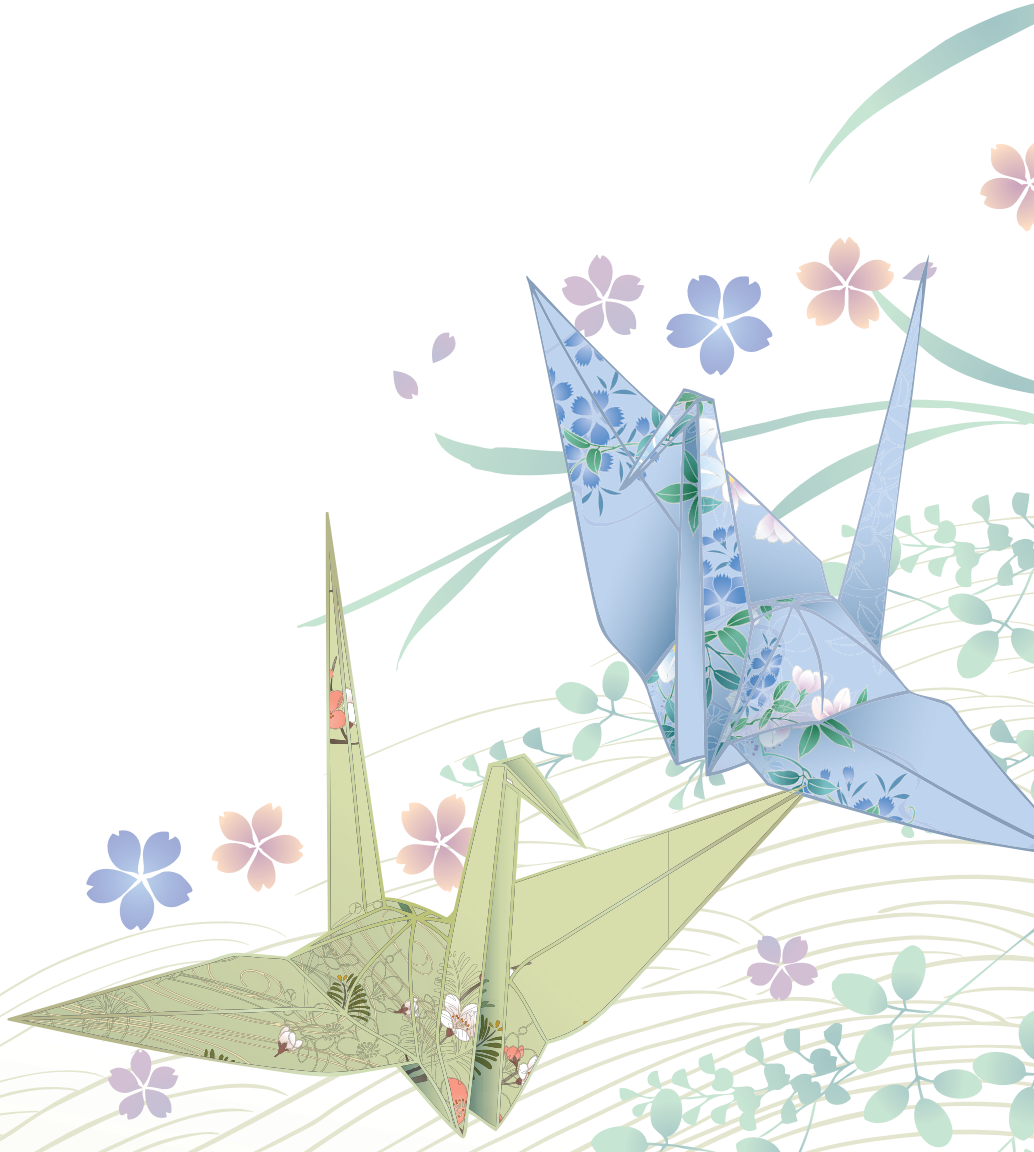
Pharmaceuticals and Medical Devices Agency, Japan

ANNUAL REPORT FY 2016



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

THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY ANNUAL REPORT FY 2016 (April 2016 – March 2017)

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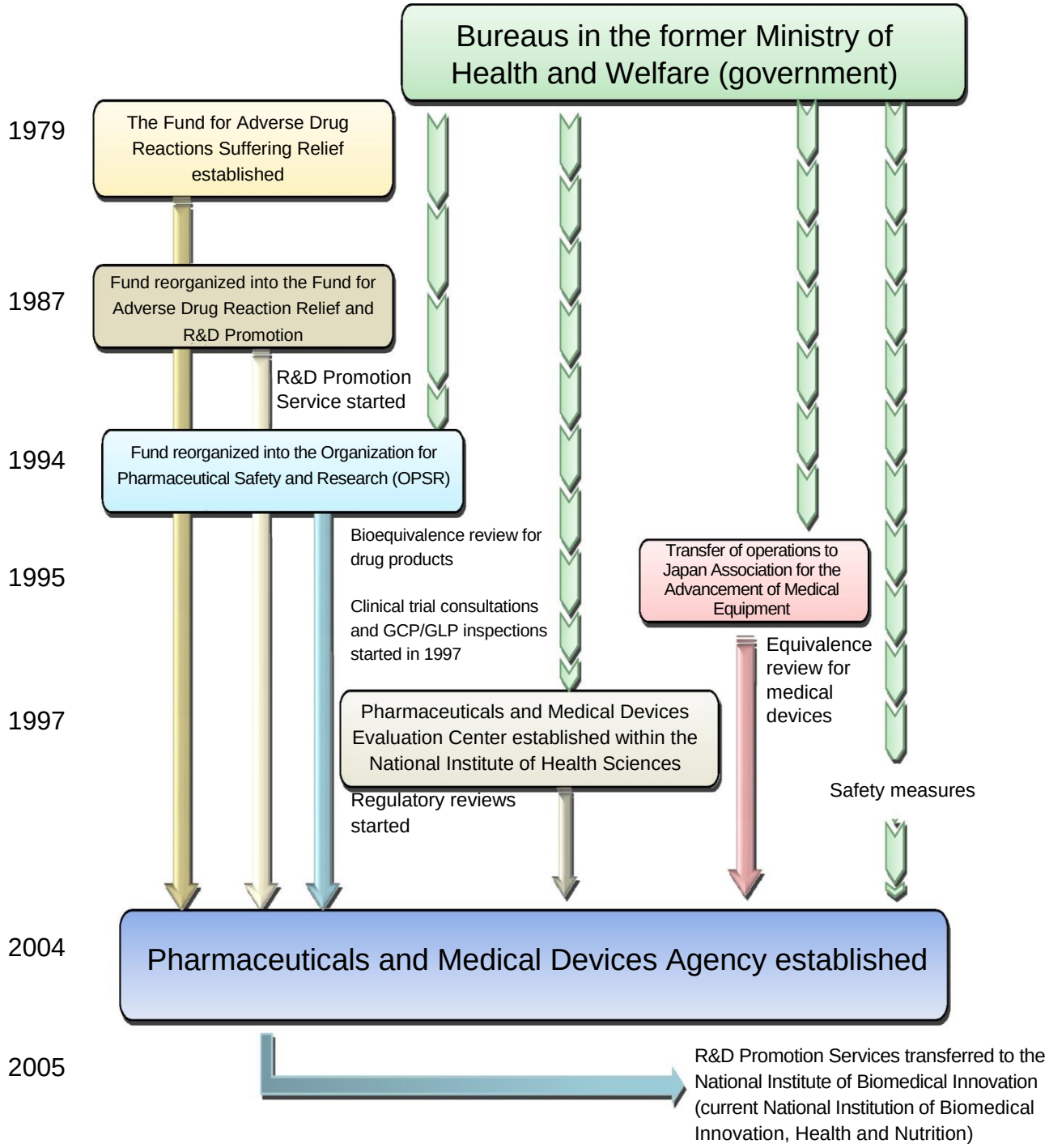
I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

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 cellular and tissue-based 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 cellular and tissue-based 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).
- PMDA provides face-to-face guidance and advice on clinical trial plans to support the development of drugs, medical devices, and regenerative medical products (Consultations and Pharmaceutical Affairs Consultation on R & D Strategy).
- 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 cellular and tissue-based 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 cellular and tissue-based 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 information to develop various standards, such as the Japanese Pharmacopoeia (JP) and certification standards of medical devices, which are set forth in the PMD Act (Research for Standards Development).

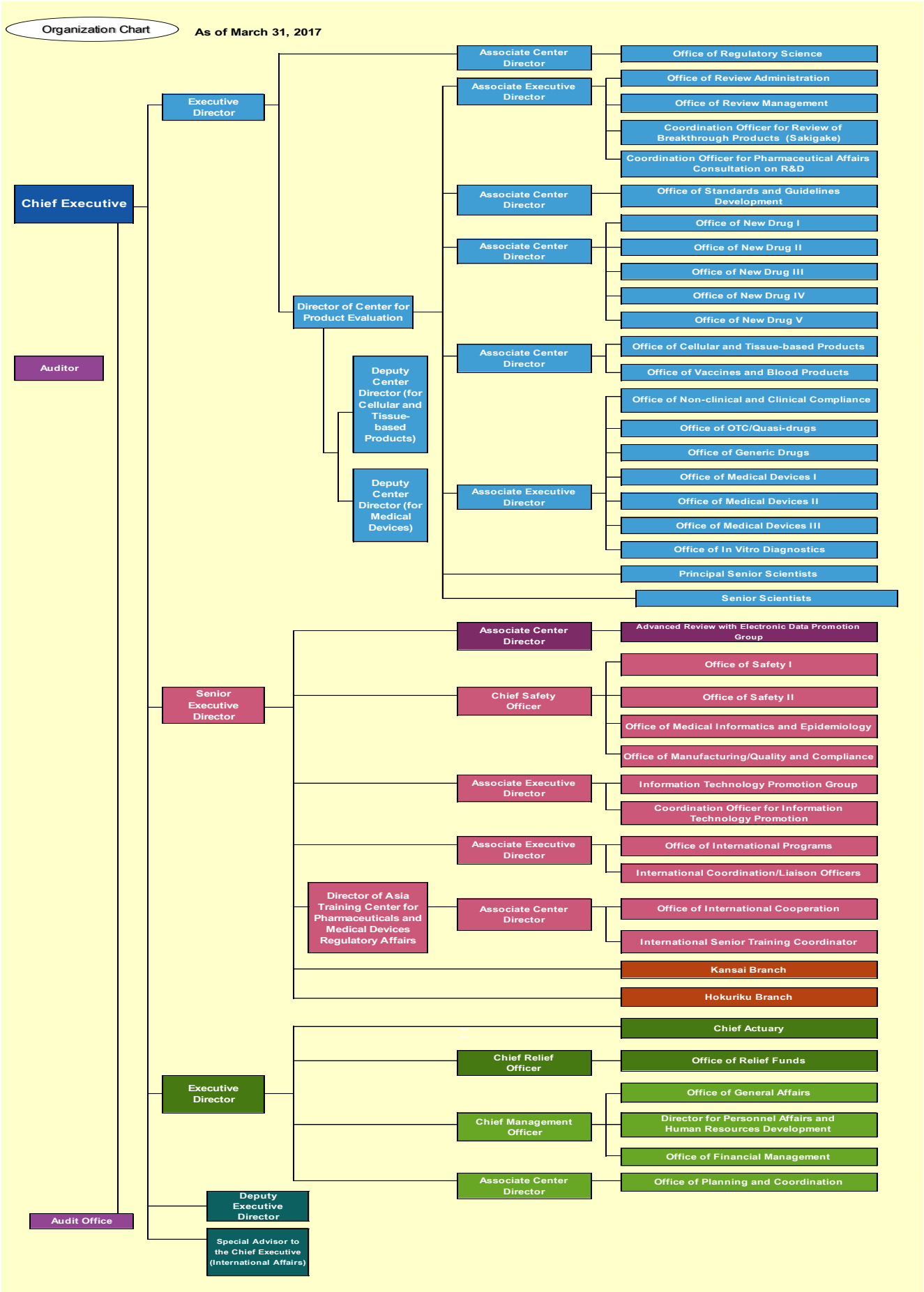
2.3. Safety Measures

- PMDA provides the following services designed to improve the safety of marketed drugs, medical devices, and cellular and tissue-based products, and also to ensure that patients and healthcare professionals can properly use drugs, medical devices, and cellular and tissue-based 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 and 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 cellular and tissue-based products widely to healthcare professionals, patients, companies, etc., in a timely manner (Information Provision).

- PMDA utilizes electronic medical records to conduct safety measures based on pharmacoepidemiological methods. These measures include quantitative assessments of the risk of adverse events, assessments of the impact on safety measures, and examination of the real-world implications of prescription drug use. PMDA is also developing medical information databases (MID-NET®) to promptly evaluate more detailed electronic medical records.

PMDA Organizational Structure (as of March 31, 2017)



II. OPERATING PERFORMANCE FOR FY 2016

PART 1 Development of the 2016 Fiscal Year Plan

1.1. Development and Implementation of the 2016 Fiscal Year Plan

- PMDA, an independent administrative agency (independent administrative agency with non-civil service status), is required to develop a Mid-term Plan to implement the Mid-term Objectives specified by the Minister of Health, Labour and Welfare, and to obtain Ministerial approval for this plan (effective period of the Third Mid-term Objectives: April 2014 to March 2019). The Mid-term Plans PMDA must develop in order to realize these objectives encompass PMDA's operational and organizational governance strategy for the relevant fiscal year (Fiscal Year Plans), and are submitted to the Minister and announced to the public following Ministerial approval.
- In addition, the 2016 Fiscal Year Plan was developed at the end of FY 2015 based on the Third Mid-term Objectives and Mid-term Plan, the results of the evaluation of PMDA's operating performance for FY 2014 provided by the Evaluation Committee for Independent Administrative Agencies of the Ministry of Health, Labour and Welfare (MHLW), and the opinions of the Commission on Policy Evaluation and Evaluation of Independent Administrative Agencies of the Ministry of Internal Affairs and Communications (MIC). The FY 2016 plan was submitted to the Minister of Health, Labour and Welfare and operations were performed in accordance with this plan following its approval.

1.2. Results of the Evaluation on Operating Performance for FY 2015

- Independent administrative agencies with non-civil service status must undergo Ministerial evaluation at the close of each fiscal year with regard to operational results during that fiscal year. (Article 32 of the Act on General Rules for Independent Administrative Agencies (Act No. 103 of 1999))
- The Minister of Health, Labour and Welfare released the Results of the Evaluation of Operating Performance for FY 2015 on September 28, 2016 prepared based on expert committee interviews concerning the results of their evaluations of independent administrative agencies as of August 15, 2016. Of the 15 criteria evaluated, PMDA received 1 "S" rating, 1 "A" rating, and 13 "B" ratings. In addition, of the criteria deemed to have be of "high importance" among these 15 evaluation criteria, PMDA's "S" rating, "A" rating, and 6 of its "B" ratings corresponded to such criteria. As no events warranting a decrease in overall rating were recognized, PMDA received an overall "B" rating ("B: Observed outcomes demonstrate progress towards achievement of the objectives specified in the Mid-term Plan") with respect to the overall assessment criteria specified in the MHLW Implementation Guidelines for the Evaluation of Independent Administrative Agencies.

  Note: List of evaluation ratings
  Individual evaluation criteria
  If quantitative indices have been defined:
  S: Agency operations demonstrate remarkable outcomes that both quantitatively and qualitatively exceed the expected objectives in the Mid-term Plan (quantitative criteria [when applicable]: achieved values of 120% or higher beyond the values targeted in the Mid-term Plan [or Fiscal Year Plan]; qualitative criteria: outstanding qualitative results)
  A: Outcomes of agency operations exceed the expected objectives in the Mid-term Plan (quantitative criteria [when applicable]): achieved values of 120% or higher beyond the values targeted in the Mid-term Plan [or Fiscal Year Plan])
  B: Outcomes of agency operations meet the expected objectives of the Mid-term Plan (quantitative criteria [when applicable]: achieved values of 100% or higher but less than 120% of the values targeted in the Mid-term Plan [or Fiscal Year Plan])

C: Outcomes of agency operations fail to meet the expected objectives of the Mid-term Plan and improvement is required (quantitative criteria [when applicable]: achieved values of 80% or higher but less than 100% of the values targeted in the Mid-term Plan [or Fiscal Year Plan])

D: Showing outcomes below the expected targets in the Mid-term Plan and drastic improvement, including discontinuation of the services, is required (quantitative criteria [when applicable]: achieved values of less than 80% of the values targeted in the Mid-term Plan [or Fiscal Year Plan], or where the competent minister deems it necessary to issue an improvement order or other necessary remedial measures)

If suitable quantitative indices cannot be defined:

S: -

A: Meets the target level established for highly difficult targets

B: Meets the target level (excluding items categorized under “A”)

C: Fails to meet the target level (excluding items categorized under “D”)

D: Fails to meet the target level, and drastic revision of operations are necessary (including cases where the competent minister deems it necessary to issue an improvement order or other necessary remedial measures)

General evaluation criteria

S: Agency operations demonstrate remarkable overall outcomes that both quantitatively and qualitatively exceed the expected objectives in the Mid-term Plan

A: Overall outcomes of agency operations exceed the expected objectives in the Mid-term Plan

B: Overall outcomes of agency operations generally achieve the expected objectives in the Mid-term Plan

C: Overall outcomes of agency operations fail to meet the expected objectives in the Mid-term Plan and improvement is required

D: Overall outcomes of agency operations fail to meet the expected objectives in the Mid-term Plan and drastic improvement, potentially including partial discontinuation of operations, is required

- The Results of the Evaluation on Operating Performance for FY 2015 were published on the PMDA website and reported to the Advisory Council at its meeting held on November 2, 2016.

Results of the Evaluation on Operating Performance for FY 2015

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

* 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.

Note: A comprehensive Ministerial evaluation for FY 2015 was conducted with respect to the items specified by the Independent Administrative Agency System Evaluation Committee, in accordance with the Guidelines for Evaluation of Incorporated Administrative Agencies.

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. Operations were performed with thorough operational progress management by executive directors, associate center directors, etc.

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

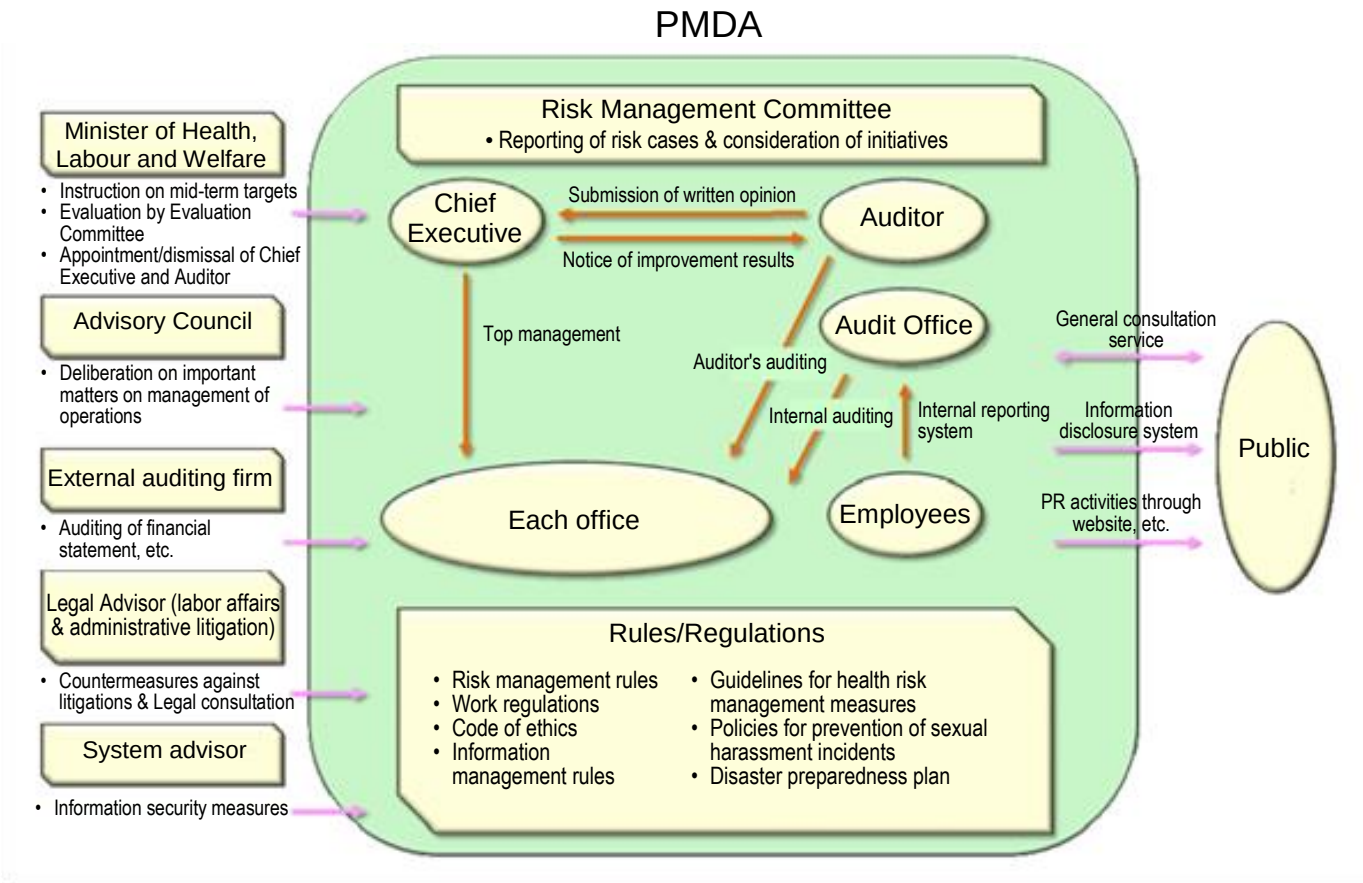
- PMDA plans to reinforce its strategic planning capacities with respect to all operations, implement a systemic approach to operational management (e.g., risk management, inspection of operations), and build an organizational system in which management decisions by the Chief Executive are promptly reflected in operations.
- To this end, the Executive Directors' Meeting was held on a periodic basis (usually every other week). The Executive Directors' Meeting is the highest decision-making body organized by executives and employees at a level above associate center directors. It reviews the basic policy on management of operations, establishment and dissolution of the organization, and important matters regarding the management of operations.
- In addition, PMDA regularly (typically once per week) held Board of Directors Meeting, 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 one meeting of Headquarters of Information Systems Management (headed by the Chief Executive) and 8 meetings of the Committee on Investment in Information Systems, and shared relevant information 8 times at Board of Directors Meeting. On such occasions, related office directors received explanations as necessary.
  In the Committee on Investment in Information Systems, all (74) systems including their operation and maintenance until the next Mid-term Plan period were checked in detail in terms of effects on activities, scale of investment, etc., based on the investment decision process developed in FY 2015.
- In light of its severe fiscal situation, PMDA implemented zero-based budgeting for FY 2017 with no safe harbor in order to improve the condition of its balance sheet, and decided to make efforts to implement the FY 2017 budget as efficiently and effectively as possible while continuing to perform its operations in a stable and sustainable manner. The agency thus introduced a conservative budget by rationalizing and streamlining operations and reducing incidental expenses.
- A budget ceiling was introduced to reduce the total budget for FY 2017. The budgets for IT system-related expenses were allocated with a focus on urgently required items with attention to information security, in order to suppress the total investment including expenses to update existing systems and financial burdens for subsequent fiscal years, from the medium- to long-term viewpoint to the end of FY 2023. Further, cost reduction targets were set for items other than IT systems, depending on the nature of each expense; the budget for discretionary expenses was reduced to a level below the actual spending in FY 2015. (The budget for mandatory [non-discretionary] expenses, such as personnel cost for executives and employees and public dues,

was not reduced.) In addition, a contingency reserve was prepared that can be used in case of an unforeseeable budget deficit due to external factors unpredictable at the stage of budget drafting. As a result, the FY 2017 budget was reduced by 3.62 billion yen (-10.9%) over the FY 2016 budget.

- Following reorganization and under the leadership of the Chief Executive, the Financial Management Committee, held 14 meetings in FY 2016 to regularly monitor PMDA's financial condition, in order to maintain sound fiscal performance and effective operations. As in previous years, the Committee received reports on the status of cash flow analysis of the declared amount of contributions, and of the user fees paid to each division in each month. In addition, the committee conducted more detailed financial analyses and discussed financial prospects in the future.
  To strengthen fiscal governance, the status of the most recent monthly closing was reported to the Advisory Council at all meetings of the council.
- PMDA had planned to use retained earnings at the end of Second Mid-term period, to strengthen the system for the Third Mid-term Plan period. However, financial prospects deteriorated because of (1) a reduction in user fees due to a reduced number of approval applications following steady resolution of drug/device lag, (2) increased safety measures, and (3) strengthened information security measures. Consequently, PMDA revised the review/consultation fees and the rate of contributions for safety measures.
- A financial soundness project team was established to ensure that PMDA continues to play its roles securely during the Fourth and subsequent Mid-term Plan periods. To this end, the project team discussed short-, medium-, and long-term measures to review financial expenditures, to strengthen the financial base, and to ensure effective budget implementation. The measures discussed by the project team are considered in the process of planning and implementing the budget for each fiscal year, through the Plan-Do-Check-Action (PDCA) cycle, to ensure financial soundness.
- The project team carefully examined the fiscal outlook and discussed short- or medium-to-long-term measures.
- In March 2017, a "Employees' Voices" was held to discuss policies for addressing staff opinions, requests, and the like.
- Meetings of the Health Committee were held every month to discuss various measures for maintaining and promoting the health of employees.
- PMDA held one idea exchange session on new drugs and one idea exchange session on safety measures in November 2016 with members of the pharmaceutical industry.
  As for medical devices and in vitro diagnostics, PMDA also cooperated with MHLW to operate and hold regular idea exchange forums focusing on medical device regulatory affairs issues (July 2016).
- PMDA's Risk Management Committee met monthly to facilitate discussion among PMDA's management regarding potential risks and corresponding countermeasures.
  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 best practices in accordance with the risk management rules, risk management manual, and guidance on incident prevention.
- The Office of Audit, which reports directly to the Chief Executive, has continued to conduct internal audits and management of PMDA's internal reporting systems.
- In order to ensure hazard and emergency readiness in the event of safety risks resulting from natural disasters such as earthquakes and fires, PMDA has informed all executives and employees of its disaster response manual (revised in January 2017) and disaster preparedness plan.
- PMDA worked on the revision of the Pharmaceuticals and Medical Devices Agency's Business Continuity Plan (BCP) to Prepare for Large-Scale Natural Disasters, which specifies the range of

important operations that PMDA should continue to conduct in the event of a large-scale natural disaster such as an earthquake in the Tokyo metropolitan area.

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 shape the policies of PMDA's PR activities and to control the progress of the activities so that PMDA will be able to implement PR activities more effectively.

- The Osaka prefectural government and other local governments located in the Kansai Innovation Comprehensive Global Strategic Special Zone, had made a request for the “arrangement of the PMDA-WEST function.” In response to the request, PMDA established the Kansai Branch Office in Osaka in October 2013. The office mainly conducts Pharmaceutical Affairs Consultation on R&D Strategy and on-site GMP inspections in the Kansai region. In June 2016, the office started to offer various kinds of consultations (face-to-face consultations) with the use of a video-conference system.
- In July 2016, a report was published by the Advisory Panel on Promotion of Venture Companies that Play an Important Role in Medical Innovation, set up by the Minister of Health, Labour and Welfare. The report states that PMDA should launch a new office within a year to support practical application of seed-stage resources owned by small-scale business operators including medical ventures. PMDA thus established the Preparatory Office for the Practical Application of Innovation Advancements (based on instructions by the Chief Executive) in October 2016. The agency also discussed and handled measures to support commercialization of innovative drugs, medical devices, and regenerative medical products, including measures to enhance and strengthen regulatory strategy consultation activities.
- In line with the PMDA International Strategic Plan 2015 unveiled in June 2015 as a new roadmap to guide PMDA’s future international initiatives, PMDA established the PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs in April 2016.
  In addition, based on the basic policies for relocation of government-related agencies, PMDA established a Hokuriku Branch Office in Toyama Prefecture in June 2016. In the Hokuriku Branch Office, a training institute for the PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs was established. The training center provided training on GMP inspections for officers from regulatory authorities in Asian countries.

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 Dr. Masataka Mochizuki, 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 Dr. Nobuyuki Miyasaka, Professor Emeritus, Tokyo Medical and Dental University) and the Committee on Review and Safety Operations (chaired by Dr. Masataka Mochizuki, 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 2016 were as follows.

Advisory Council (FY 2016)

Agenda for the 1st Meeting (June 20, 2016)

(1) Annual Report FY 2015
(2) Financial Report FY 2015
(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 2, 2016)

(1) Selection of the chairperson and appointment of the acting chairperson
(2) Results of evaluation of operating performance for FY 2015
(3) Status of recent major initiatives
(4) PMDA's financial condition
(5) Employment status of personnel from the private sector
(6) Cash contributions etc., received by external experts commissioned for Expert Discussions.
(7) Others

Agenda for the 3rd Meeting (March 13, 2017)

(1) FY 2017 plan (draft)
(2) Budget for FY 2017 (draft)
(3) PMDA's activities in response to suggestions from the Advisory Council
(4) Employment status and extension of interim restrictions on posts of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions
(6) PMDA's financial condition of accounts for reviews, etc.
(7) Others

Committee on Relief Services (FY 2016)

Agenda for the 1st Meeting (June 16, 2016)

(1) Annual Report FY 2015
(2) FY 2016 plan
(3) PR on the Relief System for Adverse Health Effects
(4) Others

Agenda for the 2nd Meeting (December 19, 2016)

(1) Selection of the chairperson and appointment of the acting chairperson
(2) Results of evaluation of operating performance for FY 2015
(3) Operating performance so far in FY 2016 and current situation of recent major initiatives
(4) Others

Committee on Review and Safety Operations (FY 2016)

Agenda for the 1st Meeting (June 16, 2016)

(1) Annual Report FY 2015
(2) FY 2016 plan, etc.
(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 (December 26, 2016)

(1) Selection of the chairperson and appointment of the acting chairperson
(2) Results of evaluation of operating performance for FY 2015
(3) Operating performance so far in FY 2016 and initiatives to be addressed in the future
(4) Employment status of personnel from the private sector
(5) Cash contributions etc., received by external experts commissioned for Expert Discussions.

(6) 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 (Japanese-language only).

2.1.(4) Establishment of an efficient operational management system

- PMDA aims to establish an efficient operational management 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 team 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.
  (1,347 external experts are commissioned as of March 31, 2017.)
- 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.
  (122 external experts are commissioned as of March 31, 2017.)
- 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 has conducted a scheme 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, inspected, and, as necessary, revised. PMDA also used non-regular staff for routine operations.

