
				Overseas		347,800 + overseas travel expenses Article 35, Paragraph 5, Item 3 (b)-(2) and Paragraph 7	347,800 + overseas travel expenses
			Addition of products	In Japan		6,900 Article 35, Paragraph 5, Item 3 (b)-(1)	6,900
				Overseas		6,900 Article 35, Paragraph 5, Item 3 (b)-(2)	6,900
		Testing institutions	Basic	In Japan		265,900 Article 35, Paragraph 6, Item 2 (a)	265,900
				Overseas		347,800 + overseas travel expenses Article 35, Paragraph 6, Item 2 (b) and Paragraph 7	347,800 + overseas travel expenses
			Addition of products	In Japan		6,900 Article 35, Paragraph 6, Item 2 (a)	6,900
				Overseas		6,900 Article 35, Paragraph 6, Item 2 (b)	6,900
GLP inspection of regenerative medical products							
	GLP		In Japan			2,121,400 Article 35, Paragraph 4, Item 1 (a) and Paragraph 10, Item 2 (a)-(1)	2,121,400
			Overseas			2,347,900 + overseas travel expenses Article 35, Paragraph 4, Item 1 (b) and Paragraph 10, Item 2 (a)-(2) and Paragraph 11	2,347,900 + overseas travel expenses
GCP inspection of regenerative medical products							
	GCP		In Japan			653,400 Article 35, Paragraph 4, Item 2 (a)	653,400
			Overseas			944,700 + overseas travel expenses Article 35, Paragraph 4, Item 2 (b)	944,700 + overseas travel expenses
GPSP inspection of regenerative medical products							
	GPSP		In Japan			628,500 Article 35, Paragraph 4, Item 3 (a)	628,500
			Overseas			976,100 + overseas travel expenses Article 35, Paragraph 4, Item 3 (b)	976,100 + overseas travel expenses
Re-examination of regenerative medical products							
	Regenerative medical products				504,400 Article 35, Paragraph 9	642,400 + overseas travel expenses Article 35, Paragraph 10, Item 1 and Paragraph 11	1,146,800 + overseas travel expenses
	GPSP		In Japan			628,500 Article 35, Paragraph 10, Item 2 (b)-(1)	628,500
			Overseas			976,100 + overseas travel expenses Article 35, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	976,100 + overseas travel expenses

13-4. List of user fees (since November 25, 2014) for PMDA's investigation based on the Act on Securing Safety of Regenerative Medicine (Act No. 85, 2013)

Note: The lower rows in the "User fees" column indicate the applicable articles of the Cabinet Order on Fees related to the Act on Securing Safety of Regenerative Medicine (Cabinet Order No. 278).

(Yen)

Classification			Inspection	Total
Investigation into license for manufacturing specified cellular products				
	New license	On-site	144,000	144,000
			Article 8, Paragraph 1, Item 1	
		Document	98,200	98,200
			Article 8, Paragraph 1, Item 2	
	Renewal of license	On-site	97,100	97,100
			Article 8, Paragraph 2, Item 1	
		Document	48,600	48,600
			Article 8, Paragraph 2, Item 2	
Investigation into accreditation for manufacturing specified cellular products				
	New accreditation	On-site	120,500 + overseas travel expenses	120,500 + overseas travel expenses
			Article 8, Paragraph 3, Item 1	
		Document	54,200	54,200
			Article 8, Paragraph 3, Item 2	
	Renewal of accreditation	On-site	56,500 + overseas travel expenses	56,500 + overseas travel expenses
			Article 8, Paragraph 4, Item 1	
		Document	37,100	37,100
			Article 8, Paragraph 4, Item 2	

13-5. List of user fees (since January 22, 2016) under Article 4 of the Administrative Instructions for the Statement of Operating Procedures on Reviews and Related Services of the Pharmaceuticals and Medical Devices Agency

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation before the start of expanded clinical trials for drugs	per consultation	249,000	
	Consultation for electronic study data submission (with recording)	per consultation	94,500	
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	Consultation before minor change notification	per consultation	304,700	
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Preparatory interview of consultations for medical devices		per consultation	29,400	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for medical devices		per consultation	294,100	
	Pre-development consultation for medical devices (after the preparatory interview)		per consultation	264,700	
	Pre-development consultation for medical devices (additional consultation)		per consultation	147,000	
	Consultation on necessity of clinical trials for medical devices		per consultation	980,300	
	Consultation on necessity of clinical trials for medical devices (after the preparatory interview)		per consultation	950,600	
	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.)		per consultation	1,960,900	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.) (after the preparatory interview)		per consultation	1,931,500	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical literature, etc.) (additional consultation)		per consultation	980,300	
	Consultation on protocol for medical devices	Safety (1 test)	per consultation	98,000	
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	
		Exploratory clinical trial	per consultation	1,076,200	
		Exploratory clinical trial (after the preparatory interview)	per consultation	1,046,800	
		Exploratory clinical trial (additional consultation)	per consultation	539,100	
		Clinical trial	per consultation	2,353,100	
		Clinical trial (after the preparatory interview)	per consultation	2,323,700	
		Clinical trial (additional consultation)	per consultation	1,176,500	
	Consultation on data sufficiency/category of application for medical devices		per consultation	134,800	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices		per consultation	399,700	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (after the preparatory interview)		per consultation	370,300	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (additional consultation)		per consultation	197,900	

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (unevaluated protocol)	per consultation	147,000	
		Safety (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (unevaluated protocol)	per consultation	293,800	
		Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (unevaluated protocol)	per consultation	441,200	
		Safety (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Safety (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (unevaluated protocol)	per consultation	588,200	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (unevaluated protocol)	per consultation	441,200	
		Performance (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Performance (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	

Attached Table (related to Article 4)

(Yen)

				User fees		Timing of payment
Consultations						
Medical devices	Evaluation consultation for medical devices		Exploratory clinical trial	per consultation	980,300	Payment by the date of consultation application after arrangement of the consultation date
			Exploratory clinical trial (after the preparatory interview)	per consultation	950,900	
			Exploratory clinical trial (unevaluated protocol)	per consultation	1,519,700	
			Exploratory clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	1,488,100	
			Exploratory clinical trial (additional consultation)	per consultation	490,200	
			Clinical trial	per consultation	1,470,700	
			Clinical trial (after the preparatory interview)	per consultation	1,441,300	
			Clinical trial (unevaluated protocol)	per consultation	2,647,200	
			Clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	2,617,700	
			Clinical trial (additional consultation)	per consultation	733,000	
	Consultation on GCP/GLP/GPSP for medical devices			per consultation	196,000	
	Consultation on GCP/GLP/GPSP for medical devices (after the preparatory interview)			per consultation	166,600	
	Consultation on GCP/GLP/GPSP for medical devices (additional consultation)			per consultation	98,000	
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics			per consultation	29,400	
	Pre-development consultation for in vitro diagnostics			per consultation	196,000	
	Pre-development consultation for in vitro diagnostics (after the preparatory interview)			per consultation	166,600	
	Pre-development consultation for in vitro diagnostics (additional consultation)			per consultation	98,000	
	Pre-development consultation for companion diagnostics			per consultation	293,800	
	Pre-development consultation for companion diagnostics (after the preparatory interview)			per consultation	264,400	
	Pre-development consultation for companion diagnostics (additional consultation)			per consultation	147,000	
	Consultation on protocol for in vitro diagnostics		Quality	per consultation	98,000	
			Quality (after the preparatory interview)	per consultation	68,600	
			Quality (additional consultation)	per consultation	46,800	
			Performance (other than quality) (1 test)	per consultation	98,000	
			Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
			Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
			Performance (other than quality) (2 tests)	per consultation	196,000	
			Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
			Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
			Performance (other than quality) (3 or more tests)	per consultation	293,800	
			Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
			Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
			Correlation	per consultation	196,000	
			Correlation (after the preparatory interview)	per consultation	166,600	
			Correlation (additional consultation)	per consultation	98,000	
			Clinical performance study	per consultation	490,200	
			Clinical performance study (after the preparatory interview)	per consultation	458,700	
			Clinical performance study (additional consultation)	per consultation	245,100	
			Clinical performance study for companion diagnostics	per consultation	733,000	
			Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
			Clinical performance study for companion diagnostics (additional consultation)	per consultation	367,600	
	Application procedure consultation for in vitro diagnostics			per consultation	78,300	

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Quality	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (unevaluated protocol)	per consultation	147,000	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (other than quality) (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (other than quality) (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (unevaluated protocol)	per consultation	441,200	
		Performance (other than quality) (3 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (unevaluated protocol)	per consultation	293,800	
		Correlation (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	293,800	
		Clinical performance study (after the preparatory interview)	per consultation	264,400	
		Clinical performance study (unevaluated protocol)	per consultation	539,100	
		Clinical performance study (unevaluated protocol) (after the preparatory interview)	per consultation	509,700	
		Clinical performance study (additional consultation)	per consultation	147,000	
		Clinical performance study for companion diagnostics	per consultation	441,200	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical performance study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical performance study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	220,600	

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Regenerative medical products	Procedural consultation for regenerative medical products	per consultation	134,800	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for regenerative medical products	per consultation	299,800	
	Pre-development consultation for regenerative medical products (additional consultation)	per consultation	149,900	
	Non-clinical consultation for regenerative medical products (effectiveness)	per consultation	899,500	
	Non-clinical consultation for regenerative medical products (effectiveness) (additional consultation)	per consultation	449,700	
	Non-clinical consultation for regenerative medical products (safety)	per consultation	946,200	
	Non-clinical consultation for regenerative medical products (safety) (additional consultation)	per consultation	473,200	
	Quality consultation for regenerative medical products	per consultation	946,200	
	Quality consultation for regenerative medical products (additional consultation)	per consultation	473,200	
	Consultation before therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation before therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	
	Consultation after therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation after therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
regenerative medical products	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for regenerative medical products (therapeutic exploratory study)	per consultation	1,098,500	
	Prior assessment consultation for regenerative medical products (confirmatory clinical study)	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products (additional consultation)	per consultation	1,199,300	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products	per consultation	399,700	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products (additional consultation)	per consultation	197,900	
	Pre-interview for regenerative medical products (with recording)	per consultation	94,500	
	Post-consultation for regenerative medical products (with recording)	per consultation	94,500	

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
SAKIGAKE comprehensive evaluation consultation	SAKIGAKE comprehensive evaluation consultation for drugs (quality)	per consultation	2,997,700	Payment by the date of consultation application after arrangement of the consultation date
	SAKIGAKE comprehensive evaluation consultation for drugs (non-clinical)	per consultation	4,999,600	
	SAKIGAKE comprehensive evaluation consultation for drugs (clinical)	per consultation	5,994,900	
	SAKIGAKE comprehensive evaluation consultation for drugs (reliability)	per consultation	2,990,900	
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000 + overseas travel expenses	
	SAKIGAKE comprehensive evaluation consultation for medical devices (quality)	per consultation	1,499,700	
	SAKIGAKE comprehensive evaluation consultation for medical devices (non-clinical)	per consultation	2,497,800	
	SAKIGAKE comprehensive evaluation consultation for medical devices (clinical)	per consultation	2,998,800	
	SAKIGAKE comprehensive evaluation consultation for medical devices (reliability)	per consultation	1,498,600	
	SAKIGAKE comprehensive evaluation consultation for medical devices (QMS)	per consultation	1,498,600 + overseas travel expenses	
	SAKIGAKE comprehensive evaluation consultation for in vitro diagnostics (quality)	per consultation	299,100	
	SAKIGAKE comprehensive evaluation consultation for in vitro diagnostics (performance)	per consultation	999,500	
	SAKIGAKE comprehensive evaluation consultation for in vitro diagnostics (clinical performance)	per consultation	1,599,300	
	SAKIGAKE comprehensive evaluation consultation for in vitro diagnostics (QMS)	per consultation	599,000 + overseas travel expenses	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (quality)	per consultation	1,499,700	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (non-clinical)	per consultation	2,497,800	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (clinical)	per consultation	2,998,800	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (reliability)	per consultation	1,498,600	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (GCTP)	per consultation	1,498,600 + overseas travel expenses	
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	154,100	
	Consultation on quality and safety for regenerative medical products	per consultation	1,541,600	
	Consultation on quality and safety of regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	154,100	
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for regenerative medical products	per consultation	874,000	
	Consultation on R&D strategy for regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600	
Simple consultations	Generic drugs	per consultation	21,600	Payment by the date of consultation application after arrangement of the consultation date
	OTC drugs	per consultation	21,600	
	Quasi-drugs (including pest control agents)	per consultation	21,600	
	Medical devices or in vitro diagnostics	per consultation	39,400	
	Preparation of new drug applications	per consultation	21,600	
	regenerative medical products	per consultation	21,600	
	GCP/GLP/GPSP for drugs	per consultation	19,400	
	GCP/GLP/GPSP for medical devices	per consultation	19,400	
	GCP/GLP/GPSP for regenerative medical products	per consultation	19,400	
	GMP/QMS inspection	per consultation	25,400	
	GCTP inspection	per consultation	25,400	

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
GLP inspection of test facilities					
All test items	Basic fee	With animal-rearing facility	per facility	1,299,600	
		Without animal-rearing facility	per facility	799,500	
	Additional fee for target tests	General toxicity studies	per study	399,700	
		Reproduction toxicity studies	per study	199,800	
		Safety pharmacology core battery (only for drugs)	per study	199,800	
		Hemocompatibility studies (only for medical devices)	per study	199,800	
		In vitro studies	per study	199,800	
		Other studies (dependence, TK, pathology, and other studies)	per study	199,800	
	Additional fee for target classification	Drugs	per facility	199,800	
		Medical devices	per facility	199,800	
		regenerative medical products	per facility	199,800	
Additional compliance accreditation			per facility	959,300	
Additional inspection			per inspection from the second inspection onwards	396,500	
Confirmation of certification on drugs, etc.					
GMP certification on investigational products (with on-site inspection)			per product of one facility	760,900	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)			per product of one facility	15,500	
Certification of drug products			per product	15,500	
Other certifications (including GMP/QMS certification)			per matter of one product	8,700	
Use of document storage rooms					
			per day per room	3,000	Payment upon invoice sent from PMDA after the end of the period of use

* Universities/research institutions and venture companies meeting requirements specified separately.
All of the following requirements should be met in principle:

For universities/research institutions

- Having not received the following specified amount or more from the government, to proceed with the research on the seed-stage resource
  For the consultation on R&D strategy for drugs or consultation on quality and safety for regenerative medical products, 90 million yen
  For the consultation on R&D strategy for medical devices or consultation on R&D strategy for regenerative medical products, 50 million yen
- Having not received research expenses from a pharmaceutical company, medical device company, etc. under a joint research agreement, etc., toward practical application of the seed-stage resource

For venture companies

- Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less)
- Any other corporation does not hold 1/2 or more of the total number of shares or investments
- Two or more other corporations do not hold 2/3 or more of the total number of shares or investments
- For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue

On and After January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation before the start of expanded clinical trials for drugs	per consultation	249,000	
	Consultation for electronic study data submission (with recording)	per consultation	94,500	
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	Consultation before minor change notification	per consultation	304,700	
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	(New consultation categories)			
	Consultation for electronic study data submission (with recording)	per consultation	94,500	
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	Consultation before minor change notification	per consultation	304,700	
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation for electronic study data submission (with recording)	per consultation	94,500	
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	Consultation before minor change notification	per consultation	304,700	
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Drugs	Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
	Consultation for electronic study data submission (with recording)	per consultation	94,500	
	Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
	Safety consultation for drugs	per consultation	1,833,700	
	Quality consultation for drugs	per consultation	1,520,500	
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
	Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
	Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
	Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
	Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
	Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
	Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
	Consultation on drug product eligibility for priority review	per consultation	846,800	
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
	Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
	Quality consultation for generic drugs	per consultation	505,800	
	(New consultation categories)			
	Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
	Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
	Post-consultation for drugs (with recording)	per consultation	94,500	
	Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Preparatory interview of consultations for medical devices		per consultation	29,400	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for medical devices		per consultation	294,100	
	Pre-development consultation for medical devices (after the preparatory interview)		per consultation	264,700	
	Pre-development consultation for medical devices (additional consultation)		per consultation	147,000	
	Consultation on necessity of clinical trials for medical devices		per consultation	980,300	
	Consultation on necessity of clinical trials for medical devices (after the preparatory interview)		per consultation	950,600	
	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical papers, etc.)		per consultation	1,960,900	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical papers, etc.) (after the preparatory interview)		per consultation	1,931,500	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical papers, etc.) (additional consultation)		per consultation	980,300	
	Consultation on protocol for medical devices	Safety (1 test)	per consultation	98,000	
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	
		Exploratory clinical trial	per consultation	1,076,200	
		Exploratory clinical trial (after the preparatory interview)	per consultation	1,046,800	
		Exploratory clinical trial (additional consultation)	per consultation	539,100	
		Clinical trial	per consultation	2,353,100	
		Clinical trial (after the preparatory interview)	per consultation	2,323,700	
		Clinical trial (additional consultation)	per consultation	1,176,500	
	Consultation on data sufficiency/category of application for medical devices		per consultation	134,800	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices		per consultation	399,700	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (after the preparatory interview)		per consultation	370,300	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (additional consultation)		per consultation	197,900	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Preparatory interview of consultations for medical devices		per consultation	29,400	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for medical devices		per consultation	294,100	
	Pre-development consultation for medical devices (after the preparatory interview)		per consultation	264,700	
	Pre-development consultation for medical devices (additional consultation)		per consultation	147,000	
	Consultation on necessity of clinical trials for medical devices		per consultation	980,300	
	Consultation on necessity of clinical trials for medical devices (after the preparatory interview)		per consultation	950,600	
	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical papers, etc.)		per consultation	1,960,900	
	Consultation on necessity of clinical trials for medical devices (assessed by referring to clinical papers, etc.) (after the preparatory interview)		per consultation	1,931,500	
	Consultation on necessity of clinical trials for medical devices (assessed by referrig to clinical literature, etc.) (additional consultation)		per consultation	980,300	
	Consultation on protocol for medical devices	Safety (1 test)	per consultation	98,000	
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	
		Exploratory clinical trial	per consultation	1,076,200	
		Exploratory clinical trial (after the preparatory interview)	per consultation	1,046,800	
		Exploratory clinical trial (additional consultation)	per consultation	539,100	
		Clinical trial	per consultation	2,353,100	
		Clinical trial (after the preparatory interview)	per consultation	2,323,700	
		Clinical trial (additional consultation)	per consultation	1,176,500	
	Consultation on data sufficiency/category of application for medical devices		per consultation	134,800	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices		per consultation	399,700	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (after the preparatory interview)		per consultation	370,300	
	Consultation on GLP/GCP/GPSP compliance investigation for medical devices (additional consultation)		per consultation	197,900	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (unevaluated protocol)	per consultation	147,000	
		Safety (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (unevaluated protocol)	per consultation	293,800	
		Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (unevaluated protocol)	per consultation	441,200	
		Safety (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Safety (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (unevaluated protocol)	per consultation	588,200	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (unevaluated protocol)	per consultation	441,200	
		Performance (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Performance (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Safety (1 test) (after the preparatory interview)	per consultation	68,600	
		Safety (1 test) (unevaluated protocol)	per consultation	147,000	
		Safety (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Safety (1 test) (additional consultation)	per consultation	46,800	
		Safety (2 tests)	per consultation	196,000	
		Safety (2 tests) (after the preparatory interview)	per consultation	166,600	
		Safety (2 tests) (unevaluated protocol)	per consultation	293,800	
		Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Safety (2 tests) (additional consultation)	per consultation	98,000	
		Safety (3 tests)	per consultation	293,800	
		Safety (3 tests) (after the preparatory interview)	per consultation	264,400	
		Safety (3 tests) (unevaluated protocol)	per consultation	441,200	
		Safety (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Safety (3 tests) (additional consultation)	per consultation	147,000	
		Safety (4 or more tests)	per consultation	390,100	
		Safety (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Safety (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Safety (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Safety (4 or more tests) (additional consultation)	per consultation	196,000	
		Quality	per consultation	390,100	
		Quality (after the preparatory interview)	per consultation	360,700	
		Quality (unevaluated protocol)	per consultation	588,200	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Quality (additional consultation)	per consultation	196,000	
		Performance (1 test)	per consultation	98,000	
		Performance (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (1 test) (additional consultation)	per consultation	46,800	
		Performance (2 tests)	per consultation	196,000	
		Performance (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (2 tests) (additional consultation)	per consultation	98,000	
		Performance (3 tests)	per consultation	293,800	
		Performance (3 tests) (after the preparatory interview)	per consultation	264,400	
		Performance (3 tests) (unevaluated protocol)	per consultation	441,200	
		Performance (3 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (3 tests) (additional consultation)	per consultation	147,000	
		Performance (4 or more tests)	per consultation	390,100	
		Performance (4 or more tests) (after the preparatory interview)	per consultation	360,700	
		Performance (4 or more tests) (unevaluated protocol)	per consultation	588,200	
		Performance (4 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	558,800	
		Performance (4 or more tests) (additional consultation)	per consultation	196,000	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Assessment consultation for medical devices	Exploratory clinical trial	per consultation	980,300	Payment by the date of consultation application after arrangement of the consultation date
		Exploratory clinical trial (after the preparatory interview)	per consultation	950,900	
		Exploratory clinical trial (unevaluated protocol)	per consultation	1,519,700	
		Exploratory clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	1,488,100	
		Exploratory clinical trial (additional consultation)	per consultation	490,200	
		Clinical trial	per consultation	1,470,700	
		Clinical trial (after the preparatory interview)	per consultation	1,441,300	
		Clinical trial (unevaluated protocol)	per consultation	2,647,200	
		Clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	2,617,700	
		Clinical trial (additional consultation)	per consultation	733,000	
	Consultation on GCP/GLP/GPSP for medical devices		per consultation	196,000	
	Consultation on GCP/GLP/GPSP for medical devices (after the preparatory interview)		per consultation	166,600	
	Consultation on GCP/GLP/GPSP for medical devices (additional consultation)		per consultation	98,000	
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics		per consultation	29,400	
	Pre-development consultation for in vitro diagnostics		per consultation	196,000	
	Pre-development consultation for in vitro diagnostics (after the preparatory interview)		per consultation	166,600	
	Pre-development consultation for in vitro diagnostics (additional consultation)		per consultation	98,000	
	Pre-development consultation for companion diagnostics		per consultation	293,800	
	Pre-development consultation for companion diagnostics (after the preparatory interview)		per consultation	264,400	
	Pre-development consultation for companion diagnostics (additional consultation)		per consultation	147,000	
	Consultation on protocol for in vitro diagnostics	Quality	per consultation	98,000	
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	490,200	
		Clinical performance study (after the preparatory interview)	per consultation	458,700	
		Clinical performance study (additional consultation)	per consultation	245,100	
		Clinical performance study for companion diagnostics	per consultation	733,000	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	367,600	
	Application procedure consultation for in vitro diagnostics		per consultation	78,300	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Assessment consultation for medical devices	Exploratory clinical trial	per consultation	980,300	Payment by the date of consultation application after arrangement of the consultation date
		Exploratory clinical trial (after the preparatory interview)	per consultation	950,900	
		Exploratory clinical trial (unevaluated protocol)	per consultation	1,519,700	
		Exploratory clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	1,488,100	
		Exploratory clinical trial (additional consultation)	per consultation	490,200	
		Clinical trial	per consultation	1,470,700	
		Clinical trial (after the preparatory interview)	per consultation	1,441,300	
		Clinical trial (unevaluated protocol)	per consultation	2,647,200	
		Clinical trial (unevaluated protocol) (after the preparatory interview)	per consultation	2,617,700	
		Clinical trial (additional consultation)	per consultation	733,000	
	Consultation on GCP/GLP/GPSP for medical devices		per consultation	196,000	
	Consultation on GCP/GLP/GPSP for medical devices (after the preparatory interview)		per consultation	166,600	
	Consultation on GCP/GLP/GPSP for medical devices (additional consultation)		per consultation	98,000	
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics		per consultation	29,400	
	Pre-development consultation for in vitro diagnostics		per consultation	196,000	
	Pre-development consultation for in vitro diagnostics (after the preparatory interview)		per consultation	166,600	
	Pre-development consultation for in vitro diagnostics (additional consultation)		per consultation	98,000	
	Pre-development consultation for companion diagnostics		per consultation	293,800	
	Pre-development consultation for companion diagnostics (after the preparatory interview)		per consultation	264,400	
	Pre-development consultation for companion diagnostics (additional consultation)		per consultation	147,000	
	Consultation on protocol for in vitro diagnostics	Quality	per consultation	98,000	
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	490,200	
		Clinical performance study (after the preparatory interview)	per consultation	458,700	
		Clinical performance study (additional consultation)	per consultation	245,100	
		Clinical performance study for companion diagnostics	per consultation	733,000	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	367,600	
	Application procedure consultation for in vitro diagnostics		per consultation	78,300	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Quality	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (unevaluated protocol)	per consultation	147,000	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (other than quality) (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (other than quality) (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (unevaluated protocol)	per consultation	441,200	
		Performance (other than quality) (3 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (unevaluated protocol)	per consultation	293,800	
		Correlation (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	293,800	
		Clinical performance study (after the preparatory interview)	per consultation	264,400	
		Clinical performance study (unevaluated protocol)	per consultation	539,100	
		Clinical performance study (unevaluated protocol) (after the preparatory interview)	per consultation	509,700	
		Clinical performance study (additional consultation)	per consultation	147,000	
		Clinical performance study for companion diagnostics	per consultation	441,200	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical performance study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical performance study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	220,600	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Quality	per consultation	98,000	Payment by the date of consultation application after arrangement of the consultation date
		Quality (after the preparatory interview)	per consultation	68,600	
		Quality (unevaluated protocol)	per consultation	147,000	
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Quality (additional consultation)	per consultation	46,800	
		Performance (other than quality) (1 test)	per consultation	98,000	
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	68,600	
		Performance (other than quality) (1 test) (unevaluated protocol)	per consultation	147,000	
		Performance (other than quality) (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	115,500	
		Performance (other than quality) (1 test) (additional consultation)	per consultation	46,800	
		Performance (other than quality) (2 tests)	per consultation	196,000	
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	166,600	
		Performance (other than quality) (2 tests) (unevaluated protocol)	per consultation	293,800	
		Performance (other than quality) (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	98,000	
		Performance (other than quality) (3 or more tests)	per consultation	293,800	
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	264,400	
		Performance (other than quality) (3 or more tests) (unevaluated protocol)	per consultation	441,200	
		Performance (other than quality) (3 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	411,800	
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	147,000	
		Correlation	per consultation	196,000	
		Correlation (after the preparatory interview)	per consultation	166,600	
		Correlation (unevaluated protocol)	per consultation	293,800	
		Correlation (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	
		Correlation (additional consultation)	per consultation	98,000	
		Clinical performance study	per consultation	293,800	
		Clinical performance study (after the preparatory interview)	per consultation	264,400	
		Clinical performance study (unevaluated protocol)	per consultation	539,100	
		Clinical performance study (unevaluated protocol) (after the preparatory interview)	per consultation	509,700	
		Clinical performance study (additional consultation)	per consultation	147,000	
		Clinical performance study for companion diagnostics	per consultation	441,200	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical performance study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical performance study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	220,600	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Regenerative medical products	Procedural consultation for regenerative medical products	per consultation	134,800	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for regenerative medical products	per consultation	299,800	
	Pre-development consultation for regenerative medical products (additional consultation)	per consultation	149,900	
	Non-clinical consultation for regenerative medical products (effectiveness)	per consultation	899,500	
	Non-clinical consultation for regenerative medical products (effectiveness) (additional consultation)	per consultation	449,700	
	Non-clinical consultation for regenerative medical products (safety)	per consultation	946,200	
	Non-clinical consultation for regenerative medical products (safety) (additional consultation)	per consultation	473,200	
	Quality consultation for regenerative medical products	per consultation	946,200	
	Quality consultation for regenerative medical products (additional consultation)	per consultation	473,200	
	Consultation before therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation before therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	
	Consultation after therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation after therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Regenerative medical products	Procedural consultation for regenerative medical products	per consultation	134,800	Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for regenerative medical products	per consultation	299,800	
	Pre-development consultation for regenerative medical products (additional consultation)	per consultation	149,900	
	Non-clinical consultation for regenerative medical products (effectiveness)	per consultation	899,500	
	Non-clinical consultation for regenerative medical products (effectiveness) (additional consultation)	per consultation	449,700	
	Non-clinical consultation for regenerative medical products (safety)	per consultation	946,200	
	Non-clinical consultation for regenerative medical products (safety) (additional consultation)	per consultation	473,200	
	Quality consultation for regenerative medical products	per consultation	946,200	
	Quality consultation for regenerative medical products (additional consultation)	per consultation	473,200	
	Consultation before therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation before therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	
	Consultation after therapeutic exploratory study for regenerative medical products	per consultation	1,098,500	
	Consultation after therapeutic exploratory study for regenerative medical products (additional consultation)	per consultation	549,700	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
regenerative medical products	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for regenerative medical products (therapeutic exploratory study)	per consultation	1,098,500	
	Prior assessment consultation for regenerative medical products (confirmatory clinical study)	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products (additional consultation)	per consultation	1,199,300	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products	per consultation	399,700	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products (additional consultation)	per consultation	197,900	
	Pre-interview for regenerative medical products (with recording)	per consultation	94,500	
	Post-consultation for regenerative medical products (with recording)	per consultation	94,500	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Regenerative medical products	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	Payment by the date of consultation application after arrangement of the consultation date
	Prior assessment consultation for regenerative medical products (therapeutic exploratory study)	per consultation	1,098,500	
	Prior assessment consultation for regenerative medical products (confirmatory clinical study)	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products	per consultation	2,398,600	
	Pre-application consultation for regenerative medical products (additional consultation)	per consultation	1,199,300	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)	per consultation	1,098,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)	per consultation	824,500	
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	549,700	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	412,200	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products	per consultation	399,700	
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products (additional consultation)	per consultation	197,900	
	Pre-interview for regenerative medical products (with recording)	per consultation	94,500	
	Post-consultation for regenerative medical products (with recording)	per consultation	94,500	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Sakigake comprehensive evaluation consultation	Sakigake comprehensive evaluation consultation for drugs (quality)	per consultation	2,997,700	Payment by the date of consultation application after arrangement of the consultation date
	Sakigake comprehensive evaluation consultation for drugs (non-clinical)	per consultation	4,999,600	
	Sakigake comprehensive evaluation consultation for drugs (clinical)	per consultation	5,994,900	
	Sakigake comprehensive evaluation consultation for drugs (reliability)	per consultation	2,990,900 * overseas travel expenses	
	Sakigake comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000 * overseas travel expenses	
	Sakigake comprehensive evaluation consultation for medical devices (quality)	per consultation	1,499,700	
	Sakigake comprehensive evaluation consultation for medical devices (non-clinical)	per consultation	2,497,800	
	Sakigake comprehensive evaluation consultation for medical devices (clinical)	per consultation	2,998,800	
	SAKIGAKE comprehensive evaluation consultation for medical devices (reliability)	per consultation	1,498,600	
	Sakigake comprehensive evaluation consultation for medical devices (QMS)	per consultation	1,498,600 * overseas travel expenses	
	Sakigake comprehensive evaluation consultation for in vitro diagnostics (quality)	per consultation	299,100	
	Sakigake comprehensive evaluation consultation for in vitro diagnostics (performance)	per consultation	999,500	
	Sakigake comprehensive evaluation consultation for in vitro diagnostics (clinical performance)	per consultation	1,599,300	
	Sakigake comprehensive evaluation consultation for in vitro diagnostics (QMS)	per consultation	599,000 * overseas travel expenses	
	Sakigake comprehensive evaluation consultation for regenerative medical products (quality)	per consultation	1,499,700	
	Sakigake comprehensive evaluation consultation for regenerative medical products (non-clinical)	per consultation	2,497,800	
	Sakigake comprehensive evaluation consultation for regenerative medical products (clinical)	per consultation	2,998,800	
	Sakigake comprehensive evaluation consultation for regenerative medical products (reliability)	per consultation	1,498,600	
	Sakigake comprehensive evaluation consultation for regenerative medical products (GCTP)	per consultation	1,498,600 * overseas travel expenses	
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	154,100	
	Consultation on quality and safety for regenerative medical products	per consultation	1,541,600	
	Consultation on quality and safety of regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	154,100	
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for regenerative medical products	per consultation	874,000	
	Consultation on R&D strategy for regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600	

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

		User fees		Timing of payment
Consultations				
Sakigake comprehensive evaluation consultation	Sakigake comprehensive evaluation consultation for drugs (quality)	per consultation	2,997,700	Payment by the date of consultation application after arrangement of the consultation date
	Sakigake comprehensive evaluation consultation for drugs (non-clinical)	per consultation	4,999,600	
	Sakigake comprehensive evaluation consultation for drugs (clinical)	per consultation	5,994,900	
	Sakigake comprehensive evaluation consultation for drugs (reliability)	per consultation	2,990,900 * overseas travel expenses	
	Sakigake comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000 * overseas travel expenses	
	(New consultation cateogires)			
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	
	Consultation on R&D strategy for drugs (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	154,100	
	Consultation on quality and safety for regenerative medical products	per consultation	1,541,600	
	Consultation on quality and safety of regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	154,100	
	Consultation on R&D strategy for medical devices	per consultation	874,000	
	Consultation on R&D strategy for medical devices (Universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for regenerative medical products	per consultation	874,000	
	Consultation on R&D strategy for regenerative medical products (universities/research institutions and venture companies meeting the requirements specified separately*)	per consultation	87,400	
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600	

On and after January 22, 2016

Attached Table (related to Article 4)

(Yen)

					User fees		Timing of payment
Consultations							
Simple consultations	Generic drugs				per consultation	21,600	Payment by the date of consultation application after arrangement of the consultation date
	OTC drugs				per consultation	21,600	
	Quasi-drugs (including pest control agents)				per consultation	21,600	
	Medical devices or in vitro diagnostics				per consultation	39,400	
	Preparation of new drug applications				per consultation	21,600	
	regenerative medical products				per consultation	21,600	
	GCP/GLP/GPSP for drugs				per consultation	19,400	
	GCP/GLP/GPSP for medical devices				per consultation	19,400	
	GCP/GLP/GPSP for regenerative medical products				per consultation	19,400	
	GMP/QMS inspection				per consultation	25,400	
	GCTP inspection				per consultation	25,400	
(Deleted)							
GLP inspection of test facilities							
All test items	Basic fee		With animal-rearing facility		per facility	1,299,600	
			Without animal-rearing facility		per facility	799,500	
	Additional fee for target tests		General toxicity studies		per study	399,700	
			Reproduction toxicity studies		per study	199,800	
			Safety pharmacology core battery (only for drugs)		per study	199,800	
			Hemocompatibility studies (only for medical devices)		per study	199,800	
			In vitro studies		per study	199,800	
			Other studies (dependence, TK, pathology, and other studies)		per study	199,800	
	Additional fee for target classification		Drugs		per facility	199,800	
			Medical devices		per facility	199,800	
			regenerative medical products		per facility	199,800	
Additional compliance accreditation					per facility	959,300	
Additional inspection					per inspection from the second inspection onwards	396,500	
Confirmation of certification on drugs, etc.							
GMP certification on investigational products (with on-site inspection)					per product of one facility	760,900	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)					per product of one facility	15,500	
Certification of drug products					per product	15,500	
Other certifications (including GMP/QMS certification)					per matter of one product	8,700	
Use of document storage rooms					per day per room	3,000	Payment upon invoice sent

* Universities/research institutions and venture companies meeting requirements specified separately.
All of the following requirements should be met in principle:
For universities/research institutions
- Having not received the following specified amount or more from the government, to proceed with the research on the seed-stage resource
  For the consultation on R&D strategy for drugs or consultation on quality and safety for regenerative medical products, 90 million yen
  For the consultation on R&D strategy for medical devices or consultation on R&D strategy for regenerative medical products, 50 million yen
- Having not received research expenses from a pharmaceutical company, medical device company, etc. under a joint research agreement, etc., toward practical application of the seed-stage resource

For venture companies
- Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less)
- Any other corporation does not hold 1/2 or more of the total number of shares or investments
- Two or more other corporations do not hold 2/3 or more of the total number of shares or investments
- For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue

Before January 22, 2016

Attached Table (related to Article 4)

(Yen)

					User fees		Timing of payment
Consultations							
Simple consultations	Generic drugs				per consultation	21,600	Payment by the date of consultation application after arrangement of the consultation date
	OTC drugs				per consultation	21,600	
	Quasi-drugs (including pest control agents)				per consultation	21,600	
	Medical devices or in vitro diagnostics				per consultation	39,400	
	Preparation of new drug applications				per consultation	21,600	
	regenerative medical products				per consultation	21,600	
	GCP/GLP/GPSP for drugs				per consultation	19,400	
	GCP/GLP/GPSP for medical devices				per consultation	19,400	
	GCP/GLP/GPSP for regenerative medical products				per consultation	19,400	
	GMP/QMS inspection				per consultation	25,400	
	GCTP inspection				per consultation	25,400	
Assessment for designation of priority consultation products							
Assessment for designation of drugs for priority consultation					per application	842,200	Request to PMDA after advanced payment
Assessment for designation of medical devices or in vitro diagnostics for priority consultation					per application	842,200	
GLP inspection of test facilities							
All test items	Basic fee		With animal-rearing facility		per facility	1,299,600	
			Without animal-rearing facility		per facility	799,500	
	Additional fee for target tests		General toxicity studies		per study	399,700	
			Reproduction toxicity studies		per study	199,800	
			Safety pharmacology core battery (only for drugs)		per study	199,800	
			Hemocompatibility studies (only for medical devices)		per study	199,800	
			In vitro studies		per study	199,800	
			Other studies (dependence, TK, pathology, and other studies)		per study	199,800	
	Additional fee for target classification		Drugs		per facility	199,800	
			Medical devices		per facility	199,800	
			regenerative medical products		per facility	199,800	
Additional compliance accreditation					per facility	959,300	
Additional inspection					per inspection from the second inspection onwards	396,500	
Confirmation of certification on drugs, etc.							
GMP certification on investigational products (with on-site inspection)					per product of one facility	760,900	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)					per product of one facility	15,500	
Certification of drug products					per product	15,500	
Other certifications (including GMP/QMS certification)					per matter of one product	8,700	
Use of document storage rooms					per day per room	3,000	Payment upon invoice sent

* Universities/research institutions and venture companies meeting requirements specified separately.
All of the following requirements should be met in principle:
For universities/research institutions
- Having not received the following specified amount or more from the government, to proceed with the research on the seed-stage resource
  For the consultation on R&D strategy for drugs or consultation on quality and safety for regenerative medical products, 90 million yen
  For the consultation on R&D strategy for medical devices or consultation on R&D strategy for regenerative medical products, 50 million yen
- Having not received research expenses from a pharmaceutical company, medical device company, etc. under a joint research agreement, etc., toward practical application of the seed-stage resource

For venture companies
- Being a small or medium-sized company (with 300 employees or less, or capitalized at 300 million yen or less)
- Any other corporation does not hold 1/2 or more of the total number of shares or investments
- Two or more other corporations do not hold 2/3 or more of the total number of shares or investments
- For the preceding fiscal year, profits of the term have not been reported, or profits of the term have been reported but without operating revenue

On and after May 15, 2015

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Drugs		Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
		Consultation for electronic study data submission (with recording)	per consultation	94,500	
		Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
		Safety consultation for drugs	per consultation	1,833,700	
		Quality consultation for drugs	per consultation	1,520,500	
		Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
		Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
		Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
		Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
		Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
		Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
		Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
		Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
		Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
		Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
		Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
		Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
		Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
		Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
		Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
		Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
		Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
		Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
		Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
		Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
		Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
		Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
		Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
		Consultation on drug product eligibility for priority review	per consultation	846,800	
		Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
		Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
		Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
		Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
		Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
		Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
		Quality consultation for generic drugs	per consultation	505,800	
		Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
		Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
		Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
		Post-consultation for drugs (with recording)	per consultation	94,500	
		Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	
In vitro diagnostics	Consultation on protocol for in vitro diagnostics	Clinical performance study for companion diagnostics	per consultation	733,000	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	367,600	
	Consultation on evaluation for in vitro diagnostics	Clinical performance study for companion diagnostics	per consultation	441,200	
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical performance study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical performance study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	220,600	
SAKIGAKE comprehensive evaluation consultation		SAKIGAKE comprehensive evaluation consultation for drugs (quality)	per consultation	2,997,700	
		SAKIGAKE comprehensive evaluation consultation for drugs (non-clinical)	per consultation	4,999,600	
		SAKIGAKE comprehensive evaluation consultation for drugs (clinical)	per consultation	5,994,900	
		SAKIGAKE comprehensive evaluation consultation for drugs (reliability)	per consultation	2,990,900 + overseas travel expenses	
		SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000 + overseas travel expenses	