2.1.(6) Development of databases

- In October 2016, PMDA started to accept electronic data for new product applications transmitted through an electronic data system; the system allows applicants to transfer data rapidly. Up until now, obstructions that may influence operations have not occurred. This system has a database that contains all electronic application data to be used in cross-product analyses in the future. All application data have been, and will be, stored in the database.

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

- A registry of IT devices was established in FY 2015. In FY 2016, using the register, PMDA (1) estimated the budget for IT systems for the current and next Mid-term Plan periods, (2) sorted out issues to address in order to enhance the efficiency of the systems and strengthen their functions, and (3) discussed how future information systems should be.

  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 2016, PMDA improved the efficiency of its services by optimizing IT systems and by reducing unnecessary expenditure. As in FY2015, PMDA made efforts to reduce procurement costs by through approaches such as general competitive bidding, resulting in a 41.5% reduction against the FY 2014 figure.

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 2016, PMDA promoted streamlining of efficiency of its services, such as optimization of systems, promotion of digitalization, 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 approaches such as general competitive bidding, resulting in a 12.0% reduction against the FY 2014 figure.

2.2.(3) Competitive bidding

- In FY 2016, the ratio of competitive contract schemes, including competitive requests for proposals and invitations to bid, to total contracts increased by 5.3% in terms of number of bids and increased by 4.8% in terms of monetary value compared with FY 2015.

  The increased ratio of competitive contracts in number is due to an increase of 12 competitive contracts and a decrease of 6 non-competitive optional contracts compared with FY 2015.

  In FY 2016, the monetary value of both competitive and optional contracts decreased substantially. The percent decrease in the monetary value, however, was larger for optional contracts than for competitive contracts, resulting in an increased ratio of competitive contracts in terms of monetary value.

		FY 2015	FY 2016	Change
General competitive bidding (including competitive planning competition and invitations to bids)		101 bids (76.6%)	113 bids (81.88%)	12 bids (5.28%)
		5,285 million yen (87.3%)	3,041 million yen (92.10%)	-2,244 million yen (4.80%)
Non-competitive optional contracts		31 bids (23.5%)	25 bids (18.12%)	-6 bids (-5.38%)
		766 million yen (12.7%)	261 million yen (7.90%)	-505 million yen (-4.80%)
	Excluding contracts in relation to office lease	22 bids (16.7%)	21 bids (15.22%)	-1 bid (-1.48%)
		537 million yen (8.9%)	171 million yen (5.18%)	-366 million yen (-3.72%)
Total		132 bids 6,051 million yen	138 bids 3,302 million yen	6 bids 2,749 million yen

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

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

- PMDA established its Contract Review Committee in accordance with the Inspection/Review of the Contract Status of Independent Administrative Agencies ordinance (adopted by the Cabinet on November 17, 2009). The Committee consists of external experts as well as internal auditors. During Committee meetings, PMDA underwent a pre-inspection regarding the appropriateness of the transaction schemes and adjustment measures for ensuring the competitiveness of procurement and similar cases involving contracts planned to be executed during FY 2016. The Committee held 4 meetings in FY 2016 and summaries of its reviews are available on the Committee's website. In addition, PMDA established an internal Committee for Discussion on Rationalization of Procurements, etc., in accordance with the Promotion of Rationalization of Procurements, etc. in Independent Administrative Agencies ordinance (adopted by the Minister of Internal Affairs and Communications, dated May 25, 2015). The Committee addresses urgent procurement cases where there is rational justification and where such cases are preliminarily investigated based on criteria similar to those applied by the Contract Review Committee, and subsequently reports its results to the Contract Review Committee.

2.2.(5) Collection and management of contributions

- Contributions from marketing authorization holders (MAHs) in industry enable PMDA to secure the major part of the financial resources necessary for PMDA's Relief Service 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 compensation. Contributions to the relief fund for infections acquired through biological products ("infection contributions") are made and declared 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 designated its target collection rates for owed contributions related to ADRs, infections, and post-marketing safety measures to be no less than 99%. In FY 2016, the collection rates achieved for ADR, infection, and post-marketing safety measure-related contributions were 99.8%, 100%, and 99.8%, respectively.
- The rate of ADR contributions and for relief for infections, are revised every five years, with the next revision in FY 2018. PMDA therefore modified the basic calculation rate for the liability reserve in FY 2016. Accordingly, the MHLW revised a ministerial notification specifying the value rates of additional contributions. The revised value rates will be effective on April 01, 2017. Also, the rate of contributions for post-marketing safety measures was changed, to cover the cost of improving information security and enhancing safety measures related to medical devices. The adjusted contribution rate became effective on April 01, 2017.

FY 2016 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.	693	693	100%	4,193
	MAHs of pharmacy-compounded drugs	4,983	4,974	99.8%	5
	Total	5,676	5,667	99.8%	4,198
Infection contributions	MAHs of approved biological products, etc.	100	100	100%	102
Post-marketing Safety measures etc., contributions	MAHs of drugs, etc.	3,147	3,141	99.8%	3,231
	MAHs of pharmacy-compounded drugs	4,983	4,974	99.8%	5
	Total	8,130	8,111	99.8%	3,236

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

- PMDA took the following efforts 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 dispatched 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 2016, the contribution rate applied to such MAHs was set at 0.27/1000 and the collected amount was 4,198 million yen.

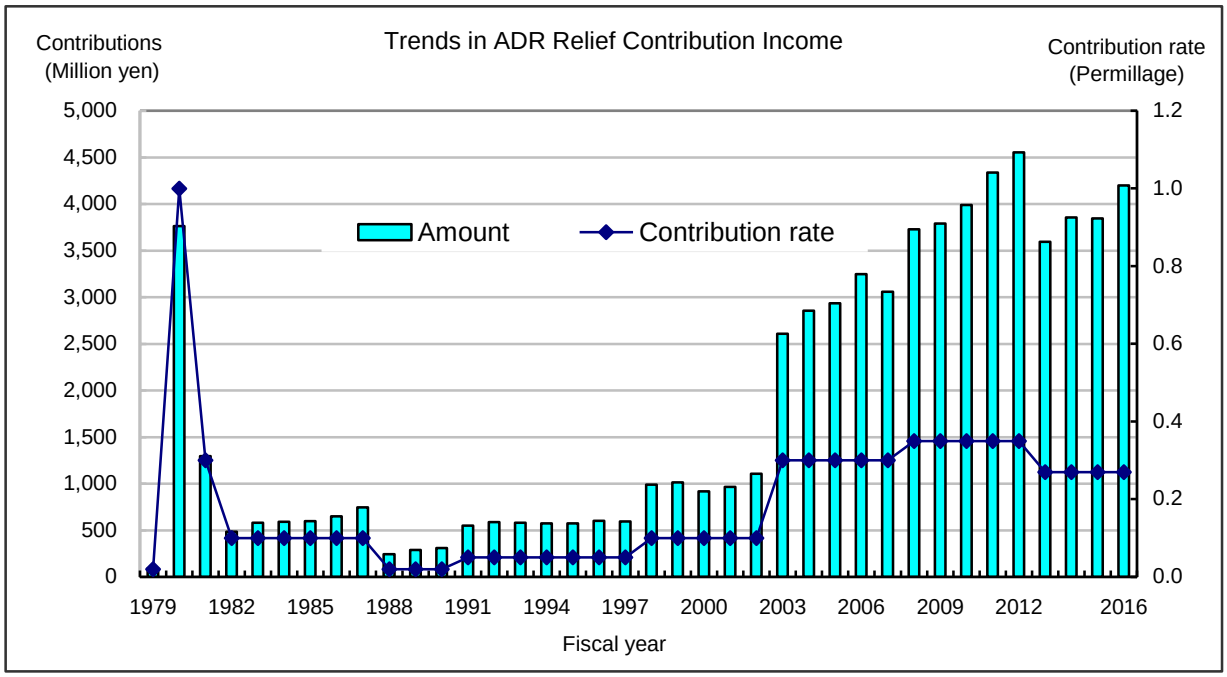
(Million yen)

Fiscal year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Contributions from MAHs of approved drugs*	4,548 [688]	3,590 [688]	3,852 [692]	3,841 [688]	4,193 [693]
Contributions from MAHs of pharmacy-compounded drugs	6 [6,186]	6 [5,866]	6 [5,658]	5 [5,439]	5 [4,974]
Total	4,554	3,596	3,857	3,847	4,198
Contribution rate	0.35/1000	0.27/1000	0.27/1000	0.27/1000	0.27/1000

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

** The figures for FY 2012, 2013, and 2014 represent the amount of contributions paid by MAHs of drug. The figures for FY 2015 and 2016 represent the amount of contributions paid by MAHs of approved drugs and MAHs of approved regenerative medical products related to ADR contributions. The figures in brackets represent the number of MAHs.*

- 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 2016, the contribution rate applied to such MAHs was set at 0.1/1000 and the collected amount was 102 million yen.

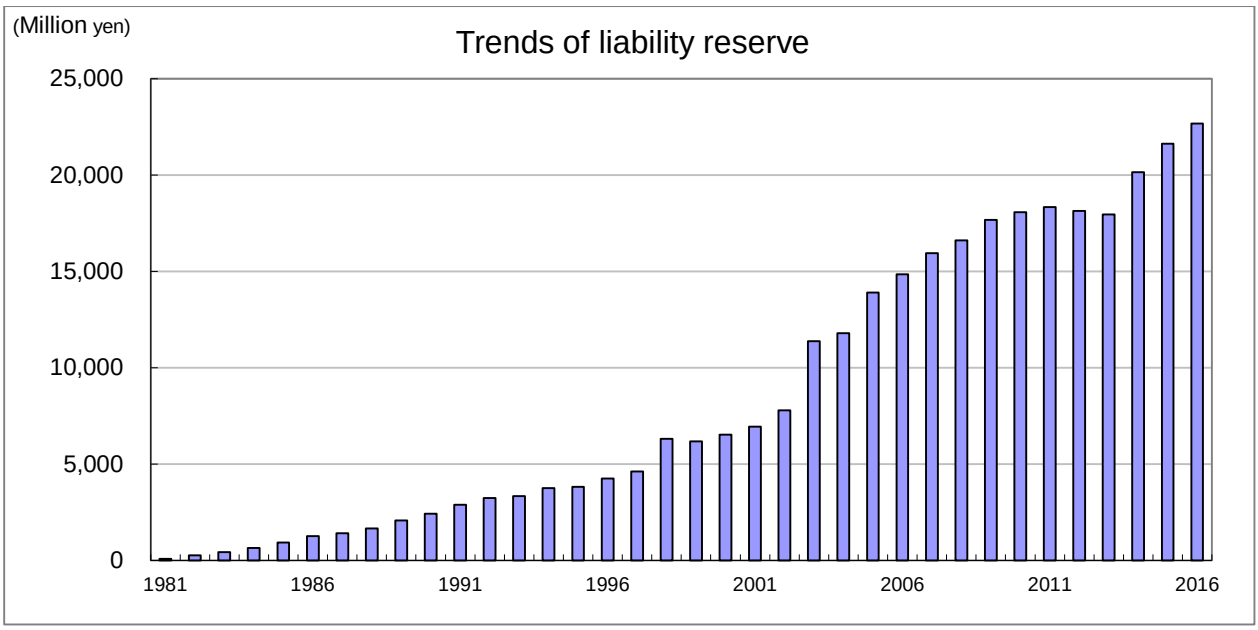
(Million yen)

Fiscal year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
MAHs of approved biological products, etc.*	866 [92]	869 [94]	93 [92]	93 [96]	102 [100]
Contribution rate	1/1000	1/1000	0.1/1000	0.1/1000	0.1/1000

** The figures for FY 2012, 2013, and 2014 represent the amount of contributions paid by MAHs of approved biological products. The figures for FY 2015 and 2016 represent the amount of contributions paid by MAHs of approved biological products and MAHs of approved regenerative medical products related to infection contributions. The figures in brackets represent the number of MAHs.*

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 2016 was 22,666 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 2016, 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 3,236 million yen.

(Million yen)

Fiscal year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
MAHs of drugs, etc.*	2,768 [2,970]	2,810 [3,023]	2,972 [3,099]	2,952 [3,139]	3,231 [3,147]
MAHs of pharmacy-compounded drugs	6 [6,186]	6 [5,866]	6 [5,658]	5 [5,439]	5 [4,983]
Total	2,774	2,816	2,977	2,958	3,236
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, *in vitro* diagnostics, and regenerative medical products)	0.22/1000 (Drugs excluding *in vitro* diagnostics) 0.11/1000 (Medical devices, *in vitro* diagnostics, and regenerative medical products)

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

** The figures for FY 2012, 2013, and 2014 represent the amount of contributions paid by MAHs of drugs (including in vitro diagnostics) and medical devices. The figures for FY 2015 and 2016 represent the amount of contributions paid by MAHs of drugs, medical devices, regenerative medical products, and in vitro diagnostics. The figures in brackets represent the number of MAHs.*

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).
- In FY 2016, PMDA made efforts to reduce the amount of paper printed by copiers. As a result, the amount and cost of paper was reduced by 7.1% and 25.8%, respectively, over FY 2015. PMDA also drastically reduced unnecessary expenditures by cutting various clerical costs and by using its offices more efficiently.

  The total budget for FY 2017 was reduced by introducing a rigorous budget ceiling system. PMDA will make efforts to implement the budget efficiently without waste by properly controlling budget execution.

  In addition, a Working-style reform project was started, and overtime work was reduced by improving the efficiency of operations.

2.3. Improvement of Services to the Public

2.3.(1) General inquiry service

- Based on the General Inquiry Guidelines that specify 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 gathered input from the public (Public Voices) and has disclosed them on its website at regular intervals. The input gathered is used to improve the agencies operational management practices
- In FY 2016, PMDA received 2,700 inquiries, of which 828 (approximately 30%) were related to applications and consultations for drugs, medical devices, etc.

	Inquiry	Complaint	Opinion/ request	Others	Total
FY 2016	2,673 (823)	3 (0)	23 (5)	1 (0)	2,700 (828)

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 left.

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 addresses complaints from relevant companies regarding product reviews and product safety operations.
- In FY 2004, PMDA established a system where, if an applicant files a complaint or other claim 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 2016.

- 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. Further, the website has a table that lists notifications issued by the MHLW. The list includes only those relevant to the Agency's operations or those that should be broadly disseminated to the public.
- The PMDA website was completely redesigned in March 2015. It was upgraded in FY 2016 based on users' requests/demands to enhance the user-friendliness of the website's search functions with respect to package inserts and similar materials.

2.3.(4) Proactive PR activities

- The PMDA Public Relations Strategic Plan (announced on July 11, 2008; revised on April 1, 2015) was developed with the aim of systematically promoting the Agency's PR overall activities. In line with the Plan, PMDA intends to take a proactive approach to information provision through implementing PR activities anticipated to be useful to individual stakeholders and improve its services to the public. In FY 2016, the following activities were implemented in accordance with this Plan.
  - PMDA distributed leaflets, designed to introduce PMDA to the general public, at events, etc.
  - 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 28 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 February 2017 to introduce the PMDA's roles and explain a recent activity, Rational Medicine Initiative—Toward Rational Medicine.
  - PMDA issued an e-mail magazine to introduce PMDA's operations to prospective employees. The Chief Executive delivered lectures and speeches as public relations activities in Japan and overseas (24 times in Japan and 5 times overseas).

2.3.(5) Disclosure requests for internal agency documents

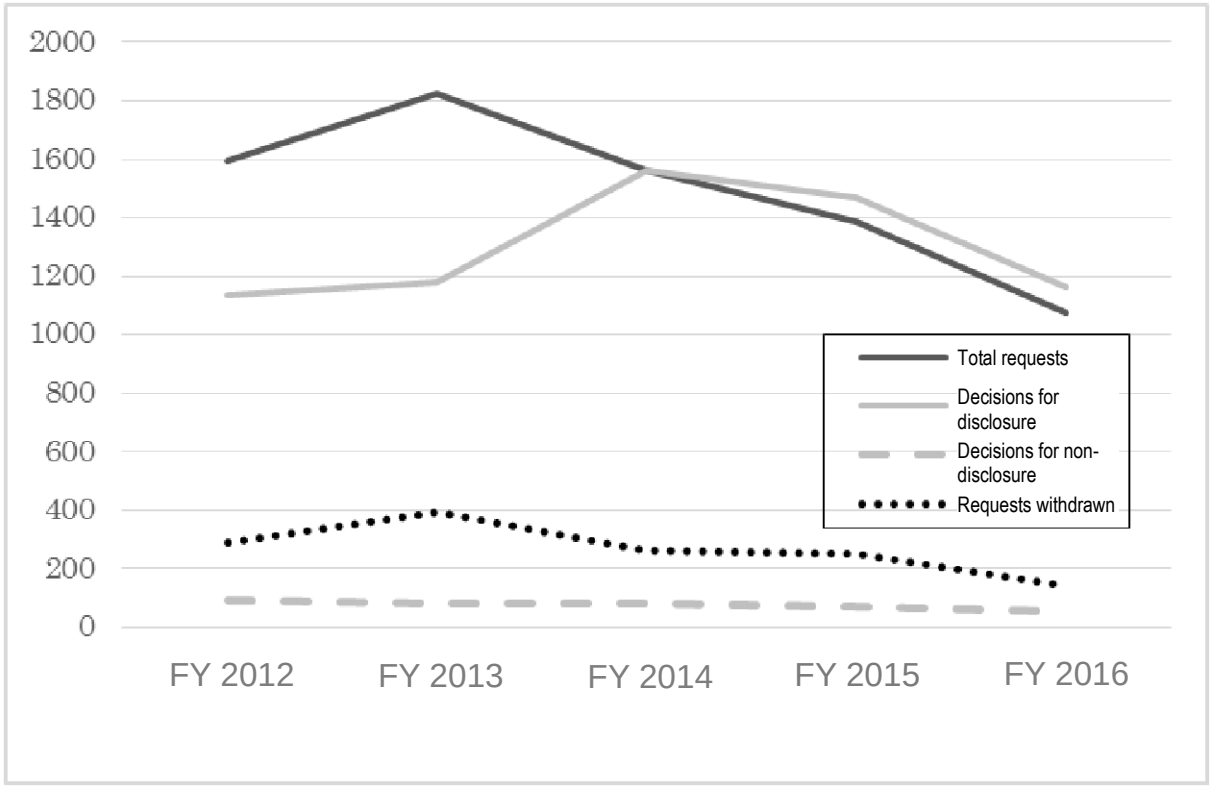
- The status of requests (over the last 5 years) for disclosure of documents under the Act on Access to Information Held by Independent Administrative Agencies is shown below. In FY 2016, the number of requests decreased by 22.3% and the number of disclosures decreased by 20.1% compared to FY 2015. PMDA appropriately processed requests in accordance with the relevant laws and regulations.

Number of Requests for Disclosure of Internal Agency Documents

	Total requests	Requests withdrawn	Decisions*					Objections made	Carry-over into FY 2017**
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2012	1,593	287	147	988	0	81	10	5	–
FY 2013	1,823	394	73	1,104	7	72	4	0	–
FY 2014	1,562	262	176	1,384	0	82	1	0	–
FY 2015	1,385	249	66	1,404	0	70	2	5	–
FY 2016	1,076	142	70	1,092	6	47	0	0	222

* *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 2017" 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 2012	FY 2013	FY 2014	FY 2015	FY 2016	Examples Product application
Review	1,410	1,675	1,457	1,295	990	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post-marketing Safety	176	131	97	82	70	ADR reports etc.
Others	7	17	8	8	16	
Total	1,593	1,823	1,562	1,385	1,076	

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 below table describes the status of requests for disclosure of personal information made within the previous five years as permitted under the Act on the Protection of Personal Information Held by Independent Administrative Agencies.

Number of Requests for Disclosure of Personal Information

	Total requests	Requests withdrawn	Decisions					Objections made	Carry-over to FY 2017
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist		
FY 2012	3	1	0	2	0	0	0	0	–
FY 2013	6	0	0	4	0	0	0	0	–
FY 2014	8	1	0	9	0	0	0	0	–
FY 2015	8	0	2	4	0	0	0	0	–
FY 2016	8	0	8	1	1	0	0	0	0

2.3.(7) Auditing

- PMDA undergoes audits conducted by an accounting auditor in accordance with the general rules for independent 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 2016, PMDA conducted internal audits on the status of document management and retention, held articles and assets, held cash and deposits, PASMO card use (a brand of IC smart card used for public transportation, etc.), funds disbursement for competitive research etc., and the status of compliance with rules restricting work assignments of personnel with prior work history 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 2015 (including the utilization of user fees and contributions) in government gazettes and on its website. PMDA also released its budget for FY 2016 on its website.

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

- The Minister of Internal Affairs and Communications adopted a policy entitled, “Promotion of Rationalization of Procurements, etc. in Independent Administrative Agencies” on May 25, 2015. In accordance with this policy, the Committee for Discussions on Rationalization of Procurements, etc. developed the Plan to Rationalize Procurement, etc. by the Pharmaceuticals and Medical Devices Agency for FY 2016, as was also done during FY 2015. The purpose of this Plan is to ensure fairness and transparency through application of the “PDCA cycle” in view of the characteristics of the clerical and business operations, and to streamline procurement processes autonomously and continuously. The plan was posted on the website in June 2016.

2.4. Personnel Matters

2.4.(1) Personnel evaluation system

- According to the Mid-term Objectives, PMDA is required to evaluate personnel fairly and consistently by taking factors related to the performance of individual employees into consideration. Moreover, in implementing the Third Mid-term Plan (FY 2014 to FY 2018), PMDA also intends to adjust its personnel evaluation system such that the results of evaluations and the attainment of individual goals are appropriately reflected in remuneration, pay raises, and promotions, to enhance employee morale.
- To this end, PMDA reflected the results of personnel evaluation during the period from April 2015 to March 2016 in pay raises etc., as of July 2016. 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.
- Interviews between secondary evaluators and evaluees are conducted, to familiarize evaluators with daily working conditions and to promote good communication and relationships between evaluators and evaluees (since FY 2013).

2.4.(2) Systematic implementation of staff training

- The science and technology of drug and medical device development are dynamic and advance at a rapid pace. As such, highly specialized and current expertise is necessary in the course of PMDA’s review, safety, and relief service operations.
- Thus, to improve the quality of operations, PMDA must systematically provide training opportunities tailored to the objectives of each specific operation geared towards not only technical staff but also administrative staff who support organizational management. PMDA’s staff training programming is divided into two courses: (1) the General Training Course, which concerns staff duties, issues that must be understood by all staff, and various other topics (e.g., IT best practices and business etiquette) deemed necessary due to the specialized nature of PMDA’s operations; and (2) the Specialized Training Course, which focuses on development of expertise in quality, efficacy, and safety evaluations as well as other more technical matters related to the products regulated by PMDA. Commensurate with educational background and prior work experience, staff have the

option to participate in both courses to aid in cultivating the knowledge and expertise needed for their work assignments.

In addition, to provide efficient and effective and role-specific training offerings, PMDA recruits the support of a variety of external organizations and subject matter experts, enriching training content and thereby improving staff capabilities. PMDA also encourages employees to participate in both domestic and overseas academic conferences and other similar events to improve their breadth of knowledge and technical expertise.

To conduct each training course, the Training Committee formulates plans based on staff need. All training programs are reviewed for quality and effectiveness, and each offering has earned high scores pertaining to participant satisfaction and acquisition of knowledge/skills. The various training programs offered to date are listed below.

1) General Training Course programs

(i) New staff training sessions were conducted between April and May 2016. The major subjects are as follows:
- Operations of each office, related systems/procedures
- Interpersonal skills (e.g., business etiquette, communication skills, motivation techniques)
- Document management, reduction of unnecessary expenditures, etc.

(ii) PMDA provided training programs tailored to different job levels—i.e., follow-up training, training for mid-level staff, and training for managerial-level staff. In FY 2016, the executive directors began to deliver lectures during follow-up training programs and training programs for mid-level staff, in order to raise the staff awareness. In addition, all managerial-level staff received new training programs (on mentoring, work-style reforms, labor management) in addition to conventional training programs (on the roles of managers).

(iii) One-on-one English conversation lessons (e.g. practical business English for international conferences, etc.) and TOEIC-IP tests were administered to improve employees' English language skills. PMDA also offers subsidies for expenses for attending English conversation schools, correspondence courses in English language, and similar enrichment activities related to language study.

(iv) PMDA required all executives and employees to undergo a new training program concerning legal and compliance matters in addition to risk management training, in order to increase awareness and understanding of legal and compliance obligations, such as the protection of personal and/or proprietary information. PMDA also designed and provided a new training program on ethics that was attended by all staff, in order to further reinforce employees' awareness and understanding of ethical concerns.

(v) Lecturers invited from patient advocacy groups, such as those related to victims of adverse drug reactions, gave presentations on three occasions during training programming.

(vi) In order to encourage more efficient use of electronic materials, a total of 51 employees underwent IT literacy training (concerning Microsoft Office software, etc.) in an e-learning format.

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 staff.

(ii) On-site training programs included visits to drug/medical device manufacturing facilities (4 facilities, a total of 46 employees participated) and medical institution IRBs (a total of

23 employees participated). Hands-on training related to medical devices (3 facilities, 37 employees) was also provided. In addition, 3 employees visited the IRB of the National Cancer Center, and 3 other employees visited the outpatient oncology pharmacist department at the National Cancer Center Hospital East.

(iii) Experts invited from Japanese or overseas regulatory authorities, industry, and universities provided special training in technical fields (13 sessions). Training programs concerning applications of biostatistics in clinical study design (10 sessions) and pharmacoepidemiological study design (11 sessions) were also provided. Pharmacoepidemiological training offerings were further enhanced by increasing the number of sessions, including 3 sessions given by external experts. CDISC overview training (8 sessions) and pharmacokinetics/clinical pharmacology and modeling & simulation training (3 sessions) were newly established and implemented with the start of acceptance of electronic data of clinical studies. Joint training with AMED was also conducted (1 session; 19 participants).

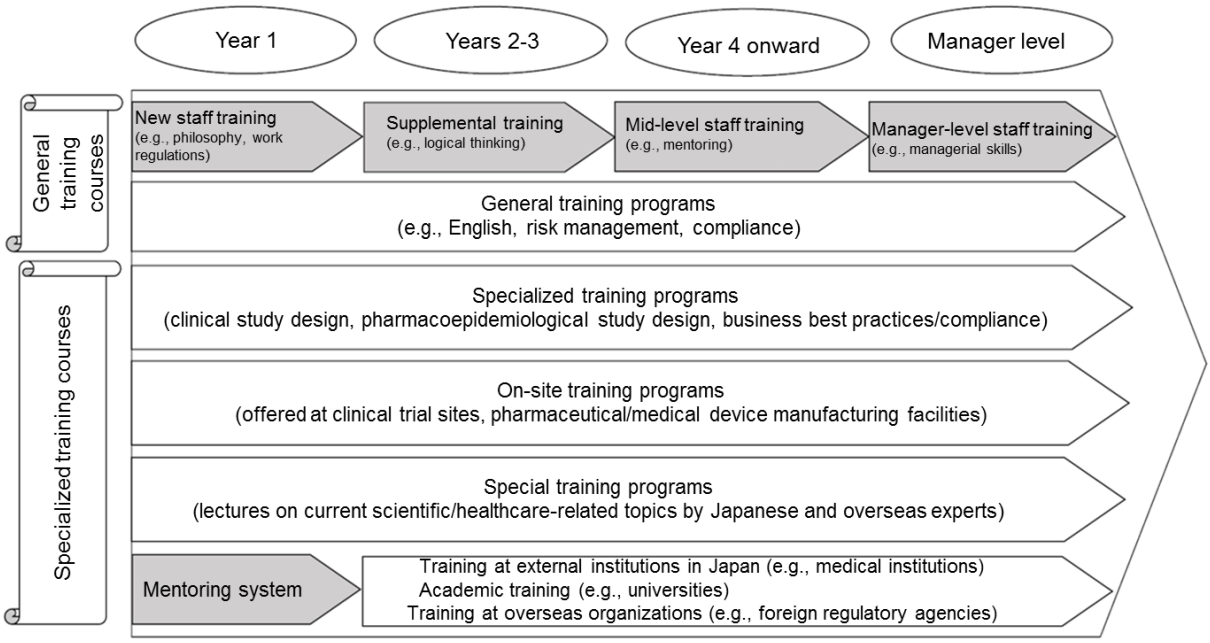
(iv) PMDA provided radioactivity technology training, including hands-on training in radioactivity measurement, to offer opportunities for learning about technical knowledge and skills in radioactivity (2 employees). The on-site training programs on safety studies were assessed for their necessity and cost-effectiveness and, as a result, were replaced by study visits to GLP facilities.

(v) Nine employees were dispatched to technical training programs conducted by external institutions (e.g., the Pharmaceuticals Promotion Association's Standard Course, the National Institute of Public Health, and the Union of Japanese Scientists and Engineers). Technical training programs concerning basic knowledge of medical devices and Class I and II medical device BME (Biomedical Engineering) were also provided (18 employees).

(vi) Four employees were dispatched to 2 medical institutions to receive practical training with pharmacists. Three employees were dispatched to 2 medical institutions to receive practical training from medical technologists at hospitals to learn clinical best practices.

(vii) To improve the workflow management skills of administrative staff, 1 employee each enrolled in an accounting training course and a contract management training course provided by the Accounting Center at the Ministry of Finance. Employees also attended other external courses, including a labor management course (3 employees), an entry level course of bookkeeping (3 employees), and a preparatory course for a Japanese business law qualification examination (4 employees).

Training and Human Resource Development



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

2.4.(3) Appropriate allocation of personnel

- 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 also conducts medium- and long-term rotation of personnel.
- In order to develop human resources in a planned manner and reinforce its overall functions, PMDA developed and launched a Career Development Program (CDP) in October 2016. (CDP was developed by modifying and refining the conventional Career Path programs [formulated in March 2011].) As a part of the CDP, PMDA created a new personnel rotation policy that focuses on the expertise of employees, to realize optimal human resource allocation so that individual employees can use their skills and abilities more effectively. In FY 2016, personnel changes were implemented in line with the conventional PMDA Career Paths, and also information was collected for personnel allocation based on the new policy after formulation of the CDP.

2.4.(4) Open recruitment of human resources

- The recruitment of capable staff with appropriate professional expertise while also considering PMDA's neutrality and impartiality are essential tasks to ensure the efficient and accurate execution of PMDA's review, safety, and relief service operations.
- 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 2016 by making use of its website as well as job information websites.

Employment through Open Recruitment in FY 2016 *(as of April 1, 2017)*

1) Technical (specialist) employees (open recruitment conducted twice [once for persons to be employed on April 1, 2018])
   - Number of applicants: 381
   - Number of persons employed: 35 (including 6 to be employed on April 1, 2018)

2) Administrative regular staff members [open recruitment conduced once]
   - Number of applicants: 129
   - Number of new hires: 4

FY 2016 Recruitment Activities

- Information sessions on career opportunities
  - April 2016: Three sessions in Tokyo and one session each in Osaka, Nagoya, Sendai, and Fukuoka (total 475 participants)
  - March 2017: Three sessions in Tokyo and one session in Osaka (total 333 participants)
- Activities performed in collaboration with directors/employees
  - Lectures at universities etc., and a business introduction during the lectures given by directors/employees
  - Attendance in on-campus seminars at university, etc.
  - Encouragement of alumni-student visit activities by young PMDA employees
  - Attendance in joint seminars, etc. sponsored by job hunting support websites
- Recruitment tools
  - Brochures for recruitment, posters for recruitment
  - The brochures and posters were sent out to approximately 400 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 posted on online job boards, etc.
  - Websites presenting job offers for new graduates (*My Navi 2018* and *Rikunavi 2018*)
  - Posting of recruitment advertisements on joint job recruitment systems for universities, etc. such as *Career+ UC* and *Kyujin-uketsuke NAVI*
  - Staff were recruited as needed in 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 Staff

	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	FY 2017 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	906	1,065
Review Department	350	389	415	438	460	492	532	560	578	
Safety Department	82	123	133	136	140	152	165	185	190	
Relief Department	32	34	34	33	33	33	36	37	39	

Note 1: The "Total" includes 6 executives (including 1 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 Coordination 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, Coordination Officer for the Practical Application of Innovation Advancements, 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, Senior Scientists, and International Senior Training Coordinator, and International Training Coordinator.

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 interactions with private industry. 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 staff regulations require that new hires submit a signed and handwritten guarantee ensuring full compliance with staff regulations, staff allocation policy, policy concerning restrictions regarding re-employment after resignation, role restrictions on staff with family members employed in a related industry, and applicable law. PMDA conducts appropriate personnel management through the creation and maintenance of its staff handbook, Q&A reference documents, and other information, and distributing these materials to staff. PMDA also regularly offers a variety of training programs for both new and existing staff designed to maintain awareness and understanding of these policies.
- PMDA also mandates that applicable employees submit for its review reports concerning actual and potential conflicts of interest as well as any donations or financial support received under its staff code of ethics.
- PMDA has established mechanisms for the effective prevention and smooth resolution of workplace bullying and harassment-related incidents. These mechanisms include the placement of a staff counselor in each office. These measures are taken in accordance with regulations

relating to the prevention of harassment and PMDA's manual on resolving workplace bullying and harassment incidents.

2.4.(6) Compensation policy optimization

- PMDA compared its personnel compensation system for FY 2015 against that for national government employees in order to facilitate public understanding of its compensation levels, and released the results on its website.
- Based on the recommendations of the National Personnel Authority in FY 2016, PMDA revised the overall compensation system, including its protocols for providing dependent allowances, in addition to narrowing disparities in compensation standards between PMDA and the private sector.

2.4.(7) Development of better workplace

- To promote the work-life balance, efforts were made to reduce overtime as a Work-Style Reform. The total monthly overtime hours decreased by approximately 41% from March 2016 (18,682 hours) to March 2017 (11,114 hours), with a 10-hour reduction in the average per employee (27 hours in March 2016; 17 hours in March 2017). PMDA will continue to make efforts to achieve the following targets: no employees work $\geq$45 hours of overtime per month (to be achieved by June 2017) or $\geq$35 hours of overtime per month (to be achieved by December 2017), except in case of irregularity or urgency.
- The "Flexible Working Hours System," proposed by the Work-Life Balance Promotion Committee, was introduced on a trial basis.

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 internal security.
- Specifically, the ID card based-"access control system" installed at each office can log every entry through designated doors and prevent non-staff from freely entering.

  In May 2010, in order to reinforce security, PMDA designated restricted floors in its office locations which cannot be accessed by elevators unless the passengers (PMDA executives and employees, etc.) have appropriate ID cards.
- PMDA has also established additional office access restrictions, and has taken all reasonable efforts to thoroughly inform its staff of these restrictions through the PMDA internal intranet and new staff training programming.

2.5.(2) IT security measures

- In accordance with its FY 2016 plan, PMDA strove to further improve the security of its IT systems and adjusted various system configurations based on the results of an IT audit and guidance information provided by the National Center for Incident Readiness and Cybersecurity Strategy (NISC). In order to strengthen security measures, PMDA also introduced a security management service intended to detect, analyze, and report illegal communications in shared local area network (LAN) systems.

- In addition, PMDA ensured that related staff received cautionary advice (information on suspicious mail) from NISC provided by MHLW, and implemented security measures as necessary.
- PMDA conducted IT security audits and offered IT security training programs in accordance with the FY 2015 PMDA Information Security Policy.
- PMDA has recorded and stored data backups for its IT systems at remote locations since FY 2007.
- In conjunction with its expanded use of secure e-mail services for audio transcription and recording activities during industry consultation sessions, PMDA has taken steps to further strengthen its "Electronic certificate issuance service for PMDA secure E-mail IDs" network security protocol, which was first implemented in January 2016. This service maintained stable functionality in FY 2016.

Numbers of Users/Issued Certificates within the Secure E-mail System

		Number of registered companies	Total certificates issued
Electronic certificate issuance service (Class 1+ secure PMDA e-mail ID)	Outside PMDA	75	837
	Within PMDA		1,517
Electronic certificate issuance service (PMDA secure e-mail ID)	Outside PMDA	18	100
	Within PMDA		137

Note: The numbers of registered companies and certificates issued as of the end of FY 2016

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 (1) to provide adequate and swift relief to victims of adverse health effects caused by drugs and regenerative medical products and infections resulting from use of biologics and regenerative medical products; and (2) 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 while exercising due care with respect to 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.

- The PMDA website contains a trial web page entitled "Patient Reports of Adverse Drug Reactions." The purpose of the web page is to improve safety measures for drugs, by identifying trends in occurrence of adverse drug reactions. The web page has a link to the "Relief Systems for Adverse Health Effects" web page.

(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 the ease of use by claimants, physicians, etc., PMDA has amended the instructions for how to fill out the forms of various medical certificates. The revised forms and instructions are available on PMDA's website.

  ♦ Downloading of claim forms: http://search.pmda.go.jp/fukusayo_dl/ (Japanese only)

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 2016

(i) As a PR campaign on TV, 30- and 15-second commercials were aired through 33 nationwide TV stations including *TV Asahi network, TBS network*, and *TV Tokyo network*, to familiarize the general public with the Relief Systems. The commercials appeared during the "Drugs and Health Weeks" (for 2 weeks from October 17, 2016). Also, through 33 nationwide TV stations, 30- to 60-second publicity infomercials (spot commercials) were run. The 30-second commercial was aired a total of 5 times during the month of October 2016 in a medical information TV program by *BS Asahi*.

The TV commercial videos are available on the special website featuring its original mascot character Doctor Q.

(ii) As a radio PR campaign, a 40-second commercial was broadcast during the month of October 2016 on *TBS Radio*. Also, a 30-second commercial was broadcast during the month of November 2016 in a radio program organized by the Japan Medical Association.

(iii) A 1/6 page monochrome advertisement was placed in 4 national morning papers (*Yomiuri, Asahi, Sankei,* and *Nikkei*) on October 17, 2016. The *Mainichi* morning paper on October 21, 2016 carried the advertisement and a full-page article on a talk between the President of Japan Medical Association and the Chief Executive of PMDA, as a special program.

(iv) Web advertisements for the general public:

- During the 3-month period from October 17, 2016 to January 17, 2017, a banner advertisement was placed on major web portals and the websites of newspapers and magazines by making use of the display networks[*1] of Yahoo! JAPAN and Google.
- The commercial videos were uploaded on Facebook during the period when the videos were broadcast on TV.

Advertisements for healthcare professionals:

- A listing advertisement was placed for 3 months from October 17, 2016 on Yahoo! JAPAN and Google.
- A banner advertisement was placed during the month of November 2016 on special websites for physicians, pharmacists, or nurses.
- A banner advertisement was placed on websites accessed by hospitals and clinics, using Demand-Side-Platform (DSP).[*2]

(v) The 30-second commercial was shown on in-store or in-hospital TV monitors in 746 medical institutions and 546 pharmacies nationwide in November 2016.

(vi) An advertisement was placed in 8 major medical newspapers/journals/magazines during the month of November 2016 (one advertisement per newspaper etc.). *Medical Asahi*, a medical journal, published a talk between the President of Japan Medical Association and the Chief Executive of PMDA. The talk was organized as a special program by the *Mainichi Newspaper*.

(vii) A news release on the Relief Systems was published on 43 websites of newspapers, magazines etc.

(viii) A total of 3,000 copies of the leaflet and an offprint of the talk published in the *Mainichi Newspaper* were distributed to the secretariats of 15 academic conferences held between November 2016 and March 2017.

[*1] A banner advertisement was placed on the websites of major Internet media/content providers (e.g., Yahoo! JAPAN or Google) and the websites of newspapers and magazines.

*2 DSP is a system that distributes banner ads to limited internet users based on IP addresses of computers. PMDA's banner ads were placed on various websites accessed by the computers in hospitals, general clinics, dental clinics, etc.

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 2016, in response to requests from medical and related institutions, PMDA dispatched staff to give lectures at 34 medical institutions and 26 related organizations to explain the Relief Systems. PMDA also sent PR materials to 123 medical institutions.

PMDA has been distributing the following questionnaires to medical institutions receiving lecture presentations from PMDA staff: (a) a questionnaire designed to identify the level of awareness about the Relief Systems and to collect comments and suggestions for improvements to PMDA staff lectures (administered immediately after training sessions); and (b) a questionnaire to evaluate how medical institutions have changed their attitudes and systems after receiving the 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 prefectures (Tokyo, Osaka, Hyogo, and Fukuoka).

(iii) Academic conferences

PMDA conducted the following PR activities at academic conferences:

- ♦ Oral presentations:
  - Japan Pharmaceutical Association Congress of Pharmacy & Pharmaceutical Science
  - Meeting of Eastern Branch of the Japan Society of Hepatology
  - DIA 2016 52nd Annual Meeting etc.

- ♦ Booth exhibitions:
  - Annual Meeting of the Japan Stroke Society
  - Annual Meeting of the Japanese Society of Hematology
  - Annual Meeting of the Japanese Society for AIDS Research, etc.

- ♦ Leaflet distribution:
  - Annual Meeting of the Japanese Society of Psychiatry and Neurology
  - Annual Meeting of the Japan Society for Clinical Immunology
  - Annual Meeting of the Tokyo Division of Japanese Dermatological Association, etc.

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

PMDA informed 19 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 gave lectures on the Relief System and distributed leaflets at the 18th 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: "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 Request for Cooperation for the System” in the “Pharmaceuticals and Medical Devices Safety Information No. 337 (October 2016).”

(vi) With the cooperation of 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 the 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 included flyers concerning the Relief System with its brochures entitled, "Pharmaceuticals and Medical Devices Safety Information Reporting System." The posters included with the brochures were distributed to relevant organizations and other stakeholders.

(ix) Information on the Relief Systems was provided in a leaflet "Useful Information on Medicines" distributed during the "Drugs and Health Week." (The leaflet is published by MHLW and the Japan Pharmaceutical Association.)

(x) PMDA asked 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) PMDA surveyed the level of awareness of the Relief Systems among the general public and healthcare professionals, in order to make PR activities more effective.

Survey period: Late December 2016 to early January 2017.

(xii) The claim forms for relief benefits were modified to gather information regarding how claimants knew the Relief Systems:

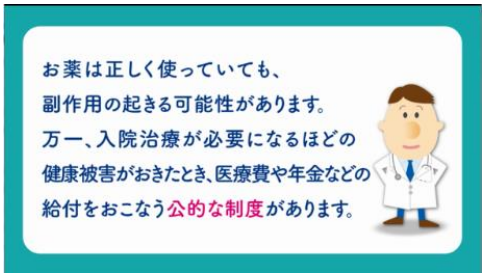
- In April 2016, all claim forms for relief benefits were modified to include a multiple-choice question asking claimants how they knew (or who informed them of) the Relief Systems, with the following options: “Physicians,” “Dentists,” “Pharmacists,” “Other medical institution staff,” “Newspaper, TV, etc.,” and “Other.” The most common answer in FY 2016 was “Physicians”

(424 answers [38.4%]), followed by “Other (Internet)” (146 answers [13.2%]), “Newspaper/TV, etc.” (134 answers [12.1%]), and “Pharmacists” (94 answers [8.5%]) (multiple answers allowed).

- In June 2014, the adverse drug reaction reporting form (which is sent from healthcare professionals to PMDA, as part of the Pharmaceuticals and Medical Devices Safety Information Reporting System) was modified to include a question asking healthcare professionals whether the patient involved will claim relief benefits for the adverse reaction concerned. In FY 2016, PMDA received 2,506 answers (multiple answers allowed): “The patient plans to claim benefits” (74 answers [3.0%]); “Already informed the patient of the Relief Systems” (135 answers [5.4%]); “The patient has no plan to claim benefits” (1,591 answers [63.5%]); “Not covered by the Relief Systems” (686 answers [27.4%]); and “Unknown/Other” (541 answers [21.6%]).

Home page of the special website

TV commercial



Newspaper Ad

◆ **Promoting the Relief Systems through a talk article: Posted in the *Mainichi Newspaper***

広告 企画・制作 毎日新聞社広告局

患者と医療を守る「医薬品副作用被害救済制度」とは

「世界最速」となった日本の新薬承認

「かかりつけ医」を持つことが安心の第一歩

世界が注目し始めた日本独自の制度

独立行政法人 医薬品医療機器総合機構
理事長 近藤 達也氏

こんどう・たつや　1968年、東京大医学部卒業。69年、同大脳神経外科入局。77年、マックス・プランク研究所（西独）に留学。その後、国立病院医療センター脳神経外科医長、国立国際医療センター病院長を経て2008年4月から現職。13年から内閣官房健康・医療戦略参与。

公益社団法人 日本医師会
会長 横倉 義武氏

よこくら・よしたけ　1969年、久留米大医学部卒業。同年、同大第2外科助手。77年、ミュンスター大学教育病院（西独）に留学。その後、医療法人弘恵会ヨコクラ病院院長、福岡県医師会会長などを経て2012年から現職。15年からヨコクラ病院理事長。

公益社団法人 日本医師会

47都道府県の医師会の会員による学術専門団体。医学や医術の向上などを目的に、医師の研修や医療の発展、保険医療を充実させるための活動を行っている。会員は約16万7000人、開業医、勤務医がほぼ同数を占める。

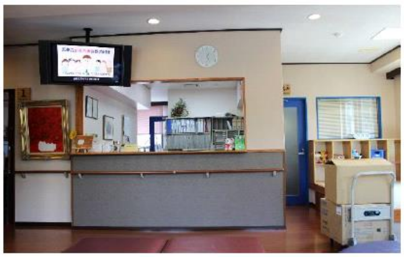
医薬品副作用被害救済制度

医療機関で処方された医薬品や、薬局等で購入した医薬品を適正に使用したにもかかわらず発生した副作用により入院治療が必要な程度の重篤な健康被害を受けた方の救済を図るため、医療費、年金などの給付を行う制度。救済給付に必要な費用は製薬企業がその社会的責任に基づいて納付する拠出金が原資となっている。2015年度の救済給付請求は1566件、患者への支給総額は20億円余りに達する。

独立行政法人 医薬品医療機器総合機構（PMDA）

医薬品と医療機器等の有効性や安全性について科学的に判断し、「審査」「安全」「救済」の三つの業務を担う機関。医薬品副作用被害救済・研究振興調査機構など3機関が統合し、2004年に発足した。

Promoting the Relief Systems through TV monitors in hospitals and pharmacies



Advertorials in healthcare journals

◆ Promoting the Relief Systems through a talk article: Posted in Medical Asahi

提供：医薬品医療機器総合機構

医薬品副作用被害救済制度

医薬品によって思いがけない副作用が起きた際に患者を救済する「医薬品副作用被害救済制度」が注目を集めています。1980年にスタートしたこの日本独自の公的制度の重要性がより高まっている背景や、国民および医療業界にもたらすメリット、そして薬の副作用の被害を最小限に抑えるための医師、患者の対策などについて、制度を運営する独立行政法人医薬品医療機器総合機構（PMDA）の近藤達也理事長と、公益社団法人日本医師会の横倉義武会長が語り合いました。

―今、患者と医療を守るために―

“世界最速”となった日本の新薬承認 速やかな未知の副作用への対応

―近年、日本での新薬承認のスピードが劇的に速くなっています。

近藤 いまでは世界最速と言ってもいいほどです。「ドラッグラグ」（海外で使用承認された薬が日本で長期間使えないこと）も大幅に解消され、いくつかの新薬は欧米をはじめとする世界に先行して日本で使えるようになりました。

横倉 近藤先生がPMDAの理事長になられて、大きく状況が変わりました。

近藤 薬は医療の重要な柱なので、その承認が遅いというのはやはりよくない。承認のスピードアップのために最も重視したのは、製薬企業との情報交換を密にすることです。米国食品医薬品局の手法を参考に、承認申請の前から新薬の狙いを聞き、効率的な審査方法を考えることで、形式的な無駄を排しました。

横倉 今はインターネットを通じて患者さんが海外の情報を早いうちから入手します。海外で使われている薬が日本で承認されていないと、不満を持たれるケースもあるでしょうから、ありがたいことです。

近藤 ただし、優れた薬を正しく使ったとしても、副作用の発生を防げないケースがあるのは事実です。日本では、公的医療保険制度のもとで、国民に大きな経済負担をかけることなく、短期間で広く承認後の新薬が使われます。素晴らしいことですが、世界で最初に大規模に薬が使用され、臨床試験等では現れなかった副作用が初めて見つかる可能性も高まってきました。そのような背景もあり、戦後の複数の大きな副作用被害を教訓に創設された医薬品副作用被害救済制度の重要性が増しているのです。

横倉 1961年に導入された国民皆保険も、経済発展の最中で先達が「国民のために」とつくったもの。約20年後に始まった医薬品副作用被害救済制度と“国民目線”という原点は同じですね。

近藤 仰る通りで、PMDAではリスクを抑制する「審査」、継続的にリスクを最小化する「安全」、発生した被害に対する「救済」という3つの業務から成り立つ「セイフティ・トライアングル」により、国民目線で総合的なリスクマネジメントを行っています。

医師は治療の経過を徹底的にチェックし 患者は地域に「かかりつけ医」を

―処方薬の残りを自己判断で使ったり、薬を個人輸入したりして起きるトラブルも多いと聞きます。

横倉 薬には用法・用量という決まりがあり、必ず医師が患者さんに合わせて薬を処方しますが、使い方を誤ると害になります。「体調が悪い時などは薬をたくさん飲んだ方がいい」と考える患者さんもおられますが、かえって副作用を起こす可能性が高まるでしょう。

近藤 最近は効果が高く、鋭く効く一方で、副作用を慎重にチェックしなければならない薬が増えているように感じます。

横倉 皮膚疾患や呼吸に影響を与える肺線維症、あるいは不整脈を引き起こすものなどもあります。そのような薬は、効果と副作用を医師がしっかりチェックしながら使用することが欠かせない。一般論ですが、新薬の使用を始めた時は1週間以内の診察が必要だと思います。

近藤 「薬が効いているか」「副作用が出ていないか」といった個々の判断は「かかりつけ医」にしかできません。患者さんには、不安な症状が出たら、なるべく早く「かかりつけ医」のもとを訪れていただきたいですね。

横倉 そういった意味でも、「かかりつけ医」を持つことが非常に重要となります。自らの健康状態を把握してもらっていれば安心です。「かかりつけ医」ならば、処方した薬を飲んだ患者さんに異変が生じた時に、素早く気付くことができます。医薬品副作用被害救済制度は任意のワクチン接種や薬局で販売されている薬による健康被害も救済対象になっていますから、市販薬で体調が悪くなった場合も、「かかりつけ医」に相談するとよいでしょう。

医療の信頼を守るセイフティネット 再生医療への展開で世界も注目

―医師にとっての医薬品副作用被害救済制度の価値とは？

横倉 長く使われ、安全といわれている薬であっても、患者さんの体調や重複して飲んだ薬との関係で予期せぬ副作用が生じることがあるように、副作用の発生はゼロにはなりません。そんな万が一の場合でも、患者さんを迅速にしっかりとケアすることができます。直接的には患者さんを守る制度ですが、避けがたい副作用に対するセイフティネットとして、我が国の医療の信頼を守ることにもつながるのです。

近藤 実は医薬品副作用被害救済制度は、いまだ一般の方にはなじみの薄い制度です。万が一副作用が生じた時には、制度の紹介、手続きの助言など、現場に立つ医師の皆さんの力をお借りすることが多くなります。患者さんと制度との橋渡し役になっていただけると幸いです。

―制度の創設から35年。時代に即した変化も起きているのでしょうか。

近藤 2014年11月からPMDAでは「再生医療等製品」に関する承認と被害救済の制度を世界に先駆けて導入しています。もちろん、京都大学の山中伸弥先生の成果を踏まえてのことです。

横倉 iPS細胞（人工多能性幹細胞）ですね。

近藤 通常、再生医療に関わる新しい製品を審査する場合、大規模な臨床試験を行い、有効性・安全性についての十分な結果を得た上で承認に進みます。しかし、この分野は進歩が速い。患者さんに恩恵がある仕組みを考えるなら、「効果がある」と判断した製品は、迅速な承認を経て一定の条件および期限付きで使用できるようにした方がよいのです。この方針を取った時、支えになるのが救済制度。いざという時に患者さんをしっかりケアできるシステムがあるからこそ、この世界初の試みが実現しました。

横倉 患者さんのメリットを考えた上で、副作用が起きてもちゃんとカバーできる。やはり国民目線を徹底しているということでしょう。

近藤 いまでは各国が医薬品副作用被害救済制度に関心を持ち始めており、台湾、韓国、それに北欧諸国も我が国をモデルに制度づくりを進めているところです。これからも多くの方の支援をいただき、制度をより発展させていきたいと思います。

医薬品副作用被害救済制度

医療機関で処方された医薬品や、薬局等で購入した医薬品を適正に使用したにもかかわらず発生した副作用により、入院治療が必要な程度の重篤な健康被害を受けた方の救済を図るため、医療費、年金などの給付を行う制度。救済給付に必要な費用は、製薬企業がその社会的責任に基づいて納付する拠出金が原資となっている。2015年度の救済給付請求は1,566件、患者への支給総額は20億円余りに達する。

独立行政法人 医薬品医療機器総合機構理事長 近藤 達也（こんどう たつや）

1968年、東京大医学部卒業。69年、同大脳神経外科入局。77年、マックス・プランク研究所（西独）に留学。その後、国立病院医療センター脳神経外科医長、国立国際医療センター病院長を経て2008年4月から現職。13年から内閣官房健康・医療戦略参与。

公益社団法人 日本医師会会長 横倉義武（よこくら よしたけ）

1969年、久留米大医学部卒業。同年、同大第2外科助手。77年、ミュンスター大学教育病院（西独）に留学。その後、医療法人弘恵会ヨコクラ病院院長、福岡県医師会会長などを経て2012年から現職。15年からヨコクラ病院理事長。

救済制度相談窓口 救済制度についての詳細は、PMDAにご相談ください。
0120-149-931 受付時間［月～金］午前9:00～午後5:00（祝日・年末年始を除く）
詳しくは 副作用 救済 検索 http://www.pmda.go.jp/kenkouhigai_camp/

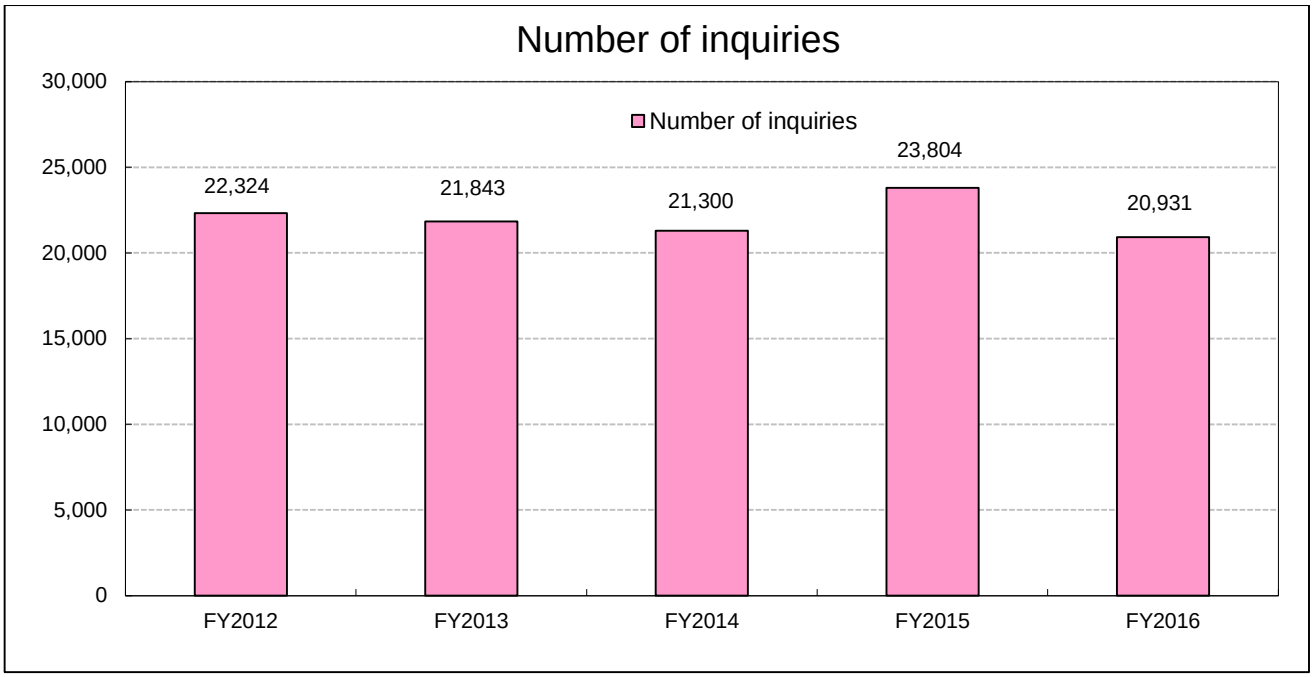
独立行政法人 医薬品医療機器総合機構
東京都千代田区霞が関3-3-2 新霞が関ビル

この記事は、朝日新聞出版「メディカル朝日」2016年11月号に広告として掲載したものです。（2016年9月対談実施）

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

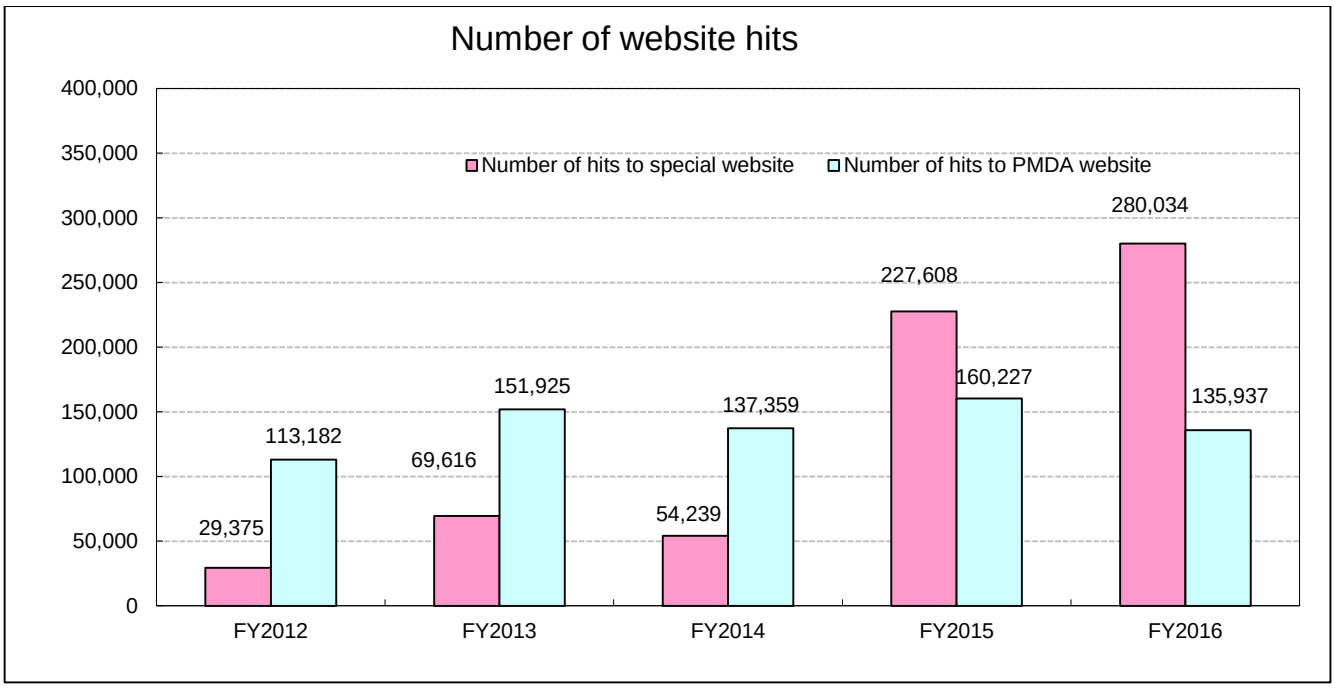
- In FY 2016, the Relief System Inquiry Service received 20,931 inquiries, which represents 87.9% versus FY 2015 (23,804 inquiries).

Fiscal year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Versus FY 2015
Number of inquiries	22,324	21,843	21,300	23,804	20,931	87.9%



- In FY 2016, the PMDA website was accessed 135,937 times, which represents 84.8% versus FY 2015 (160,227 hits).
- The special website for the Relief Systems was accessed 280,034 times, which represents 123% versus FY 2015 (227,608 hits).