Before May 15, 2015

Attached Table (related to Article 4)

(Yen)

			User fees		Timing of payment
Consultations					
Drugs		Procedural consultation for drugs	per consultation	143,800	Payment by the date of consultation application after arrangement of the consultation date
		(New consultation categories)			
		Consultation on bioequivalence testing, etc. for drugs	per consultation	571,900	
		Safety consultation for drugs	per consultation	1,833,700	
		Quality consultation for drugs	per consultation	1,520,500	
		Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,360,500	
		Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,277,200	
		Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,669,400	
		Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,257,400	
		Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,114,900	
		Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,339,200	
		Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	6,183,300	
		Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	4,644,800	
		Pre-application consultation for drugs (non-orphan drugs)	per consultation	6,183,200	
		Pre-application consultation for drugs (orphan drugs)	per consultation	4,642,000	
		Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,664,800	
		Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,664,800	
		Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	826,800	
		Additional consultation for drugs (non-orphan drugs)	per consultation	2,752,100	
		Additional consultation for drugs (orphan drugs)	per consultation	2,067,900	
		Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700	
		Prior assessment consultation for drugs (quality)	per consultation	3,136,500	
		Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,120,000	
		Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,120,000	
		Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,120,000	
		Prior assessment consultation for drugs (phase I study)	per consultation	3,584,300	
		Prior assessment consultation for drugs (phase II study)	per consultation	4,625,900	
		Prior assessment consultation for drugs (phase II / III study)	per consultation	7,185,300	
		Consultation on drug product eligibility for priority review	per consultation	846,800	
		Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	173,500	
		Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,114,900	
		Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,142,800	
		Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	948,300	
		Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	414,600	
		Consultations on bioequivalence of generic drugs	per consultation	1,026,000	
		Quality consultation for generic drugs	per consultation	505,800	
		Pre-application consultation for switch OTC drugs	per consultation	1,544,000	
		Consultation on key points of clinical trial protocols for OTC drugs	per consultation	516,800	
		Consultation on appropriateness of development of new OTC drugs	per consultation	204,800	
		Post-consultation for drugs (with recording)	per consultation	94,500	
		Consultation on GCP/GLP/GPSP for drugs	per consultation	289,200	
In vitro diagnostics	Consultation on protocol for in vitro diagnostics	Clinical evaluation study for companion diagnostics	per consultation	733,000	
		Clinical evaluation study for companion diagnostics (after the preparatory interview)	per consultation	703,600	
		Clinical evaluation study for companion diagnostics (additional consultation)	per consultation	367,600	
	Consultation on evaluation for in vitro diagnostics	Clinical evaluation study for companion diagnostics	per consultation	441,200	
		Clinical evaluation study for companion diagnostics (after the preparatory interview)	per consultation	411,800	
		Clinical evaluation study for companion diagnostics (unevaluated protocol)	per consultation	809,000	
		Clinical evaluation study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	779,600	
		Clinical evaluation study for companion diagnostics (additional consultation)	per consultation	220,600	
		(New consultation categories)			

Mid-term Targets of the Pharmaceuticals and Medical Devices Agency (PMDA)
(Provisional Translation)

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

Instruction No. 0307-73 (dated March 7, 2014) of
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare (MHLW)

Targets to be achieved by the Pharmaceuticals and Medical Devices Agency in its operation management shall be established as below, based on the provision of Article 29, Paragraph 1 of the Act on General Rules for Incorporated Administrative Agency for Incorporated Administrative Agency (Act No. 103, 1999),.

March 7, 2014

Minister of Health, Labour and Welfare
Norihisa Tamura

Part 1
Effective Period for Mid-term Targets
The effective period for Mid-term Targets according to Article 29, Paragraph 2, Item 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999) shall be 5 years, from April 2014 through March 2019.

Part 2
Matters Regarding Improvement in Operation Management of the Overall Corporation and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public
The targets related to the overall corporation regarding improvement in efficiency of operations, as stipulated in Article 29, Paragraph 2, Item 2 of the Act on General Rules for Incorporated Administrative Agency, and the targets regarding improvement in the quality of services and other operations rendered to the public, as stipulated in Article 29, Paragraph 2, Item 3 of the Act on General Rules for Incorporated Administrative Agency, shall be as follows.

1) Efficient and Flexible Management of Operations

a) The Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the "PMDA") 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 controls including the way of implementing duties in accordance with instructions from accounting auditors, and proactively disclose measures taken.
- Examine the way of internal control by utilizing professional knowledge from experts of third-parties.
- PMDA shall refer to the matters that were notified to each evaluation committee of the incorporated administrative agencies of the government ministries, which are opinions on the report (*Internal Control and* Evaluation *in Incorporated Administrative Agencies*) released by the Study Group on Internal Control and Evaluation in Incorporated Administrative Agencies held by the Ministry of Internal Affairs and Communications, and opinions on evaluation results of the operating performance in incorporated administrative agencies from the Ministry of Internal Affairs and Communications and the Evaluation Committee of Incorporated Administrative Agencies.

b) Promote computerization of the operations to increase efficiency of the operation management system.

c) Based on a re-examination of systems control operation of the common information and the review operation, PMDA shall control costs by re-examining the system configuration of the overall PMDA and its procurement method, in order to reduce system costs, to ensure transparency of system procurement, and to streamline operation management.
For this reason, PMDA shall promote approaches to optimize operations and systems by integrating the individual review systems and by establishing a system to promote information sharing among review services, post-marketing safety measures, and relief services for adverse health effects, based on the Optimization Plan for Operations and Systems established at the end of FY 2007.

2) Improvement of Operation Management

a) By continuously improving the operation and increasing efficiency in management, the following reduction in the budget for the Mid-term Plan is expected to have been achieved by the end of the effective period for Mid-term Targets, regarding general administrative expenses (excluding personnel expenses) in which the administrative subsides are to be applied.
- No less than 15% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase in personnel, etc.).

b) By increasing efficiency in operations, the following reduction, regarding operating expenses (excluding personnel expenses, and single fiscal-year expenses, etc., that were paid for the establishment of operations) in which the administrative subsidies are to be applied, is expected to be made by the end of the effective period for Mid-term Targets.
- No less than 5% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase of personnel, etc.).

c) Yearly administrative subsidies are to be rigorously calculated with consideration of its debt balance.

d) Promote efficiency and improvements of operations by consolidating the management of the marketing authorization holder's product data, etc. of contributions for adverse drug reaction (ADR), contributions for relief for infections, and contributions for post-marketing safety measures.

e) As a general rule, contracts shall be concluded through open competitive bidding, etc., and the following approaches shall be made.
- Fully secure competitiveness and transparency even when contracts are not concluded by open competitive bidding such as planning competition and invitation to bids.
- Conduct bids and conclude contracts appropriately, by having them thoroughly checked by auditors and accounting auditors as well as by utilizing opinions of experts.

f) Provide and disseminate genuinely useful information from the public perspective
Let the public be aware of the services and role of PMDA by disseminating and providing information from the public's perspective, which enables the public and patients to readily access to the information they need. Enhance the consultation system and ensure transparency of operations and its details in order to improve the services rendered to the public.

g) Analyze issues of the operation system
Analyze the issues of the operation system appropriately and revise them if necessary.

h) Considerations related to financial base
Consider a financial base that is appropriate for the role of PMDA and take necessary measures.

Part 3
Matters Regarding Improvement in Operation Management of Each Division and Matters Regarding Improvement in 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 for Adverse Health Effects (hereinafter referred to as "relief services"), it is important not only to fully disseminate more people the Adverse Drug Reaction Relief System and the Relief System for Infections Acquired through Biological Products (hereinafter referred to as "relief systems") and appropriately operate them, but also adequately and promptly provide relief for those suffering from ADR and infections acquired through biological products or regenerative medical products (hereinafter, including cellular and tissue-based products and gene therapy products). Based on this concept, the following targets shall be achieved.

1) Enhance Public Relations and Dissemination of Information Regarding the Relief Systems

a) Conduct proactive public relations so that the relief systems are definitely utilized when necessary.
b) Make more efficient operations by reducing the number of cases where inadequate operations of claim documents, etc., result in need of extra processing time.

2) Promptly Process Relief Benefit Claims by Investigating and Organizing the Facts of the Claims

a) Promptly process relief benefit claims
b) Set up standard administrative processing times* and steadily achieve those standards.
* Standard administrative processing time includes a certain period for medical and pharmaceutical judgments of the Ministry of Health, Labour and Welfare. However, administrative processing time shall exclude the period when processing could not be continued because additional or supplementary documents and investigations of the claimant or medical institutions were required to make medical and pharmaceutical judgments.

3) Promote Appropriate Information Transmission in cooperation with Divisions

Cooperation shall be promoted among the divisions of PMDA, and information especially regarding cases of relief payment shall be appropriately disseminated to the Review Divisions and the Safety Measures Divisions, with attention to ensuring protection of personal information.

4) Implement Appropriate Health and Welfare Services

Steadily implement health and welfare services.

5) Appropriately Provide Healthcare Allowances to SMON Patients and Patients infected with HIV through Blood Products

Appropriately conduct services regarding healthcare allowances to SMON patients and HIV-positive patients infected with blood products.

6) Appropriately Pay Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

Appropriately conduct services regarding payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus.

2. Reviews and Related Services

In the review services and post-marketing safety measures, PMDA shall enable better pharmaceuticals and medical devices, etc., to be provided to medical settings more promptly and safely, so that the public can use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

Along with this conception, and based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14,2013) and the Healthcare and Medical Strategy (an agreement among the Chief Cabinet Secretary, Minister of Health, Labour and Welfare, and Minister of Internal Affairs and Communications on June 14, 2013), Act to Ensure Quality, Efficacy, and Safety of Pharmaceuticals and Medical Devices (Act No. 145, 1960) that were revised as a result of the Act for Partial Revision of the Pharmaceutical Affairs Act, (Act No. 84, 2013), as well as the Act to Ensure Safety of Regenerative Medicine (Act No. 85, 2013), etc., PMDA shall accelerate reviews speed for s and medical devices, aim to achieve elimination of review lag*, and aim to improve the quality of the reviews, etc. Pharmaceutical Affairs Consultation on R&D Strategy, etc., shall also be enhanced as a support to eliminate the developmental lag*.
In order to achieve these targets, PMDA's financial resources shall be utilized in enhancing the system.
*Drug lag and device lag are defined as delay of approvals of pharmaceuticals and medical devices, respectively, from United States in Japan. Drug lag or device lag can be divided into review lag, which are differences in review time (time from application to approval) between the United States and Japan, and development lag, which are differences in time at which the companies submit applications to the regulatory agencies of the United States and Japan (from the Japan Revitalization Strategy [approved by the Cabinet on June 14, 2013]).
The overall lag shall be eliminated by eliminating the review lag and development lag.

Following measures shall be promoted in order for the above mentioned measures to be implemented appropriately and smoothly, while maintaining cooperation with MHLW.

1) Make pharmaceuticals, medical devices, etc. accessible by the public more quickly

Efforts shall be made to enable the public and healthcare professionals to promptly gain advantage of advanced and safe pharmaceuticals and medical devices, etc., based on their needs so that they can receive the maximum benefit from them.
PMDA shall proactively support and cooperate with MHLW and its approaches, including acceleration of clinical trials, to promote development of pharmaceuticals and medical devices that are still unapproved in Japan but are of high medical need, in order to reduce development lag.

a) Conduct various measures, while evaluating and verifying their state of progress, and take additional measures when necessary.
b) In order to achieve reduce review lag while improving the quality of reviews, PMDA shall improve the services by setting time reduction targets (targets at ordinary times without any exceptional cases such as substantial changes in the systems or social conditions) for the processing time of applications (regulatory review time for products approved in the respective years) that were submitted after April 1, 2004. PMDA shall develop a review system to achieve these targets.
c) Promote multiregional clinical trials by cooperating with the United States, Europe, and Asian countries.
d) Prioritize clinical trial consultations for pharmaceuticals and medical devices that are expected to be highly useful by enhancing pre-application consultations, so as to reduce review period. Correctly understand the accurate needs of companies at the stage of development and reevaluate system of the consultation service whenever necessary.

e) Improve PMDA's own scientific levels for skills of consultations and reviews, with consideration of the rapid development of the latest technologies such as biotechnology, genomics, and regenerative medicine, and shall take necessary measures for the consultations and reviews along with the development of new pharmaceuticals, new medical devices, and regenerative medical products that utilize the latest technologies.

f) Take necessary measures to accelerate reviews for generic drugs, etc., as in the case of new pharmaceuticals.

g) Take measures to accelerate reviews for behind-the-counter (BTC) drugs*, over-the-counter (OTC) drugs, and quasi-drugs as with new pharmaceuticals.

* Behind-the counter (BTC) drugs are defined as switch OTC drugs and powerful OTC drugs which require pharmacist's intervention.

h) Set targets to aim for eliminating review lag for medical devices, as with new pharmaceuticals, and take measures to accelerate reviews. Develop a review system to achieve these targets.
Regarding reviews of improved medical devices and generic medical devices, PMDA shall take measures to systematically and intensively review items which had taken long time for the reviews after submission, and shall make efforts to reduce the applicant's time (the time within the review time that is necessary for the applicants to reply to inquiries from the regulatory side).

i) Take measures to accelerate reviews for regenerative medical products by enhancing the relevant review divisions necessary to conduct accurate and prompt reviews, while introducing conditional and time-limited approval system as well as setting target review times.

j) Appropriately and efficiently conduct conformity inspections.

k) Conduct appropriate and efficient GMP/QMS/GCTP (Good gene, Cellular and Tissue Practice) etc. inspections.

2) Provide Support to be the First in the World to Facilitate Practical Use of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medical Products

Make the following approaches in order to be first in the world to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products.

a) Establish and update review standards for innovative products.

b) Proactively conduct Pharmaceutical Affairs Consultation on R&D Strategy, etc.

c) Operate the approval system based on the characteristics of regenerative medical products.

3. Safety Measures

In the review services and post-marketing safety measures, PMDA shall promptly and safely provide superior pharmaceuticals and medical devices, etc., to medical settings in order to enable the public to use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

In accordance with this concept, utilize finances including PMDA's own financial resource and enhance the system when necessary to improve post-marketing safety measures of pharmaceuticals and medical devices, etc., based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.

a) Systematically and continuously conduct comprehensive evaluations of information on ADR, Malfunction, and Adverse Reaction (here in after ADR, etc.), by substantially enhancing assemble of information on ADR, etc., and its evaluation analysis system in order to accurately respond to the advanced and specialized evaluation of information on ADR, etc. Furthermore, find out new relationships among multiple ADR information, and establish an efficient and effective evaluation system for safety information such as researching and utilizing methods to identify and analyze new safety information, and improved it when necessary, by using IT technology.

b) Have healthcare professionals and companies increase utilization of feedback information on the analysis results of collected safety information, etc., and enhance methods of disseminating information on appropriate use to the patients, in order to enhance the rigorous system for disseminating safety information to improve safety measures at medical institutions. At the same time, PMDA shall also establish standards that enable the accomplishments of safety measures to be more accurately understood in a manner in which the public are able to understand easily.

c) Conduct appropriate post-marketing safety measures based on the Risk Management Plan of pharmaceuticals.

d) Cooperation shall be promoted among the relief services and the review services to enable appropriate assessment of safety.

e) Establish a system that enables confirmation of the current status and effectiveness of post-marketing safety measures taken by PMDA in companies and medical institutions, etc.

f) Appropriately collect information on Adverse Reaction reports regulated in the Preventive Vaccination Act and appropriately conduct investigations and analyses.

4. Promotion of Regulatory Science, Globalization, etc.

Note: Regulatory science = Science for coordinating results of science and technology into the most desirable form for harmonizing people and society, by conducting accurate and evidence-based estimations, evaluations, and decisions in order for the results of science and technology to be used for people and society. (from the Science and Technology Basic Plan, adopted by the Cabinet on August 19, 2011)

a) Enhance regulatory science research
Develop an environment and system for conducting regulatory science research (hereinafter referred to as the "RS research") aimed at improving the quality of the services provided by PMDA. Make efforts to train human resources to be experts in RS research through conducting it, and make efforts to contribute to increase the efficiency of development of pharmaceuticals, etc., through establishment of guidelines, etc.

b) Response to globalization
Reinforce partnerships with foreign regulatory agencies, promote global harmonization activity to proactively collect foreign information, and make efforts to promote dissemination of information in English.
Furthermore, enhance the English website of PMDA, and enhance measures in order for Asian countries to increase their understanding of Japanese regulations and standards regarding pharmaceutical applications, etc.

c) Enhance staff training
By enhancing staff training, PMDA shall establish a group of engineering supervisors that have a global level in review services and post-marketing safety measures so as to increase the quality of the services, and shall make efforts to train human resources to be experts in RS research.

d) Promote interaction with external researchers and investigative research
Promote investigative research by proactively interacting with external researchers in order to contribute to activate development and to establish guidelines regarding innovative seed-stage resources.

e) Promptly facilitate practical use of pharmaceuticals for intractable diseases and orphan diseases.

f) Promote further transparency of review services and post-marketing safety measures such as revealing in public review reports.
g) Develop an information system basis that ensures reliability and increases efficiency of review services and post-marketing safety measures.

Part 4
Matters Regarding Improvement in Financial Affairs

The following is the target for improving financial affairs specified in Article 29, Paragraph 2, Item 4 of the Act on General Rules for Incorporated Administrative Agency.

For matters specified in Part 2, items 1) and 2) of this Mid-term Targets, a Mid-term budget shall be developed with an estimation of cost reductions, and PMDA shall operate based on this budget.

Part 5
Important Matters Regarding Other Operation Management

The following are important targets regarding other operation management specified in the Article 29, Paragraph 2, Item 5 of the Act on General Rules for Incorporated Administrative Agency.

1) Matters Regarding Personnel Affairs

a) Secure enough personnel necessary to reviews and post-marketing safety measures, based on the Act for Partial Revision of the Pharmaceutical Affairs Act, etc., that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.
In order to avoid any suspicion of inappropriate relationships with pharmaceutical companies, etc., PMDA shall take appropriate measures in employment, allocation, post-retirement reemployment, etc., of executives and employees, while thoroughly ensuring its neutrality, etc.
PMDA shall make efforts to adjust the salary levels of the employees to achieve an appropriate and efficient level, taking into consideration competitiveness for stable securement of excellent human resources.

b) Appropriately develop personnel capacities by having them interact with external institutions to increase their expertise, and appropriately conduct personnel evaluations based on their work performance. PMDA shall also increase motivation of the personnel through these measures, etc.

2) Ensure Security

Ensure security of the offices, etc. and take all measures to thoroughly manage information, in order to thoroughly protect information of personal, corporate, etc.

3) Matters Regarding Disposition of the Reserve Funds Specified in Article 31, Paragraph 1 of the Act on the Pharmaceuticals and Medical Devices Agency

Appropriately dispose the reserve funds that are still left even after adjusting profit and loss according to Article 44 of the Act on General Rules for Incorporated Administrative Agency at the end of the last fiscal-year of the effective period for the Second Mid-term Targets.

4) Other Matters

Steadily conduct approaches based on the government policy indicated in past Cabinet decisions, etc.

Mid-term Plan of the Pharmaceuticals and Medical Devices Agency (PMDA)
(Provisional Translation)

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

Notification No. 0331-44 (dated March 31, 2014) of
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

To achieve the Mid-term Targets of the Pharmaceuticals and Medical Devices Agency assigned on March 7, 2014 by the Minister of Health, Labour and Welfare based on the provisions of Article 29, Paragraph 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999), the Pharmaceuticals and Medical Devices Agency (PMDA) has developed the following Mid-term Plan based on the provisions of Article 30, Paragraph 1 of the same act.