Fiscal year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Versus FY 2015
Access to PMDA website	113,182	151,925	137,359	160,227	135,937	84.8%
Access to special website	29,375	69,616	54,239	227,608	280,034	123.0%



<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

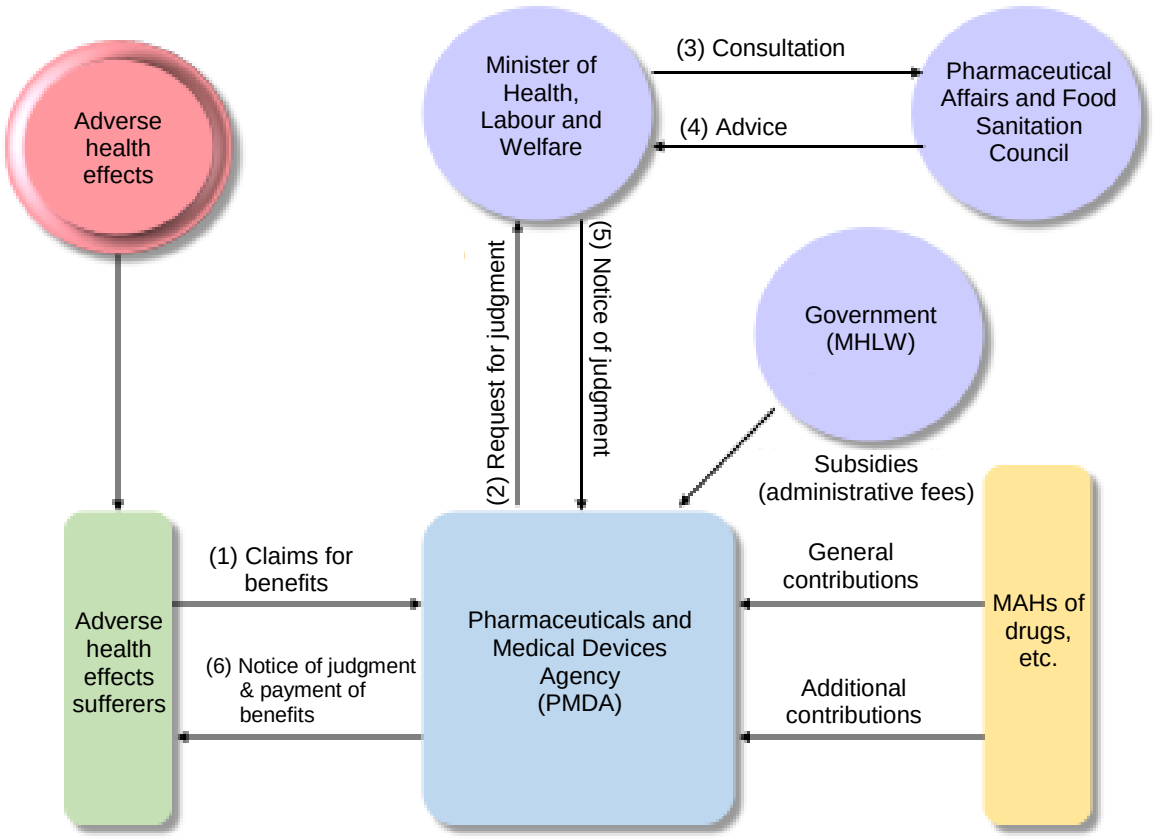
3.1.(4) Promotion of efficient database-backed services

- 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 at least 60% of claims should be judged (approved/rejected) within 6 months of filing. To achieve this target, in FY 2016, PMDA strove to process benefit claims received as quickly as possible, as in previous years.

  In FY 2016, 1,843 claims were submitted (a marked increase from the 1,566 claims submitted in FY 2015) and 1,754 were judged. Of the 1,754 claims, 1,182 (67.4%) were judged within 6 months of filing, exceeding the annual target by upwards of 60%).

  In FY 2016, 334 claims related to HPV were filed (an increase from 152 claims in FY 2015) and 314 were judged.

  HPV-associated claims

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FT 2014	FY 2015	FY 2016	Total
Number of claims filed	2	10	7	25	39	152	334	569
Number of claims judged	0	5	9	8	4	75	314	415

(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 2016 is shown below.

Fiscal Year			FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims filed			1,280	1,371	1,412	1,566	1,843
Number of claims judged			1,216	1,240	1,400	1,510	1,754
	Approved		997	1,007	1,204	1,279	1,340
	Rejected		215	232	192	221	411
	Withdrawn		4	1	4	10	3
	Within 6 months	Number of claims	553	754	867	915	1,182
		Achievement rate[*1]	45.5%	60.8%	61.9%	60.6%	67.4%
Claims in progress[*2]			779	910	922	978	1,067
Median processing time (months)			6.2	5.8	5.7	5.6	5.3

*[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 under review at the end of each fiscal year.*

b. Number of claims by type of benefit

The numbers of claims filed in FY 2016 by type of benefit are shown below.

Fiscal Year		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims filed		1,280	1,371	1,412	1,566	1,843
Types of benefit	Medical expenses	1,101	1,200	1,221	1,341	1,595
	Medical allowances	1,168	1,252	1,290	1,428	1,693
	Disability pensions	83	88	95	109	111
	Pensions for raising handicapped children	1	7	12	7	8
	Bereaved family pensions	46	49	41	37	56
	Lump-sum benefits for bereaved families	53	54	65	61	71
	Funeral expenses	98	105	103	100	128

Note: More than one type of benefits may be claimed within a single claim.

c. Approval by type of benefit

The number of approved claims and amounts of benefits paid in FY 2016 by type of benefit are shown below.

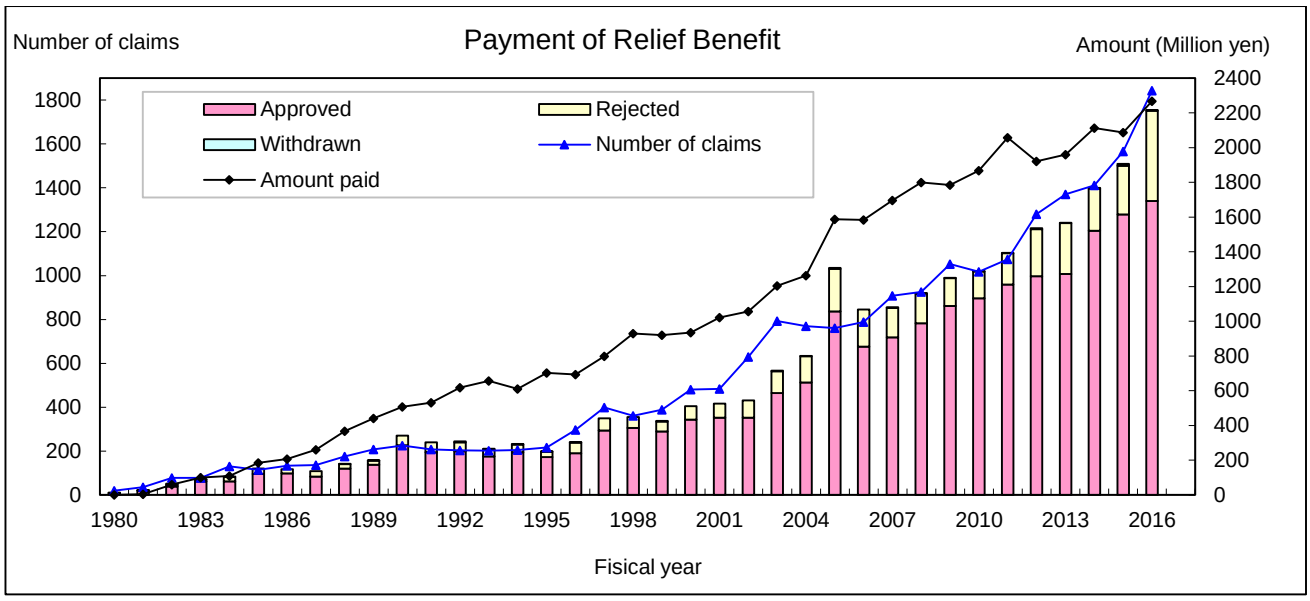
(Unit: Thousand yen)

Type	FY 2012		FY 2013		FY 2014	
	No. of claims	Amount paid	No. of claims	Amount paid	No. of claims	Amount paid
Medical expenses	892	97,905	886	95,025	1,108	123,987
Medical allowances	947	75,326	945	82,730	1,151	95,457
Disability pensions	28	861,595	39	905,233	37	943,939
Pensions for raising handicapped children	0	43,744	3	40,785	2	38,965
Bereaved family pensions	32	602,068	31	603,130	31	585,626
Lump-sum benefits for bereaved families	32	227,696	32	220,032	45	310,806
Funeral expenses	62	12,438	59	12,249	72	14,507
Total	1,993	1,920,771	1,995	1,959,184	2,446	2,113,286

Type	FY 2015		FY 2016	
	No. of claims	Amount paid	No. of claims	Amount paid
Medical expenses	1,146	118,235	1,190	136,997
Medical allowances	1,220	112,040	1,269	120,109
Disability pensions	47	1,002,305	53	1,082,599
Pensions for raising handicapped children	8	43,675	6	42,153
Bereaved family pensions	23	580,934	31	607,497
Lump-sum benefits for bereaved families	32	218,891	38	263,243
Funeral expenses	53	10,822	73	14,944
Total	2,529	2,086,902	2,660	2,267,542

Note 1: "No. of claims" is the number of approved claims. "Amount paid" is the amounts of benefits paid to both new and existing recipients.

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



d. Number of current status reports from pension recipients

In FY 2016, PMDA received 588 (571) current status reports from pension recipients: 343 (329) from those receiving disability pension, 36 (42) from those receiving pensions for raising handicapped children, and 209 (200) from those receiving reports of bereaved family pension.

* The figures in parentheses represent the number of reports received in FY 2015.

(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 medicine products on or after November 25, 2014) that were determined to have been used in accordance with their approved labeling and prescribing information. 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 relief service for infections

The performance for FY 2016 is shown below.

Fiscal Year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims filed	4	7	3	6	1
Number of claims judged	6	4	7	2	5
Approved	4	4	6	1	3
Rejected	2	0	1	1	2
Withdrawn	0	0	0	0	0
Claims in progress[*1]	2	5	1	5	1
Achievement rate[*2]	83.3%	100.0%	42.9%	50.0%	20.0%
Median processing time (months)	4.7	4.3	6.3	7.5	10.0

*[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 2016 by type of benefit are shown below.

Fiscal Year		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims		4	7	3	6	1
Types of benefit	Medical expenses	2	6	2	5	1
	Medical allowances	4	7	3	5	1
	Disability pensions	0	0	0	0	0
	Pensions for raising handicapped children	0	0	0	0	0
	Bereaved family pensions	0	0	1	2	0
	Lump-sum benefits for bereaved families	0	1	1	0	0
	Funeral expenses	0	1	2	2	0

Note: More than one type of benefits may be claimed within a single claim.

c. Approval by type of benefit

The number of approved claims and amounts of benefits paid in FY 2016 by type of benefit are shown below.

(Unit: Thousand yen)

Type	FY 2012		FY 2013		FY 2014		FY 2015		FY 2016	
	No. of claims	Amount paid	No. of claims	Amount paid	No. of claims	Amount paid	No. of claims	Amount paid	No. of claims	Amount paid
Medical expenses	2	83	3	258	5	336	1	0	3	92
Medical allowances	4	282	4	356	6	566	1	170	3	210
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,362	–	2,353	–	2,338	–	2,393	–	1,005
Lump-sum benefits for bereaved families	–	–	–	–	–	–	–	–	–	–
Funeral expenses	–	–	–	–	–	–	–	–	–	–
Total	6	2,726	7	2,967	11	3,239	2	2,563	6	1,306

Note: As benefit amounts are rounded to the nearest thousand yen, the figures in 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 concerning 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 provides healthcare professionals with simple and clear suggestions on how to use drugs safely 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

- 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 who require such services in addition to relief benefits. (These services are offered in accordance with the PMD Act.)

(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 2016, PMDA summarized the Team's operating performance during FY 2015, prepared an investigative research report, and conducted investigative research targeting 75 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 (75 volunteers in FY 2016).

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 results of the survey on adverse health effects caused by reactions to drug products indicated 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 numerous 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 2016, 99 consultations were performed.

(iii) Distribution of benefit recipient cards

In January 2010, PMDA began issuing credit card sized certificates to recipients of adverse reaction relief benefits for their convenience at their request. 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 2016, PMDA issued such certificates to 857 recipients.

(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 2016, PMDA summarized the operating performance for FY 2015, prepared an investigative research report, and conducted research in 154 subjects.

Research Method

Among individuals with hepatitis C caused by treatment for congenital diseases, those with serious infections are asked to complete a survey form to provide detailed data on their daily living. The data are analyzed and evaluated (154 volunteers in FY 2016).

Research Team

Team Leader: Kugahisa Teshima, Professor, Graduate School of Social Service, Japan College of Social Work
Namiki Izumi, 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

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)

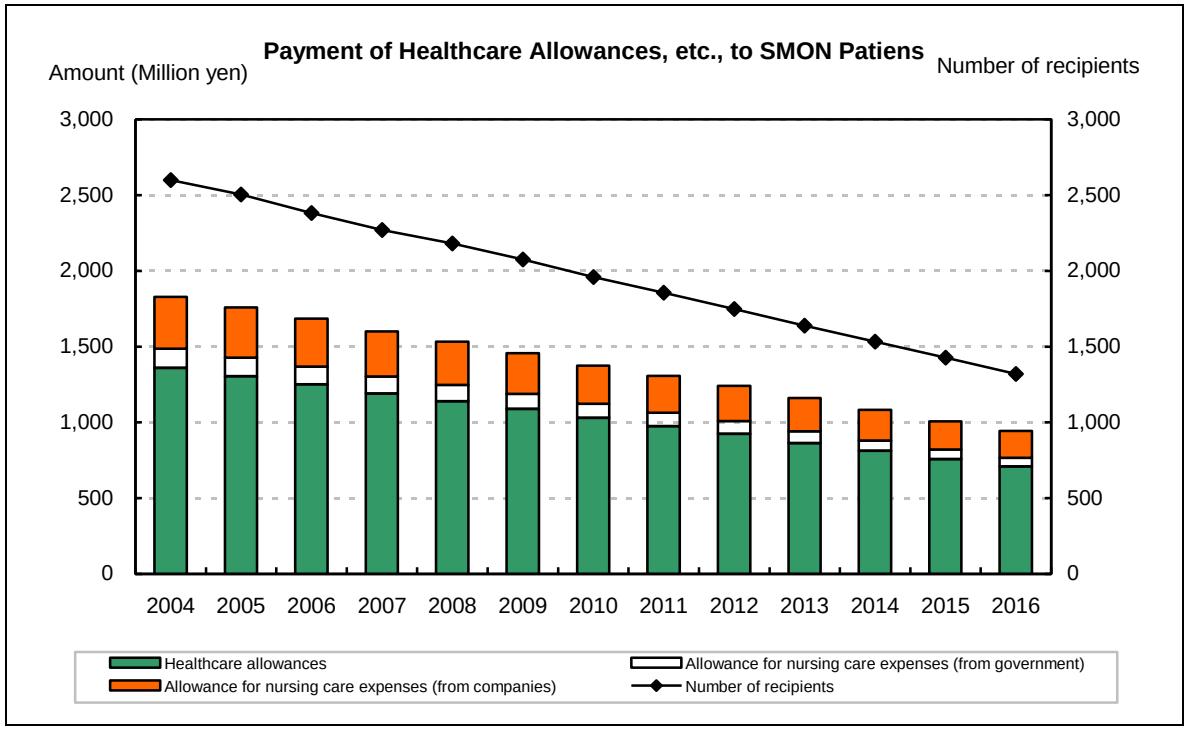
- PMDA provides healthcare allowances and nursing care expenses to patients with SMON (Subacute myelo-optico-neuropathy) for whom an out of court settlement was reached. In FY 2016, a total of 943 million yen was paid to 1,319 patients.

  * SMON due to Quinoform products

  SMON is a disease caused by Quinoform products (antiflatulents) that leads to numbness, walking difficulty, visual disturbance, etc. According to a research group, approximately 10,000 individuals are estimated to have been affected by SMON.

Fiscal year		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of recipients		1,748	1,639	1,533	1,428	1,319
Amount paid (thousand yen)		1,241,368	1,160,944	1,082,992	1,006,135	942,828
Break down	Healthcare allowances	924,669	864,462	811,727	757,285	709,290
	Allowance for nursing care expenses (from companies)	233,050	219,630	201,919	185,319	176,639
	Allowance for nursing care expenses (from government)	83,650	76,902	69,346	63,532	56,899

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 2016, 513 HIV-positive patients received allowances under the

investigative research, 111 patients with AIDS under the healthcare support service, and 2 patients with AIDS received special allowances. In total, 626 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

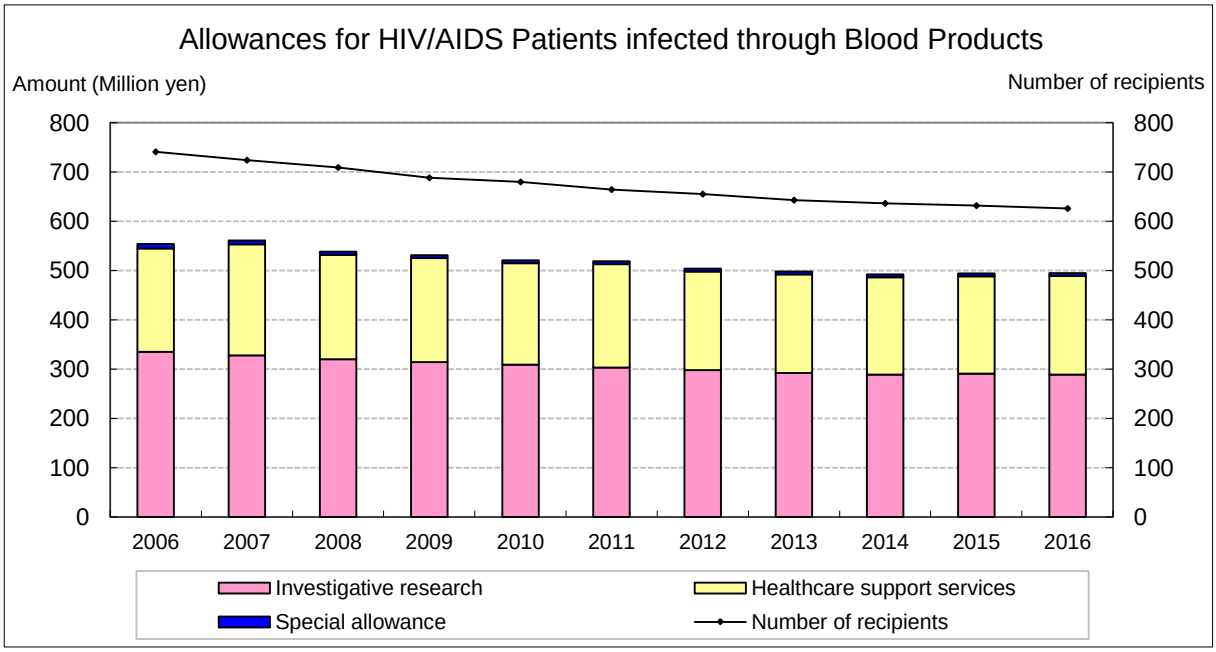
* HIV infection due to blood products

Patients with hemophilia, etc. were infected with HIV after receiving unheated blood coagulation-factor products manufactured from blood donated by people in the US.

Fiscal Year	FY 2012		FY 2013		FY 2014	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	540	297,790	529	292,349	524	288,736
Healthcare support services	112	199,500	112	199,650	110	197,400
Special allowance	3	6,362	2	6,232	2	6,190
Total	655	503,652	643	498,230	636	492,325

Fiscal Year	FY 2015		FY 2016	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	520	290,935	513	288,703
Healthcare support services	110	197,400	111	199,650
Special allowance	2	6,336	2	6,384
Total	632	494,671	626	494,737

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



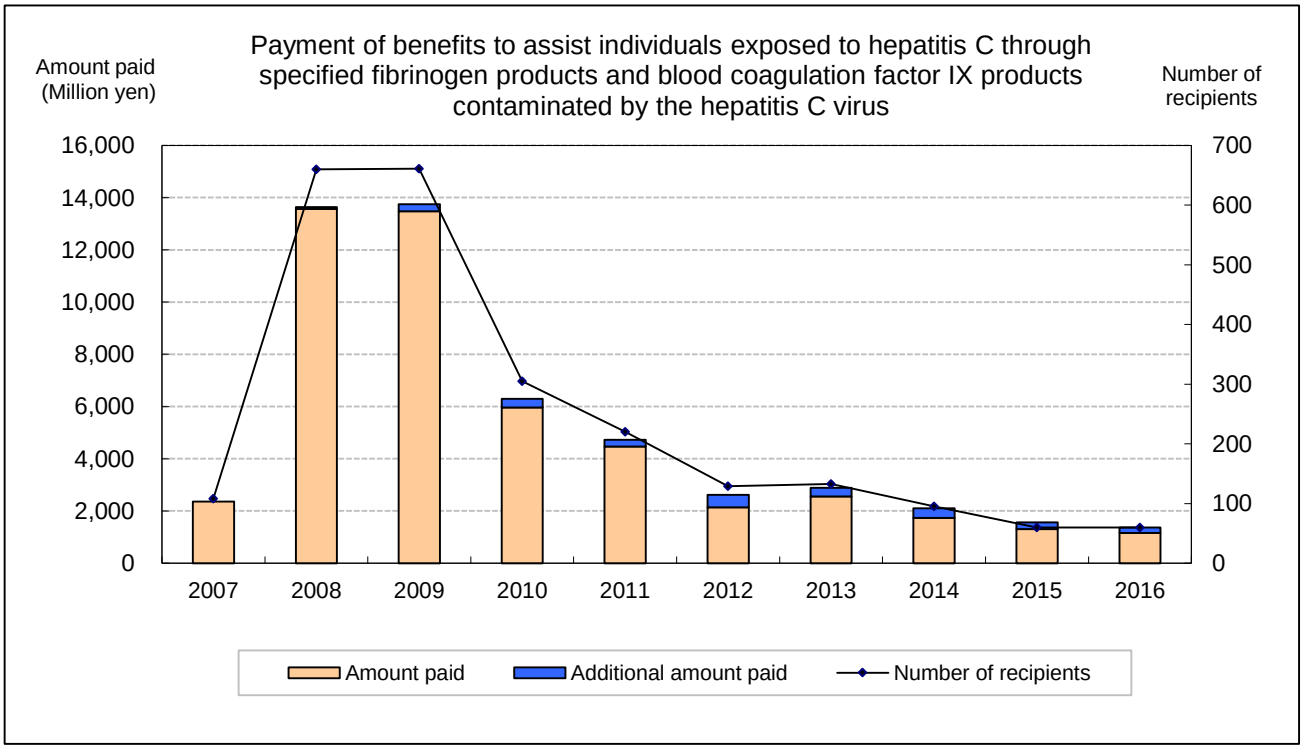
3.1.(9) Appropriate provision of benefits to individuals with hepatitis C caused by specified fibrinogen products and specified blood coagulation factor IX products

- 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 2016, 60 patients received benefits (1.16 billion 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	FY 2016
Number of recipients	129	133	95	60	60
(Number of these recipients receiving additional payment)	(28)	(18)	(20)	(14)	(14)
Amount paid (thousand yen)	2,624,000	2,888,000	2,100,000	1,308,000	1,156,000
(Amount of additional payment)	(488,000)	(332,000)	(368,000)	(252,000)	(208,000)
Number of inquiries	982	473	660	834	1,087



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, and 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 medical products through 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, which consists of external experts in related fields such as medicine, dentistry, pharmaceutical sciences, and engineering, was established in FY 2012 to more appropriately manage products employing advanced scientific techniques and technologies. In FY 2016, 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 accelerating reviews and improving the quality of reviews, based on the “Japan Revitalization Strategy” 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 has been significantly improved since 1997. In FY 2004, PMDA was founded to consolidate review functions while the final authority regarding medical product approvals 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 thoroughly re-examined and integrated into a single "independent administrative agency, the Pharmaceuticals and Medical Devices Agency."

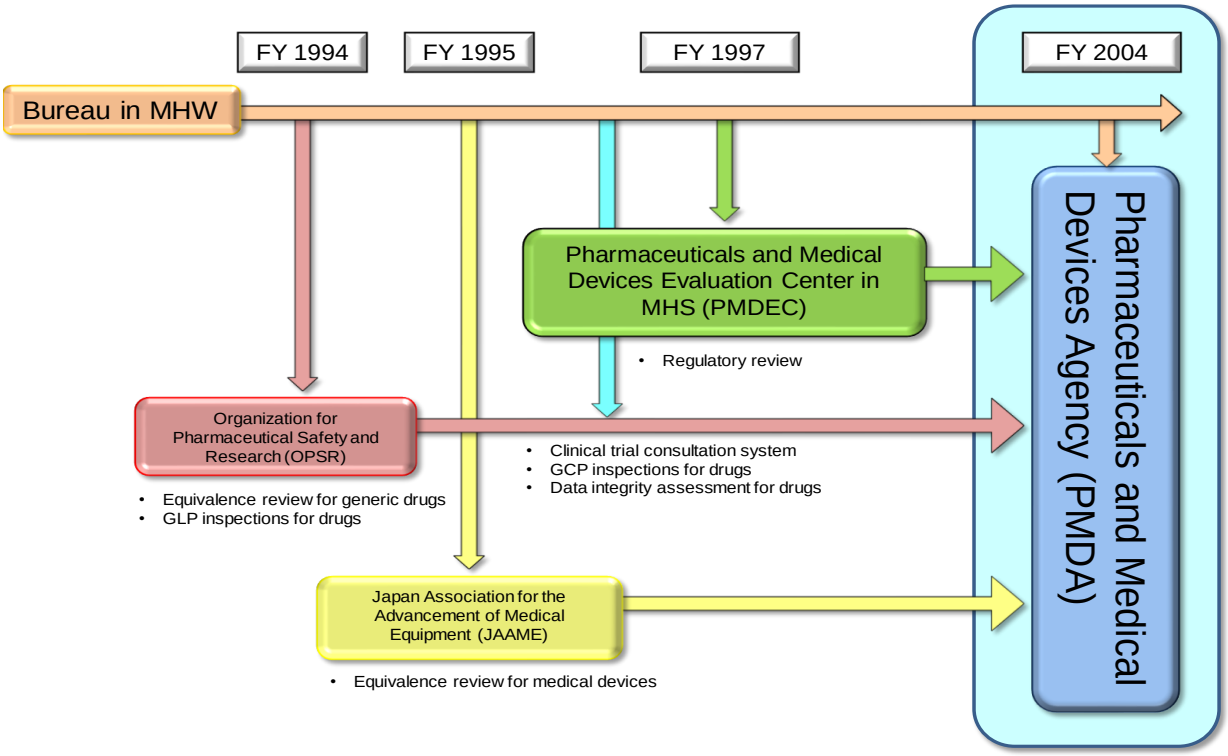
  2) Substantial increase in the number of staff including reviewers.

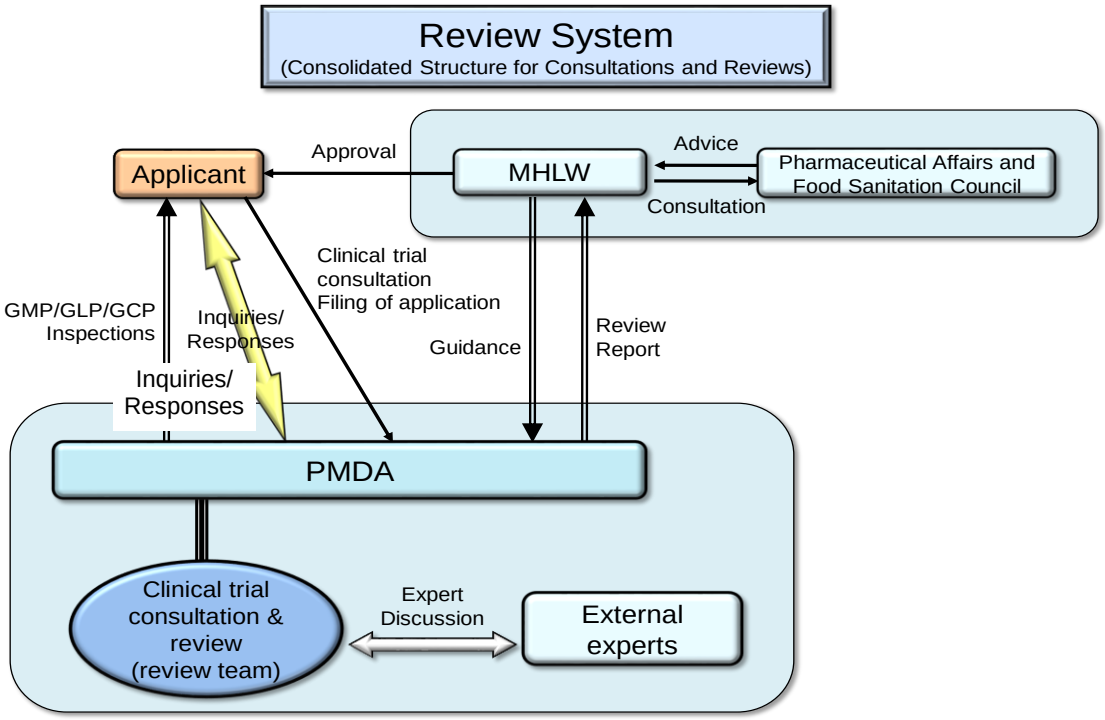
  3) Introduction of a coherent system in which the process from clinical trial consultations until reviews is conducted by the same team with the same staff members.

  4) Enhancement of reviews of biological and biotechnology-derived products.

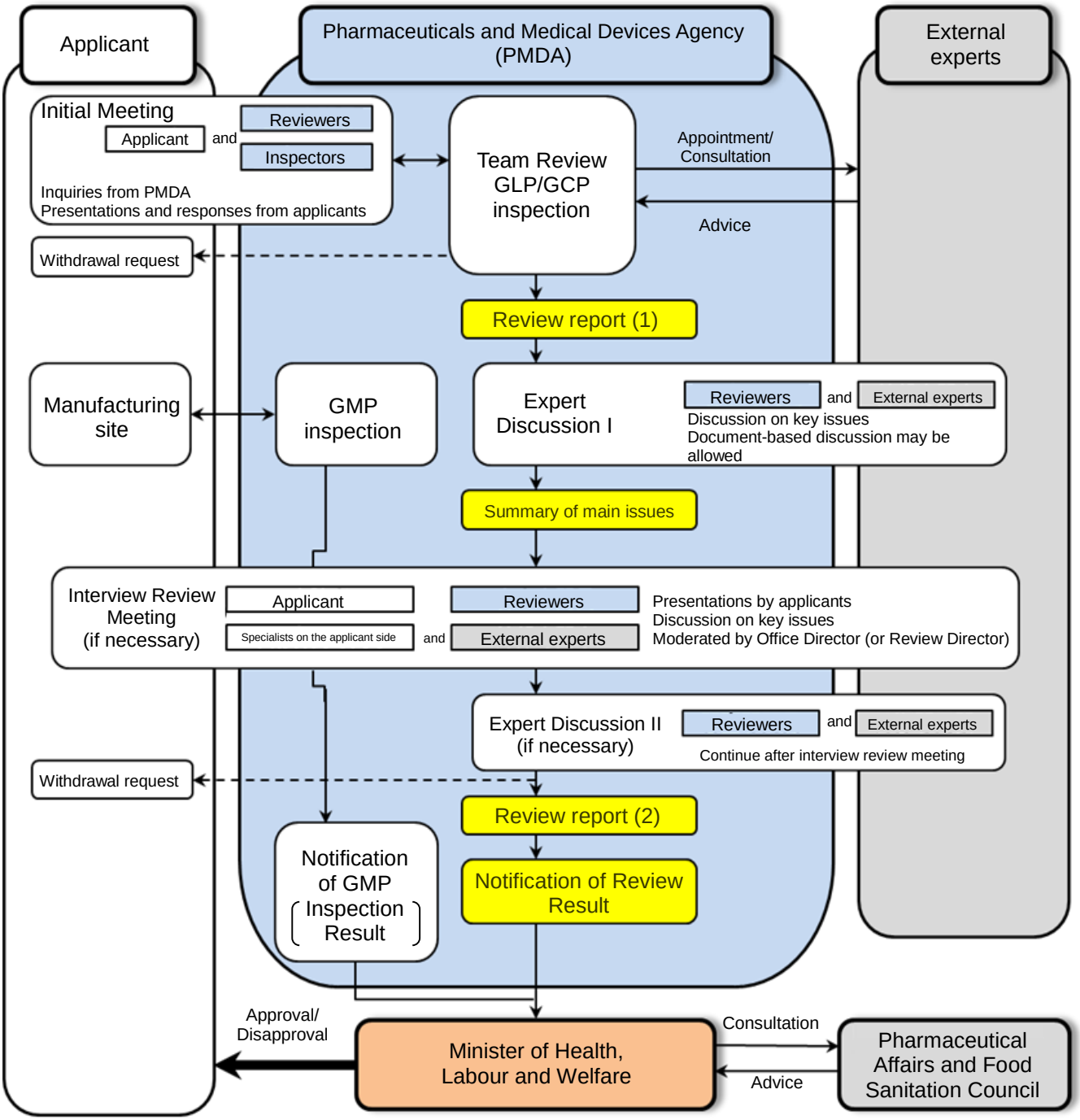
  5) Reinforcement of functions for reviewing medical devices.