March 7, 2014

Tatsuya Kondo, Chief Executive,
Pharmaceuticals and Medical Devices Agency

Development toward global PMDA based on the PMDA Philosophy

PMDA was established in April 2004, after several times of reorganization by integrating the services of review and post-marketing safety measures, and has its roots in the “Fund for Relief Services for Adverse Drug Reactions”, which was established following tragic pharmaceutical-induced sufferings caused by pharmaceuticals such as thalidomide and diseases such as subacute myelo-optical neuropathy (SMON). Based on this history, and in order to carry out its mission to promptly provide the public with more effective and safer pharmaceuticals and medical devices, PMDA has been dedicating itself to improve its services for review, post-marketing safety measures, and relief services for adverse health effects. Essential targets have been accomplished by accelerating reviews and enhancing post-marketing safety measures in its efforts during the first and second terms. PMDA will need to further strengthen and enhance its system to aim to be a world-class institution responsible for reviews and post-marketing safety measures, in order to equal the United States and Europe in the future.

PMDA will promote comprehensive risk management through “Safety Triangle”, a system based on three major services, which are the review, post-marketing safety measures for pharmaceuticals and medical devices, and relief services for adverse health effects, to secure safety and efficacy, based on the following organizational philosophy of action (PMDA Philosophy).

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 pharmaceuticals 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 global community by promoting global harmonization.
5) We conduct services in a way that is trusted by the public based on our experiences from the past.

In promoting its risk management, PMDA will especially make efforts to develop an environment that enables judgments from an ethical perspective based on regulatory science, and to proactively contribute in improving public health and safety. PMDA will also promote cooperation with the United States, Europe, and Asian countries, etc., and approach issues from a global perspective in order to further improve health of people not only in Japan but also in the world.

Based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14, 2013), the Healthcare and Medical Strategy (an agreement among the Chief Cabinet Secretary, Minister of Health, Labour and Welfare, and Minister of Internal Affairs and Communications, etc., on June 14, 2013), the Act to Ensure Quality, Efficacy, and Safety of Pharmaceuticals and Medical Devices (Act No. 145, 1960; hereinafter referred to as the “Pharmaceutical and Medical Devices Act”), and the Act to Ensure Safety of Regenerative Medicine (Act No. 85, 2013; hereinafter referred to as the “The Act of the Safety of Regenerative Medicine”), etc., PMDA will further accelerate and improve the review services in order to promote to be the first in the world in practical use of innovative pharmaceuticals, medical devices, and regenerative medical products, while taking post-marketing safety measures, such as ensuring quality of post-marketing products and preventing occurrence and spread of health hazards.

In order to achieve these goals, the review and post-marketing safety measures in this term shall be improved by further enhancing the system and by introducing new review methods, etc., while pursuing elimination of review lag. Efforts will be made to have the public be aware of the relief services to ensure utilization of them. With these targets, the Third Mid-term Plan is to be established and implemented as follows:

Part 1

Measures to be taken in Order to Achieve Targets Related to Matters Regarding Improvement in Operation Management of the Overall Corporation and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

The following are the measures to be taken in order to achieve targets regarding improvement in efficiency of operations, as stipulated in Article 30, Paragraph 2, Item 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999; hereinafter referred to as the "Act on General Rules"), and to achieve targets regarding improvement in the quality of services and other operations rendered to the public, as stipulated in Article 30, Paragraph 2, Item 2 of the Act on General Rules.

1) Efficient and Flexible Management of Operations
   a) Manage transparent and appropriate operations through thorough compliance risk management
      - Clarify the operational targets and responsibilities of each division, and identify and resolve problems by managing the operational progress on a daily basis.
      - Develop and appropriately utilize internal control processes to achieve efficacy and efficiency of operations, reliability of financial reports, compliance with acts related to operational activities, and maintenance of assets, and proactively disclose the details of those measures that were taken.
      - Gather opinions on operational performance for each fiscal year and utilize them in managing the operations.
      - Hold advisory councils as an opportunity to exchange opinions with experts from various fields, and seek proposals and improvement measures for operations and the management system, in order to increase efficiency as well as to ensure fairness and transparency of the operations.
      - Efficiently manage the operations by flexibly allocating personnel according to situations and by effectively utilizing external experts.
      - Utilize manuals for emergency management appropriately by reviewing them from time to time in response to particular situations, in order to thoroughly manage risks in the management of operations.
      - Develop a system necessary to support the operations of the review, post-marketing safety measures, and relief service in order to respond to the expansion of the organization due to system reinforcement, and to enable reviewers to concentrate on technical and specialized operations.
   b) Standardize operation procedures
      - Standardize the procedures of each operation so that they can be conducted appropriately, which will enable utilization of non-regular staff, and as a result limit the number of regular staff members.
   c) Develop materials and information databases
      - Utilize an electronic format for documentary information whenever possible, and promote the development of databases that enable the information to be systematically organized and stored, as well as to enable material and information to be collected and analyzed.
   d) Optimize the system to improve efficiency of operations
      - Continue operations based on the basic policies of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the "Agency") for developing the system environment.
      - Based on the Optimization Plan for Operations and Systems that was established at the end of FY 2007, a system shall be developed to promote information sharing in the operations of review, post-marketing safety measures, and relief services for adverse health effects, and further approaches shall be promoted for the optimization of operations and systems, which was revised in FY 2012 for the purpose of enhancing the accounting and personnel management functions to respond to changes such as increase in personnel. Expenses for system development and improvement shall be invested systematically and efficiently by comprehensively judging at the Committee on Investment in Information Systems from such perspectives as appropriateness, cost-effectiveness, and technical difficulty.
      - Along with the Optimization Plan for Operations and Systems, increase efficiency of operations by revising the information system according to the actual status of the operations in each division.

2) Rationalize Operation Management
   a) Retrench general administrative expenses (management divisions)
      - By continuously improving the operation and increasing efficiency in management, the following reduction in the budget for the Mid-term Plan is expected to have been achieved by the end of the effective period for Mid-term Targets, regarding general administrative expenses (excluding personnel expenses) in which the administrative subsidies are to be applied.
      - No less than 15% as compared to FY 2014
      - Appropriately utilize consolidation and outsourcing for management operations such as payroll accounting, fund balancing, and calculation of travel expenses.
   c) Calculate administrative subsidies
   b) Retrench operating expenses for efficient operation management
      - By increasing efficiency in operations such as promoting computerization, the following reduction in the budget for the Mid-term Plan is expected to have been made by the end of the effective period for Mid-term Targets, regarding operating expenses (excluding personnel expenses, and single fiscal-year expenses that were paid for the establishment of operations) in which the administrative subsidies are to be applied.
      - No less than 5% as compared to FY 2014
      - Appropriately utilize consolidation and outsourcing for management operations such as payroll accounting, fund balancing, and calculation of travel expenses.
      - Yearly administrative subsidies are to be rigorously calculated with consideration of its debt balance.
   d) Stable collection of contributions
      - Have the marketing authorization holders (MAHs) of pharmaceuticals and medical devices understand the significance of the contribution system for adverse drug reaction (ADR) fund, relief for infections, and contributions to post-marketing safety measures, in order for contributions to be appropriately declared and paid, and to ensure stable collection of each contribution.
      - The collection rate for the contributions of ADR fund, relief for infections, and contributions to post-marketing safety measures shall be no less than 99%.
   e) Secure contract competitiveness and transparency
      - Contracts shall be concluded through open competitive bidding as a principle, and the following approaches shall be made.
      - Fully secure competitiveness and transparency even when contracts are not concluded by general competitive bidding such as planning competition and invitation to bids.
      - To conduct biddings and conclusion of contracts appropriately, contracts should be pre-inspected, etc., by the Contract Review Committee and thoroughly checked by auditor and accounting auditor.
   f) Provide and disseminate genuinely useful information from the public perspective
      - Take the following measures to steadily implement the PMDA Public Relations Strategic Plan.
        1. Enhance dissemination of information by improving the website so that it can be easily understood in order for the public and patients to be able to readily access information regarding safety and efficacy of pharmaceuticals and medical devices.
        2. Conduct public relations using newsletters related to PMDA.

3. Provide and publish information regarding PMDA in television and magazines.
4. Create newsletters in English and disseminate information to Foreign Correspondents' Club of Japan and to foreign media.
5. Enhance and improve the system for responding to consultations and complaints from the public.

- Enhance dissemination of information to the general public by disclosing the details of PMDA's services and achievements when appropriate, through various media including its website in order for the public to better understand the safety of pharmaceuticals and medical devices, as well as the overall services of PMDA.
- Conduct external audit in accordance with the incorporated administrative agencies system, together with systematic internal audit and accounting audit, and disclose those results.
- Disclose PMDA's overall financial standing as well as its financial standing for each account and segment in order to ensure transparency of the expenditures.

g) Analyze issues of the operation system
- Quantitatively analyze and examine issues of each division regarding the current operation processes as well as their systems as much as possible by the midpoint of the effective period for the Third Mid-term Targets, based on the understanding of the past operating performances of the relief service, review, and safety divisions, and those processes and systems shall be revised if necessary in order to confirm whether the personnel are allocated appropriately for the system enhancement and whether the operations are conducted efficiently.

h) Considerations related to financial base
- Consider a financial base that is appropriate for the role of PMDA, and take necessary measures based on the current situation where PMDA's revenue such as user fees from companies accounts for the majority of the financial base of PMDA, because the review and safety services of pharmaceuticals and medical devices greatly influence the life and safety of the public.

Part 2

Measures to be taken in Order to Achieve Targets Related to Matters Regarding Improvement in Operation Management of Each Division and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

- Make all efforts to promote the safety triangle of review, safety, and relief as a mission of PMDA -

1. Relief Fund Services for Adverse Health Effects

The Relief System for ADR and the Relief System for Infections Acquired through Biological Products (hereinafter referred to as the "relief systems") are systems unique to Japan, which, along with reviews and post-marketing safety measures, are responsible for being part of the safety triangle. The following measures shall be taken for the necessity of having the relief systems to be definitely utilized through consultations with physicians and pharmacists in case of emergencies of health damage due to ADR of pharmaceuticals or regenerative medical products, or due to infections through biological products or regenerative medical products, as well as for the necessity of continuing appropriate operations, such as prompt processing of relief benefit claims.

1) Enhance Public Relations and Dissemination of Information Regarding the Relief Systems

a) Proactively develop public relations in order for the relief systems to be definitely utilized.
- Consider and proactively conduct effective public relations regarding the relief systems.
- Continue informing more of the public regarding the relief systems by utilizing such media as websites and newspapers.
- Current measures, including dissemination of thorough information with the cooperation of relevant organizations, etc., shall be promoted, and the following measures shall be focused in order to increase the awareness by the end of the effective period for the Mid-term Targets, in order to further gain awareness and understanding from the public, health care professionals and MAHs, etc., regarding the relief systems. Surveys shall be conducted every fiscal year to find out the degree of their awareness, and those results shall be examined.
  1. Public relations activities shall be proactively conducted by utilizing the opportunities of training at medical institutions for health care professionals and opportunities of informing pharmacists regarding the systems, in order to properly make patients know the existence of relief systems by healthcare professionals including physicians and pharmacists, in case health damage occurs due to ADR or infections through biological products.
  2. Develop public relations nationwide through professional medical organizations.
  3. Conduct public relations for the general public using such media as websites, television, and newspapers.
  4. Develop effective public relations through other media aside from the above that is appropriate for promoting the relief systems.

b) Announce cases of benefit payment
- Further understanding of the current situation of benefit payment and dissemination of the relief systems to the public, healthcare professionals shall be promoted, by announcing cases of benefit payment and operational statistics on the website.

c) Disseminate information regarding the relief systems
- Review the methods of disseminating information from the perspective of making it user-friendly and easy to be understood, by revising the pamphlets and claim guidelines, by improving the content of information disseminated through the Internet, etc.

d) Ensure an efficient system for the consultation services
- Allocate regular staff for the consultation services, and ensure a system where specialized consultations can be received regarding use of the relief systems as well as the procedures to process benefit payments for ADR and infections.

2) Accelerate the Processing of Relief Benefit Claims

a) Investigate and organize the facts of the claim
- In order for relief benefit claims to be promptly processed, the facts of the claims shall be investigated and organized when received, before requesting the Minister of Health, Labour and Welfare for medical and pharmaceutical judgment.

b) Promptly process within the standard administrative processing time
- The target administrative processing time from receipt of the claim until the decision of payment (within 6 months, more than 60%) shall be maintained even in situations where the number of claims is expected to increase, by taking appropriate measures such as by enhancing the system for receiving and investigating claims, further enhancing and improving instructions for filling medical certificates, and accurately managing the time to use a system.
- Administrative processing time shall exclude the period when processing could not be continued because additional or supplementary documents and investigations of the claimant or medical institutions were necessary in order to make medical and pharmaceutical judgments.

c) Promote efficient operation with the use of databases
- Data of information related to the operation of relief services of ADR, especially information on the causative pharmaceutical, etc., and health damages shall be accumulated on the

database, and those accumulated data shall be statistically processed so that they can be analyzed from various perspectives, in order to operate a system that enables prompt and efficient payment of relief benefits using those results.
    - Upgrade the systems, develop operation support tools, and enhance systems if necessary, in order to respond to increases in relief benefit claims and to operational situations accordingly.

3) Promote Cooperation with the Review Divisions and the Safety Divisions
    - Cooperate with each division of PMDA and appropriately disseminate information, especially regarding cases of relief payment to the divisions of review and the post-marketing safety measures, with attention to ensuring protection of personal information.

4) Implement Appropriate Health and Welfare Services
    - Based on the results of a survey that investigated the current situation of health damages due to ADR, investigative research shall be continued in order to obtain information for considering measures to improve QOL of patients suffering from serious and rare health damages.
    - Steadily conduct consultations regarding mental issues.

5) Provide Healthcare Allowances for SMON Patients and HIV-positive Patients Infected with Blood Products Appropriately
    - In providing healthcare allowances to SMON patients and HIV-positive patients infected with blood products, appropriate services shall be implemented based on the details of the consignment contract, with special attention to ensuring protection of personal information.

6) Pay Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C virus Appropriately
    - In providing benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus, appropriate operations shall be implemented, with special attention to ensure protection of personal information.

2. Reviews and Related Services

Based on the Japan Revitalization Strategy and the Healthcare and Medical Strategy, as well as the Pharmaceutical and Medical Devices Act and the Regenerative Medicine Act that were revised as a result of the Act for Partial Revision of the Pharmaceutical Affairs Act, (Act No. 84, 2013), reviewing speed shall be accelerated, aiming to reduce review lag*, and the quality of the reviews shall be improved through approaches according to the characteristic of each pharmaceutical, medical device, and regenerative medical product (hereinafter, including cellular and tissue-based product and gene therapy product). Pharmaceutical Affairs Consultation on R&D Strategy shall also be enhanced as a support to eliminate the development lag*.

In order to achieve these targets, PMDA's financial resources shall be utilized in enhancing the system.

* Drug lag and device lag are defined as delay of approvals of pharmaceuticals and medical devices, respectively, from United States in Japan. Drug lag or device lag can be divided into review lag, which are differences in review time (time from application to approval) between the United States and Japan, and development lag, which are the differences in time at which the companies submit application to the regulatory agencies of the United States and Japan (from the Japan Revitalization Strategy [approved by the Cabinet on June 14, 2013]). The overall lag shall be eliminated by eliminating the review lag and development lag.

Following measures shall be promoted in order for the above mentioned measures to be implemented appropriately and smoothly, while maintaining cooperation with MHLW.

Note: The organization responsible for implementing the following measures is PMDA unless otherwise stated as MHLW, or other corporations.

1) Make pharmaceuticals, medical devices, etc. accessible by the public more quickly

New pharmaceuticals

a) Conduct accurate and prompt reviews
    - Enhance system in order to improve quality of the reviews by utilizing the Science Board and by enhancing training, with aiming to achieve elimination of review lag.
    - Steadily implement the project management system in order to improve the progress management function of the review services and to increase transparency of the progress and outlook of reviews for applicants as well.
    - Continue considering the efficiency and transparency of the review services and processes through exchange of opinions with the industry.
    - Strengthen cooperation with academia and healthcare professionals in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of pharmaceuticals.
    - Proactively support and cooperate in discussions and in requesting development for unapproved pharmaceuticals etc., at the Study Group on Unapproved and Off-label Pharmaceuticals of High Medical Need organized by MHLW.
    - Continue making approaches to reduce unapproved pharmaceuticals and off-label pharmaceuticals by enhancing database for the current status of pharmaceutical approval in major overseas nations.
    - Secure consistency between clinical trial consultations and reviews by maintaining cooperation between these two services, and flexibly organize groups to conduct accurate and prompt reviews and consultations.
    - Conduct accurate and prompt re-examinations for new pharmaceuticals. Take appropriate measures for re-evaluations as well.
    - Promote establishment of standards regarding quality of pharmaceuticals, such as the Japanese Pharmacopoeia established by MHLW, in order to conduct accurate and prompt reviews.

b) Introduce new methods for reviews and others
    - Systematically enhance the system for prior assessment consultations and respond to all consultations that were requested regarding superior pharmaceuticals of high medical need by the FY 2018.
    - Develop a system in PMDA that enables to accept electronic submission of clinical study data regarding new pharmaceutical applications after FY 2016.
    - Improve the quality of reviews and consultations by conducting PMDA-initiated analyses using the clinical trial data and by giving indications and suggestions based on those analyses results. Consider a system that enables cross-sectional analyses of products using advanced methods of analysis and prediction evaluation, and further improve reviews and consultation by establishing guidelines, etc., and increase efficiency of pharmaceutical development.

c) Targets to aim for eliminating review lag in pharmaceuticals
    - Regarding pharmaceuticals which new pharmaceutical applications were submitted after April 1, 2004, the percentile of the standard total review time from application to approval for the items approved in respective fiscal years, shall rise in stages as shown in the following table. The review time of 9 months for priority review products and 12 months for standard review products shall be achieved at 80th percentile by FY 2018.
      The review services shall be enhanced to achieve these targets.

1. Review time for new pharmaceuticals (priority review products)

Fiscal year	Percentile	Review time
FY 2014	60%	9 months
FY 2015	60%	9 months
FY 2016	70%	9 months
FY 2017	70%	9 months
FY 2018	80%	9 months

2. Review time for new pharmaceuticals (standard review products)

Fiscal year	Percentile	Review time
FY 2014	60%	12 months
FY 2015	70%	12 months
FY 2016	70%	12 months
FY 2017	80%	12 months
FY 2018	80%	12 months

- Regarding re-examination of new pharmaceuticals, the review time shall be reduced in stages regarding pharmaceuticals that are to be submitted for re-examination after FY 2014, with review results issued in respective fiscal years, and the total review time of 18 months shall be achieved at 50th percentile (median) by FY 2018. Products re-examined before FY 2014 shall also be sequentially processed.
- Regarding re-evaluations, evaluation and confirmation shall be conducted without delay by setting the appropriate standard review time to each pharmaceutical, based on the points of the application.

d) Promote multi-regional clinical trials
- In order to promote multi-regional clinical trials, appropriately respond to requests for consultations related to multi-regional clinical trials, based on the guidance regarding study design, etc.
- In order to promote multi-regional clinical trials especially in Asian countries, PMDA shall support the approaches of the Multi Regional Clinical Trial Roadmap led by MHLW at APEC RHSC, and develop an environment for conducting multi-regional clinical trials in Asian countries.
- PMDA shall promote multi-regional clinical trials in clinical trial consultations, etc., including information sharing with foreign regulatory agencies so as to increase the rate of conducting multi-regional clinical trials that Japan will participate amongst foreign clinical trials by FY 2018, to eliminate pharmaceutical development lag.

e) Conduct smooth clinical trial consultations, etc.
- Priority consultations and advance confirmation of application documents shall be continued, in order to increase opportunities to provide guidance and consultations before applications.
- Firmly maintain the time it currently takes from request for clinical trial consultation of new pharmaceuticals to direct consultation (about 2 months), while at any time accepting requests for priority clinical trial consultations so as to accelerate procedures for clinical trial consultations on new pharmaceuticals.
- Regarding categories such as prior assessment consultations, Pharmaceutical Affairs Consultation on R&D Strategy, and simple consultations, categories shall be added or altered according to the needs of the applicants by exchanging opinions with relevant industries and by analyzing the content of consultations, so as to enhance clinical trial consultations.

f) Promote evaluation of new technologies, etc.
- For pharmaceuticals developed using new technologies, concepts regarding development and evaluation shall be established in cross-sectional projects, along with guidelines if necessary, by using the knowledge of the Science Board and opinions of external experts.
- PMDA shall increase its scientific knowledge in order to lead the development of pharmaceuticals using latest technologies such as iPS cells.
- Cooperate with MHLW in establishing guidelines for evaluating products using the latest technologies, and proactively disclose the points to consider for evaluations.
- For preliminary reviews regarding the Act Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (hereinafter referred to as the “Cartagena Act”), the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.
- Enhance the Pharmaceutical Affairs Consultation on R&D Strategy by conducting consultations where suggestions can be made on development processes (roadmap) as well as confirmatory trial protocols, and by conducting consultations for pharmaceutical companies on developmental strategies.