Transition of approval review system on drugs and medical devices





Flowchart of review process



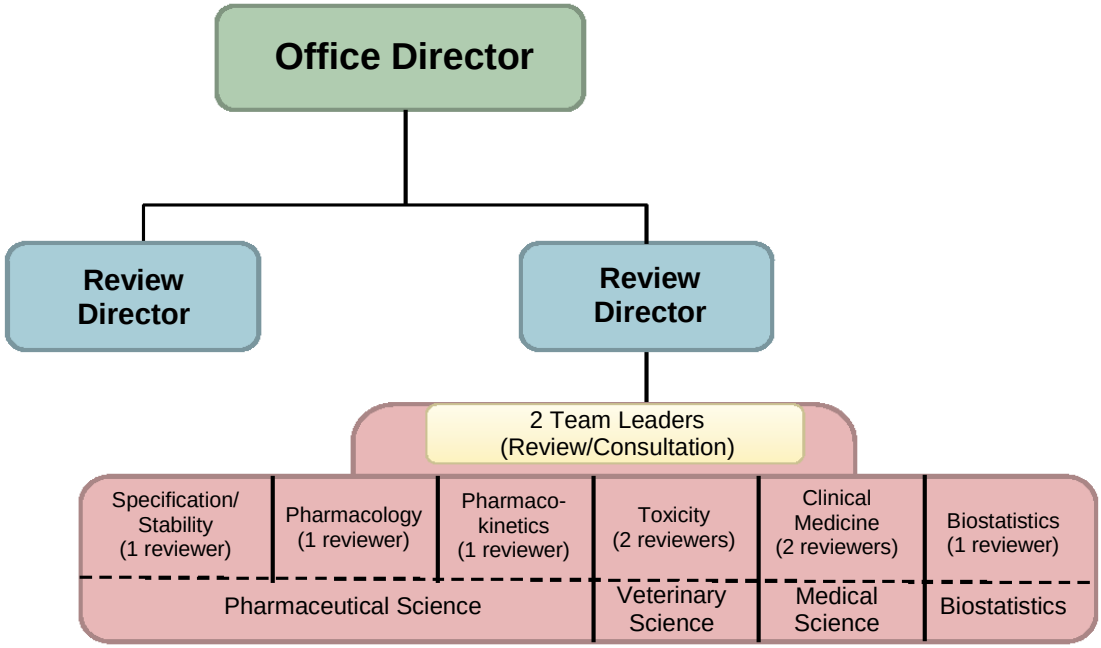
Review Performance for FY 2016 (drugs)

(1) Number of Expert Discussions conducted: 191 (154 document-based discussions, 37 meetings)

(2) Applications deliberated at the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 85
Applications reported to the Drug Committees (under PAFSC): 28

- 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 holding academic degrees in pharmaceutical science, veterinary medicine, clinical medicine, biostatistics, and other specialized fields. Each review team is typically comprised of a team leader, deputy team leader(s), and reviewers specializing in the areas of quality, toxicology, pharmacology, pharmacokinetics, clinical medicine, and biostatistics.

Organization Chart for Reviews of New Drugs



- In order to enhance its review system, PMDA increased the number of reviewers allocated to the categories receiving large numbers of new drug application filings where delays in the review process were most likely.
- 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 (including alternatives for blood products)

- PMDA conducted clinical trial consultations for new drugs based on the team-reviewed guidance plan drafted by 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 2016, based on the experience accumulated so far, this scheme was further integrated into the review system.
- The PMDA's Progress Management Committee for Reviews and Related Services is intended to ensure that PMDA executives have an accurate understanding of the progress status of reviews and related services and improve the progress as needed. The "Review Segment Committee for

Progress Management" is headed by the Director of the Center for Product Evaluation. The two committees held joint meetings to manage the progress of reviews, in order to achieve the target review times specified in the Mid-term Plan. In the meetings, the committee members shared information regarding the overall review status for new drugs and associated issues including GCP and GMP inspections, discussed measures to address challenges and future approaches, and checked the progress of reviews for new drugs and other products. (11 meetings held in FY 2016.)

At these joint meetings, (1) the PMDA executives, the Director of the Center for Product Evaluation, and the Associate Center Director provided necessary guidance after reviewing reports from the office directors of review divisions, and (2) each review segment was notified of the content of discussion regarding measures to address issues associated with the products that had required 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.
- The Investigational Committee on Medically Necessary Unapproved Drugs and Off-Label Use Drugs (chaired by Dr. Tomomitsu Hotta, Honorary President of National Cancer Center) was established in the MHLW in February 2010, and since then has been active. The purpose of committee is to request that pharmaceutical companies develop drugs and indications that have been approved in Europe and the U.S. but not approved in Japan. In FY 2016, the committee convened four times. PMDA continuously supports the 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 collected information on the approval status at the FDA and EMA, gathered and organized evidence information etc., and 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 the FDA or EMA in or after April 2009, 123 (FDA) and 91 (EMA) have not been approved in Japan as of March 2017. 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 2016.

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.
- In FY 2016, 119 products were subjected to re-examination.
- The target median review time for re-examination applications filed in or after FY 2014, is 18 months (to be achieved by FY 2018). In FY 2016, re-examination result notifications were issued for 101 products, with the median total review time being 17.1 months.

Number of Re-examinations/Re-evaluations Conducted

		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Products undergoing re-examination		50	121	86	114	119
Products undergoing re-evaluation	Efficacy re-evaluation	0	0	139	19	0
	Quality re-evaluation	0	0	0	0	0

Note: The figures represent the number of products for which a notification of re-examination/re-evaluation results was issued in respective fiscal year.

g. Development of the Japanese Pharmacopoeia draft

1) Development of the Japanese Pharmacopoeia draft

- In FY 2016, the Japanese Pharmacopoeia (JP) Draft Committee held 90 meetings. Subsequently, PMDA published on its website a draft of Supplement 1 to the Japanese Pharmacopoeia 17th edition to seek public comments: 127 official monographs (23 new articles, 87 amendments, 17 deletions), 18 general tests and general information (5 new tests, 13 amendments), 10 ultraviolet-visible reference spectra (5 new tests, 5 deletions), 10 infrared reference spectra (5 new tests, 5 deletions), and partial amendment to other general rules for preparations. Supplement 1 will be announced in the autumn of 2017.

  PMDA also published on its website a draft of Supplement 2 to the Japanese Pharmacopoeia 17th edition to seek public comments: 8 official monographs (6 new articles, 2 amendments), 1 general information (1 new information), and 1 infrared reference spectra (1 new test). Supplement 2 will be announced in the spring of 2019.

  The table below shows the number of drafts of official monographs reported to MHLW.

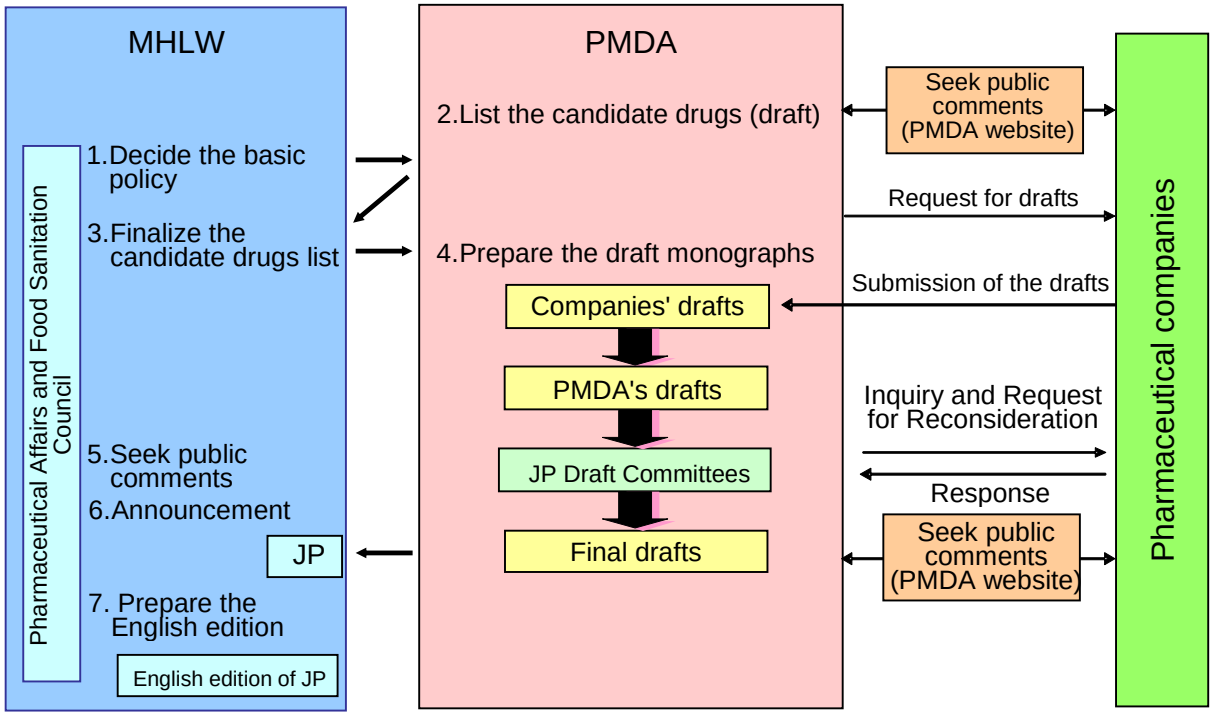
Month and year reported	Nov. 2008	Mar. 2009	Aug. 2009	Aug. 2010	Mar. 2012	Jan. 2013	Sep. 2013	Jul. 2015	Mar. 2017
New monographs	1	106	-	106	77	0	60	76	32
Amendments	1	122	2	330	176	1	172	471	114

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	FY 2006 Mar.	FY 2007 Sep.	FY 2009 Mar.	FY 2009 Sep.	FY 2010 Jul.	FY 2011 Mar.	FY 2012 Sep.	FY 2014 May	FY 2014 Feb.	FY 2016 Mar.
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

Flow of Revision of Japanese Pharmacopoeia



- The period for seeking public comments on official monographs was extended from one month to three months from December 2016, in order receive a broader range of comments on the Japanese Pharmacopoeia page on the PMDA website. Also, PMDA sought public comments in English

regarding all new official monographs in the draft of Supplement 1 to the Japanese Pharmacopoeia 17th edition (to be announced in autumn 2017).

2) Issuance of notifications, etc.

- PMDA developed a draft basic policy for preparation of the Japanese Pharmacopoeia 18th edition and reported it to the MHLW. This policy was published as a PSEHB/PED Administrative Notice dated October 19, 2016, by the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW.
- PMDA developed a guideline for preparation of the draft Japanese Pharmacopoeia 18th edition, and issued it as a notification by the Director of the Office of Standards and Guidelines Development, PMDA (PMDA/OSGD Notification No. 0118001 dated January 18, 2017).
- PMDA held a total of 6 Expert Discussion meetings on drug names and determined how to handle 75 Japanese Accepted Names (JAN). In FY 2016, PMDA received new JAN applications/notifications for 51 products and made efforts to steadily process them in order to reduce unprocessed applications/notifications.

3) Transmission of information on the Japanese Pharmacopoeia page of the PMDA website

- PMDA provided information such as the status of seeking public comments on the Pharmacopoeia and information related to the international harmonization of the Pharmacopoeia.
- Under the initiative of the WHO, PMDA participated in the development of a guideline for preparation of pharmacopoeia (Good Pharmacopoeial Practices). The guideline was posted on the website of the international harmonization of the Pharmacopoeia. Further, the PDG harmonized document (cover sheet) was posted on the website to disclose the handling status of the PDG harmonized document in the Japanese Pharmacopoeia.

4) Approaches to increased efficiency of operations

- The secretariat of the JP Draft Committee prepared JP drafts and proposed issues to be discussed before the meetings of the Chemicals Subcommittee and other subcommittees. In this way, the secretariat led and streamlined operations of the JP Draft Committee.
- The Office of Generic Drugs in PMDA and the Pharmaceutical Evaluation Division in MHLW held monthly meetings to share information before developing the drafts of the Japanese Pharmacopoeia, in order to ensure the appropriate use of the Japanese Pharmacopoeia.

h. Implementation of the master file workshop

- A workshop on the master file system was held for drug substance manufacturers, in-country representatives, MAHs, etc. The purpose of the workshop was to encourage manufactures etc. to use the system, thereby reducing delays in approval reviews and minimizing inadequacies in post-approval management. The participants were informed of recent instructions by PMDA regarding the system. PMDA also offered consultations by facsimile at the request of in-country representatives and published reference cases on the PMDA website.

(ii) Introduction of new review systems

a. Implementation of prior assessment consultations

- To 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 2016, 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 1: 1 product (number of consultation categories, 4)

  Oncology drugs: 1 product (number of consultation categories, 2)

  Bio-CMC: 1 product (number of consultation categories, 1) (*7 out of 13 cases handled)

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

- PMDA developed the Electronic Application Data System (development period: September 2014 - June 2016). The system accepts electronic submission of application data, stores the submitted electronic data, conducts statistical analyses, and performs other functions. On October 01, 2016, PMDA started to accept electronic submission of clinical study data (hereinafter referred to as “electronic application data”) through the system, receiving data for 24 products.
- On July 07, 2016, PMDA issued an Administrative Notice that provides the launch date of the Electronic Application Data System and other information. On July 14, 2016, PMDA held a briefing to ensure that persons who actually use the system in related industries are familiar with the details of the system, and with points to note when submitting electronic application data.
- PMDA continued to exchange opinions with related industries regarding various issues on electronic submission of application data. The agency provided assistance to MHLW in preparing “Partial Revision of ‘Handling of Electronic Common Technical Document Specification’” (PSEHB/PED Notification No. 0824-3 dated August 24, 2016), using knowledge acquired through discussions with overseas regulatory authorities. Partial revisions were made to “Technical Conformance Guide on Electronic Study Data Submissions” (PMDA/AREDPG Notification No. 0427001 dated April 27, 2015, by the Director of the Advanced Review with Electronic Data Promotion Group, PMDA). In addition, PMDA periodically revises “FAQ about Electronic Application Data” posted on its website.
- On August 31 and September 01, 2016, PMDA held workshops for persons who actually use the Electronic Application Data System in related industries, to inform them of the technical details of the system. On February 28, 2017, the agency held a briefing to share experiences gained after starting to accept electronic submission, to call attention to the points to note when submitting electronic application data, and to provide other information. On October 01, 2016, PMDA started to accept electronic application data, receiving data for 24 products.
- PMDA began to offer “Consultation for electronic study data submission” on May 15, 2015. The purpose of this consultation is to discuss issues associated with electronic submission before each individual product is filed for approval, to streamline the preparation of application data, and to accelerate the review process after submission. In FY 2016, PMDA provided 55 consultations.

Number of consultation for electronic study data submission

	FY 2015	FY 2016
Number of requests	13	62
Conducted	11	55

Additionally, to improve the quality of reviews and consultations, PMDA carried forward discussions of a new review process that reflected the results of the introduced pilot programs. PMDA also launched case study meetings about modeling & simulation. In the meetings, PMDA reviewers seek advice on how to examine data (submitted for approval or consultations) that have been organized using advanced analytical methods such as modeling & simulation.

- Relevant PMDA staff members were encouraged to participate in both internal and external workshops so that they can broaden their knowledge of electronic application data and improve their skills in using software.
- PMDA improved its systems to prepare for using CDISC standards for electronic submission.

(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 following tables below the status of reviews of new drugs in FY 2016 (excluding applications of drug products* that are reviewed by PMDA and approved only through the administrative process at MHLW):

* 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, as designated by the Minister of Health, Labour and Welfare)

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	60	70
Total review time [months] (Reference, 80th percentile) [months]	6.1 (9.0)	7.2 (9.1)	8.8 (9.2)	8.7 (9.5)	8.8 (9.2)
Number of approved applications	53	42	44	37	38

Reference

Regulatory review time [months]	3.8	3.6	4.0	4.0	4.0
Applicant's time [months]	1.5	3.8	5.0	4.9	5.3

Note 1: Products submitted in or after April 2004 are covered. The number of approved applications is based on active ingredients. For details, refer to the list of approved products included in "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 among the priority review products.

Note 3: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

Reference: Review times for new drugs (priority review products) excluding public knowledge-based applications for unapproved drugs

Fiscal Year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	60	70
Total review time [months] (Reference, 80th percentile) [months]	9.0 (10.0)	8.0 (9.9)	8.9 (9.2)	8.8 (9.8)	8.8 (9.3)
Regulatory review time [months]	3.4	3.4	3.8	4.0	3.9
Applicant's time [months]	4.6	4.1	5.2	5.2	5.5
Number of approved applications	25	31	37	33	32

- 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 2016, 38 priority review products (including 6 public knowledge-based applications for the "Study Group on Unapproved and Off-label Drugs of High Medical Need") were approved.
- In FY 2016, 4 applications requesting priority reviews were submitted for drugs regarded as having particularly high medical needs. In FY 2016, 5 applications were judged as "applicable" and no applications were determined to be "not applicable."
- The total review time (70th percentile) for priority review products approved in FY 2016 was 8.8 months, achieving the target review time.

  The priority review products accounted for 34% of products approved in FY 2016, showing an increase from 32% in FY 2015.

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	70	70
Total review time [months] (Reference, 80th percentile) [months]	10.3 (11.9)	11.3 (12.3)	11.9 (12.3)	11.3 (11.7)	11.6 (12.0)
Number of approved applications	81	96	73	79	74

Reference

Regulatory review time [months]	5.7	6.7	6.8	7.3	7.3
Applicant's time [months]	4.2	4.6	5.4	5.8	6.0

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

Note 2: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

- The total review time for standard review products approved in FY 2016 was 11.6 months, achieving the target review time.
- The number of applications under review at the end of FY 2016 was 87 (including 17 applications for orphan drugs and 2 public knowledge-based applications for unapproved drugs).

Review Status of New Drugs by Fiscal Year of Application

New drugs (FY of submission)	Applied	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	0	5	0
FY 2013	123	118	0	4	1
FY 2014	128	118 (2)	0	9 (3)	1 [-5]
FY 2015	125	115 (86)	0	4 (1)	6 [-89]
FY 2016	102	24 (24)	0	1 (1)	77 [+77]
Total	1,529	1,315 (112)	1	126 (5)	87 [-17]

Note 1: The figures in parentheses in "Approved" and "Withdrawn" represent the number of applications processed in FY 2016 (included in figures to the left).

Note 2: The figures in brackets represent differences from the status reported in FY 2015.

(iv) Promotion of global clinical trials

- In order to reduce 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 645 clinical trial notifications submitted in FY 2016, 240 were for global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

Fiscal Year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of notifications	138	173	181	276	240

- PMDA intends to take an active approach for global clinical trials. In FY 2016, PMDA carried out 73 consultations on global clinical trials for drugs with new active ingredients, meeting all requests for consultations.

Number of Consultations on Global Clinical Trials with New Active Ingredients

Fiscal Year	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of consultations	64	59	67	66	73

- 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 advanced by MHLW. Specifically, PMDA acted as "Roadmap Champion" to ensure the smooth progress of 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). In addition, PMDA has served as the co-chair of APEC-LSIF-RHSC since FY2015 and lead discussions.

(v) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- In accordance with the start of the SAKIGAKE designation system, priority consultation service began to cover SAKIGAKE designation drugs in FY 2015, in addition to orphan drugs. In FY 2016, PMDA handled those drugs in a similar manner.

b. Acceleration of the procedure for clinical trial consultations

- To expedite clinical trial consultations, PMDA streamlined the procedure by which applicants request consultations and PMDA receives such requests. The revised procedures apply to consultation requests submitted during or after October 2010. PMDA has consistently maintained its target period from request submission to consultation of approximately 2 months.

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

Number of Consultations

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	387	354	411	371	422
Withdrawn	20	30	38	33	61

Number of Prior Assessment Consultations for Drugs

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	19	32	32	1	7
Withdrawn	0	0	0	0	0

Number of Consultations on Drug Product Eligibility for Priority Review

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	7	10	6	7	5
Withdrawn	0	0	0	0	0

Note 1:Prior assessment consultations for drugs have been conducted since FY 2009. Consultations on drug product eligibility for priority review 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 2016, PMDA conducted 422 consultations (including 61 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. When a consultation cannot be scheduled for a desired month, the consultation is scheduled within one month before or after that month. In FY 2016, PMDA provided 410 consultations (61 withdrawals), responding to all requests for clinical trial consultation.
- 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 2016, the target was achieved in 407 of 410 consultations (99.3%).
- 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 2016

Review category	Results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs etc.)	7	1	4	5	4	9	8	6	4	3	6	7	64
Category 6-2 (Hormone drugs)	1	0	3	4	1	4	1	2	5	0	1	3	25
Category 2 (Cardiovascular drugs)	3	2	1	1	2	2	3	3	8	1	2	0	28
Category 5 (Drugs for the urogenital system etc.)	0	0	2	1	1	2	2	2	1	2	1	2	16
Radiopharmaceuticals	0	0	0	0	0	0	0	0	0	1	0	0	1
In vivo diagnostics	0	0	0	0	0	0	0	1	0	1	1	2	5
Category 3-1 (Central nervous system drugs etc.)	1	3	2	4	1	3	2	4	7	6	4	4	41
Category 3-2 (Anesthetic drugs etc.)	1	1	0	1	0	2	1	2	4	0	4	0	16
Category 4 (Antibacterial agents etc.)	2	0	3	1	5	3	2	1	1	5	1	0	24
Category 6-1 (Respiratory tract drugs etc.)	2	2	10	4	3	5	6	3	4	2	5	4	50
AIDS drugs	0	0	1	0	0	0	1	0	0	0	0	0	2
Oncology drugs	9	3	9	11	4	3	6	7	6	4	5	9	76
Bio-CMC	1	1	1	5	8	2	3	4	5	0	1	2	33
Vaccines	6	2	1	2	1	0	0	5	1	2	0	2	22
Blood products	5	3	2	1	0	0	3	1	0	0	1	1	17
Generic drugs	0	0	0	0	0	0	0	0	1	1	0	0	2
[Re-listed] Prior assessment	0	0	0	2	0	0	4	1	0	0	0	0	7
[Re-listed] Drug product eligibility for priority review	0	0	0	2	0	0	0	0	1	1	0	1	5
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	38	18	39	40	30	35	38	41	47	28	32	36	422
Withdrawal	1	7	4	2	3	7	4	7	4	5	6	11	61
Grand Total	39	25	43	42	33	42	42	48	51	33	38	47	483

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 related industries on clinical trial consultation services. As a result, in July 2016, PMDA began offering “Consultations on re-examination compliance assessment for drugs,” to assess the reliability of re-examination application data before submission of re-examination application. In August 2016, PMDA started to offer “Consultations on compliance for materials of regenerative medical products,” to provide advice or instructions regarding the eligibility of materials containing human- or animal-derived ingredients used to

manufacture regenerative medical products (i.e. materials not included in the finished products, such as culture media) from the viewpoint of safety of viruses, prions etc.

(vi) Promotion of evaluation of new technologies

a. Utilization of external experts

- As PMDA is required to enhance the expertise at its disposal in connection with its consultation and review activities, particularly in the fields of the latest technologies such as biotechnology and genomics, PMDA has continued to contract with external experts to serve as expert advisors to PMDA who will provide opinions on scientifically important matters at Expert Discussions in connection with product reviews and post-marketing safety measures.

  (As of March 31, 2017, the number of commissioned experts was 1,347 including external experts commissioned for issues relating to safety measures)

- In FY 2016, 191 Expert Discussions were conducted (154 through document-based discussions; 37 through meetings).

- PMDA utilized external experts in Expert Discussions for regulatory reviews and clinical trial consultations for biologics and regenerative medical products. PMDA also continued to exchange information regarding both biologics and regenerative medical products with overseas regulatory authorities including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) via teleconference, etc.

- In anticipation of the development of advanced drugs using new scientific technologies such as induced pluripotent stem cells (iPS cells), PMDA accumulated current knowledge by acting as a research collaborator in the “Research on Development of Next-generation Toxicity/Safety Evaluation Test System for Drugs Utilizing Human iPS Cell Differentiation Technology & International Standardization” study, a regulatory harmonization research initiative implemented by the Japan Agency for Medical Research and Development (AMED). In addition, PMDA gathered information concerning overseas studies of safety evaluation systems using iPS cells and other technologies by participating in meetings and teleconferences, such as the Steering Team of the Comprehensive *In Vitro* Proarrhythmia Assay (CiPA) Initiative.

b. Support for the development of national guidelines

- The Companion Diagnostics Working Group (within the Projects Across Multi-Offices for Standard Development) provided assistance to MHLW in preparing the following notification and administrative notice:

  (1) “Legislation Notice to Applicants for Marketing Authorization of DNA Sequencers and Related Products Utilized for Genetic Testing System” (PSEHB Notification No. 0428-1 dated April 28, 2016, issued jointly by the Counsellor of Minister's Secretariat, MHLW and the Director of Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

  (2) “Q&A for Applicants for Marketing Authorization to Handle DNA Sequencers and Related Products Utilized for Genetic Testing System” (Administrative Notice dated January 26, 2017, issued jointly by the Medical Device Evaluation Division and the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

- In addition to the above, MHLW issued 4 notifications etc. in FY 2016 with the cooperation of relevant review categories or offices in PMDA.

- In line with the initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products, in FY 2016, PMDA provided assistance in the preparation of guidelines for development and evaluation methods, issued by research groups for development/research of seed-stage resources and for development/evaluation of drugs. Specifically, the research groups in the following institutions received assistance from PMDA.
- Hokkaido University (cancers, nanotechnology), Tohoku University (pharmacogenomics), The University of Tokyo (Alzheimer's disease), National Cancer Center (malignant tumors, personalized medicine, molecular imaging), Nagoya City University (malignant tumors, personalized medicine), Kyoto University (Alzheimer's disease), Osaka University (nucleic acid medicine)

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
No. of preliminary reviews for Type 1 Use	0	0	3	2	3
Median review time [months]	-	-	0.8	0.9	2.9
No. of preliminary reviews for Type 2 Use	21	24	25	21	23
Median review time [months]	1.2	0.9	1.3	1.0	1.3

Note: "Type 1 Use" refers to cases where no measures are taken to prevent the release to the environment.
"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 2016 is shown in the table below.
- In FY 2016, PMDA provided 39 on-site introductory consultations in various prefectures throughout Japan, including Fukushima, Toyama, Aichi, Tottori, Hiroshima, and Fukuoka prefectures.
- Introductory consultations and pre-consultation meetings were also conducted at PMDA’s Kansai Branch Office. (The Kansai Branch Office was established in October 2013.)
- Since November 2014, PMDA has conducted pilot consultations concerning the product development process (roadmap) and investigator-initiated confirmatory clinical trial protocols. The purpose of the consultations is to promote the practical application of seed-stage research products originating in Japan.
- In October 2015, PMDA launched the Pharmaceutical Affairs Consultation on R&D Strategy for Medical Devices in the Special Zones, in accordance with the “Japan Revitalization Strategy, revised in 2015” (adopted by the Cabinet on June 30, 2015). This consultation service offers advice regarding the development of innovative medical devices in core clinical trial hospitals located in

the National Strategic Special Zones. The consultation service includes “Pre-consultation in Special Zones” and “Follow-up consultation in Special Zones,” in which PMDA staff members (acting as concierges) provide advice on development progress management. In FY 2016, PMDA conducted 9 Pre-consultations in Special Zones.

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	FY 2016	Total
Introductory consultations (Number of these consultations conducted at the Kansai branch[2])	118	302	237 (20)	271 (63)	221 (56)	190 (63)	1,339 (202)
Pre-consultations[3] (Number of these consultations conducted at the Kansai branch[2])	153	254	346 (26)	325 (57)	412 (60)	397 (53)	1,887 (196)

Face-to-face consultations on:	FY 2011[1]	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
Drugs	20	28	66	48	58	40	260
Medical devices	6	5	38	16	16	20	101
Regenerative medical products[4]	-	-	-	2	11	14	27
Quality and safety of regenerative medical products[5]	5 [7]	7 [13]	19 [32]	18 [44]	29 [55]	26 [64]	104 [215]
Development plan[6]	-	-	-	1	0	0	1
Total	31 [33]	40 [46]	123 [136]	85 [111]	114 [140]	100 [138]	493 [604]

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

Note 2: This consultation category was introduced on October 01, 2013.

Note 3: Pre-consultations include 10 pre-consultations 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 processes and the marketing approval documents of drugs

- Pharmaceutical companies conducted self-inspections of the manufacturing processes of their products, in accordance with “Implementation of Inspection on Consistency between Actual Manufacturing Processes and Marketing Approval Documents” (PSEHB/ELD Notification No. 0119-1 dated January 19, 2016, issued by the Director of Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). The inspections revealed differences between actual manufacturing processes and descriptions contained in approval application materials for 22,297 products in 479 companies (according to the MHLW press release

dated June 01, 2016). MHLW issued a notification that describes the procedure for resolving the differences: “Procedure after Inspection on Consistency between Actual Manufacturing Processes and Marketing Approval Documents” (PSEHB/ELD Notification No. 0212-4 dated February 12, 2016). In accordance with this notification, PMDA accepted Description Update Notifications from pharmaceutical companies.

(viii) Cooperation in the development of proper use guidelines

- PMDA provided assistance to MHLW in (1) developing the Optimal Clinical Use Guidelines of innovative drugs (developed on a trial basis) and (2) designing the conditional early approval system for new drugs, published by MHLW in January 2017.