Generic drugs, etc.

The following measures shall be taken to promote wide use of generic drugs, etc.

a) Conduct accurate and prompt reviews

1. Establish a new office for generic drugs, etc.
   - Enhance and accelerate reviews by appropriately increasing and allocating members for the generic drug, etc. group and by establishing a new office.
2. Ensure efficient and transparent reviews
   - Strengthen cooperation with academia and healthcare professionals, etc. to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of pharmaceuticals.
   - Promote establishment of standards regarding quality of pharmaceuticals, etc., such as the Japanese Pharmacopoeia, etc., established by MHLW, in order to conduct accurate and prompt reviews.
   - Recommend application by CTD/eCTD format in order to increase efficiency in reviews.
   - Ensure transparency of the reviews by preparing and disclosing review reports on new generic drugs.
   - Establish guidelines for bioequivalence testing in order to respond to the increased complexity of bioequivalence assessments and the diverse pharmaceutical products that are being developed.
   - Cooperate with relevant offices to take appropriate measures to steadily implement the risk management plan.

b) Targets for reducing review time
- Regarding pharmaceuticals which applications were submitted after April 1, 2004, the target review times for the items approved in respective fiscal years, shall be as shown in the following table. The regulatory authority shall make efforts to achieve these targets with the cooperation of the applicants.

  The review system shall be enhanced to achieve these targets.

1. Review time for new application of generic drugs
   The following targets shall be achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
New generic drugs	10 months

2. Review time of application for partial change approval in generic drugs, etc. (standard review products)
   Targets shall be achieved at 50th percentile (median) by FY 2018, based on the following plan.

Fiscal year	Total review time
FY 2014	15 months
FY 2015	14 months
FY 2016	13 months
FY 2017	12 months
FY 2018	10 months

3. Review time of application for partial change approval in generic drugs, etc. (products other than standard review products)
   The following targets shall be achieved at 50th percentile (median) by FY 2018.

Products	Total review time
Products applied for partial change approval (change in procedure of study, etc.)	6 months
Products applied for partial change approval (prompt review)	3 months

c) Conduct smooth clinical study consultations, etc.
- All consultations shall be conducted for those requested for quality consultation or bioequivalence consultation (face to face consultation).
- Enhance consultation services by considering whether setting up new consultation categories are necessary to meet the needs of the applicants.

Behind-the-counter (BTC) drugs*, over-the-counter (OTC) drugs, and quasi-drugs

The following measures shall be taken to promote public self-medication.

a) Conduct accurate and prompt reviews
- In order to conduct accurate and prompt reviews for BTC drugs, OTC drugs, and quasi-drugs, etc., the following measures shall be taken to enhance the review system, etc., including safety assessments.
  1. Enhance system for BTC drugs and OTC drugs, etc.
     - In order to respond to the establishment of BTC drugs system, etc., that was newly developed by the Act for Partial Revision of the Pharmaceutical Affairs Act and the Pharmacists Act (Act No. 103 of 2013), the review system shall be enhanced by allocating reviewers for toxicity and clinical matters (including biostatistics), and by securing human resources who have experience in post-marketing safety measures and conformity assessment.
     - Strengthen cooperation with academia and healthcare professionals, etc., in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of BTC drugs and OTC drugs.
     - Conduct accurate and prompt reviews by establishing standards regarding quality of pharmaceuticals, such as the Japanese Pharmacopoeia as well as official specification for excipients.
     - Increase efficiency and enhance the review service for Chinese herbal medicines and crude drugs.
  2. Enhance system for quasi-drugs, etc.
     - Increase the number of reviewers in order to accelerate reviews for innovative products.
     - Increase efficiency of the reviews by establishing standards for quasi-drugs, such as the Japanese Standards of Quasi-drug Ingredients established by MHLW, as well as establishing quality standards for excipients, etc.
     - Improve quality of the reviewers through training, etc.
     - Strengthen cooperation with academia and healthcare professionals, etc., in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of quasi-drugs.
       * Behind-the-counter (BTC) drugs are defined as switch OTC drugs and powerful OTC drugs which require pharmacist's intervention.

b) Targets for reducing review time
- Regarding BTC drugs, OTC drugs and quasi-drugs which applications were submitted after April 1, 2004, and were approved in respective fiscal years, the target review times shall be as shown in the following table. Approaches shall be made to achieve these targets.

1. Review time for BTC drugs and OTC drugs
   The following target shall be achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
BTC drugs and OTC drugs	7 months

2. Review time for quasi-drugs
   The following target shall be continuously achieved at 50th percentile (median) by FY 2018.

Product	Regulatory review time
Quasi-drugs	5.5 months

c) Conduct smooth consultation services
- For BTC drugs and OTC drugs, conduct consultations on the appropriateness of developing new OTC drugs, etc., pre-application consultations for switch OTC drugs, and consultations on confirming the key points of the protocols.
- For quasi-drugs, develop and conduct pre-application consultations.

Medical devices

a) Conduct accurate and prompt reviews
- Systematically enhance the review system for new medical devices in order to accelerate the reviews for innovative medical devices.
- Accelerate reviews by making efforts to conduct rational reviews based on the characteristic of medical devices which constantly being improved, etc.
- Strengthen cooperation with academia and healthcare professionals in order to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of medical devices.
- Proactively support and cooperate in requesting development for medical devices, including unapproved medical devices, at the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Need held by MHLW.

- Make efforts to smoothly operate and implement the new use-results evaluation system for medical devices.
- For new medical devices, improved medical devices, and generic medical devices, thoroughly manage the timeline for the standard review process so as to be conducted adequately.

b) Clarify review standards, etc.
- Compile and disclose the concept regarding clinical evaluation.
- In order to accelerate the reviews, cooperate with MHLW in establishing approval standards, certification standards, and review guidelines for medical devices, and disclose those standards and guidelines on the website, etc.
- Clarify, share, and establish the concept of substantial equivalence for generic medical devices.

c) Smoothly transfer specially controlled medical devices to the third party certification system
- Transfer to the third party certification system sequentially from the products whose standards have been established among specially controlled medical devices (class III).

d) Targets to aim for eliminating review lag in medical devices
- Regarding medical devices which applications were submitted after April 1, 2004, the percentile of the standard total review time from application to approval for the items approved in respective fiscal years, shall be raised in stages as shown in the following table, in order for the targets to be achieved by FY 2018. Approaches shall be made to achieve these targets by systematically and intensively completing processing of the devices that were submitted for application in the past as soon as possible, and the regulatory authority shall make efforts to improve the lag with the cooperation of the applicants.

1. Review time for new medical devices (priority review products)
Achieve 10 months at 80th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	60%	10 months
FY 2015	60%	10 months
FY 2016	70%	10 months
FY 2017	70%	10 months
FY 2018	80%	10 months

2. Review time for new medical devices (standard review products)
Achieve 14 months at 80th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	60%	14 months
FY 2015	60%	14 months
FY 2016	70%	14 months
FY 2017	70%	14 months
FY 2018	80%	14 months

3. Review time for improved medical devices (with clinical data)
Achieve 10 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	10 months
FY 2015	54%	10 months
FY 2016	56 %	10 months
FY 2017	58 %	10 months
FY 2018	60 %	10 months

4. Review time for improved medical devices (without clinical data)
Achieve 6 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	6 months
FY 2015	54%	6 months
FY 2016	56 %	6 months
FY 2017	58 %	6 months
FY 2018	60 %	6 months

5. Review time for generic medical devices
Achieve 4 months at 60th percentile by FY 2018 based on the following plan.

Fiscal year	Percentile	Review time
FY 2014	52%	4 months
FY 2015	54%	4 months
FY 2016	56 %	4 months
FY 2017	58 %	4 months
FY 2018	60 %	4 months

e) Conduct smooth clinical trial consultations, etc.
- Reconsider the consultation category and improve consultation methods in order for the consultation service to be easier to utilize, and to be efficient and effective.
- Address the relevant industries to proactively utilize the consultation service, in order to eliminate review lag and development lag.

f) Promote evaluation of new technologies, etc.
- For medical devices using new technologies, guidelines, etc., shall be established if necessary, utilizing knowledge of the Science Board and opinions of external experts.
- Make efforts to accumulate relevant knowledge, etc., in order to appropriately respond to the development of medical devices using the latest technologies.
- Cooperate with MHLW in establishing guidelines for evaluating products that were developed using the latest technologies, and proactively disclose the points to consider for evaluations.
- For preliminary reviews regarding the Cartagena Act, the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.
- Enhance the Pharmaceutical Affairs Consultation on R&D Strategy by conducting consultations where suggestions can be made on development processes (roadmap) and confirmatory trial protocol, and by conducting consultations for medical devices related companies on developmental strategies.

***In vitro* diagnostics**

a) Conduct accurate and prompt reviews
   - Appropriately increase and allocate members for the *in vitro* diagnostics group, in order to accelerate and increase transparency of the reviews.
   - Strengthen cooperation with the academia and healthcare professionals, etc., to conduct consultations and reviews based on the latest medical care trends and needs, and to promote cooperation toward appropriate use of *in vitro* diagnostics.
   - Proactively support and cooperate in requesting development of *in vitro* diagnostics, including those that are still unapproved, that were discussed at the Study Group on the Early Introduction of Medical Devices, etc., with High Medical Need held by MHLW.

b) Enhance consultation service
   - Reconsider the consultation category and improve consultation methods in order for the consultation service to be easier to utilize, and to be efficient and effective.

Regenerative medical products

a) Conduct accurate and prompt reviews
   - Enhance the services of the division of Pharmaceutical Affairs Consultation and its relevant divisions, as well as the division of biologics reviews. Strengthen cooperation with academia such as the Japanese Society for Regenerative Medicine, the National Institute of Health Sciences, and the Center for iPS Cell Research and Application (CiRA), etc., in order to conduct consultations and reviews based on the latest medical care trends and needs.
   - Conduct consultations.

b) Introduce new review methods
   - With the implementation of the Act for Partial Revision of the Pharmaceutical Affairs Act, respond appropriately to conditions related to regenerative medical products and to the introduction of time-limited approvals. Develop a system for this, along with its review process, and conduct them accurately.

c) Target review time
   - For regenerative medical products which applications were submitted based on the Pharmaceutical Medical Devices Act, standard review time (regulatory time) for the items approved in respective fiscal years shall be set to 9 months.
     The review system shall be enhanced to achieve this target.

d) Conduct smooth clinical study consultations, etc.
   - Make efforts to conduct thorough consultations so as to be understood easily, since regenerative medical products are a new field.
   - Conduct high-quality consultations by utilizing the Science Board for considering evaluation methods, etc., and highly-qualified external experts, etc., to obtain the latest knowledge.
   - PMDA shall make efforts to have applications of regenerative medical products after going through consultations such as the Pharmaceutical Affairs Consultation on R&D Strategy (as the substitute of pre-confirmation application) and pre-application consultations, and develop a system necessary to conduct prompt and smooth reviews considering the current situation of consultations and reviews.
   - In order to enable the academia and ventures to consult easily, the target details, etc., of the Pharmaceutical Affairs Consultation on R&D Strategy shall be considered for regenerative medical products, based on the current situation.

e) Promote evaluation of new technologies, etc.
   - Conduct appropriate evaluations for regenerative medical products, by utilizing the Science Board for considering evaluation methods, etc., and highly-qualified external experts.
   - Make efforts to accumulate relevant knowledge, etc., in order to be able to appropriately respond to the development of regenerative medical products using the latest technologies, such as iPS cells, etc.
   - Clarify and rationalize the review standards by promoting the initiative to facilitate development and designated research.
   - Enhance the post-marketing surveillance, considering especially the surveillance methods for those conducted after conditional and time-limited approvals, cooperating with the safety division.
   - Cooperate with the MHLW in establishing evaluation guidelines regarding products using the latest technologies, and proactively disclose the points to consider for evaluations.
   - Enhance consultations to enable proactive utilization of Pharmaceutical Affairs Consultation on R&D Strategy as the substitute of preliminary reviews conducted before clinical trials regarding regenerative medical products and gene therapy products.
   - For preliminary reviews regarding the Cartagena Act, the regulatory review time shall be 6 months for approval of first-class use and 2 months for confirmation of second-class use, with a target of achieving 50th percentile (median) for each class.

Promotion of conformity assessments and clinical trials, etc.

The following measures shall be taken to enhance, with strengthening the organization, studies related to the application such as clinical trials, and to ensure reliability of submitted application documents, with focus on an importance of ensuring the reliability of clinical trial data, etc., at the application of pharmaceuticals and medical devices.

a) Implement smooth and efficient conformity assessments for new pharmaceuticals, etc.
   - Strengthen the organization to conduct timely assessments which will not affect the time of approval. New assessment methods with efficiency and effectiveness shall also be introduced.
   - As for the items concurrently submitted with the applications in the world, etc., strengthen the coordination on partnership with foreign regulatory agencies and strengthen the organization, for example, considering the assessment in collaboration with them.
   - Make clear policy on the procedure for clinical trials in which CDISC was introduced from data gathering step.

b) Implement smooth and efficient conformity assessments for medical devices
   - Strengthen the organization to conduct timely assessments which will not affect the time of approval.
   - Strengthen the organization conduct GCP on-site assessment, in particular, focus on innovative medical devices and multi-regional clinical trials, etc.
   - Establish and disseminate detailed requirements that are necessary for applications, in order to implement conformity assessments smoothly and promptly.

c) Implement smooth and efficient conformity assessments for regenerative medical products
   - Cope with the introduction of a conditional and time-limited approval system.
   - In order to implement appropriate conformity assessments, coordinate with the division of biologics review sufficiently considering assessment methods and processes that are based on the characteristics of regenerative medical products.

d) Implement smooth and efficient GLP compliance assessment
   - Train GLP inspectors that has global competency.
   - Examine how to establish a smooth operation of the GLP regulation considering global consistency, and implement the GLP compliance assessment more appropriately and efficiently.

e) Implement smooth and efficient conformity assessment for re-examinations (including conformity assessment on use-results evaluation)
   - Implement efficient and effective GPSP on-site assessments and document-based conformity assessments.

- To enable high quality post-marketing surveillances, examine to establish such as consultation to provide guidance and advices regarding the compliance for GPSP, etc., during the re-examination period.
- Examine and disseminate effective assessment methods, to enable smooth and prompt conformity assessments for re-examination, etc.

f) Promote appropriate clinical trials, etc.
- Enlighten the further promotion for implementation of appropriate clinical trials, etc., through the conformity assessment at medical institutions and sponsors, and training course, etc., in the period of the Mid-term targets, to ensure the quality of clinical trials, etc. in Japan.
- Examine the establishment of advice system that enables individual cases on GCP, etc.

Promotion of GMP/QMS/GCTP inspection

In order for manufacturers to appropriately maintain and control manufacturing processes and the quality management system for pharmaceuticals, medical devices, and regenerative medical products, the following improvements shall be made to improve inspectional quality.

a) Conduct efficient GMP inspections
- In response to accelerated reviews and increased numbers of bio-products, methods to improve GMP inspection efficiency shall be considered and conducted. This includes system enhancements to conduct timely inspections and clarify application time, while not affecting the time of approval.
- Increase the efficiency of inspections by using the assessment results of other regulatory agencies under PIC/S etc., in risk evaluation to decide if inspections shall be conducted on-site or off-site.
- In response to globalization of active pharmaceutical ingredients supply, partnerships with foreign regulatory agencies shall be reinforced and inspectional information shall be exchanged. A system to enhance on-site inspections at manufacturers overseas, especially in Asian countries, shall be developed.
- Quality of inspections shall be improved by having reviewers accompany the GMP inspection team and by promoting cooperation between GMP inspectors and reviewers.
- Enhance staff training for GMP inspectors by letting them proactively participate in training and meetings conducted overseas. Overseas training will increase staff with knowledge of global GMP harmonization and practices.

b) Conduct smooth and efficient QMS inspections
- QMS inspection and related operations streamlined by the Act for Partial Revision shall be established.
- Promote cooperation between the review groups and the QMS inspection group.
- Standardize inspection methods with other domestic and overseas inspection agencies, such as registered certification bodies.
- Build expertise in global QMS harmonization and practices, through enhancing training for QMS inspectors and let them proactively participate in training and meetings conducted overseas, etc.
- Share inspection information with relevant domestic authorities to efficiently use resources.

c) Conduct smooth GCTP inspections
- For accurate and prompt GCTP (Good gene, Cellular and Tissue Practice) inspections by PMDA that will start after enactment of the Act for Partial Revision, appropriate inspection methodology and necessary resources shall be established and secured.
- For buildings/facilities conformity assessments and relevant on-site inspections by PMDA into establishments that are processing cell/tissue products, that will start after enactment of the Regenerative Medicines Safety Act. Necessary resources shall be immediately secured and managed and current domestic and overseas situation regarding production of such products shall be figured out.

d) Increase efficiency of inspectional efficiency by utilizing the Kansai Branch and by conducting GMP inspections.

Establishment of control function for the registered certification bodies

1) Improve the quality of certification bodies by ensuring the quality of the inspectors and by conducting appropriate training, etc., for those bodies.

2) Provide Support to be the First in the World to Facilitate Practical Use of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medical Products

a) Establish and update review standards regarding innovative products
- Utilize the Science Board, the initiative to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products, and regulatory science research (hereinafter referred to as the “RS research”), etc., in order to establish guidelines and guidance and to consider RS research, etc., that PMDA shall make approaches on.
- Establish guidelines and guidance, etc., in cross-sectional projects regarding development and evaluation of pharmaceuticals, etc., that uses new technologies, and make necessary approaches in order to smoothly implement them.

b) Proactively conduct Pharmaceutical Affairs Consultation on R&D Strategy, etc.
- Conduct consultations where suggestions can be made on development processes (roadmap) and confirmatory trial protocol. Conduct consultations for pharmaceutical companies on developmental strategies as well.
- Promote medical innovations by utilizing the Kansai Branch to fully educe technological capacity of Japan regarding biopharmaceuticals, medical devices, and regenerative medical products, etc.
- Regarding PMDA’s function to mediate between clinical study and practical use, support, etc., shall be proactively provided through Pharmaceutical Affairs Consultation on R&D Strategy, etc., in establishing exit strategies, with the cooperation of the Japan National Institutes of Health, etc.

c) Operation of approval system based on the characteristics of regenerative medical products
- In order to appropriately cope with conditions related to regenerative medical products as well as the system for time-limited approval that were both introduced by the enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act, information dissemination and utilization of the consultations shall be promoted, by enhancing Pharmaceutical Affairs Consultation on R&D Strategy and by cooperating with relevant academia and industry.

3. Safety Measures

Utilize finances including PMDA’s own financial resource and enhance system necessary to improve post-marketing safety measures of pharmaceuticals, medical devices, etc., based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, the final recommendation by the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, the discussions held by the Investigational Sub-committee on Revision of Pharmaceutical Regulatory Systems of the Health Science Council, etc.

The following measures shall be taken in order to promote appropriate and efficient approaches mentioned above, with close cooperation with MHLW.

Note: The organization responsible for implementing the following measures is PMDA unless otherwise stated to be MHLW, etc., or other corporations, etc.

1) Enhance Collection of ADR and Malfunction Information
   - Establish a system in which patients can easily report ADR, based on opinions, etc., from the patients and patients' families, etc., who have reported them, and officially commence accepting and evaluating ADR reports, including reports on OTC drugs and Switch OTC and powerful drugs.
   - Accept reports from MAHs as well as healthcare professionals, and take measures to increase reports from healthcare professionals with the cooperation of MHLW.
   - Enhance and improve the systems to report information on ADR and malfunctions, etc., based on the current situation of global development such as ICH E2B and on the advancement of information technology, etc., and promote efficient and effective collection of safety information, etc.
   - Enhance measures to collect information on ADR of quasi-drugs and cosmetics.

2) Systematize Information of ADR, etc., and Its Evaluation Analysis
   - In order to appropriately respond to the evaluation approach for ADR which is increasingly sophisticated and specialized, substantially enhance current framework to assemble and analyze information on ADR. For this purpose, it is necessary to increase the number of staff members in each group organized according to pharmaceutical effect classification and area of medical practice that correspond to the review divisions. Measures, such as utilizing IT technology, shall also be taken to carefully investigate the overall domestic reports on ADR and infections.
   - Modify a PMDA-initiated system step-by-step to follow-up on ADR reported from medical institutions, and ensure its application for all reports that needs investigation by FY 2018.
   - Standardize and increase transparency of the process from obtaining information of ADR to take post-marketing safety measures including revision of package inserts, and increase accuracy and expediting of the process.
   - Steadily accelerate the process taken to prepare post-marketing safety measures by setting a target time, and by increasing efficiency of the process with standardization. For the target time, consider, reducing the current median time from the first meeting with the MAHs until notification of investigation results.
   - Modify submission process for package inserts to enable MAHs to smoothly submit package inserts.

   Establish a system to check contents of submitted package inserts and ensure that the submitted information is based on the latest knowledge.
   - Respond promptly to consultations from MAHs when it voluntarily develop or revise either package inserts or communication tools for healthcare professionals and patients.
   - Respond promptly to medical safety consultations from MAHs regarding safer use of pharmaceuticals and medical devices at clinical practice.

3) Establish Database, etc., for Medical Information
   - Conduct pharmacoepidemiological analyses using electronic medical information, such as the Medical Information Database Network, and improve those analysis methods to promote its utilization for risk/benefit assessments of pharmaceuticals and for post-marketing safety measures.
   - Promote MAHs to utilize the Medical Information Database Network for post-marketing safety measures, with its conditions of utilization determined by MHLW for post-marketing surveillance, etc., based on results of utilization obtained through pilot studies.
   - Data accumulation shall be promoted in order to improve the quantity and quality of the Medical Information Database Network as well as to improve post-marketing safety measures.
   - In order to promptly and safely provide useful medical devices and regenerative medical products, discussions up to the previous effective period for the Mid-term Targets shall be put into consideration to enhance the system of collecting post-marketing information, for example, by establishing a patient registry system for confirming long-term safety, with the cooperation of relevant academia and companies, etc.
   - Promote investigational research regarding utilization of pharmacogenomics in post-marketing safety measures.

4) Establish a System for Post-marketing Safety Measures by Providing Information Feedback, etc.
   - Regarding line listing of ADR, the time from ADR reporting to disclosure shall remain as within 4 months.
   - ADR reports from medical institutions shall be promptly disclosed in the line listing for those that have been investigated by PMDA.
   - The instructions for revising the package inserts shall be published on the website within 2 days after issuance of those instructions.
   - Disseminate information related to cases of ADR and malfunction, etc., for those that served as the basis for revising package inserts for prescription pharmaceuticals and medical devices, etc.
   - Consider with MHLW about measures to enable medical institutions to discern the urgency and importance of the disseminated information more easily.
   - Enhance dissemination of information to promote appropriate use of generic drugs.
   - Regularly disseminate medical safer information so that pharmaceuticals and medical devices, etc., will be used safely at clinical settings.
   - Collect medical safety information from vocational groups, etc., and enhance dissemination of the information.
   - Aim for a wider use of the Pharmaceuticals and Medical Devices Information E-Mail Alert Service by enhancing the content of the service and by increasing the number of registries at an early period before the end of FY 2018 by more than 1.5 times that at the end of FY 2013, by means of strongly promoting registry of healthcare professionals working at medical institutions and pharmacies with the cooperation of relevant organizations, and so on.
   - Let healthcare professionals, including physicians and pharmacists, etc., increase understanding of the information that PMDA provides.

5) Enhance Dissemination of Information to the Public Regarding Safety of Pharmaceuticals and Medical Devices, etc.
   - Improve the method of disseminating information on the website regarding safety of pharmaceuticals and medical devices, etc., in order to respond to changes in the environment in which pharmaceuticals, medical devices, and regenerative medical products are provided, such as internet marketing of OTC drugs.
   - Promptly release important safety information in a manner that is easy to understand from the patients' perspective.
   - Enhance dissemination of information to patients by further increasing patient's awareness of the Pharmaceutical Guide for Patients and by increasing its convenience.
   - Enhance dissemination of information that can be used for medication instructions for patients.
   - Conduct consultations services for general consumers and patients for a safe and secure use of pharmaceuticals and medical devices, etc.
   - Further improve the contents of information to the public, etc.

6) Conduct Appropriate Post-marketing Safety Measures Based on the Risk Management Plan of Pharmaceuticals
   - Consultation and instruction systems shall be strengthened and enhanced to appropriately conduct pharmacovigilance activities and risk minimization activities, based on the new Risk Management Plan (RMP) of pharmaceuticals.
   - The new pharmaceuticals review divisions and the safety divisions shall cooperate together through discussions with the applicant in confirming RMP before reviews of new pharmaceuticals concludes.
   - Regarding generic drugs, the generic drugs review division and the safety divisions shall cooperate together in order to confirm in the reviews the pharmacovigilance activity and the risk minimization activity that the MAHs are required to conduct.
7) Enhance Safety Measures in Response to the Introduction of New Review Service, and a Safety Management System Consistent from the Review Stage
   - Safety management system shall strengthen cooperation with the relief services and maintain consistency from the review stage. Information from the relief services shall be utilized in the post-marketing safety measure operation, with special attention to ensuring protection of personal information.
   - The safety divisions and the review divisions shall share information on adverse reactions caused by regenerative medical products (including time during conditional and time-limited approvals), and shall cooperate in taking post-marketing safety measures.
   - Information on malfunctions of new medical devices and certified medical devices shall be shared among the safety divisions, the review divisions, and the registered certification body assessment division, for taking post-marketing safety measures.
   - The system of safety management shall be enhanced in order to maintain consistency from the review stage, by allocating multiple risk managers for each field according to the number of new pharmaceutical products.
   - The management function of the overall post-marketing safety measures shall be enhanced and the groups shall coordinately cooperate, to conduct appropriate operation.
   - For products which need investigation on all cases as an approval condition, safety and efficacy information obtained from post-marketing surveillance shall be promptly provided to the public and health care professionals?
8) Enhance Follow-ups of the Safety Measures Conducted
   - Conduct investigations to confirm the current status of post-marketing safety measures in MAHs, for example, whether information is definitely conveyed from the MAHs to medical institutions, and to confirm whether information from MAHs is conveyed and utilized within medical institutions and pharmacies. Based on the investigation results, information regarding methods of utilizing safety information in medical institutions and pharmacies shall be disseminated as best practices to use pharmaceuticals and medical devices safely.
   - Investigate the status of whether the information provided from PMDA is utilized by general consumers and healthcare professionals, and analyze their needs and satisfaction level, to reflect them in the information service improvement.
9) Data Collection, Investigation, and Analysis on Adverse Reactions Reports in Accordance with the Preventive Vaccination Act
   - Adverse reactions shall be promptly disclosed on the website for those that were reported from medical institutions and were investigated by PMDA.
   - Details of adverse reactions reports shall be investigated in accordance with the Preventive Vaccination Act, with special attention to ensuring protection of personal information, and investigations and analyses shall be conducted in order to ensure safety of vaccination.

4. Promotion of Regulatory Science and Globalization, etc.

In order to promptly provide clinical settings with necessary pharmaceuticals and medical devices, etc., it is essential for the quality, efficacy, and safety of pharmaceuticals and devices to be accurately estimated, evaluated, and determined based on scientific rationale and to be ascertained from an ethical perspective on whether to allow the public to use them. Regulatory science (RS) pursue this, and it has become increasingly important to be promoted, and research needs to be conducted on establishing prompt and accurate evaluation methods, etc., based on the latest results of technology, by utilizing external experts and by improving PMDA's capability.

In the midst of global development, manufacturing, distribution, and marketing of pharmaceuticals and medical devices, the services of PMDA have increasingly become globalized. Under these circumstances, improvement in medical services as well as establishment of PMDA's global standing shall be made by cooperating with MHLW, the United States, Europe, and Asian countries, etc., and by proactively promoting global activities based on the PMDA International Strategic Plan, PMDA International Vision, and Road map for the PMDA International Vision.

Note: Regulatory science = Science for coordinating results of science and technology into the most desirable form for harmonizing people and the society, by conducting accurate and evidence-based estimations, evaluations, and decisions in order for the results of science and technology to be used for the people and the society (from the Science and Technology Basic Plan, adopted by the Cabinet on August 19, 2011).

1) Promotion of Regulatory Science
   1. Utilize the Science Board
      - Proactively utilize the Science Board comprising external experts from the fields of medical science, dentistry, pharmaceutics, and engineering, to strengthen cooperation and communication with universities, research institutions, etc., and clinical settings regarding evaluation methods for innovative pharmaceuticals, medical devices, and regenerative medical products, and to make approaches to advanced technology products more adequately, for example, by utilizing Pharmaceutical Affairs Consultation on R&D Strategy.
   2. Enhance regulatory science research
      - Establish a system in PMDA to enable electronic submission of clinical study data for new pharmaceuticals that are to be submitted after FY 2016.
        Conduct PMDA-initiated cross-sectional analyses on cross-sectional clinical study data, etc., using advanced methods of analysis and prediction evaluation, and consider a system that increases the efficiency of pharmaceutical development through establishment of guidelines, etc.
      - As a part of RS research aimed at improving the quality of PMDA's services, a system and environment shall be developed by cooperating with external organizations (NIHS, academia, etc.) when necessary, so PMDA can take initiative in reaching solutions for issues that become evident through its services and issues of making practical use of the latest technologies.
      - Develop an environment to easily engage in RS research, to promote and enhance designated research.
      - Promote RS research, and encourage those results to be presented at conferences or to be submitted to scientific journals. Through RS research, train human resources to be experts in it.

- As for cross-sectional activities, establish the concept of developing and evaluating pharmaceuticals to enable exchange of opinions between industry, government, and academia, and to establish guidelines and GRP, etc.

3. Enhance staff training
   - Besides improving the quality of review, etc., and post-marketing safety measures, from the perspective of developing experts in RS research, status of the current training programs shall be evaluated for their implementation status, and their content shall be improved and conducted steadily.
   - Enhance staff training to raise staff members with abilities to take the initiative in discussions at global negotiations and conferences, and to cooperate with foreign countries in establishing standards and guidelines, etc.
   - Enhance on-site training at clinical settings and at manufacturing sites of companies, etc., as it is necessary, when conducting reviews, etc., and post-marketing safety measures, to have experience in clinical settings and increase in knowledge of manufacturing processes and quality controls for pharmaceuticals and medical devices.
4. Promote Interaction and investigative research with external researchers
   - Proactively accept personnel from universities and research institutions in the field to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products conducted by MHLW, while also dispatching staff from PMDA in order to help promote the development of innovative seed-stage resources and to establish guidelines.
   - Develop and enhance education and research guidance systems that are conducted by directors and staff members at joint graduate school program, including regulations for those systems. These approaches will target increasing staff members who have a doctoral degree, etc.

2) Response to Globalization

1. Reinforce partnerships with the United States, Europe, Asian countries, and global organizations, etc.
   - Cooperation with the United States FDA, the European Commission, EMA, and Swissmedic, etc., in promoting bilateral conferences based on confidentiality agreement and promoting exchange of information.
   - Establish partnerships with other countries in America, Europe, and Asia, and global organizations.
   - Continue dispatching liaison personnel to the United States, Europe, and Switzerland as much as possible, while promoting further dispatches to other countries in America, Europe, and Asia, etc., and global organizations, etc., as well.
   - Utilize the liaison personnel dispatched to foreign countries to proactively collect information from their dispatched country, and to strengthen cooperation with those countries.
   - Regarding GLP, GCP, GMP, and QMS inspections, further strengthen cooperation with foreign countries by proactively exchanging information on inspection notifications and investigation reports, etc.
   - Respond to globalization of pharmaceutical distribution by enhancing globalization measures, for example, by promoting support in issuing an English version of the Japanese Pharmacopoeia as soon as possible, by disseminating information in English, and by promoting partnerships with the pharmacopoeias of Europe, the United States and Asia, etc.
   - Reinforce partnerships with regulatory agencies in the United States and Europe in order to conduct accurate reviews and consultations based on the latest science and technology, and to take post-marketing safety measures based on the latest information.
   - Promote cooperation necessary to deepen mutual understanding regarding pharmaceutical regulations with the regulatory agencies in Asian countries, which are becoming increasingly important as sites of clinical development and manufacturing of pharmaceuticals, etc.
   - Make necessary efforts for the pharmaceuticals and medical devices approved in Japan to be accepted by regulatory agencies in foreign countries, by enhancing information dissemination regarding review and post-marketing safety measures in Japan, etc.
2. Enhance approaches toward global harmonization
   - Contribute to the establishment of global standards and provide cooperation at global conferences regarding establishment of standards, such as at ICH and International Medical Device Regulators Forum (hereinafter referred to as “IMDRF”), etc., by proposing new topics, taking the initiative in establishing global standards, and proactively stating opinion on topics initiated by other countries. Promote harmonization with other global standards, such as standards for establishing application data that were defined in these conferences, and the ISO and others.
   - For medical devices, continue promoting activities of the Harmonization by Doing (HBD) conducted with the United States and promote exchange of information.
   - Promote globalization of the Japanese Pharmacopoeia through global harmonization of pharmacopoeia, etc., at the Pharmacopoeial Discussion Group (PDG).
   - Participate in discussions at IGDRP, where global collaboration is held for generic drugs, and promote cooperation with foreign countries regarding reviews for generic drugs.
   - Cooperate with MHLW in discussions at the International Cooperation on Cosmetics Regulation (ICCR) in order to promote cooperation with foreign countries.
   - Participate in and contribute to global cooperation activities such as WHO and OECD.
   - Consider accepting a wider range of submission data for new pharmaceutical applications that are in English.
3. Promote interaction of personnel
   - In order to promote establishment of networks with foreign regulatory agencies, have staff members proactively participate in global academic meetings and conferences, and increase opportunities to dispatch staff to organizations other than FDA, EMA, and Swissmedic.
   - Promote personnel interactions through PMDA training seminars with Asian countries, etc., and global organizations, etc., and accepting trainees, etc., in order to establish a system to regularly exchange information related to reviews and post-marketing safety measures. Also have Asian countries, etc., increase their understanding of Japanese regulations, etc., and standards regarding pharmaceutical applications, etc., through symposiums co-hosted by multiple countries, etc.
4. Train and enhance human resources to acquire global perspectives and communication skills
   - In order to train human resources to be globally involved in establishing guidelines such as ICH and IMDRF, staff training programs shall be established and conducted, including attendance at meetings and global conferences where guidelines are established, and research opportunities at foreign institutions and graduate schools, etc.
   - Improve linguistic ability by continuing and enhancing English training for executives and staff members, etc.
5. Enhance and improve global public relations and information dissemination
   - Enhance system to improve ability of disseminating information globally.

- Enhance and improve the content of PMDA's website in English to promote exchange of opinions and information with foreign countries. To be more specific, proactively release English versions of pharmaceutical regulations, details of services, review reports, and safety information, etc. Make certain that review reports are translated into English especially for products having significance in disseminating information, such as products that are the first in the world to be approved. (Forty products per year by the end of FY 2014. Thereafter, targets will be set in each fiscal year plan, with consideration of the utilization status of relevant people and the application status of pharmaceuticals and medical devices, etc.)
- Continuously conduct lectures and present booth exhibits, etc., at global conferences.

3) Measures for Intractable Diseases and Orphan Diseases, etc.
- Develop review guidelines and enhance consultation services regarding pharmaceuticals for intractable diseases and orphan diseases.
- Take necessary measures to operate notifications and guidance regarding companion diagnostics pharmaceuticals, etc., smoothly.
- Take necessary measures through discussions with foreign regulatory agencies regarding points to be considered in developments, etc., using biomarkers.
- In order to promote utilization of pharmacogenomics in pharmaceutical development, PMDA shall take initiative in establishing evaluation guidelines at ICH, cooperate and share information with foreign regulatory agencies to establish a system that enables the 3 regions, including FDA and EMA, to make recommendations together, and thereby contributing to the development of global methods.

4) Provide Information Including Review Reports, etc.
- In order to promote transparency of the services, PMDA shall proactively promote efforts to enhance disclosure of information by cooperating with MHLW to promptly provide information related to review reports, including results of priority reviews, and other review services, in an easily accessible manner for the public and healthcare professionals, and by enhancing the content of information related to review.
- Both the regulatory authority and the applicants shall make efforts to reveal in public review reports of new pharmaceuticals and new medical devices under the concept of rational use on the website immediately after approval, and also take appropriate measures to release re-examination reports of pharmaceuticals, etc. The outlines of the documents related to new pharmaceuticals and new medical devices shall also be released on the website within three months after approval.
- In addition to the integration of the services of releasing information, such as the service of information disclosure based on the Act on Access to Information Held by Independent Administrative Agencies, and the service of revealing in public review reports, so that PMDA can cope with the yearly increasing disclosure requests of documents, PMDA shall further improve efficiency of the services with the cooperation of relevant divisions.

5) Ensuring Fairness when Utilizing External Experts
- Utilize external experts with relevant knowledge. When utilizing external experts, PMDA shall ensure neutrality and fairness in both the review, etc., and post-marketing safety measures services based on fair rules, and shall review those rules when necessary.

6) Improving the Quality of Review and Safety Services by Enhancing the Information System
- Improve the quality of services by enhancing the function of information system to cope with the changes in review and post-marketing safety measures services where increase of the amount of information to be handled and deepening of the correlation and accuracy of information are expected.
- Consider Enhancing computerization of review procedures, including eCTD, and improving the IT literacy of the staff.

Part 3
Budget, Income and Expenditure Plan and Cash Flows Plan

1. Budget: see Attachment 1

2. Income and expenditure plan: see Attachment 2

3. Cash flows plan: see Attachment 3

Part 4
Limit of Short-term Borrowing

1) Limit of Borrowing
2.2 billion yen

2) Expected Reasons for Short-term Borrowing
a) Shortage of funds due to delayed receipt of administrative subsidies, subvention, and agent service fees, etc.
b) Unexpected retirement payments.
c) Shortage of funds due to other unexpected situations.

Part 5
Plans for Transferring or Mortgaging Important Property if Applicable

None

Part 6
Use of Surplus Funds

Surplus funds can be allocated to the review account for the following purposes.
- Resources for expenditure related to operational improvement.
- Financial resources for training and research, etc., to improve personnel qualifications and service quality.
Regarding the ADR relief account and the infection relief account, surplus funds shall be adjusted as reserve funds, as specified in the provision of Article 31, Paragraph 4 of the Act on the Pharmaceuticals and Medical Devices Agency (Act No. 192, 2002).

Part 7
Other Matters Regarding Operation Management Specified in the Ordinance of the Competent Ministry, etc.
The following measures shall be taken for matters regarding operation management, etc., specified in Article 4 of the Ministerial Ordinance Regarding Operation Management, Finance, and Accounting of the Pharmaceuticals and Medical Devices Agency (MHLW Ministerial Ordinance No. 55, 2004), etc.

1) Matters Regarding Personnel Affairs

a) Plans regarding personnel affairs of staff members

- In order to increase regular staff, PMDA shall employ highly specialized and capable human resources, mainly through open recruitment based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the final proposals of the Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings.

  Note: Standards regarding personnel affairs
  The number of regular staff at the end of the term shall not exceed 141.9% of that at the beginning of the term.

  Reference 1) Number of regular staff members at the beginning of the term: 751
  Number of regular staff members at the end of the term: 1,065

  Reference 2) Total personnel expenses for effective period for the Mid-term Targets: 36,535 million yen (estimate)
  Note that the above amount is equivalent to the expenses for the executive compensation and basic pay, miscellaneous allowances, and overtime work pay for staff members.