Drug name	Indication	Date of issue
Opdivo Intravenous Infusion 20 mg Opdivo Intravenous Infusion 100 mg	Unresectable, advanced or recurrent non-small cell lung cancer	Feb. 14, 2017
	Unresectable malignant melanoma	Feb. 14, 2017
	Recurrent or distant metastatic head and neck cancer	Mar. 28, 2017
	Unresectable or metastatic renal cell carcinoma	Apr. 18, 2017
	Relapsed or refractory classical Hodgkin lymphoma	Apr. 18, 2017
Keytruda Injection 20 mg Keytruda Injection 100 mg	PD-L1-positive, unresectable, advanced or recurrent non-small cell lung cancer	Feb. 14, 2017
	Unresectable melanoma	Feb. 14, 2017
Repatha SC Injection 140 mg Syringe Repatha SC Injection 140 mg Pen	Familial hypercholesteremia, hypercholesteremia The product should be used only in patients with high cardiovascular risk who have had an inadequate response to HMG-CoA reductase inhibitors.	Mar. 31, 2017
Praluent 75 mg Solution for Injection in Pre-filled Syringe Praluent 75 mg Solution for Injection in Pre-filled Pen Praluent 150 mg Solution for Injection in Pre-filled Syringe Praluent 150 mg Solution for Injection in Pre-filled Pen	Familial hypercholesteremia, hypercholesteremia The product should be used only in patients with high cardiovascular risk who have had an inadequate response to HMG-CoA reductase inhibitors.	Mar. 31, 2017

Generic drugs, etc.

- PMDA implemented or considered the following measures to accelerate reviews of generic drug products, etc.

(i) Appropriate and prompt reviews

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

a. Consultations and reviews based on medical care needs

- Members of PMDA's staff have participated in academic conferences and symposia held both in Japan and overseas, and have also exchanged opinions with healthcare professionals in order to better understand their needs. PMDA has also held consultations and conducted 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 the 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 CTD/eCTD for marketing applications, in order to increase the efficiency of review services. Where possible, companies submitted a trial version of CTD, for new applications filed in FY 2016. The companies submitting a trial version of CTD received individual feedback from PMDA regarding areas for improvement in CTD preparation. The submission of CTD will be mandatory, in principle, from March 2017, in accordance with the PSEHB/ELD Notification issued by MHLW on March 11, 2016. Accordingly, PMDA published an approval application checklist to ensure that new application data submitted in FY 2016 contain information equivalent to that of CTD.
- PMDA discussed the contents of the trial version of review reports to be prepared for new generic drugs, based on the opinions exchanged with stakeholders in FY 2016.
- PMDA discussed the development of a guidance concerning bioequivalence studies for drugs that cannot be evaluated based on the existing guidelines for bioequivalence studies. Accordingly, PMDA developed guidance materials concerning 2 basic concepts pertaining to bioequivalence studies of aqueous eye drops and powder inhalants. This guidance was published by MHLW (PSEHB/ELD Notification dated March 11, 2016). In FY 2016, PMDA discussed other dosage forms, such as suspension-type ophthalmic solutions and intranasal solutions.

(ii) Approaches to shorten review times

- PMDA established the following target regulatory review times for applications submitted on or after April 1, 2004 (and approved thereafter), and has made efforts to achieve these targets while asking for the cooperation of applicants.

- In order to carry out prompt and accurate reviews of generic drugs, PMDA performed its operations in accordance with its SOPs and its Procedures for the Review of Generic Prescription Drugs.

  Data detailing the rate of realization of the target review times were periodically collected and provided to reviewers in PMDA. The progress of operations was assessed at joint meetings of the Progress Management Committee for Reviews and Related Services and the Review Segment Committee for Progress Management.

- The approval status of generic drugs in FY 2016 is 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 [months]
New generic drugs	10

Results

	FY 2014	FY 2015	FY 2016
Approved products	1,325	635	731
Median regulatory review time [months]	6.1	8.2	8.2

Note: Products submitted for approval in or after April 2004 are covered.

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 [months]	15	14	13	12	10

Results

	FY 2014	FY 2015	FY 2016
Approved products	586	701	537
Median total review time [months]	15.5	13.0	11.7

Note: Products submitted for approval in or after April 2004 are covered.

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 time for the 50th percentile (median) of applications by FY 2018.

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

Results

		FY 2014	FY 2015	FY 2016
Change of test methods, etc.	Approved products	1,367	1,594	1,676
	Median total review time [months]	7.3	6.9	7.0
Expedited review	Approved products	168	305	248
	Median total review time [months]	4.0	4.8	4.3

Note: Products submitted for approval in or after April 2004 are covered.

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

Fiscal Year	Applied	Approved	Withdrawn, etc.	Under review
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	3,502	3,235	281	3,382
FY 2016	3,160	3,192	254	3,096

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 2016 was 8.2 months, achieving the target (10 months). For partial change approval applications of generic drugs, the median total review time for standard review products was 11.7 months, achieving the target (13 months). The median total review time for partial change applications (change of test methods etc.) was 7.0 months (target, 6 months) and that for partial change applications (expedited review) was 4.3 months (target, 3 months); PMDA will make every effort to achieve these targets by FY 2018 by taking measures such as improving the review system from the next fiscal year.

Document-based Compliance Assessments for Generic Drugs by Fiscal Year

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Generic drugs	1,188	1,086	1,080	1,045	870

- PMDA conducted 870 assessments of generic drug application data to examine whether the data comply with GLP, GCP, GPSP, and other standards. In the assessments, the application data were checked against raw data such as test records, laboratory notebook, and case report forms.

(iii) Efficient implementation of clinical trial consultations

- In January 2012, PMDA began providing the following clinical trial consultations for generic drugs on a pilot basis: "Quality consultation for generic drugs" and "Consultation on the bioequivalence of generic drugs." In FY 2016, 56 consultations were conducted. The applications for consultation have been increasing with the increasing recognition of the usefulness of clinical trial consultations in the development of generic drugs. PMDA adapted to this increase in consultation requests by improving its operations.

Number of Consultations for Generic Drugs

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	10	17	24	48	56
Withdrawn	0	1	1	8	4

Note: PMDA began providing consultations focusing on generic drug products in FY 2011.

Number of Consultations for Generic Drugs by Consultation Category in FY 2016

Consultation category	Conducted	Withdrawn
Consultations on bioequivalence of generic drugs	51	2
Quality consultations for generic drugs	5	2
Total	56	4

(iv) Assessment of consistency between actual manufacturing practices and descriptions contained in application materials of approved drug products

- 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

- Staff members with experience in conducting safety or compliance-related operations provided advice and guidance to other staff in accordance with the degree and nature of their expertise. 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. Also, PMDA issued a notification to ensure that document-based compliance assessments are conducted smoothly.

  PMDA's Office of OTC/Quasi-drugs performed toxicological and clinical reviews of new BTC/OCT drugs in close collaboration with other Offices while obtaining the advice of expert PMDA staff as necessary.

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

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

- PMDA made efforts to improve the quality of its 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

- In order to improve the efficiency of review, PMDA requested that applicants submit the "Checklist for application data for marketing approval of quasi-drugs, etc." on a trial basis for applications filed in FY 2016.

- PMDA supported MHLW in the process of the revision of Japanese Standards of Quasi-drug Ingredients and insecticide guidelines, by assisting MHLW in holding meetings of the Review Committee on Japanese Standards of Quasi-drug Ingredients and the Review Committee on Revision of Insecticide Guidelines. PMDA supported the holding of meetings of the "Quasi-drugs Guidance Review Committee," to encourage the use of alternative methods for animal experiments, promoted by the Japanese Center for the Validation of Alternative Methods (JaCVAM).

- 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 established target review times for applications for BTC, OTC, and quasi-drugs submitted on or after April 1, 2004, and has since conducted reviews to achieve these targets.

- In order to conduct prompt and accurate reviews of products in these categories, PMDA executed operations in accordance with its SOPs, the Procedures for Review of OTC Drugs, Procedures for Review of Insecticides/Rodenticides, and the Procedures for Review of Quasi-drugs. Each of these procedures specify the standard methods and protocols associated with each type of regulatory review.

  Data on the achievement of the target review times were periodically collected and provided to reviewers in PMDA. The progress of operations was assessed at joint meetings of the Progress Management Committee for Reviews and Related Services and the Review Segment Committee for Progress Management.

- At the Review Segment Committee for Progress Management and other occasions, PMDA clarified review schedule by presenting target times of initial inquiries, Expert Discussion, and Drug Committees, to contribute to progress management for novel BTC/OTC drugs. In addition, applicants delaying responding to initial inquiries from PMDA were instructed to report the reason for the delay and to answer the inquiries as quickly as possible. The Expert Discussion discussed 5 OTC ingredients (12 products), among which 2 new active ingredients (4 products) and 1 ingredient (4 products with a new dosage) were discussed and approved by the Drug Committee.
- Similarly to its handling of BTC and OTC drugs, PMDA clarified target processing times for applications for quasi-drugs (e.g., target times for the Cosmetics and Quasi-Drug Committees) to accelerate review process. The Expert Discussion discussed 5 new quasi-drugs, among which 2 quasi-drugs with a new active ingredient were discussed and approved by the Drug Committee.
- The approval status of BTC drugs, OTC drugs, and quasi-drugs in FY 2016 is 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 and OTC drugs	7 months

Results

BTC and OTC drugs	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Approved products	881	916	844	752	646
Median regulatory review time [months]	4.1	4.9	6.3	5.5	4.3

Note: Products submitted for approval in or after April 2004 are covered. The calculation excluded 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 [months]
Quasi-drugs	5.5 months

Results

Quasi-drugs	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Approved products	1,968	2,028	1,779	2,495	1,924
Median regulatory review time [months]	4.9	4.9	4.9	4.7	4.4

Note 1: Products submitted for approval in or after April 2004 are covered. The calculation excluded 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

Category	Fiscal Year	Applied	Approved	Withdrawn, etc.	Under review
BTC drugs OTC drugs	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	716	752	126	1,686
	FY 2016	700	646	115	1,625
Quasi-drugs	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
	FY 2016	2,062	1,924	137	2,190

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 times for approved products in FY 2016 were 4.3 months for BTC and OTC drugs (target, 7 months) and 4.4 months for quasi-drugs (target, 5.5 months). Target realization was achieved 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. In addition, pre-application consultations for OTC Switch drugs and consultations on key points of clinical trial protocols became fully available from May 2015. Based on discussions done at the "Review Committee on Diversion from Ethical to BTC/OTC" conducted at MHLW, PMDA will exchange opinions with the industry and discuss the establishment of a consultation system for such drugs in the future.

Consultations for OTC Drugs

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	4	21	21	15	23
Withdrawn	0	0	0	1	0

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2016

Consultation category	Conducted	Withdrawn
Pre-application consultation for OTC switch drugs	2	0
Consultation on key points of clinical trial protocols for OTC drugs	4	0
Consultation on appropriateness of development of new OTC drugs	17	0
Total	23	0

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

- In order to expand pre-application consultation services for quasi-drugs, PMDA exchanged views with concerned parties (e.g., the Japan Cosmetic Industry Association) regarding the development of new consultation services. Accordingly, in FY 2017 PMDA will launch, on a trial basis, new types of consultations on the development of quasi-drugs (i.e., “human study plan confirmation consultation,” “new inactive ingredient development consultations”).

(iv) Assessment of consistency between actual manufacturing practices and descriptions contained in application materials of approved drug products

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

Medical devices

- Various measures were implemented or considered to accelerate reviews of new medical devices in following with the "Cooperation Plan to Accelerate Reviews of Medical Devices" (March 2014) (successor to the "Action Program to Accelerate Reviews of Medical Devices" [December 2008]), the "Japan Revitalization Strategy," and the "Healthcare and Medical Strategy."

(i) Appropriate and prompt reviews

a. Clinical trial consultation and review structures

- To enhance its review system to become capable of achieving its new targets, PMDA increased the number of reviewers allocated to the categories receiving large numbers of medical device application filings where delays in the review process were most likely.
- Reviews of new medical devices and improved medical devices were conducted by review teams consisting of experts holding 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.

  Review teams are typically comprised of a team leader and reviewers specializing in biological, physicochemical, electrical safety, and clinical evaluations.

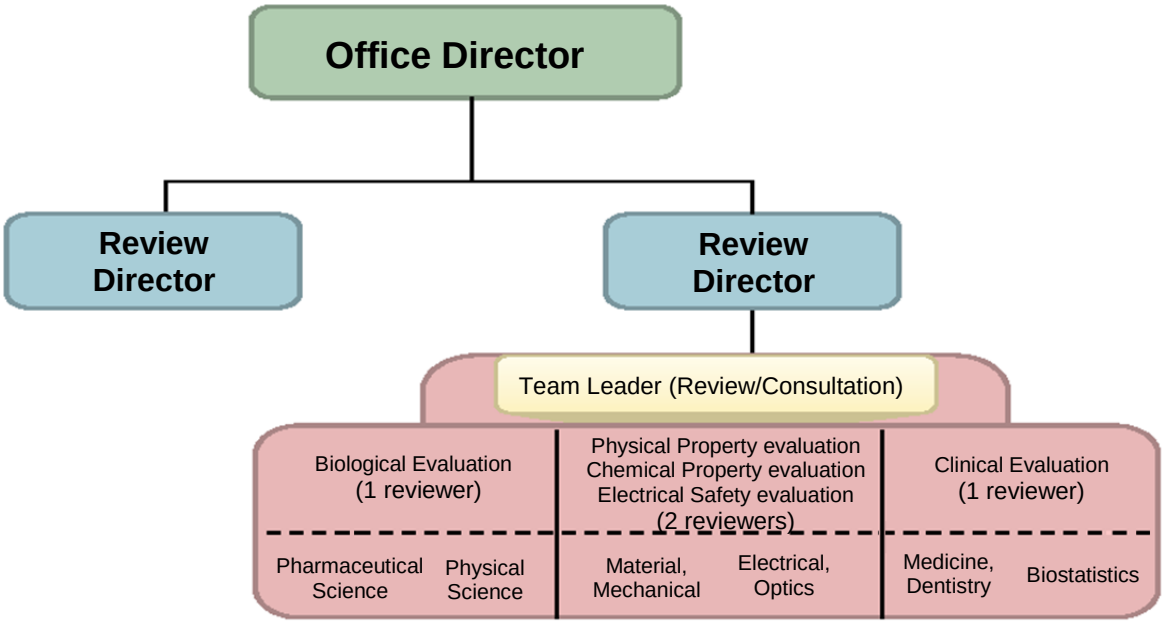
Note:

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 (hereinafter, the "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 PMD 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 PMD 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 PMD Act)*

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 a more smooth and flexible review/consultation system, PMDA has restructured these review categories into new review areas (see tables below) since October 1, 2015, while maintaining the 3-track system for new, improved, and generic devices.

  Through the restructuring of review categories, PMDA has been making efforts to share information, to standardize the level of reviews, and to harmonize reviewers' awareness between the new/improved device review teams and the generic devices review team. Further, (a) the number of reviewers has increased for each review category, (b) individual reviewers have improved their ability to conduct high-level reviews, and (c) relevant rules have been established to enhance the environment for review services. As a result, the review teams were able to handle a sudden increase in applications/consultations, leading to a reduction in the review time as compared with FY 2015.

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 on April 1, 2015.

Since 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 • 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
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 for gastrointestinal and urinary systems, obstetrics and gynecology
	Dentistry and Oral Medicine	Mainly for dentistry
Office of Medical Devices III	Ophthalmology and Otorhinolaryngology	Mainly for 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 (viii) Biological device team, Office of Cellular and Tissue-based Products (Evaluation of virus safety of biological products)		

- Expert Discussions were held as necessary to support reviews performed by PMDA's review teams with opinions from external experts. In addition, innovative medical devices and other products, were discussed at the Committee on Medical Devices and *In-vitro* Diagnostics convened by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) at MHLW.

Review Performance for FY 2016 (medical devices and* in vitro *diagnostics)

(1) Number of Expert Discussions conducted: 88 (71 document-based discussions, 17 meetings)
(2) Applications deliberated at the Committees on Medical Devices and *in vitro* Diagnostics (under PAFSC): 11
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 297 (269 medical devices, 28 *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 2016, PMDA promoted the system based on the experiences in the previous fiscal year.

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

- The “Progress Management Committee for Reviews and Related Services” is intended to ensure that PMDA executives have an accurate understanding of the progress status of reviews and related services and improve the progress as needed. The "Review Segment Committee for Progress Management" is headed by the Director of the Center for Product Evaluation. The two committees held joint meetings, in order to manage the progress of reviews to achieve the target review times specified in the Mid-term Plan. In the meetings, the committee members shared information regarding the progress of operations, and discussed how to address issues associated with new medical device reviews, by assessing relevant information comprehensively.

  At these joint meetings, necessary guidance was provided on an ongoing basis by the Director of the Center for Product Evaluation and the Associate Center Director 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 extended review.

- To accelerate review times, timelines were managed strictly in accordance with the "On the Standard Review Timeline for New Medical Device Applications" (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 Device Applications (with Clinical Data)" (PFSD/ELD/OMDE Notification No. 0328-4 dated March 28, 2014), and "On the Standard Review Timeline for Improved Medical Device (without Clinical Data) and Generic Medical Device Applications" (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 3 documents concerning basic points to consider related to its review processes: "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)," 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 October 2006, MHLW established the “Study Group on the Early Introduction of Medical Devices etc., with High Medical Need (chaired by Dr. Soichiro Kitamura, then President-Emeritus of the National Cerebral and Cardiovascular Center),” to encourage medical device manufacturers to develop medical devices that had already obtained approval in Europe and the U.S. but not in Japan. Under this Study Group, a working group was established to discuss and evaluate individual issues. The Study Group and the working group have held active discussions. In 2016, the Study Group convened twice and the working group convened five times. PMDA supported the operation of the Study Group. As a result of the discussions by the Study Group, PMDA conducted clinical trial consultations and product reviews, leading to the approval of one medical device in FY 2016. The meetings of the working group were held at PMDA, which served as the secretariat, engaging in various activities, such as preparing documents, communicating with the working group members, and seeking the opinions of academic societies and companies.

  In 2015, the following changes were introduced to this scheme, to further promote the introduction of medical devices with high medical needs into Japanese clinical practice:

  (1) Under this scheme, MHLW had accepted the request for the development of “medical devices, etc. approved in the U.S. and Europe but not in Japan.” In addition to this, MHLW began to accept the request for the development of “medical devices, etc. that have not been approved in the US and Europe but meet certain requirements and are intended to be marketed in Japan and overseas.”

  (2) The working group had previously held 2 meetings, which was changed to 1 meeting. Small working groups were established for individual clinical areas.

  (3) To promote the development of devices designated as having “high medical need,” the development progress of such devices is monitored and reported to the Study Group.

In the previous selection scheme, the required selection time (time from a meeting of the working group to selection at the Study Group) was 8 months at minimum, but in the current selection scheme, the required time is 3 months at minimum.

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 PMD Act, PMDA worked on the efficient operation and implementation of the use-results evaluation system for medical devices (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, 26 medical devices (including 8 medical devices selected for use-results survey) were approved in FY 2016.

- 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, 9 medical devices subject to re-examination were processed in FY 2016.

(ii) Introduction of new review systems

a. 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 26 of 28 products approved in FY 2016 was not more than 2 months, excluding the period for GCP/GLP inspections.

b. 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 2016.

  The table below shows the number of approval or certification standards reported to MHLW in FY 2016 to be established or revised. Approval standards included 1 established standard and 1 revised standard. Certification standards included 156 revised standards for designated controlled medical devices, 1 established standard for designated specially controlled medical devices (medical devices of Class III risk level), and 1 established standard for review guidelines.

FY (for reporting)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
Approval standards	13	5	2	6	6	5	4	0	3	2	46
Certification standards (designated controlled medical devices)	14	86	64	294	84	67	82	129	99	156	1075
Certification standards (designated specially controlled medical devices)	-	-	-	-	-	-	-	3	7	1	11
Review guidelines	1	2	6	0	0	0	0	0	0	1	10

The following table shows the number of standards established by MHLW in FY 2016 based on the reports from PMDA. One certification standard was established for designated specially controlled medical devices (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	FY 2016	Total
Approval standards	0	17	8	10	-2※1	5	3	0	0	4	0	-1*1	0	44
Certification standards (designated controlled medical devices)	363	9	24	0	17	68	274	67	2	3	109	0	-1*2	935
Certification standards (designated specially controlled medical devices)	-	-	-	-	-	-	-	-	-	-	3	7	1	11
Review guidelines	0	0	0	0	3	1	4	0	0	0	0	0	0	8

*Note *1 Two established approval standards were switched to certification standards in FY 2008 and another in FY 2015, resulting in a negative number.*

*Note *2 In FY 2016, one established certification standard was integrated with certification standards for designated specially controlled medical devices, resulting in a negative number.*

List of Certification Standards for Medical Devices (FY 2016)

Established: Certification standards,1; Approval standards,0; Review guidelines, 0	
Date of issue	Name of standard
MHLW Ministerial Announcement No. 159 March 31, 2017	Certification standards for anesthetic vaporizers

- The PMDA web page concerning the information service on medical device standards provides current information on certification and approval standards as well as links to their components, including: JIS, ISO/IEC, MHLW Notifications, Japanese Medical Device Nomenclature (JMDN), etc. In FY 2016, as part of the Medical Device International Standardization Strategy Promotion Project, PMDA published information in English, including English translations of certification standards for device products designated as specially controlled medical devices, in order to further enhance the contents of its English website, as it has done in previous years. PMDA also added English translations of approximately 4,100 definitions of term names, and 8 review guidelines (previously available in Japanese only) to its English website. The information on the web page is updated periodically, in principle 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 addressed procedures for changing raw materials for 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 Medical Product Evaluation], MHLW, dated November 20, 2014), "Handling of Applications for Dental Implants" (PFSB/ELD/OMDE Notification No. 0713-1, dated July 13, 2012).

c. Equivalence review of generic medical devices

- PMDA conducted equivalence reviews for generic medical devices filed in FY 2016 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 Medical 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 strove to identify and summarize problems that needed to be resolved.

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

- PMDA has made every effort and sought the cooperation of applicants, to achieve the review time targets (see "a" through "e" presented below) by FY 2018, for medical device applications submitted on or after April 1, 2004. The target percentile values are gradually increased.
- 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.

- Each review office introduced “team-based review” to the reviews of generic medical devices, as a result of the restructuring of PMDA’s organization in October 2015. Further, PMDA organized 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 device, 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.
- Harmonization by Doing (HBD) is a cooperative effort among the industries, the governments, and academia in Japan and the US. PMDA participated in HBD and discussed (a) the conduct of global clinical trials, (b) support for the development of medical devices, and (c) the utilization of post-marketing data. In FY 2016, a sub-working group (HBD for children) was established to support the development of pediatric devices lagging behind in their development in both Japan and the US. In February 2017, an HBD session on CRT (Cardiovascular Research Technologies) was held in Washington, D.C. In the session, pediatricians, related companies, and regulatory authorities in Japan and the US discussed (a) problems in the development of pediatric devices and (b) future action policies. In addition, as part of the HBD activities, PMDA participated in scientific sessions held in academic conferences such as CVIT (Japanese Association of Cardiovascular Intervention and Therapeutics) held in February 2015 in Tokyo, and TCT (Transcatheter Cardiovascular Therapeutics) held in October 2016 in Washington, D.C. In these sessions, the industries, the governments, and the academia discussed problems and solutions in the development of individual new medical devices, how to use post-marketing registries, and other issues.
- PMDA worked to achieve its target total review times through these measures. The status of reviews for medical devices in FY 2016 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	60	70
Total review time [months] (Reference, 80th percentile) [months]	9.3 (20.8)	9.0 (10.0)	8.8 (8.9)	7.9 (8.2)	8.0 (8.0)
Number of cases	5	14	5	8	1

Reference

Regulatory review time [months]	7.2	5.1	4.0	4.2	3.2
Applicant’s time [months]	3.4	3.5	3.3	3.8	4.8

Note 1: Applications submitted for approval in or after April 2004 are covered.

Note 2: The figures in “regulatory review time” and “applicant's time” represent their respective percentile values. The sum of “regulatory review time” and “applicant's time” may not equal “total review time.”

- 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 2018, 1 priority review product (new medical device) was approved.
- As for the approval status of priority review products in FY 2016, the total review time (70th percentile) was 8.0 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	60	70
Total review time [months] (Reference, 80th percentile) [months]	12.7 (15.5)	6.3 (14.8)	5.6 (10.6)	10.1 (11.9)	12.0 (14.0)
Number of cases	41	80	62	48	24

Reference

Regulatory review time [months]	*5.4*	*4.0*	*3.5*	*5.0*	*7.8*
Applicant's time [months]	*5.0*	*1.6*	*2.2*	*4.3*	*4.3*

Note 1: Applications submitted for approval in or after April 2004 are covered.

Note 2: The results in FY 2016 exclude standalone medical device software newly categorized as "medical devices" from November 25, 2014 (according to the PMD Act) that was submitted for approval during the transitional period (from November 25, 2014 to February 24, 2015).

Note 3: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

- As for the approval status of standard reviews for new medical devices in FY 2016, the total review time (70th percentile) was 12.0 months, and the achievement rate for the target total review time (14 months) was 79.2%, substantially higher than the target. In total, 24 applications were approved in FY 2016, and 22 applications were under review at the end of FY 2016.

Review Status of New Medical Devices by Fiscal Year of Submission

New medical devices (FY of submission)	Applied	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	26 (2)	2	0 [-2]
FY 2011	42	40	2	0
FY 2012	64	63	1 (1)	0 [-1]
FY 2013	72	72	0	0
FY 2014	99	93 (3)	4 (2)	2 [-5]
FY 2015	30	28 (11)	0	2 [-11]
FY 2016	30	11 (11)	1 (1)	18 [+18]
Total	676	529 (27)	125 (4)	22 [-1]

Note 1: The figures in "Applications" represent the number of applications for new medical devices.

Note 2: The figures in "Approved" include the number of approved improved medical devices.

Note 3: The figures in parentheses indicate applications processed in FY 2016 (included in values to the left).

Note 4: The figures in brackets indicate differences from FY 2015.

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	52	54	56
Total review time [months] (Reference, 60th percentile) [months]	17.3 (19.8)	11.6 (13.2)	9.9 (10.5)	11.0 (11.6)	10.0 (11.6)
Number of approved applications	44	63	35	53	43

Reference

Regulatory review time [months]	7.9	5.7	5.0	5.3	6.3
Applicant's time [months]	8.8	5.5	5.0	4.8	4.7

Note 1: Applications submitted for approval in or after April 2004 are covered.

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.

Note 3: The results in FY 2016 exclude devices to be used in combination with "new medical devices" that were submitted for approval around the same time.

Note 4: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

- As for the approval status of improved medical devices (with clinical data) in FY 2016, the total review time (56th percentile) was 10.0 months, and the achievement rate for the target total review time (10 months) was 58.1%, achieving the target. The number of approvals in FY 2016 was 43, 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 (with Clinical Data) by Fiscal Year of Submission

Improved medical devices (with clinical data) (FY of submission)	Applied	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	3 (1)	0 [-1]
FY 2013	46	42 (2)	4 (1)	0 [-3]
FY 2014	45	40 (4)	4 (2)	1 [-6]
FY 2015	27	24 (16)	2 (2)	1 [-18]
FY 2016	49	17 (17)	0	32 [32]
Total	303	249 (39)	20 (6)	34 [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: The figures in "Approved" include the number of approved products includes those approved under other application categories for medical devices.

Note 3: The figures in parentheses indicate applications processed in FY 2016 (included in values to the left).

Note 4: The figures in brackets indicate differences from FY 2015.

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	52	54	56
Total review time [months]	9.7	7.5	6.0	6.0	5.8
(Reference, 60th percentile) [months]	(11.1)	(9.2)	(7.4)	(7.0)	(5.9)
Number of approved applications	229	231	213	233	218

Reference

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

Note 1: Applications submitted for approval in or after April 2004 are covered.

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.

Note 3: The results in FY 2015 and FY 2016 exclude standalone medical device software newly categorized as "medical devices" from November 25, 2014 (according to the PMD Act) that was submitted for approval during the transitional period (from November 25, 2014 to February 24, 2015).

Note 4: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

- As for the approval status of improved medical devices (without clinical data) in FY 2016, the total review time (56th percentile) was 5.8 months, and the achievement rate for the target total review time (6 months) was 71.6%, achieving the target. The number of approved applications in FY 2016 was 218, showing a decrease 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 Submission

Improved medical devices (without clinical data) (FY of submission)	Applied	Approved	Withdrawn	Under review
FY 2009	137	122	15	0
FY 2010	165	141	24	0
FY 2011	176	160	16	0
FY 2012	210	198	11	1
FY 2013	190	177	12 (1)	1 [-1]
FY 2014	259 [-1]	215 (18)	4 (1)	40 [-20]
FY 2015	219	201 (105)	9 (4)	9 [-109]
FY 2016	217	97 (97)	3 (3)	117 [+117]
Total	1,573	1,311 (220)	94 (9)	168 [-13]

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 figures in "Approved" include the number of applications approved under other medical device categories.

Note 4: The figures in parentheses indicate applications processed in FY 2016 (included in values to the left).

Note 5: The figures in brackets indicate differences from FY 2015.

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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	52	54	56
Total review time [months]	4.0	3.9	3.9	4.4	3.5
(Reference, 60th percentile) [months]	(6.0)	(5.3)	(4.5)	(5.0)	(3.6)
Number of approved applications	1,216	958	920	868	825

Reference

Regulatory review time [months]	1.6	1.8	1.9	2.0	1.9
Applicant's time [months]	2.3	2.1	1.8	2.3	1.4

Note 1: Applications submitted for approval in or after April 2004 are covered.

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.

Note 3: The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

- As for the approval status of generic medical devices approved in FY 2016, the total review time (56th percentile) was 3.5 months, and the achievement rate for the target total review time (4 months) was 79.2%, which was lower than the target.

Review Status of Generic Medical Devices by Fiscal Year of Submission

Generic medical devices (FY of submission)	Applied	Approved	Withdrawn	Under review
FY 2009	1,126	1,038	88	0
FY 2010	1,020	919 (1)	100 (2)	1 [-3]
FY 2011	995	931	64	0
FY 2012	1,075	1,031 (1)	43 (2)	1 [-3]
FY 2013	921	879 (5)	24 (1)	18 [-6]
FY 2014	946 [-1]	895 (14)	44 (5)	7 [-20]
FY 2015	785 [-5]	751 (185)	20 (10)	14 [-200]
FY 2016	931	628 (628)	8 (8)	295 [+295]
Total	7,799	7,072 (834)	391 (28)	336 [+63]

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 cancelled application was deleted from the number of applications in FY 2016 and 5 cancelled applications were deleted from the number of applications in FY 2015.

Note 3: The figures in "Approved" include the number of applications approved under other medical device categories.

Note 4: The figures in parentheses indicate applications processed in FY 2016 (included in values to the left).