- Improve qualification and capacity of the staff members by interacting with the government, research institutions, and universities with a consideration of a mobilization of human resources, and reduce proportion of transferees from the government with a consideration of appropriate balance.
  Therefore, PMDA shall strive to make reductions in accordance with the Basic Policy for Review of System/Organization of Incorporated Administrative Agencies (adopted by the Cabinet) established on December 7, 2010, and shall disclose those statuses every year.
  PMDA shall also systematically make approaches to steadily increase staff members, including specialized technical employees, etc., as specified in Part 7-1). Employment terms shall also be revised systematically to make a more attractive work environment.
  To ensure employment of highly specialized human resources, PMDA shall determine strategic methods, including an increase in number of fixed-term staff and introduce an annual salary system.
- In order to avoid any suspicion of inappropriate relationships with pharmaceutical companies, etc., PMDA shall appropriately manage personnel by establishing certain restrictions in employment, allocation, and post-retirement reemployment, etc., for executives and employees.

b) Develop a comfortable working environment

- Consider developing a comfortable working environment for employees by improving working environment such as a promotion of work-life balance. Make approaches that enable a good balance between family life and career and that allows especially the women staff members, accounting for about half of the total employees, to keep fulfilling their abilities.

c) Adjust salary standards

- Based on the Basic Policy Regarding Reform of Incorporated Administrative Agency (adopted by the Cabinet on December 24, 2013), PMDA shall take necessary measures to adjust the salary standards of the employees to achieve an appropriate and efficient level, taking into consideration the salary standards of national government employees as well as its competitiveness to stably securing distinguished human resources.
  PMDA shall also inspect its state of approaches for adjusting salary standards every year from the following perspectives and shall disclose those results.
  1) Appropriateness in salary standards of the employees when compared to the national government employees in view of factors such as their office locations and academic backgrounds, etc.
  2) Room to improve the causes of high salary standards, for example, high proportion of employees dispatched form the government.
  3) Ability to thoroughly explain the appropriateness of the current salary standards when the large government spending, the accumulated losses, and the salary standards of private companies engaged in similar services are pointed out.
  4) Competitive salary standards of PMDA's staff members compared to the standards in the relevant fields, such as pharmaceutical companies and research institutes at universities, etc., when we need to secure human resources with highly specialized knowledge and experience in technical matters.
  5) Other explanations for the salary levels must be rational to gain sufficient public consent.

d) Improve qualifications of the staff members

- In order to improve the quality of the services, PMDA shall improve qualification of the staff members by systematically providing opportunities for training according to targets of the services, etc., by enhancing training conducted with the cooperation of companies, and by interacting with MHLW, as well as domestic and foreign universities and research institutions, etc.
- Training for new staff members shall especially be enhanced in order to ensure effectiveness of enhancing system by increasing staff numbers.
- Enhance staff training programs for administrative staff members who are on main career tracks, so as to improve the quality of staff members at clerical positions supporting the organizational management.
- Implement a personnel evaluation system that allows motivation of the staff members to increase, and appropriately reflect those evaluations and the status of achieving their goals on their salary, pay raise, and promotion.
- Strategically allocate the staff members in view of their future career development to maintain their specialization as well as the continuity of operations.

2) Ensure Security

- Continue enhancing the internal control system for security and confidentiality reasons by thoroughly controlling entrances and exits 24 hours a day, using the entrance and exit control system at the office.
- Continue ensuring security of information related to the information system.
- Continue ensuring the document control system based on the property of the stored documents.

3) Matters Regarding Facilities and Equipment

None

4) Matters Regarding Disposition of the Reserve Funds Specified in Article 31, Paragraph 1 of the Act on the Pharmaceuticals and Medical Devices Agency

In cases where there are still reserve funds for the review account even after adjusting profit and loss according to Article 44 of the Act on General Rules at the end of the last fiscal-year of the effective period for the Second Mid-term Targets, the amount approved by the MHLW out of those reserve funds can be applied to the financial resources of the review service and post-marketing safety measures service, as specified in Article 15 of the Act on Pharmaceuticals and Medical Devices Agency.

5) Other Matters

Steadily conduct approaches based on the government policy indicated in past Cabinet decisions, etc.

Attachment 1

Budget

Budgets for Mid-term Plan (FY 2014 - FY 2018) (Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commissioned payment account	Total
Income							
Administrative subsidies			6,350				6,350
Governmental subsidies	883	707	1,854				3,444
Contributions	20,322	553	16,043	18,390			55,308
User fees			60,151				60,151
Commissioned operations			926		5,410	3,262	9,598
Management income	1,671	312					1,983
Miscellaneous income	7	1	146		8	5	167
Total	22,883	1,572	85,471	18,390	5,418	3,268	137,001
Expenditure							
Operating expenses	16,501	1,300	81,659	18,585	5,380	3,243	126,667
Personnel expenses	1,254	130	38,056	85	188	99	39,813
Administrative expenses	15,247	1,170		18,500	5,192	3,143	43,252
Expenses for reviews and related services			29,533				29,533
Expenses for safety measures, etc.			14,069				14,069
General administrative expenses	541	74	10,526	12	38	25	11,216
Personnel expenses	270		3,626				3,897
Non-personnel expenses	271	74	6,899	12	38	25	7,319
Total	17,043	1,374	92,184	18,597	5,418	3,268	137,883

<Note 1>

Personnel expenses were calculated as expenses based on self-financial resources for increases in and after FY 2015.

<Note 2>

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

Rules of Calculation of the Running Expenses Grant for Accounts for Reviews, etc.

The rules of calculation of the running expenses grant in the target mid-term period (FY 2014 - FY 2018) are as follows.

1. FY 2014

Expenses required for implementation of services are individually estimated and calculated.

2. In or after FY 2015

The following calculation formula is used:

Running expenses grant	=	Service division personnel expenses	+	Expenses	+	Special factor	-	Self-generated income

○ Service division personnel expenses = Basic salaries, etc. (A) + Termination benefits (S)

A: Personnel expenses including basic salaries, various benefits, and contribution to mutual aid association (excluding termination benefits) which are calculated by using the following formula:

$A = [\{P1 \times \alpha \times \beta\} + \{P2 \times \beta\} + P3]$

A: Basic salaries, etc. for the said fiscal year
P1: Those influenced by salary raises and salary revisions among basic salaries in the preceding fiscal year
P2: Those influenced by salary revisions among basic salaries in the preceding fiscal year
P3: Those not influenced by salary raises and salary revisions among basic salaries in the preceding fiscal year
α: Salary raise resource rate in view of running status, etc.
β: Salary revision rate in view of running status, etc.

S: Amount of termination benefits for the said fiscal year corresponding to persons expected to terminate in the said fiscal year and persons expected to terminate in the preceding fiscal year or before

○ Expenses = ((General administrative expenses (B) × γ1 × δ) + (Operating expenses (R) × γ2 × δ))

B: Non-personnel expenses related to the management division in the preceding fiscal year
R: Non-personnel expenses related to services in the preceding fiscal year
γ1: Efficiency coefficient (general administrative expenses)
γ2: Efficiency coefficient (operating expenses)
δ: Consumer price index

○ Special factor = A measure required in association with law/regulation revision, etc. or a demand for fund occurring due to a reason unpredictable at present which is determined in the process of budget-making for every fiscal year.

○ Self-generated income = The estimated mount of an income that may occur from clerical works/projects implemented with the running expenses grant as the financial resource

[Notes]

1. For α, β, δ, γ1, and γ2, concrete discrete values are determined for the said fiscal year in the process of budget-making for the year in view of the followings:
   δ (consumer price index): The actual value in the preceding fiscal year is used.
2. Budgets for the overall mid-term plan were estimated,
   [1] Assuming that the increase rate is 0 for α, β, and δ.
   [2] Assuming that γ1 (efficiency coefficient) is -3.75% in FY 2015, -3.90% in FY 2016, -4.05% in FY 2017, and -4.23% in FY 2018.
   [3] Assuming that γ2 (efficiency coefficient) is -1.25% in FY 2015, -1.27% in FY 2016, -1.28% in FY 2017, and -1.30% in FY 2018.

Income and Expenditure Plan

Income and Expenditure Plan for the Mid-term Plan (FY 2014 - FY 2018) (Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commissioned payment account	Total
Expenditure							
Ordinary expenses	24,163	1,495	93,471	18,600	5,422	3,269	146,420
Operating expenses	16,346	1,233	75,708	18,585	5,383	3,243	120,498
Relief benefits	12,270	155					12,425
Operating expenses for health and welfare	197	621					818
Operating expenses for reviews			29,719				29,719
Operating expenses for safety measures			11,317				11,317
Specified relief benefits				18,390			18,390
Benefits (healthcare allowances, etc.)					5,118		5,118
Benefits (special allowances, etc.)						1,294	1,294
Operating expenses for research and study						1,768	1,768
Administrative expenses	2,619	331		117	93	88	3,249
Personnel expenses	1,260	126	34,673	78	172	92	36,399
General administrative expenses	542	78	10,520	12	38	25	11,214
Personnel expenses	272		3,306				3,577
Non-personnel expenses	270	78	7,214	12	38	25	7,636
Depreciation expenses	241	16	7,243	4	1	1	7,507
Provision for liability reserve	7,030	163					7,192
Miscellaneous losses	5	5					10
Income							
Ordinary income	22,876	1,572	85,713	18,600	5,418	3,268	137,447
Governmental subsidies	883	707	1,854	207			3,651
Contributions	20,322	553	16,043				36,918
User fees			60,151				60,151
Commissioned operations					5,410	3,262	8,672
Other governmental grants			926				926
Administrative subsidies			6,350				6,350
Reversal of asset offset subsidies			89	4			92
Reversal of asset offset administrative subsidies			207				207
Reversal of asset offset gifts received							
Financial income (no operating income)	1,671	312					1,983
Gain on reversal of specified relief fund deposit received				18,390			18,390
Miscellaneous income		1	92		8	5	107
Net income (△net loss)	△ 1,287	77	△ 7,759	0	△ 4	△ 1	△ 8,974
Reversal of appropriated surplus							
Gross income (△gross loss)	△ 1,287	77	△ 7,759	0	△ 4	△ 1	△ 8,974

<Note 1>

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 Act for Pharmaceuticals and Medical Devices Agency.

<Note 2>

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

Cash Flow Plan

Cash Flow Plan for the Mid-term Plan (FY 2014 - FY 2018) (Unit: million yen)

Classification	Amount						
	Adverse drug reactions relief account	Infection relief account	Review account	Specified relief account	Commission and loan account	Commissioned payment account	Total
Cash Outflows							
Cash outflows from operating activities	16,462	1,210	86,230	18,599	5,430	3,304	131,234
Relief benefits	12,251	155					12,406
Operating expenses for health and welfare	197	621					818
Operating expenses for reviews			29,012				29,012
Operating expenses for safety measures			10,811				10,811
Specified relief benefits				18,390			18,390
Benefits (healthcare allowances, etc.)					5,131		5,131
Benefits (special allowances, etc.)						1,294	1,294
Operating expenses for research and study						1,768	1,768
Administrative expenses	2,275	243		114	86	119	2,837
General administrative expenses	266	69	6,882	12	31	25	7,286
Personnel expenses	1,472	121	39,525	83	183	97	41,480
Cash outflows from investing activities	20,532	2,664	5,357				28,552
Payments for purchases of investment in securities	20,000	2,500					22,500
Payments for purchases of intangible fixed assets	532	164	5,357				6,052
Cash outflows from financial activities							
Amount carried forward to the next mid-term plan period	438	422	9,440	123	40	96	10,559
Total	37,431	4,296	101,026	18,721	5,471	3,400	170,345
Cash Inflows							
Cash inflows from operating activities	22,906	1,575	86,332	18,423	5,433	3,268	137,937
Governmental subsidies	885	708	1,854				3,447
Administrative subsidies			6,350				6,350
Contributions	20,322	553	16,043	18,422			55,340
User fees			60,975				60,975
Commissioned operations			382		5,423	3,262	9,067
Miscellaneous income	1,698	315	728	1	10	6	2,757
Cash inflows from investing activities	14,100	2,500					16,600
Cash inflows from financial activities							
Amount brought forward at the beginning of the mid-term plan period	426	221	14,694	299	37	132	15,808
Total	37,431	4,296	101,026	18,721	5,471	3,400	170,345

<Note>

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

Attachment 4

Budgets for Fiscal Year Plan (FY 2015)

(Unit: million yen)

Classification	Amount of money								
			Review account						
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Total	Specified relief account	Commission and loan account	Commissioned payment account	Total
Income									
Administrative subsidies			525	743	1,268				1,268
Governmental subsidies	178	142	234	180	414				734
Contributions	3,815	98		3,079	3,079	4,928			11,920
User fees			10,952		10,952				10,952
Commissioned operations			228		228		1,098	643	1,970
Management income	373	74							448
Miscellaneous income	2	0	34	9	43	0	2	1	48
Total	4,368	314	11,974	4,011	15,985	4,928	1,100	644	27,340
Expenditure									
Operating expenses	3,022	245	12,576	4,833	17,409	8,362	1,092	638	30,767
Personnel expenses	251	27	5,246	1,300	6,546	16	37	17	6,893
Administrative expenses	2,771	218	7,330	3,533	10,863	8,345	1,055	621	23,874
General administrative expenses	136	20	2,132	482	2,614	3	9	6	2,788
Personnel expenses	69		690	149	840				908
Non-personnel expenses	67	20	1,441	333	1,775	3	9	6	1,880
Total	3,157	265	14,708	5,315	20,023	8,365	1,100	644	35,555

Note: The figures in "Total" have been rounded off in principle and therefore may not be the exact sum of individual figures.

Income and Expenditure Plan for Fiscal Year Plan (FY 2015)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commissioned payment account	Total
Ordinary expenses	4,275	369	14,090	4,671	-33	18,727	8,365	1,103	643	33,482
Relief benefits	2,221	31								2,252
Operating expenses for health and welfare	36	124								160
Operating expenses for reviews			4,263			4,263				4,263
Operating expenses for safety measures				2,061		2,061				2,061
Specified relief benefits							8,316			8,316
Benefits (healthcare allowances, etc.)								1,038		1,038
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									348	348
Provision for liability reserve	1,112	109								1,221
Other administrative expenses	763	83	7,546	2,093		9,639	46	54	32	10,618
Personnel expenses	234	25	4,745	1,215		5,960	15	33	16	6,285
Depreciation expenses	34	5	924	540		1,464	0	1	0	1,504
Retirement benefit expenses	8	1	197	38		235	0	1	0	245
Provision for accrued bonuses	7	1	283	55		338	1	2	1	350
Other expenses	480	51	1,396	246		1,642	29	16	15	2,233
General administrative expenses	141	21	2,279	515	-33	2,761	3	9	7	2,943
Personnel expenses	64		633	136		769				833
Depreciation expenses	0		162	0		162				162
Retirement benefit expenses	2		24	5		28				31
Provision for accrued bonuses	2		33	9		42				45
Other expenses	73	21	1,427	366	-33	1,760	3	9	7	1,873
Financial expenses	0		2	0		2				2
Miscellaneous losses	1	1		1		1		2	1	6
Ordinary income	4,343	314	11,941	4,045	-33	15,953	8,365	1,100	644	30,719
Governmental subsidies	178	142	183	95		278				598
Administrative subsidies			525	707		1,232				1,232
Other governmental grants							49			49
Contributions	3,815	98		3,079		3,079				6,992
User fees			10,952			10,952				10,952
Gain on reversal of specified relief fund deposit received							8,316			8,316
Commissioned operations			228			228		1,098	643	2,059
Reversal of asset offset subsidies			9	145		153	0			154
Reversal of asset offset administrative subsidies			0	19		19				19
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	350	75								424
Miscellaneous income			44	0	-33	10		2	1	13
Ordinary net income (△ net loss)	68	-54	-2,149	-625		-2,775	0	-3	1	-2,762
Current net income before tax (△ net loss)	68	-54	-2,149	-625		-2,775	0	-3	1	-2,762
Current net income (△ net loss)	68	-54	-2,149	-628		-2,775	0	-3	1	-2,762
Reversal of appropriated surplus	-	-	2,149	625		2,775	-	-	-	2,775
Current gross income (△ gross loss)	68	-54	0	0		0	0	-3	1	12

Note: The figures in "Total" have been rounded off in principle and therefore may not be the exact sum of individual figures.

Cash Flow Plan for Fiscal Year Plan (FY 2015)

(Unit: million yen)

Classification	Amount									
			Review account							
	Adverse drug reactions relief account	Infection relief account	Review segment	Safety segment	Adjusted	Total	Specified relief account	Commission and loan account	Commissioned payment account	Total
Cash Outflows										
Cash outflows from operating activities	3,288	303	14,449	4,481	△ 29	18,901	8,366	1,123	654	32,634
Relief benefits	2,217	30								2,247
Operating expenses for health and welfare	36	124								160
Operating expenses for reviews			7,003			7,003				7,003
Operating expenses for safety measures				2,696		2,696				2,696
Administrative expenses	637	70					30	17	16	771
Specified relief benefits							8,316			8,316
Benefits (healthcare allowances, etc.)								1,042		1,042
Benefits (special allowances, etc.)									255	255
Operating expenses for research and study									348	348
General administrative expenses	68	20	1,492	342		1,834	3	9	6	1,941
Personnel expenses	308	26	5,681	1,395		7,077	16	35	16	7,478
Repayment money	1	1		1		1		2	1	6
Other cash outflow from operating activities	22	31	272	47	△ 29	290	1	18	12	373
Cash outflow from investing activities	4,033	611	1,653	1,219		2,873			2	7,519
Amount carried forward to next fiscal year	2,649	332	6,119	1,900		8,019	158	47	132	11,336
Total	9,970	1,246	22,221	7,600	△ 29	29,792	8,524	1,169	787	51,488
Cash Inflows										
Cash inflows from operating activities	4,373	317	12,041	4,018	△ 29	16,030	4,944	1,105	644	27,412
Contributions	3,815	98		3,079		3,079	4,944			11,936
Administrative subsidies			525	743		1,268				1,268
Governmental subsidies	178	142	234	180		414				734
User fees			10,997			10,997				10,997
Commissioned operations			173			173		1,103	643	1,920
Amount of interests received	373	74								448
Miscellaneous incomes			69	16		85		1	1	88
Other incomes	6	3	42		△ 29	13	0	0	0	22
Cash inflows from investing activities	3,399	600								3,999
Amount carried forward from preceding fiscal year	2,199	329	10,180	3,582		13,763	3,580	64	143	20,078
Total	9,970	1,246	22,221	7,600	△ 29	29,792	8,524	1,169	787	51,489

Note: The figures in "Total" have been rounded off in principle and therefore may not be the exact sum of individual figures.

Basic Implementation Policy for the Third Mid-term Plan

The Executive Board Decision
November 25, 2014

1. Goals for PMDA to attain by the end of the third mid-term period

In order to meet the public expectations at a higher level in ever-changing business environment, PMDA, as the one and only organization that performs three regulatory operations (review, safety, and relief services) in Japan, aims for the goals described below by the end of the effective period of the mid-term plan, in accordance with the Third Mid-term Plan based on the universally applicable "PMDA Philosophy."

PMDA aims to:

○ Provide fast and high-quality review, safety measures, and relief services for adverse health effects, using the latest scientific knowledge in accordance with the concept of regulatory science;

○ Collaborate with regulatory authorities of other countries and take the lead to promote international harmonization;

○ Contribute to improvement of medical standards in terms of ensuring the efficacy, safety, and quality of medical products and assuring their reliability, in collaboration with academia, etc.;

○ Act and communicate in a way that will earn trust of stakeholders including the general public; and

○ Enhance the standardization, efficiency, and advancement of operations and thereby reduce workload of applicants, persons receiving consultation, and employees of PMDA, while creating a comfortable work environment attracting highly qualified and competent employees and allowing them to pursue long-term careers with PMDA.

2. Basic strategic perspective and policy for implementing the Third Mid-term Plan

○ In order to ensure high-quality and reliable operations, PMDA will:

- Respond to reform of the systems appropriately;
- Improve quality of reviews and enhance transparency of review results;
- Deepen the possessed scientific knowledge and sophisticate the efficiency and efficacy of data analysis; and
- Reinforce the consultation for practical application of promising seed-stage resources in academia and companies.

○ In order to play its expected roles and to increase its presence, PMDA will:

- Enhance its contribution to the international harmonization of regulations and standards and strengthen commitment particularly to Asian countries;
- Strengthen the training function for transferring knowledge and technique/methods of conformity audit and quality control, etc., to stakeholders; and
- Reinforce provision of information about the operations and achievements of PMDA in a clear and transparent manner.