Note 5: The figures in brackets indicate differences from FY 2015.

(iv) Efficient conduct of clinical trial consultations

a. Conduct of priority consultations

- During FY 2016, there were no requests for designation for priority consultation or consultation on GLP/GCP compliance for priority consultation medical device products.

b. Implementation of clinical trial consultations and improvements to consultation service offerings

Number of Consultations

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	165	162	196	203	276
Withdrawn	3	11	11	4	7

Number of Prior Assessment Consultations for Medical Devices

	FY 2012	FY 2013	FY 2014
Conducted	3	1	3
Withdrawn	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 number of prior assessment consultations for medical devices was 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.

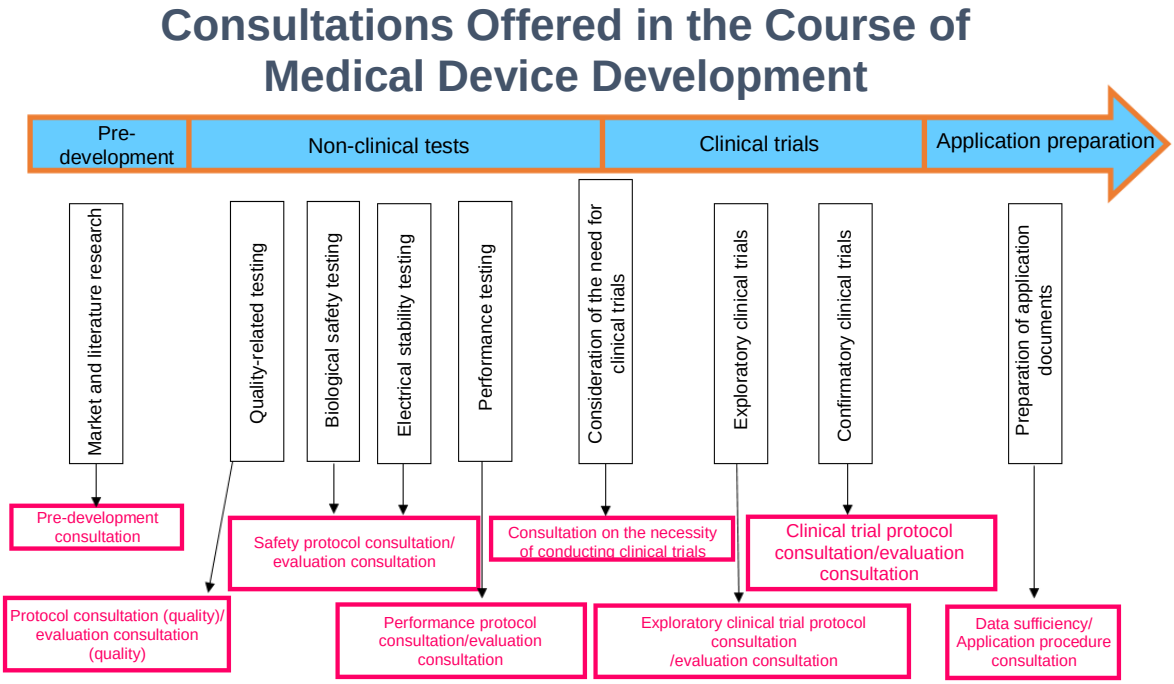
Number of Consultations for Medical Devices by Category in FY 2016

Consultation category*	Face-to-face consultations conducted	Withdrawn
Pre-development consultation for medical devices	16	0
Pre-development consultation for medical devices (preliminary consultation completed)	119	2
Consultation on necessity of clinical trials for medical devices	1	0
Consultation on necessity of clinical trials for medical devices (preliminary consultation completed)	3	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)	16	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)	1	0
Protocol consultation for medical devices (safety) (1 trial) (preliminary consultation completed)	2	0
Protocol consultation for medical devices (safety) (2 trials) (preliminary consultation completed)	1	0
Protocol consultation for medical devices (safety) (4 or more trials) (preliminary consultation completed)	2	0
Protocol consultation for medical devices (performance) (1 trial)	3	1
Protocol consultation for medical devices (performance) (1 trial) (preliminary consultation completed)	8	0
Protocol consultation for medical devices (performance) (2 trials) (preliminary consultation completed)	5	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)	5	0
Protocol consultation for medical devices (exploratory clinical trial) (preliminary consultation completed)	4	0
Protocol consultation for medical devices (clinical trial)	4	0
Protocol consultation for medical devices (clinical trial) (preliminary consultation completed)	31	0
Protocol consultation for medical devices (clinical trial) (additional consultation)	4	0
Safety evaluation consultation for medical devices (1 trial) (protocol not evaluated)	1	0
Safety evaluation consultation for medical devices (1 trial) (protocol not evaluated) (preliminary consultation completed)	1	0
Safety evaluation consultation for medical devices (2 trials) (protocol not evaluated)	1	0
Safety evaluation consultation for medical devices (2 trials) (protocol not evaluated) (preliminary consultation completed)	2	0
Safety evaluation consultation for medical devices (3 trials) (protocol not evaluated)	1	0
Safety evaluation consultation for medical devices (4 or more trials) (protocol not evaluated)	3	0
Safety evaluation consultation for medical devices (4 or more trials) (protocol not evaluated) (preliminary consultation completed)	4	0
Quality evaluation consultation for medical devices (protocol not evaluated)	2	0
Quality evaluation consultation for medical devices (protocol not evaluated) (preliminary consultation completed)	3	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)	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)	0	1
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)	4	0
Clinical trial evaluation consultation for medical devices (protocol not evaluated)	4	0
Clinical trial evaluation consultation for medical devices (protocol not evaluated) (preliminary consultation completed)	5	1
Clinical trial evaluation consultation for medical devices (preliminary consultation completed)	3	0
Data sufficiency/application category consultation for medical devices	8	0
Total	276	7

** This table shows only the categories of the consultations actually implemented in FY 2016.*

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.
- 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.*

(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, 2017, the number of commissioned experts is 11 including experts in safety measures.)
- The number of Expert Discussions conducted in FY 2016 was 88 (71 document-based discussions, 17 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 subcommittee "Subcommittee on Artificial Intelligence."

b. Support for the development of national guidelines

- PMDA supported the preparation of the guidance documents for the evaluation of bioabsorbable vascular stents, published as "Publication of the Guidance for the Approval Process of Brand-new Medical Devices and Regenerative Medical Products" (PSEHB/MDED Notification No. 0630-1 dated June 30, 2016, issued by the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). The guidance document is available on the PMDA website. In addition, PMDA participated in the working group for preparing guidance documents for (a) microanalytical apparatuses, (b) medical devices with a new function using a biological material, and (c) blood flow analysis simulation software. The agency participated in the discussion of the contents of the documents.
- The "Initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products for FY 2016" addresses various topics, including 7 medical device-related topics: (1) cancers, electromagnetic/ultrasonic wave treatment devices; (2) orthopedics and dental area, combination products; (3) cancers, next-generation endoscopic systems; (4) minimally-invasive treatment devices; (5) quantitative assays, domestically produced artificial valves; (6) next-generation ventricular assist devices; (7) circulatory diseases, and next-generation treatment devices. PMDA facilitated personnel exchanges by dispatching reviewers and other employees to research institutions such as universities, in order to facilitate the development of guidelines that will support the practical application of these 7 topics. In addition, PMDA discussed 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

- To prevent delays in the development of innovative medical devices arising from financial difficulties 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 company. No fee subsidy applications related to this project were submitted in FY 2016.

In vitro diagnostics

(i) Appropriate and prompt reviews

- PMDA launched its Office of In Vitro Diagnostics on April 1, 2015, in accordance with the Collaborative Plan to Accelerate Reviews of *In Vitro* Diagnostics (March 2014). PMDA also increased its number of reviewers on staff to strengthen the review system to achieve future targets.
- In October 2006, MHLW established the Study Group on the Early Introduction of Medical Devices, etc. with High Medical Need. The Study Group discusses how to encourage MAHs to seek approval for *in vitro* diagnostic products that are marketed in Europe and/or the U.S. but not yet in Japan. Under the umbrella of the Study Group, a sub-working group held a meeting in PMDA in FY 2016 to examine issues related to diagnostic products. PMDA served as the secretariat of the working group, engaging in various activities such as preparing documents, communicating with working group members, and seeking the opinions of academic societies and companies.
- PMDA provided support to MHLW in preparing the following notification and Administrative Notice:

  (1) "Procedures for Marketing DNA Sequencers, etc. used in Genetic Testing Systems" (PSEHB Notification No. 0428-1 dated April 28, 2016, issued jointly by the Counsellor of Minister's Secretariat, MHLW, and the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

  (2) "Q&A about Procedures for Marketing DNA Sequencers, etc. used in Genetic Testing Systems" (Administrative Notice dated January 26, 2017, issued jointly by the Medical Device Evaluation Division, MHLW, and the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

Review Status of In Vitro Diagnostics

In vitro diagnostics (FY of submission)	Applied	Approved	Withdrawn	Under review
FY 2004 In or before Mar. 31	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	7	0
FY 2012	165	155	10 (1)	0 [-1]
FY 2013	136	123 (4)	13	0 [-4]
FY 2014	163	152 (19)	7 (4)	4 [-23]
FY 2015	196	175 (101)	5 (3)	16 [-104]
FY 2016	149	75 (75)	3 (3)	71 [+71]
Total	2,891	2,586 (199)	186 (11)	119 [-61]

Note 1: The figures in parentheses indicate applications processed in FY 2016 (included in values to the left).

Note 2: The figures in brackets indicate differences from FY 2016.

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 its clinical trial consultation categories pertaining to *in vitro* diagnostic products (implemented on November 25, 2014) to better accommodate the diverse range of needs arising during each stage of development, and to enhance the efficiency and effectiveness of consultations, while also considering requests from industry and the agency's previous experiences.

Number of Consultations

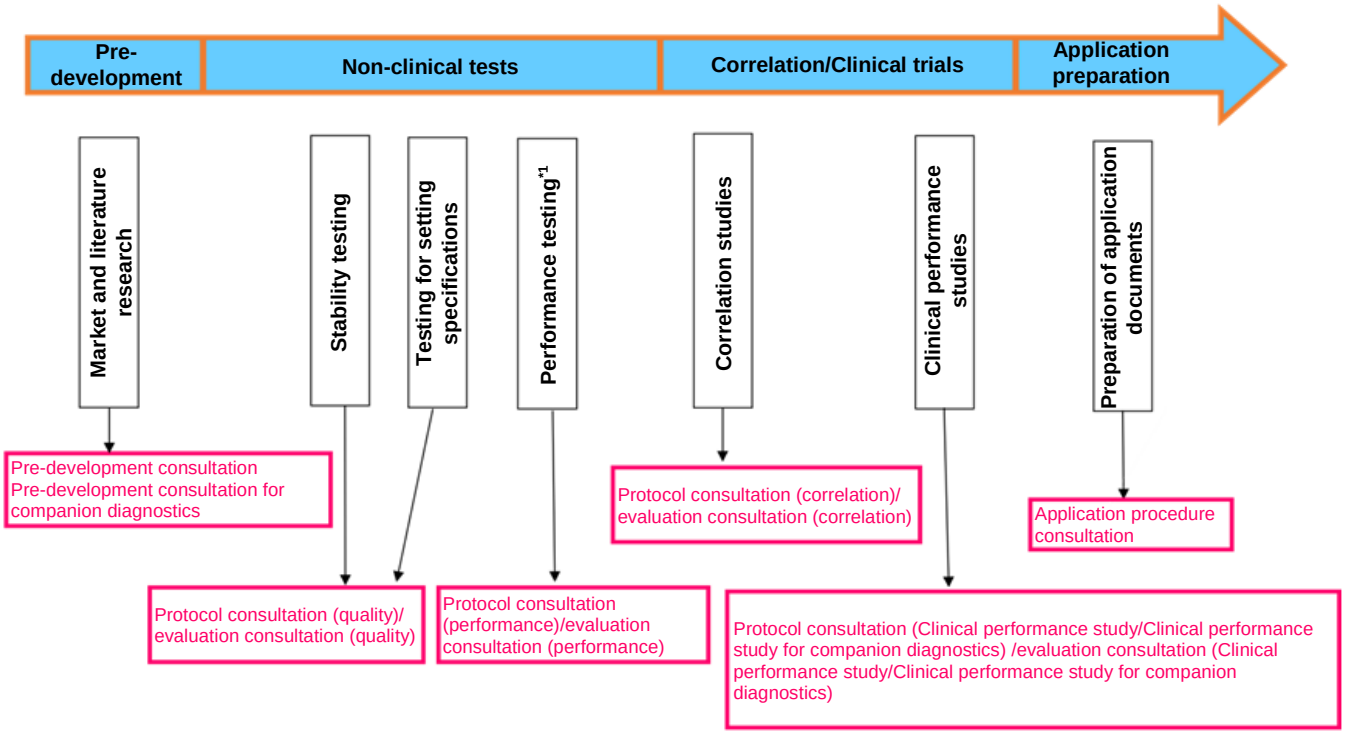
	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Conducted	8	7	25	45	43
Withdrawn	0	1	0	0	1

Number of Consultations for In Vitro Diagnostics by Category in FY 2016

Consultation category*	Face-to-face consultations conducted	Withdrawn
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)	3	0
Protocol consultation for *in vitro* diagnostics (quality)	1	0
Protocol consultation for *in vitro* diagnostics (quality) (preliminary consultation completed)	3	1
Protocol consultation for *in vitro* diagnostics, clinical performance test for companion diagnostics (preliminary consultation completed)	4	0
Protocol consultation for *in vitro* diagnostics (performance other than quality) (3 or more trials)	1	0
Protocol consultation for *in vitro* diagnostics (correlation) (preliminary consultation completed)	4	0
Protocol consultation for *in vitro* diagnostics (clinical performance test)	2	0
Protocol consultation for *in vitro* diagnostics (clinical performance test) (preliminary consultation completed)	12	0
Evaluation consultation for *in vitro* diagnostics, clinical performance studies for companion diagnostics (protocol not evaluated)	2	0
Performance (other than quality) evaluation consultation for *in vitro* diagnostics (2 trials) (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
Performance (other than quality) evaluation consultation for *in vitro* diagnostics (3 or more trials) (protocol not evaluated) (preliminary consultation completed)	1	0
Clinical performance evaluation consultation for i*n vitro* diagnostics (protocol not evaluated)	1	0
Clinical performance evaluation consultation for *in vitro* diagnostics (preliminary consultation completed)	1	0
Total	43	1

** This table shows only the categories of the consultations actually implemented in FY 2016.*

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 displayed above, other categories such as additional consultations are also available.*

Regenerative medical products

(i) New review systems and appropriate and prompt reviews

- With the enactment of the PMD Act, PMDA improved its review processes related to regenerative medical products to ensure the appropriate introduction of a conditional time-limited authorization for regenerative medical products. To ensure consistency between guidance provided during clinical trial consultations and actual review practices, PMDA allows for team flexibility while maintaining communication between consultation teams and review teams.

(ii) Setting of target review time

- The target standard regulatory review time (i.e., the time from initial submission to final approval) for regenerative medical products in FY 2016 was 9 months; product reviews were carried out in consideration of this target. In FY 2016, PMDA processed 1 regenerative medical product application; the total review time was 8.1 months (regulatory review time: 2.7 months). Thus, PMDA achieved a 100% success rate with respect to realization of the target regulatory review time (9 months).
- 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 [months]
Regenerative medical products	9

Results

	FY 2014	FY 2015	FY 2016
Total review time [months]	-	11.9/10.8	8.1
Regulatory review time [months]	-	3.3/2.2	2.7
Applicant's time [months]	-	8.6/8.5	5.5
Number of approved applications	0	2	1

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

- To conduct faster and more efficient reviews, PMDA communicated with related parties at meetings of academic societies such as the Japanese Society of Regenerative Medicine, and encouraged these organizations to take advantage of consultations offered by PMDA. PMDA developed consultation services tailored to the requirements of its 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	FY 2016
Conducted	6	18	28
Withdrawn	0	1	2

Number of Prior Assessment Consultations regarding Regenerative Medical Products

	FY 2014	FY 2015	FY 2016
Conducted	0	1	0
Withdrawn	0	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 proactive approach to its utilization of its Science Board, which retains highly knowledgeable external experts to contribute to reconsiderations of current evaluation methods. PMDA conducted Pharmaceutical Affairs Consultations on R&D Strategy based on viewpoints presented in the following reports prepared by the Science Board:
    - “Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products” dated August 14, 2015 (CPC Subcommittee);

- "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.

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 at international academic conferences and other similar events.

b. Knowledge accumulation

- 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 it is also able to gather information regarding the practical application of such products.

c. Support for 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 2016, guidelines on the evaluation of the following topics).
  - Cell-based products: 7 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], Mie University [cancer immunotherapy])
  - Gene therapy products: 2 topics (The University of Tokyo [virotherapy for malignant tumor], National Center for Child Health and Development [virotherapy for WAS])
  - Other products: 1 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 2016, PMDA participated as an observer in group meetings regarding the regeneration of human (autologous) epidermis (skin) (outsourced to Yoji Sato; chairperson, Hajime Matsumura), 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 review process was 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 with the enactment of the PMD Act in November 2014; and provision of relevant information at academic conferences. As a result, 52 clinical trials concerning regenerative medical products, including several investigator-initiated trials by academia, had been initiated by the end of FY 2016 with the support of PMDA [for the results of Pharmaceutical Affairs Consultations on R&D strategy, see 3.2.(1) New drugs (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 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 considered implementing a risk-based inspection method. Specifically, this method would select clinical trial sites for inspection based partly on the progress of clinical trials (according to clinical trial notifications). This risk-based inspection method has been applied to some trial sites.
- PMDA sent a questionnaire to the companies participating in a pilot survey on 2 types of inspection control sheet used to promote effective inspection: (1) GCP control sheet (tentative name) that records operational processes performed by a sponsor, and (2) the safety information control sheet (tentative name) for operations related to safety information conducted by a sponsor. PMDA held a discussion with industry organizations about the control sheets based on the results of the questionnaire, and decided to introduce the full-scale use of the GCP control sheet starting in FY 2017. To ensure that the GCP control sheet is used efficiently by sponsors, PMDA published the following materials on its website: (1) guidelines about how to enter data on the sheet; (2) a sample of the completed GCP sheet. Further, the agency held briefing sessions for the industry on the use of the GCP control sheet.
- PMDA conducted a pilot survey to evaluate the feasibility of on-site GCP inspections, of overseas trial sites, that allows sponsors to be present during some part of the inspection. The survey showed that such inspection can be conducted smoothly at overseas trial sites. Accordingly, PMDA modified a part of the procedures for on-site GCP inspection, to allow the presence of a sponsor during some part of inspection if requested by the sponsor.
- PMDA's Office of Non-clinical and Clinical Compliance obtained information, at an early stage, regarding products to be submitted 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 exchanged opinions with FDA and EMA in the anticipation that GCP inspection reports will be exchanged between PMDA and these regulatory authorities. PMDA's participation in the EMA-FDA GCP initiative was proposed. (The initiative aims to contribute to efficient GLP/GCP/GPSP inspection and data integrity assessment.) PMDA thus made preparations for the pilot participation in the initiative.
- PMDA discussed how to conduct inspection of clinical trials that adopt CDISC standards. In view of the results of the FY 2015 pilot survey, PMDA improved its operational systems and provided training sessions. The agency then began to use electronic data, in a complementary manner, before the conduct of inspection.

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

- The Offices of Medical Devices and the 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 2016, PMDA conducted a GCP on-site inspection of the manufacturer of 1 new medical device under the proper procedures and systems.
- PMDA participated in working-level meetings of “Cooperation Plan for Expediting Medical Device Reviews” to exchange opinions with industry on specific requirements for inspections to facilitate expeditious reviews of medical devices.
- PMDA agreed with industry on the content of the “Points to Consider for Smooth Implementation of Document-based Compliance Assessments of Medical Devices (Non-clinical studies).” The document was prepared based on the “Cooperation Plan for Expediting Medical Device Reviews”, which is available on the PMDA website.

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

- In FY 2016, PMDA conducted inspections of regenerative medical products submitted for approval in FY 2015 or FY 2016, in accordance with the inspection procedure for drugs.

(iv) Efficient GLP inspections and data integrity assessments

- Currently, a staff member of the Office of Non-clinical and Clinical Compliance serves as the chair of the OECD GLP working group. The member accompanied many GLP inspections conducted in Japan, and informed inspectors of the difference between Japanese inspection methods and international GLP inspection methods. In this way, the member trained Japanese inspectors so that they can become GLP inspectors who meet international standards.
- At the GLP training sessions in FY 2016, PMDA had a dialogue with the industry and explained (a) how to apply GLP to regenerative medical products and (b) how to handle certain situations that often raise questions. The purpose of these activities was to promote the efficient operation of “Instructions for GLP Inspection in laboratories conducting tests on Drugs, Medical Devices, and Regenerative Medical Products,” revised in FY 2014.
- PMDA participated in the GLP working group of the OECD (a staff member of PMDA served as the chairperson for this fiscal year) and dispatched 1 trainee to the OECD office, thereby introducing 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 2016, 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 discussed how to conduct GLP/GCP/GPSP compliance assessments in cases where electronic medical record data are included in the re-examination application data, at meetings of a working group with the pharmaceutical industry. (The working group discuss the use of databases of pharmacoepidemiology and electronic medical data.) In addition, PMDA continued to have a dialogue with the industry on consultations services for “re-examination compliance inspection consultation for drugs,” which was launched in July 2016.

- "The use-results evaluation system for medical devices" was recently launched. To promote the efficient conduct of the system, PMDA prepared the following documents based on the opinions from the industry: (a) "Checklist for medical device GPSP compliance inspections"; (b) "Items to be inspected in document-based compliance inspections." The documents are available on the PMDA website.

  Office of Non-clinical and Clinical Compliance and Office of Medical Devices shared information regarding the progress of the inspection into re-examination products.

- PMDA provided 8 re-examination compliance inspection consultations for drugs.

(vi) Proper conduct of clinical trials, etc.

- To further promote the proper execution of clinical trials, etc., 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. As for the re-examination compliance inspections for medical devices, PMDA provided information regarding GLP/GCP/GPSP compliance assessments (e.g., points to consider) at a briefing session hosted by the medical device industry in June 2016, at a lecture session on safety management in December 2016, and at lecture session hosted by a medical device-related organization in October and November 2016.

- As a sub-researcher, PMDA participated in a study group of Health and Labour Sciences Research, and conducted research on operation of GCP, to contribute to the efficient implementation of clinical trials. In particular, PMDA prepared a schedule, a draft revision of guidance, and a draft notification, in order to introduce ICH-E6 guidelines into Japan.

- In FY 2014, PMDA launched a new consultation categories concerning GCP/GLP/GPSP compliance assessments. In FY 2016, PMDA provided 50 consultations for drugs, 25 for medical devices, and 4 for regenerative medical products.

- PMDA accepted 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Tokyo	1,254	1,189	1,242	1,140	1,043
Osaka	471	404	448	352	368
Total	1,725	1,593	1,690	1,492	1,411

- Office of Non-clinical and Clinical Compliance discussed how to use the disease registries developed by MHLW to improve the infrastructure for clinical studies, and made efforts to promote the use of medical information databases. On the basis of these activities, the Office discussed how to ensure reliability (for example, through the use of medical information databases in the applications for approval or re-examination) in collaboration with related PMDA's Offices and external organizations.

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

		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Document-based assessments		2,737	2,610	2,396	2,332	2,066
	New drugs	286	364	370	389	381
	Generic drugs	1,188	1,086	1,080	1,045	870
	Medical devices	1,263	1,160	946	894	812
	Regenerative medical products	-	-	0	4	3
GCP on-site inspections		197	242	236	201	204
	New drugs	187	222	221	191	191
	Generic drugs	9	15	10	7	11
	Medical devices	1	5	5	1	1
	Regenerative medical products	-	-	0	2	1
Document-based assessments for re-examination		127	80	81	136	230
	New drugs	112	71	74	120	176
	New medical devices	15	9	7	16	54
On-site GPSP inspections for re-examination		112	71	74	120	176
	New drugs	112	71	74	120	176
	New medical devices	0	0	0	0	0
Document-based assessments for re-evaluation		0	0	0	19	0
On-site GPSP inspections for re-evaluation		0	0	0	19	0
GLP inspections		39	21	40	36	24
	Drugs	29	18	27	22	17
	Medical devices	10	3	13	9	4
	Regenerative medical products	-	-	0	5	3

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 2013 represent the numbers of products for which both inspection/assessment and review/re-examination were completed.

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 and/or Ministerial Ordinance on QMS for Medical Devices and *In vitro* Diagnostics, 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).
- With the enactment of the PMD Act in November 2014, manufacturing of medical devices and *in vitro* diagnostics was changed 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, rather than for individual products. By doing so, 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. If an approved/certified medical device or in vitro diagnostic was scheduled to undergo the “every-5-year QMS inspection” within 1 year of the enactment of the PMD Act, the MAH of the medical device or in vitro diagnostic was 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.) As a result, the number of applications for QMS inspections, especially for renewal inspections, rapidly increased within 1 year of the enactment of the PMD Act. PMDA took actions to address this situation by reviewing the administrative system. Currently, PMDA has devised measures including adjustments of application time and inspection period with applicants and started reviewing the measures to avoid a rapid increase in the number of applications for renewal inspections in the future.
- With the introduction of the laws/regulations for re-manufacturing single-use medical devices (SUDs), PMDA has begun to support the preparation of draft revision of the QMS ministerial ordinance, and to discuss matters related to on-site QMS inspections to be conducted each year.
- In 2015, a certain MAH was determined to have manufactured blood products for many years applying processes different from those described in the corresponding marketing approval documents for those products, and systematically created falsified and altered records to conceal this fact. Faced with this problem, PMDA began to conduct unannounced on-site GMP inspections as a safeguard against similar instances of fraud, in accordance with the related MHLW notification (PSEHB/CND Notification No. 0115-3 dated January 15, 2016, issued by the Director of Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In FY 2016, PMDA conducted 11 unannounced on-site inspections.
- In 2014, the Ministerial Ordinance on GCTP and the Regulations for Buildings and Facilities for Pharmacies and Manufacturing Establishments were established and came into effect. To promote

efficient manufacturing and quality control at manufacturing sites, PMDA supported the preparation of guidelines and a document providing examples on how to deal with the regulations.

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

Note 1: GMP (Good Manufacturing Practice)
Note 2: QMS (Quality Management System)
Note 3: GCTP (Good Gene, Cellular, and Tissue-based Products Manufacturing Practice)

b. Establishment of the inspection system

- PMDA had 50 GMP/GCTP/QMS inspectors (including inspectors in the Kansai Branch) at the end of FY 2016.

  In the Office of Manufacturing/Quality and Compliance, inspectors had been divided into several groups, each led by an Inspection Director to ensure that GMP/QMS inspections are conducted on a group-by-group basis. To further improve the efficiency of inspections, since January 1, 2016, each inspector has been assigned to either of the two divisions of the Office: (1) Division of Pharmaceuticals; (2) Division of Medical Devices.

  In FY 2014, Japan joined the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S: An international framework on GMP inspections, centering on European countries). In response to this, PMDA established the “inspection quality assurance group” in Office of Manufacturing/Quality and Compliance, to supervise quality management of drugs and quasi-drugs. 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 2016 is shown below:

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

	FY2011				FY2012			
	Applied	Completed	Withdrawn	In progress	Applied	Completed	Withdrawn	In progress
Drugs*	1,538	1,283 (185)	31	908	1,582	1,593 (198)	40	821
In vitro diagnostics	73	85 (0)	1	6	64	48 (0)	0	16
Quasi-drugs	0	0 (0)	0	2	6	2 (0)	2	3
Medical devices	697	765 (36)	24	57	999	954 (81)	3	37
Regenerative medical products	-	-	-	-	-	-	-	-
Total	2,308	2,133 (221)	56	973	2,651	2,597 (279)	45	877

	FY2013				FY2014			
	Applied	Completed	Withdrawn	In progress	Applied	Completed	Withdrawn	In progress
Drugs*	1,508	1,415 (168)	75	875	1,877	1,672 (163)	51	1,030 (0)
In vitro diagnostics	52	67 (1)	0	7	65	38 (1)	0	27 (0)
Quasi-drugs	3	3 (1)	0	4	5	6 (0)	0	2 (0)
Medical devices	988	883 (61)	11	193	755	512 (42)	18	225 (86)
Regenerative medical products	-	-	-	-	0	0 (0)	0	0 (0)
Total	2,551	2,368 (231)	86	1,079	2,702	2,228 (206)	69	1,284 (86)

	FY2015				FY2016			
	Applied	Completed	Withdrawn	In progress	Applied	Completed	Withdrawn	In progress
Drugs*	1,719	1,647 (165)	67	1,039	1,818	1,783 (171)	122	959
In vitro diagnostics	1 179	1 (0) 146 (33)	0 1	0 50	0 54	0 (0) 83 (44)	1 1	0 20
Quasi-drugs	2	2 (0)	0	2	1	3 (0)	0	0
Medical devices	70 2,333	178 (25) 1,854 (326)	7 38	1 436	0 739	1 (0) 951 (251)	10 11	0 210
Regenerative medical products	9	8 (3)	1	0	1	0 (0)	0	1
Total	4,313	3,836 (552)	114	1,528	2,613	2,821 (466)	145	1,190

**) 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 and FY 2016 include applications made under the former Act (upper) and those made under the new Act (lower). One application after the revised Act includes the average of three institutions; this prevents a simple comparison of figures between the new and former Acts, or between drugs, quasi-drugs, and regenerative medical products.

- The processing times of GMP/GCTP/QMS inspections in FY 2016 are shown below:

Median Processing Time of GMP/GCTP/QMS Inspections

	FY 2011		FY 2012		FY 2013	
	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*	176	90	147	77	118	71
In vitro diagnostics	100	36	83	38	106	66
Quasi-drugs	219	71	-	-	272	71
Medical devices	21	44	113	21	106	56
Regenerative medical products	-	-	-	-	-	-
	FY 2014		FY 2015		FY 2016	
	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*	172	76	172	81	163	84
In vitro diagnostics	147	102	160/120	38/72	772/128	30/57
Quasi-drugs	166	96	422	158	141	74
Medical devices	118	74	114/140	60/85	601/105	35/49
Regenerative medical products	-	-	84	54	-	-

** Excluding in vitro diagnostics.*

The figures in "In vitro diagnostics" and "Medical devices" in FY 2015 and FY 2016 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 building and facility inspections conducted in FY 2016 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	15 (9)	9 (4)	25 (11)	26 (18)	19 (11)
In vitro diagnostics	1 (1)	3 (3)	0 (0)	-	-
Medical devices	2 (1)	0 (0)	2 (2)	-	-
Regenerative medical products	-	-	1 (1)	1 (1)	-
Total	18 (11)	12 (7)	28 (14)	27 (19)	19 (11)

** Excluding in vitro diagnostics.*

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

- 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 2016 is shown below:

Number of For-cause Inspections (Manufacturers in Japan)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	13	6	5	7	15
In vitro diagnostics	1	1	0	0	0
Medical devices	0	0	0	0	0
Regenerative medical products	-	-	0	0	3
Total	14	7	5	7	18

** Excluding in vitro diagnostics.*

- PMDA conducts simple consultations concerning GMP/GCTP/QMS inspections. The number of such consultations conducted in FY 2016 is shown below.