○ In order to make full use of limited resources, PMDA will:

- Promote prioritization/rationalization of operations and systematic implementation while accommodating any situational change in a flexible manner;
- Increase the productivity of individual employees and thereby enhance the performance of PMDA as a whole;
- Work on development or modification of IT systems and cost reduction in order to standardize and streamline operations; and
- Establish appropriate systems for personnel management and training in order to be able to secure competent personnel and to train them.

Balance Sheet (corporate basis)

(As of March 31, 2016)

(Unit: yen)

Account item	Amount		Account item	Amount	
Assets			Liabilities		
I Current assets			I Current liabilities		
Cash and deposits		21,774,387,348	Deposit subsidy, etc.		109,001,445
Securities		3,205,423,103	Accrued benefits		342,002,085
Expenses for work-in-process reviews, etc.		1,430,428,089	Accounts payable		2,991,362,419
Prepaid expenses		8,125,798	Advances received		8,803,457,251
Accounts due		594,066,750	Deposits received		138,554,683
Accrued income		44,433,080	Lease obligations		30,650,990
Other current assets		2,645,523	Allowance		
			Accrued bonuses	518,708,735	518,708,735
Total of current assets		27,059,509,691	Total of current liabilities		12,933,737,608
			II Fixed liabilities		
II Fixed assets			Per contra liabilities for property acquisition		
Tangible fixed assets			Administrative subsidies for assets as per contra	108,191,348	
Tools, equipment and fixtures	2,693,471,963		Governmental subsidies, etc. for assets as per contra	523,051,250	
Cumulative total of depreciation	-1,329,776,271	1,363,695,692	Amount of received goods for assets as per contra	115,940	631,358,538
Building and accompanying facilities	31,320,000		Deposits of specific relief funds		
			Long-term deposit subsidy, etc.	154,411,164	
Cumulative total of depreciation	-150,902	31,169,098			
			Deposit contribution	3,820,736,642	3,975,147,806
Construction in progress		451,299,600	Long-term lease obligations		31,441,684
Total of tangible fixed assets		1,846,164,390	Allowances		
			Allowances for retirement benefits	1,766,355,986	1,766,355,986
Intangible fixed assets			Liability reserve		21,617,323,983
Software		4,787,165,744			
			Total of fixed liabilities		28,021,627,997
Software in progress		1,011,782,800			
			Total of liabilities		40,955,365,605
Telephone subscription right		286,000	Net assets		
Total of intangible fixed assets		5,799,234,544			
			I Capital funds		
Investments and other assets			Government investment		1,179,844,924
Investment securities		34,658,545,534	Total of capital funds		1,179,844,924
Rental deposit		13,272,360	II Capital surplus		
			Capital reserves		4,670,640
Total of investments and other assets		34,671,817,894			
			Cumulative total of depreciation that are not recorded as expenses (△)		-670,455,915
Total of fixed assets		42,317,216,828	Loss on retirement or sale of fixed assets that are not recorded as expenses (△)		-98,706,116
			Total of capital surplus		-764,491,391
			III Retained earnings		28,006,007,381
			Total of net assets		28,421,360,914
Total of assets		69,376,726,519	Total of liabilities and net assets		69,376,726,519

Profit and Loss Statement (Corporate basis)

(From April 1, 2015 to March 31, 2016)

(Unit: yen)

Account item	Amount		
Ordinary expenses			
Adverse reaction relief benefits		2,086,901,672	
Infection relief benefits		2,562,800	
Operating expenses for health and welfare		127,477,101	
Operating expenses for reviews		3,668,141,458	
Operating expenses for safety measures		1,510,770,898	
Specific relief benefits		1,308,000,000	
Benefits for healthcare allowances, etc.		1,006,135,300	
Benefits for special allowances, etc.		203,736,000	
Investigative research		290,935,200	
Provision of liability reserves		1,480,491,002	
Other operating expenses			
Personnel expenses	6,040,879,634		
Depreciation expenses	1,683,453,617		
Retirement benefit expenses	-8,923,678		
Provision for accrued bonuses	338,773,285		
Estate rental fees	1,496,622,233		
Other expenses	567,649,524	10,118,454,615	
General administrative expenses			
Personnel expenses	789,280,485		
Depreciation expenses	223,536,921		
Retirement benefit expenses	6,638,930		
Provision for accrued bonuses	56,500,967		
Estate rental fees	267,081,468		
Other expenses	929,783,809	2,272,822,580	
Financial expenses			
Interest paid		2,117,249	
Miscellaneous losses		21,915,303	
Total of ordinary expenses			24,100,461,178
Ordinary revenues			
Administrative subsidies		1,321,978,520	
Reversal of provision for deposits of specific relief funds			
Revenues from contributions		1,308,000,000	
User fees		10,884,792,885	
Contributions		6,897,298,200	
Revenue from governmental subsidies		637,942,397	
Commissioned operations for government		63,878,218	
Commissioned operations for others		1,646,000,897	
Return of administrative subsidies for assets as per contra		18,673,172	
Return of subsidies, etc. for assets as per contra		144,705,447	
Return of amount of received goods for assets as per contra		33,148	
Return of liability reserves		4,337,165	
Financial revenue			
Interest on securities	419,384,542	419,384,542	
Miscellaneous gains		16,015,073	
Total of ordinary revenues			23,363,039,664
Ordinary losses			-737,421,514
Extraordinary losses			
Loss on retirement of fixed assets		1	1
Current net losses			-737,421,515
Reversal of reserve carried forward from the previous Mid-term target period			2,104,400,565
Current gross profit			1,366,979,050

Cash Flow Statement (Corporate basis)

(From April 1, 2015 to March 31, 2016)

(Unit: yen)

Account item	Amount of money
I. Cash flow from operating activities	
Expenditure for adverse reaction relief benefits	-2,101,529,789
Expenditure for infection relief benefits	-2,558,200
Expenditure for operating expenses for health and welfare	-128,845,445
Expenditure for operating expenses for reviews	-3,730,214,111
Expenditure for operating expenses for safety measures	-1,508,643,855
Expenditure for specific relief benefits	-1,308,000,000
Expenditure for benefits for healthcare allowances, etc.	-1,015,689,728
Expenditure for benefits for special allowances, etc.	-202,523,800
Expenditure for expenses for investigative research	-289,957,600
Expenditure for personnel expenses	-7,186,094,470
Expenditure for money refunded for settlement of subsidies, etc.	-68,114,121
Other operating expenditures	-3,467,599,139
Income from administrative subsidies	1,268,297,000
Income from governmental subsidies	750,779,000
Income from contributions	7,374,294,200
Income from user fees	11,681,827,234
Income from commissioned operations for government	63,878,218
Income from commissioned operations for others	1,716,819,072
Other incomes	132,042,679
Subtotal	1,978,167,145
Interest paid	-2,117,249
Interest received	450,874,818
Cash flow from operating activities	2,426,924,714
II. Cash flow from investing activities	
Expenditure for acquisition of investment securities	-5,155,455,000
Income from redemption of investment securities at maturity	4,000,000,000
Expenditure for acquisition of tangible fixed assets	-516,034,200
Expenditure for acquisition of intangible fixed assets	-1,861,862,012
Expenditure for payment of lease deposits	-4,558,200
Cash flow from investing activities	-3,537,909,412
III. Cash flow from financing activities	
Expenditure for repayment of finance lease obligations	-34,738,051
Cash flow from financing activities	-34,738,051
IV. Increase in funds	-1,145,722,749
V. Beginning-of-term balance of funds	22,920,110,097
VI. End-of-term balance of funds	21,774,387,348

Government Service Implementation Cost Statement (Corporate basis)

(From April 1, 2015 to March 31, 2016)

(Unit: yen)

Account item	Amount of money		
I. Operating expenses			
(1) Expenses in the profit and loss statement			
Adverse reaction relief benefits	2,086,901,672		
Infection relief benefits	2,562,800		
Operating expenses for health and welfare services	127,477,101		
Operating expenses for reviews	3,668,141,458		
Operating expenses for safety measures	1,510,770,898		
Specific relief benefits	1,308,000,000		
Benefits for healthcare allowances, etc.	1,006,135,300		
Benefits for special allowances, etc.	203,736,000		
Expenses for investigative research	290,935,200		
Provision of liability reserves	1,480,491,002		
Other operating expenses	10,118,454,615		
General administrative expenses	2,272,822,580		
Financial expenses	2,117,249		
Miscellaneous losses	21,915,303		
Loss on retirement of fixed assets	1	24,100,461,179	
(2) (Exemption) Self-generated income, etc.			
Income from contributions	-8,205,298,200		
Income from user fees	-10,884,792,885		
Income from commissioned operations for government	-63,878,218		
Income from commissioned operations for others	-1,646,000,897		
Return of liability reserves	-4,337,165		
Financial revenue	-419,384,542		
Miscellaneous gains	-16,015,073	-21,239,706,980	
Total of operating expenses			2,860,754,199
II. Amount equivalent to depreciation that are not recorded as expenses			11,515,254
III. Estimated amount of non-allowance bonuses			12,950,842
IV. Estimated increased amount of non-allowance retirement benefits			68,345,726
V. Opportunity costs			
Opportunity costs of investments by the government or local governments, etc.			0
VI. Government service implementation costs			2,953,566,021

Notes

I. Important Accounting Policies

From FY 2015, Amendments to Accounting Standards for Incorporated Administrative Agencies, Annotations of Accounting Standards for Incorporated Administrative Agencies (amended on January 27, 2015), and Q & A on Accounting Standards for Incorporated Administrative Agencies and Annotations of Accounting Standards for Incorporated Administrative Agencies (amended in February 2016) (hereafter referred to as “Amendments”) were employed to generate financial statements.

However, regarding the Accounting Standards for Incorporated Administrative Agencies No.43 (annotation #39), an interim measure is applied as specified in a supplemental provision No.8 in Amendments of Act on General Rules for Incorporated Administrative Agencies, and segment information is published under the current segments until the term of the interim measure has expired.

Interim measures are also applied to the Amendment to Accounting Standards for Incorporated Administrative Agencies No.81 (annotations #60 and #61) and No.81 (annotation #60) before the amendment is used.

1. Criteria for allocation of revenue from administrative subsidies

The percentage-of-expense method has been employed as an interim measure due to the time required for the development of systems for the management of operations exercising control over quotas and actual activity expenses by departments tasked with operational and administrative duties.

2. Evaluation criteria and evaluation methods for securities

Held-to-maturity bonds

They are handed by the amortized cost method (straight-line method).

3. Evaluation criteria and evaluation methods for expenses for work-in-process reviews, etc.

They are handled by the lower-of-cost-or-market method based on specific identification method.

4. Methods of accounting for depreciation

(1) Tangible fixed assets

[1] Tangible fixed assets other than lease assets

The straight-line method has been employed.

Durable years of main assets are as follows.

Tools, equipment and fixtures	2 - 18 years
Building and accompanying facilities	15 - 22 years

An amount equivalent to depreciation of particular depreciable assets (Accounting Standards for Incorporated Administrative Agencies No. 87) is shown to be deducted from the capital surplus as cumulative total of depreciation that are not recorded as expenses.

[2] Lease assets

Lease assets related to non-ownership-transfer finance lease transactions

The straight-line method, in which the lease period is durable years and the residual value is zero, has been employed.

(2) Intangible fixed assets

The straight-line method has been employed.

Software is used within the corporate body based on an available period (5 years) within the corporate body.

5. Criteria for allocation of allowances and estimated amounts related to bonuses

Amounts occurring for the current term are allocated from among the expected amounts of payment of bonuses for the next term to executives, regular employees, etc.

However, allowances are not allocated for amounts which are funded from the administrative subsidies and governmental subsidies from among the said expected amounts of payment.

6. Criteria for allocation of allowances and estimated amounts related to retirement benefits

To prepare for retirement benefits for executives and regular employees, the allowances and estimated amounts are allocated based on the expected amounts of retirement benefit obligations at the end of the current fiscal year. Actuarial differences are to be collectively amortized in the next fiscal year after the occurrence. However, allowances related to retirement benefits are not allocated for amounts which are funded from the administrative subsidies.

Change of accounting policies

PMDA changed the method for calculating discount rates, in accordance with the “Amendments” enforced in FY 2015. The former method calculates discount rates based on the approximate value of the mean remaining working years. The new method calculates discount rates based on single weighted average discount rate that reflects estimated periods for calculating retirement benefits and the amount of retirement benefits to be paid according to the periods. This change causes no impact on profit or loss or on government service implementation cost of FY2015.

7. Criteria for allocation of liability reserves

To prepare for the payment of relief benefits in the future, amounts specified in the statement of operation procedures are allocated pursuant to the provisions of Article 30 of the Act on Pharmaceuticals and Medical Devices Agency (Act No.192 of 2002).

8. Method of allocating opportunity costs in government service implementation cost statements

The opportunity cost was calculated at a rate of 0%, based on the administrative notice “Handling of Opportunity Cost Calculation in Statement of Administrative Service Execution Costs in FY 2015 Financial Statements by introduction of ‘Quantitative and Qualitative Monetary Easing with a Negative Interest Rate (points to be considered)’” dated April 1, 2016 issued by Administrative Management Bureau, Ministry of Internal Affairs and Communications and public accounting room in legal division at Budget Bureau, Ministry of Finance.

9. Methods of accounting for lease transactions

Finance release transactions for which the total of lease fees is 3 million yen or more are handled by accounting method according to the method for usual sales transactions.

Finance release transactions for which the total of lease fees is less than 3 million yen are handled by accounting method according to the method for usual lease transactions.

10. Methods of accounting for consumption tax, etc.

These are handled by the tax-included method.

II. Items to note

1. Notes for balance sheets

(1) Notes regarding matters including current prices of financial products

[1] Items related to the status of financial products

Deposits are to be deposits for settlement.

Also, investments in financial products for purposes of funds management are limited to long-lived deposits, public and corporate bonds, and similar categories of securities. As investment securities, the PMDA holds only public bonds, FILP agency bonds, and class A or higher corporate bonds and does not hold stocks, etc. based on rules such as the provisions of Article 47 of the Act on General Rules for Incorporated Administrative Agencies.

[2] Items related to matters including current prices of financial products

Balance sheet amounts, current prices, and amounts of difference between them on closing date are as follows.

(Unit: yen)

Classification	Balance sheet amount (*)	Current price on closing date (*)	Amount of difference
A. Cash and deposits	21,774,387,348	21,774,387,348	0
B. Securities and investment securities	37,863,968,637	39,434,150,000	1,570,181,363
C. Accounts payable	(2,991,362,419)	(2,991,362,419)	0

(*) Those allocated in liabilities are shown in parentheses.

Notes: Method of calculating current prices of financial products and items related to securities, etc.

A. Cash and deposits

Current prices approximate book values, and therefore are based on these book values.

B. Securities and investment securities

Current prices are based on prices at the stock exchange or prices offered by correspondent financial institutions.

Items to note for securities are as follows.

1) Held-to-maturity bonds with current price

(Unit: yen)

Classification	Balance sheet amount	Current price on closing date	Amount of difference
Bonds with current prices exceeding balance sheet amount	36,823,848,112	38,396,930,000	1,573,081,888
Bonds with current prices not exceeding balance sheet amount	1,040,120,525	1,037,220,000	-2,900,525
Total	37,863,968,637	39,434,150,000	1,570,181,363

2) Scheduled amounts of redemption after closing date for held-to-maturity bonds

(Unit: yen)

Classification	≤ 1 year	> 1 year ≤ 5 years	> 5 years ≤ 10 years	> 10 years
Government bonds	0	5,100,000,000	5,300,000,000	0
Government-guaranteed bonds	1,400,000,000	5,000,000,000	10,500,000,000	0
Local government bonds	0	0	700,000,000	0
Corporate bonds	1,300,000,000	1,200,000,000	2,900,000,000	0
FILP agency bonds	500,000,000	2,800,000,000	1,000,000,000	0
Bonds issued by agency under a special act	0	0	0	0
Total	3,200,000,000	14,100,000,000	20,400,000,000	0

C. Accounts payable

The accounts are settled in short period and current prices, approximate book values, are therefore based on these book values.

(2) Estimated amount of non-allowance bonuses

Estimated amount of bonuses to be covered by the administrative subsidies and governmental subsidies: 82,975,354 yen

(3) Estimated amount of non-allowance retirement benefits

Estimated amount of retirement benefits to be covered by the administrative subsidies: 73, 305,585 yen

2. Notes for profit and loss statements

(1) Expenses for health and welfare services are expenses required for investigative research conducted to improve the QOL (Quality of Life) of people such as those covered by the system who suffered a serious and rare adverse drug reaction for which supports are not necessary sufficient when taking general measures intended for disabled people. These expenses consist of rewards for cooperation for investigation, etc.

(2) Expenses for reviews and related services are expenses required for the operation of reviews and related services for drugs, medical devices, etc. These expenses consist of rewards, travel expenses, expenses at government offices in charge of clerical tasks, etc. Also, expenses for safety measures, etc. are expenses required for the operation of post-marketing safety measures for drugs, medical devices, etc. These expenses also consist of rewards, travel expenses, expenses at government offices in charge of clerical tasks, etc.

(3) Expenses for investigative research are expenses required for investigative research of persons infected with HIV through blood products for the purpose of contributing to the prevention of the onset and spread of AIDS. All of these expenses are classified as healthcare expenses for HIV-infected persons.

(4) Income from user fees is income paid by applicants for drug or medical device product approval, and is utilized as a financial resource for conducting review services for drugs and other regulated products.

(5) Income from contributions is income paid by drug and medical device marketing and manufacturing authorization holders as a financial resource for conducting relief services for victims of regulated product-related adverse health effects and post-marketing safety operations.

3. Notes for cash flow statements

Relationship between the end-of-term balance of funds and money amounts of accounting items shown in the balance sheet

Cash and deposits: 21,774,387,348 yen

End-of-term balance of funds: 21,774,387,348 yen

4. Notes for government service implementation cost statements

The estimated increased amount of non-allowance retirement benefits includes 59,265,400 yen for executives and regular employees temporally transferred from the government.

5. Notes for asset retirement obligations

The PMDA has obligations for restoration to original state at the time of leaving business office based on the real estate leasehold contract, but the actual period of use of lease assets related to these obligations are not clear.

As such, it is difficult to predict when these obligations will be implemented, and it is not possible to reasonably estimate asset retirement obligations. For this reason, asset retirement obligations that match these obligations have not been allocated.

6. Notes for allowances for retirement benefits

(1) Outline of the retirement benefits system employed

The PMDA has established a retirement lump sum grants system as a defined-benefit system.

(2) Reconciliation between beginning-of-term and end-of-term retirement benefit obligations of FY 2015.

(Unit: yen)

Classification	April 1, 2015 - March 31, 2016
[1] Beginning-of-term retirement benefit obligations	1,575,538,051
[2] Service expenses	203,435,784
[3] Interest expenses	15,143,851
[4] Actuarial difference of the current term	423,539,039
[5] Retirement benefits paid	-27,761,700
[6] End-of-term retirement benefit obligations ([1] + [2] + [3] + [4] + [5])	2,189,895,025

(3) Reconciliation of retirement obligation and allowances for retirement benefits reported on the balance sheet

(Unit: yen)

Classification	As of March 31, 2016
[1] Retirement benefit obligations	2,189,895,025
[2] Unrecognized actuarial difference	-423,539,039
[3] Allowance for retirement benefits ([1] + [2])	1,766,355,986

(4) Profit and Loss of retirement benefit

Classification	April 1, 2015 - March 31, 2016
[1] Service expenses	206,545,782
[2] Interest expenses	15,416,991
[3] Amortization expenses for actuarial difference	-224,403,821
[4] Retirement benefit funded from the administrative subsidies	156,300
[5] Retirement benefits expenses ([1] + [2] + [3] + [4])	-2,284,748

Note: Retirement benefit expenses for workers temporally transferred from other institutions are included: [1] 3,109,998 yen for service expenses; and [2] 273,140 yen for interest expenses.

(5) Items related to basic calculation of actuarial

Classification	As of March 31, 2016
Discount rate	0.2%
Method of periodic allocation of estimated amounts of retirement benefits	Straight-line attribution
Amortized period of actuarial difference	1 year
	Actuarial differences are to be collectively amortized in the next fiscal year after the occurrence.

III. Important Acts of Bearing Obligation

There are no corresponding events.

IV. Important Subsequent Events

There are no corresponding events.

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