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	38	44	32	33	36
In vitro diagnostics	0	0	0	4	0
Quasi-drugs	0	0	0	0	0
Medical devices	8	3	51	64	34
Regenerative medical products	-	-	-	3	0
Total	46	47	83	104	70

** Excluding in vitro diagnostics.*

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

- The following tables show the number of on-site inspections of foreign manufacturing sites, conducted in FY 2005:

On-site Inspections of Foreign Drug Manufacturing Sites by Region

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
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
FY 2016	6	6	67	0	79

Note: Breakdown of FY 2016:

Europe: France, Belgium, Italy, Austria, and Hungary
North, Central, and South America: the United States
Asia/Oceania: China, India, South Korea, Thailand, Taiwan, and Singapore

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

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
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
FY 2016	0	0	2	0	2

Note 1: Breakdown of FY 2016:

Asia, Oceania: South Korea and Singapore

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 2016 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 Foreign Manufacturing Sites

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	530	383	384	356	686
In vitro diagnostics	68	79	23	-	-
Quasi-drugs	62	58	58	33	69
Medical devices	1,751	1,453	722	-	-
Regenerative medical products	-	-	0	0	0
Total	2,411	1,973	1,187	389	755

** 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 2016 is shown below:

Number of For-cause Inspections at Foreign Manufacturing Sites

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	4	2	1	0	0
In vitro diagnostics	0	0	0	0	0
Medical devices	1	1	0	0	0
Regenerative medical products	-	-	0	0	0
Total	5	3	1	0	0

** Excluding in vitro diagnostics.*

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

Region	Country	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Europe	France	5	6	1	3	2	1	3	0	1
	Denmark	2	2	0	0	0	2	0	0	0
	Ireland	5	3	2	0	1	1	0	0	0
	UK	1	3	0	0	1	1	0	0	0
	Netherlands	1	5	0	0	2	0	0	0	0
	Spain	1	1	0	0	0	0	1	0	0
	Italy	5	3	2	0	1	2	3	0	1
	Belgium	2	4	3	1	0	2	3	0	1
	Austria	2	2	0	1	2	0	1	0	2
	Finland	0	2	0	0	1	0	0	0	0
	Germany	3	7	0	3	1	0	1	0	0
	Sweden	1	0	0	0	0	1	0	0	0
	Romania	1	0	0	0	0	1	0	0	0
	Czech	0	0	0	0	1	0	0	0	0
	Ukraine	0	0	0	0	1	0	0	0	0
	Lithuania	0	0	0	0	1	0	0	0	0
	Slovenia	2	1	0	0	0	0	0	0	0
	Portugal	0	0	3	0	0	0	0	0	0
	Greece	0	0	0	1	0	0	0	0	0
	Turkey	0	0	1	0	0	0	1	0	0
	Iceland	0	0	0	0	0	1	0	0	0
	Hungary	0	0	0	0	0	0	3	0	1
	Cyprus	0	0	0	0	0	0	1	0	0
	Latvia	0	0	0	0	0	0	2	0	0
	Slovakia	0	0	0	0	0	0	1	0	0
	Subtotal	31	39	12	9	14	12	20	0	6
North, Central, and South America	USA	14	18	23	6	14	8	3	2	6
	Canada	2	2	1	0	0	1	0	0	0
	Mexico	1	0	0	1	0	0	0	0	0
	Argentina	2	0	0	0	0	0	0	0	0
	Brazil	0	0	0	0	0	1	0	0	0
	Subtotal	19	20	24	7	14	10	3	2	6
Asia/Oceania	China	11	25	10	20	16	18	23	27	30
	India	12	4	7	4	4	3	4	19	18
	Singapore	4	0	0	0	0	2	0	0	1
	South Korea	3	9	10	18	14	11	13	10	11
	Indonesia	0	0	0	0	1	0	0	3	0
	Taiwan	2	6	1	1	2	6	6	2	6
	Thailand	0	2	0	1	0	2	1	0	1
	Vietnam	0	0	1	1	0	0	3	0	0
	Israel	0	0	0	0	1	0	0	0	0
	New Zealand	0	1	0	0	0	0	0	0	0
	Malaysia	0	0	0	0	0	0	1	0	0
Subtotal		32	47	29	45	38	42	51	61	67
Grand Total		82	106	65	61	66	64	74	63	79

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

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 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Europe	Ireland	6	0	4	1	3	0	1	0	0
	UK	1	0	0	1	0	1	2	0	0
	Italy	2	0	2	1	1	0	1	0	0
	Netherlands	1	0	1	0	0	0	0	0	0
	Switzerland	1	1	0	0	0	1	0	0	0
	Spain	1	0	0	0	1	0	0	0	0
	France	1	1	1	1	4	0	0	0	0
	Denmark	0	1	0	0	0	0	0	0	0
	Austria	0	0	0	0	1	0	0	0	0
	Belgium	0	0	0	0	1	0	0	0	0
	Turkey	0	0	0	0	0	1	0	0	0
	Subtotal	13	3	8	4	11	3	4	0	0
North, Central, and South America	USA	16	27	19	12	21	8	4	0	0
	Mexico	1	0	0	1	0	0	1	0	0
	Brazil	0	1	0	0	0	0	0	0	0
	Canada	0	0	0	1	1	4	0	0	0
	Costa Rica	0	0	0	1	0	0	0	0	0
	Subtotal	17	28	19	15	22	12	5	0	0
Asia	China	0	3	0	0	1	1	6	0	0
	South Korea	0	0	1	0	0	5	8	4	1
	Thailand	0	0	0	0	1	0	0	0	0
	Singapore	0	2	0	0	0	2	1	1	1
	Philippines	0	0	0	0	2	0	0	0	0
	Israel	0	0	0	1	0	1	0	0	0
	Taiwan	0	0	0	0	0	1	3	3	0
	UAE	0	0	0	0	0	1	0	0	0
	Malaysia	0	0	0	0	0	0	1	1	0
	India	0	0	0	0	0	0	1	0	0
	Subtotal	0	5	1	1	4	11	20	9	2
Grand Total		30	36	28	20	37	26	29	9	2

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

Note 2:Puerto Rico was included in the USA.

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

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 monthly meetings with the Review Division (Offices of New Drugs) 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.
- In FY 2015, MHLW issued a notification directing medical device manufacturers to file applications for QMS inspections within 10 days of submitting applications for marketing approval of "generic medical devices" and "improved medical devices (without clinical data)." This procedural

adjustment enabled PMDA to confirm whether an application for a QMS inspection has been submitted after submission for marketing approval. In addition, the Office of Manufacturing/Quality and Compliance informed the review offices of PMDA about the progress of QMS inspections every week, and exchanged information with the offices at regular meetings. As a result, QMS inspections were conducted in line with the progress of reviews, without affecting the time of marketing approval.

e. For-cause inspections of registered certification bodies

- PMDA has served as the regulatory authority governing registered certification bodies, in accordance with the revision of the relevant system in November 2014. In FY 2016, PMDA conducted inspections of Japanese certification bodies: 1 on-site inspection at registration, 10 on-site inspections at registration renewal, and 2 periodic on-site inspections.
- There was a case in which a medical device requiring approval was certified wrongly. MHLW therefore conducted unannounced on-site inspections (3 inspections of registered certification bodies, 2 inspections of MAHs). PMDA accompanied and supported the inspections.

f. Inspection of MDSAP-recognized auditing organizations

- In June 2015, Japan announced that it would formally participate in MDSAP.[Note] PMDA therefore began the inspection of MDSAP-recognized auditing organizations (16 inspections conducted in FY 2016).

Note) The Medical Device Single Audit Program (MDSAP) is 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. Establishment of the inspection system

- In accordance with the Act on the Safety of Regenerative Medicine (enforced in 2014), PMDA conducts compliance assessments of 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. These compliance assessments are carried out at the request of the Health Policy Bureau in MHLW or Regional Bureau of Health and Welfare.

  In addition, PMDA has to conduct for-cause inspections when requested to do so by the Health Policy Bureau of the MHLW. In FY 2016, PMDA received no request for-cause inspections from MHLW.

  To maintain a sufficient number of inspectors, PMDA started to provide a training program 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				FY 2016			
	Application	Completed	Withdrawn	In progress	Application	Completed	Withdrawn	In progress	Application	Completed	Withdrawn	In progress
Application for manufacturing licensure (in Japan)	19	0	0	19	43	37 (36)	2	4	13	7 (7)	1	5
Application for manufacturing licensure (outside Japan)	0	0	0	0	4	1 (1)	1	2	2	1 (1)	0	1
Total	19	0	0	19	47	38 (37)	3	6	15	8 (8)	1	6

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

Administrative Processing Period for Inspection related to Manufacturer Licensing/Accreditation

	FY 2014		FY 2015		FY 2016	
	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)
Application for manufacturing licensure (in Japan)	-	-	134	83	142	64
Application for manufacturing licensure (outside Japan)	-	-	166	136	133	114

Number of For-cause Inspections Conducted by PMDA

Region	FY 2014	FY 2015	FY 2016
Japan	0	0	0
Outside Japan	0	0	0
Total	0	0	0

Number of On-site Inspections of Foreign Facilities by Region

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
FY 2014	-	-	-	-	-
FY 2015	0	0	2	0	2
FY 2016	0	0	2	0	2

Number of On-Site Inspections of Foreign Facilities by Region

Region	Country	FY 2014	FY 2015	FY 2016	Total
Europe	-	-	-	-	0
	Subtotal	-	0	0	0
North, Central, and South America	-	-	-	-	0
	Subtotal	-	0	0	0
Asia	South Korea	-	2	2	4
	Subtotal	-	2	2	4
Grand Total		-	2	2	4

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

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

- The 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. In April 2016, the third term of the Science Board started. For details of the use of the Science Board, see 3 4.(1) (ii).
- 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.
- To ensure the proper execution of 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 the research purpose, how the research is related to PMDA's operations, and on comments from the Regulatory Science Research Evaluation Committee. In FY 2016, 7 projects (1 new project and 6 ongoing projects) were selected as designated research and the results of 4 of these projects were published in academic journals or lecture meetings (2 published in papers, 2 lectures).
- PMDA supported the development of evaluation guidelines through the activities of 10 working groups (WG) in the Projects Across Multi-offices to Develop Standards etc. (hereinafter referred to as "Projects Across Multi-offices"). The Projects aim 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 2016, PMDA supported the Companion Diagnostics WG in the preparation of one notification (draft) and one administrative notice (draft).
- The Companion Diagnostics WG in Projects Across Multi-offices exchanged ideas with the FDA. The WG prepared a concept paper regarding the policy for evaluation of companion diagnostic systems using next-generation DNA sequencers. The paper is available on the PMDA website. PMDA exchanged ideas with related industrial groups on a total of 3 occasions regarding issues concerning the development of companion diagnostics.

- The Pediatric Drugs 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, and also exchanged ideas with related industrial groups regarding the development of pediatric drugs. On November 28, 2016, PMDA held a workshop, “Toward promotion of development of pediatric drugs—what we can do now for the future of children.” During the workshop, the industry, academia, and government discussed and exchanged ideas. Further, Pediatric Drugs WG gave presentations and participated in panel discussions in workshops and international academic conferences, thereby explaining how reviews and consultations are regarded in Japan and exchanging ideas with participants from foreign regulatory authorities, in order to promote international harmonization.
- The Orphan Drug WG in Projects Across Multi-offices exchanged ideas with related industrial groups regarding the development of orphan drugs.
- The Omics WG in Projects Across Multi-offices participated in workshops and in its program preparatory committee on safety biomarkers hosted by related industrial groups, and exchanged ideas with participants from the industry, academia, and government.
- The ICH Q12 WG and the Innovative Manufacturing Technology WG in Projects Across Multi-offices exchanged ideas with the FDA and EMA.
- The Clinical Innovation Network (CIN) WG in Projects Across Multi-offices exchanged ideas among the industry, academia, and government through cooperation with the research project of the Japan Agency for Medical Research and Development (AMED). The AMED has been discussing (a) the use of patient registries for clinical study design, epidemiological research, and reliability standards, etc.; and (b) the creation of patient registries for muscular dystrophy, amyotrophic lateral sclerosis (ALS), cancer/rare fractions, and brain surgical therapy.

(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.
- In July 2016, MHLW issued a report titled “Advisory Panel on Promotion of Venture Companies that Facilitate Medical Innovation.” In response to this, PMDA launched the “Preparatory Office for the Practical Application of Innovation Advancements” in October 2016.
- 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.

  The Osaka Prefectural government and pharmaceutical industry associations representing the Kansai region requested that PMDA improve the convenience of its service offerings for applicants in the Kansai region. In response, in June 2016, PMDA’s Kansai Branch Office began offering “face-to-face” consultations using video conferencing technology. In total, 41 consultations were conducted by the end of FY 2016 (during the 10-month period between June 2016 and March 2017).
- On August 19, 2015, PMDA and AMED concluded their “Agreement on Collaboration between Pharmaceuticals and Medical Devices Agency and Japan Agency for Medical Research and Development.” The agreement is aimed at the creation and practical application of innovative drugs,

and medical devices at an early stage. As a collaborative effort based on the Agreement, PMDA and AMED agreed in principle that research projects adopted by AMED that have advanced to the stage of practical application should adhere to the Pharmaceutical Affairs Consultation on R&D Strategy. PMDA and AMED discussed how and when the 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 launched on a trial basis for drugs, medical devices, *in vitro* diagnostics, and regenerative medical products. To manage this system, PMDA has improved its organizational setup through methods including the introduction of “Review Partners (concierges)” and the “SAKIGAKE comprehensive assessment consultation” service intended for pre-evaluation of designated products.
- At the request of MHLW, the review offices of PMDA pre-evaluated products submitted for consideration for the SAKIGAKE designation. Based on the results of these pre-evaluations, MHLW designated the following as SAKIGAKE products: 6 drugs (in October 2015), 2 medical devices (in February 2016), and 3 regenerative medical products (in February 2016). The manufacturer of 1 of the 2 medical devices applied for SAKIGAKE comprehensive assessment consultation (QMS) in April 2017; PMDA plans to conduct an on-site assessment of quality and manufacturing controls with respect to this product. The application for the other medical device product was withdrawn. In February 2017, 3 medical devices, 1 *in vitro* diagnostic, and 3 regenerative medical products were newly designated as SAKIGAKE products. A list of SAKIGAKE-designated products to date as well as a summary of their features is available on the PMDA website. Review Partners have begun to manage the progress for these designated products on a product-by-product basis.

3.3 Safety Measure Services

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

- 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 it promptly provides easy-to-understand safety information, to ensure that reviews and safety measures function in an integrated manner.
- Every year, PMDA receives various types of case reports from industry: approximately 450,000 reports on serious adverse reactions and infections attributable to drugs (from Japanese and foreign companies); approximately 52,000 reports on medical device malfunctions and infections attributable to medical devices (from Japanese and foreign companies); approximately 120 reports on regenerative medical product malfunctions and infections attributable to such products; approximately 1,800 case reports on suspected malfunctions, etc. of equipment parts of combination drugs (from Japanese and foreign companies); and approximately 210 reports on adverse reactions attributable to quasi-drugs/cosmetics. PMDA records the information obtained from these reports into a database that is shared with MHLW. PMDA also 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. In particular, 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 pharmaceutical ingredients, 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs	198	160	100	87*2	152
Medical devices	15	14	4	28	6
Regenerative medical products	-	-	0*1	0	0
Medical safety	6	6	6	6	6

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

**2 A 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 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs	Directions for revision to precautions in package insert	198	160	100	87[*1]	152
	Releasing PMDSI reports	36	40	29	28[*2]	32
Medical devices	Directions for revision to precautions in package insert or issuance of self-check notifications[*3]	16 (4)	11 (3)	4 (2)	28 (3)	6 (1)
	Releasing PMDSI reports	1	4	1	1	0
Regenerative medical products	Directions for revision to precautions in package insert or issuance of self-check notifications	-	-	0[*4]	0	0
	Releasing PMDSI reports	-	-	0[*4]	0	0

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

**2 A 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 cases after enactment of the PMD Act on November 25, 2014*

PMDSI: Pharmaceuticals and Medical Devices Safety Information

- The precautions in the package inserts for benzodiazepines (hypnotics, anxiolytics, and antiepileptic drugs) were revised to replace a statement meaning, “Long-term, high-dose therapy may result in dependency” with a new statement meaning, “Dependency may occur even in patients receiving the approved dosage.”
- Package inserts for certain selective neurotransmitter reuptake inhibitor (SNRIs [antidepressants]) products were amended to lift restrictions on automobile operation while receiving SNRI therapy.
- As collaborative activities with the review offices, PMDA’s 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.
- PMDA has made efforts to adequately collect, organize, and examine reports on adverse drug reactions, case reports on medical device malfunctions, etc., that have been submitted by marketing authorization holders (MAHs) and medical institutions. For example, PMDA holds periodical liaison meetings with MHLW, promotes the participation of employees in academic conferences, and collects relevant information. In addition to these activities, in FY 2016 PMDA carried out the following actions:

  a. In the first quarter of FY 2016, PMDA initiated practical application of the ICH-E2B (R3) guideline, which sets forth standards for next-generation international data exchange regarding adverse drug reaction reporting.

  b. To support electronic reporting by MAHs, PMDA provided a test environment where MAHs can send test files.

c. Following the MHLW's issuance of a notification on handling, etc. of electronic transmissions in compliance with ICH-E2B (R3), PMDA issued a director's notification on points to consider for reports of adverse reactions, etc. attributable to quasi-drugs and cosmetics.

d. To improve the usability of the electronic case reporting system for medical device malfunctions, PMDA upgraded the malfunction data management system to increase the number of characters that can be entered, and took other measures.

○ Collection of adverse reaction reports etc.

1-1) Number of reports relating to drugs

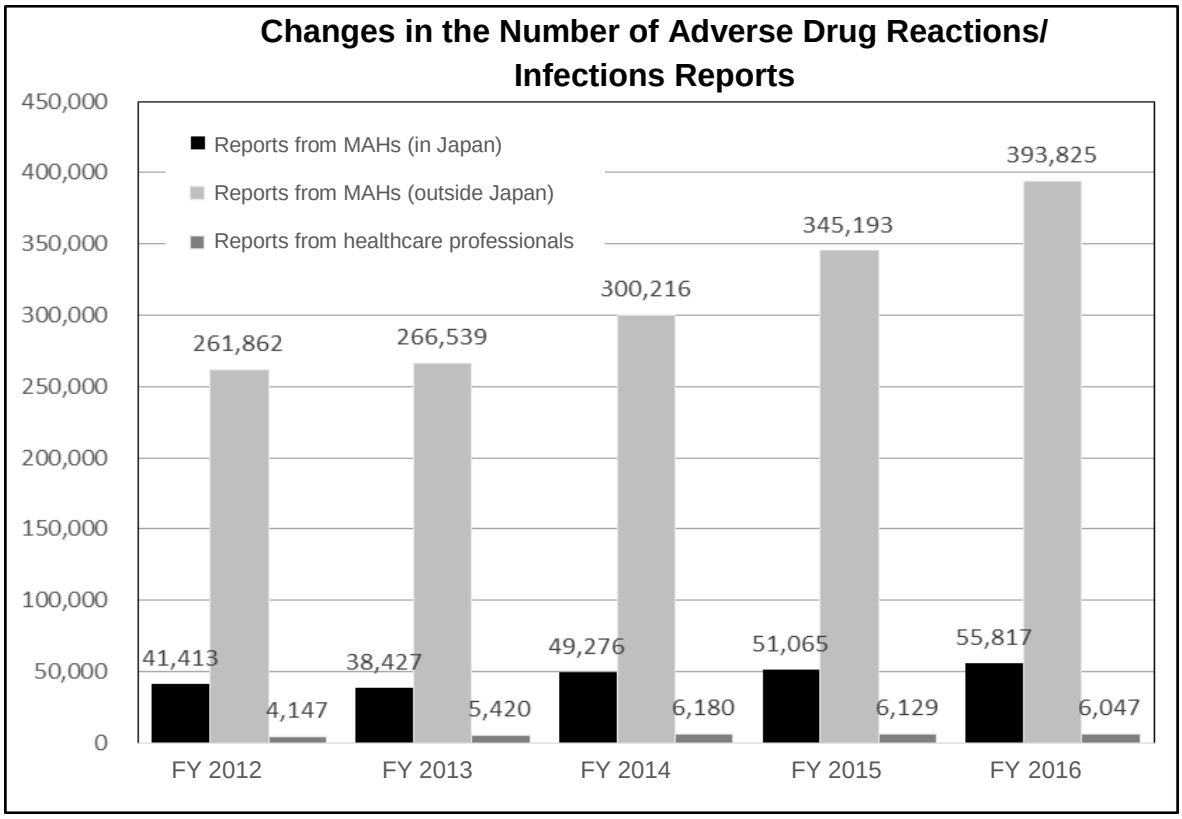
	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Reports from MAHs	306,410	308,383	352,908	399,852	453,296
(adverse drug reactions, in Japan)	(41,254)	(38,329)	(49,198)	(50,977)	(55,728)
(infections caused by drugs, in Japan)	(159)	(98)	(78)	(88)	(89)
(adverse drug reactions, outside Japan)	(261,823)	(266,506)	(300,191)	(345,161)	(393,767)
(infections caused by drugs, outside Japan)	(39)	(33)	(25)	(32)	(58)
(research reports)	(884)	(962)	(1,099)	(1,219)	(1,117)
(foreign safety measure reports)	(1,134)	(1,317)	(1,219)	(1,273)	(1,397)
(periodic infection reports)	(1,117)	(1,138)	(1,098)	(1,102)	(1,140)
Reports from healthcare professionals	4,147	5,420	6,180	6,129	6,047
([1] Safety information reporting system)	(3,304)	(4,067)	(4,782)	(4,891)	(4,956)
([2] Vaccines*)	(843)	(1,353)	(1,398)	(1,238)	(1,091)
Total	310,557	313,803	359,088	405,981	459,343

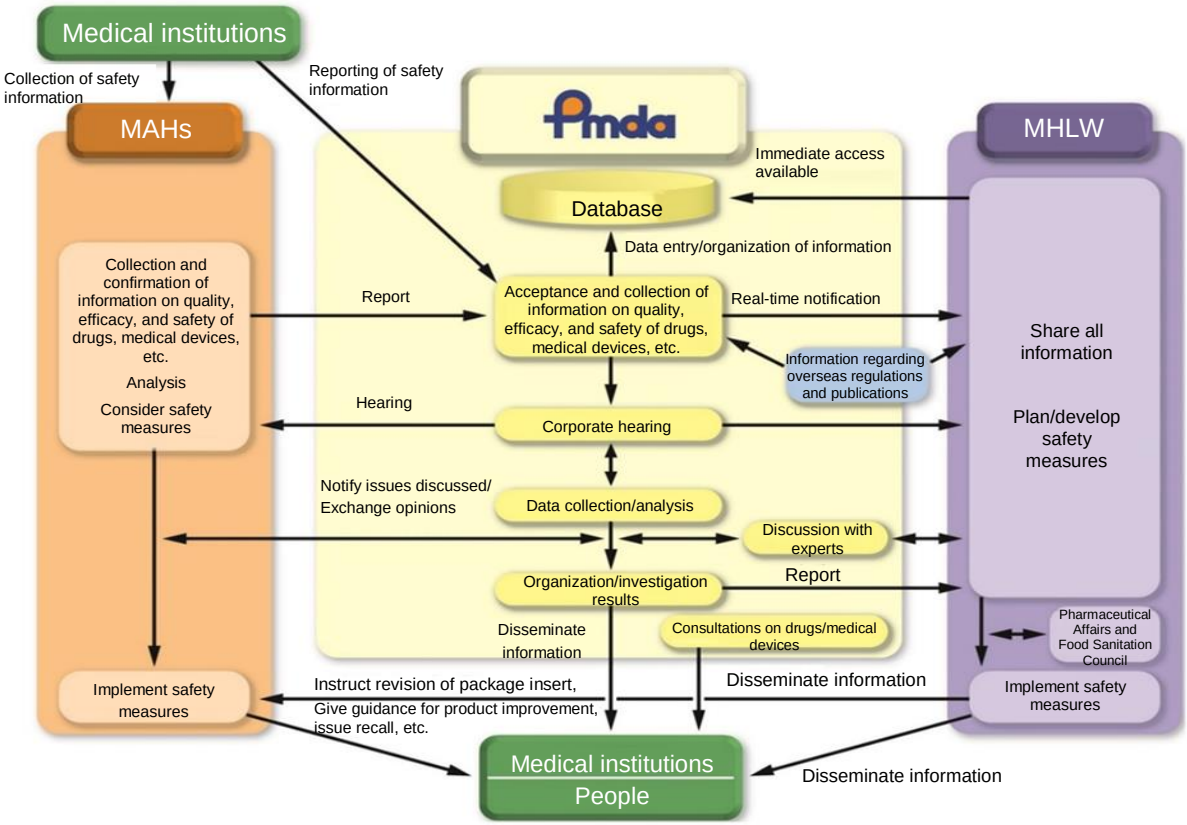
** The figures in FY 2012 indicate the total numbers of reports on suspected adverse reactions following vaccination with cervical cancer vaccine, Hib vaccine, pediatric pneumococcal conjugate vaccine, and influenza vaccines. The figures in FY 2013 to FY 2016 indicate the total numbers of reports on suspected adverse reactions following vaccination with all vaccines.*

		FY 2014	FY 2015	FY 2016
Cases of malfunctions of combination drugs (in Japan)	Reports from MAHs	0	38	661
	Reports from healthcare professionals	-	-	4
Cases of malfunctions of combination drugs (outside Japan)	Reports from MAHs	0	60	1,126

Note: The transitional period (during which reporting was not mandatory) was from November 25, 2014 to November 24, 2016. Reporting was made mandatory on November 25, 2016. The number of reports in FY 2014 is the number of reports after enactment of the PMD Act on November 25, 2014.

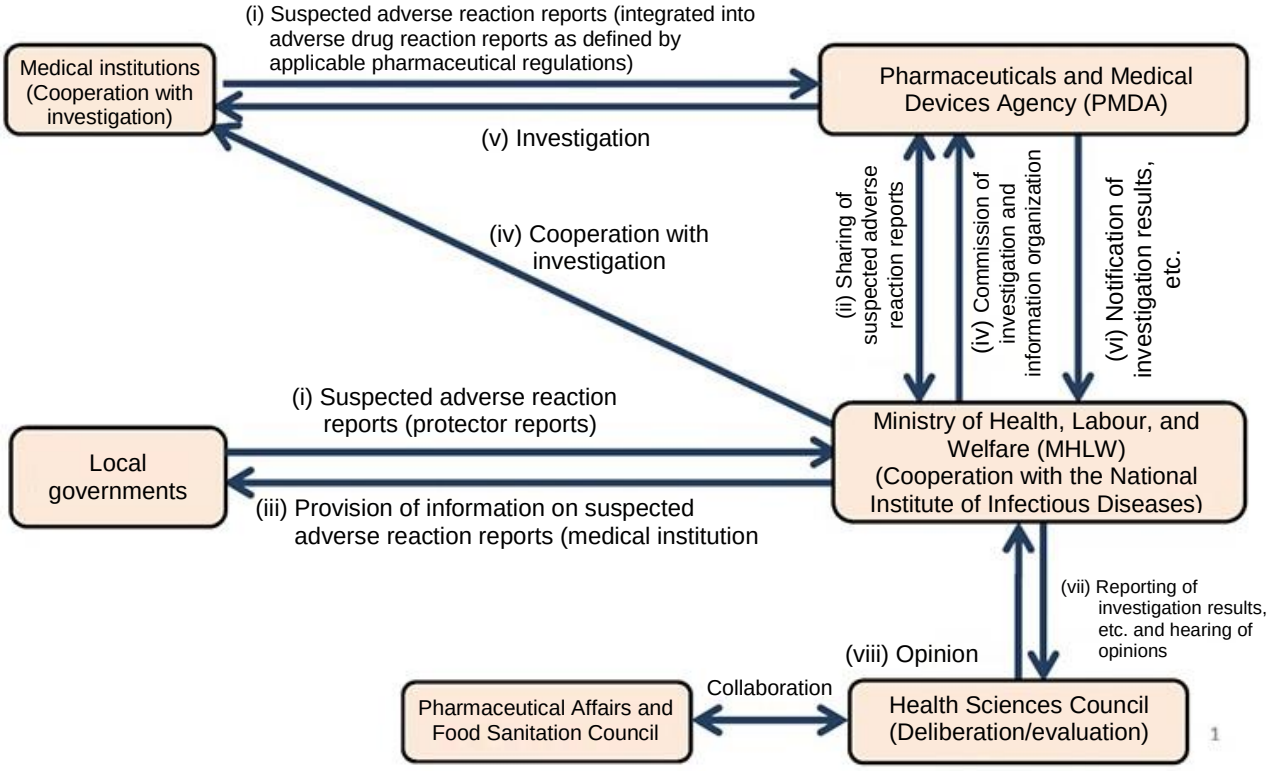
	FY 2014	FY 2015	FY 2016
Quasi-drugs	561	323	146
Cosmetics	116	114	71


Changes in the Number of Adverse Drug Reactions/ Infections Reports
450,000
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
41,413
261,862
4,147
38,427
266,539
5,420
49,276
300,216
6,180
51,065
345,193
6,129
55,817
393,825
6,047
FY 2012
FY 2013
FY 2014
FY 2015
FY 2016


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 measures
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
Plan/develop safety measures
Hearing
Corporate hearing
Notify issues discussed/ Exchange opinions
Data collection/analysis
Discussion with experts
Organization/investigation results
Report
Disseminate information
Consultations on drugs/medical devices
Pharmaceutical Affairs and Food Sanitation Council
Implement safety measures
Instruct revision of package insert, Give guidance for product improvement, issue recall, etc.
Disseminate information
Implement safety measures
Medical institutions
People
Disseminate information

1-2) Reports on suspected adverse reactions following vaccination based on the Preventive Vaccination Act

Pursuant to the provisions of Article 14 of the Preventive Vaccination Act (Act No. 68 of 1948), PMDA has been conducting projects for investigating and organizing “suspected adverse reaction reports” (changed from “adverse reaction reports” on October 01, 2016). As of November 25, 2014, suspected 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 2016, PMDA received 1,091 suspected adverse reactions reports. Upon receiving suspected 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. As for reported cases of suspected adverse reactions to vaccine products, PMDA conducted interviews as needed with physicians who diagnosed symptoms suspected to be adverse reactions and those who administered vaccinations. In the cases of deaths and symptoms suspected to be particular serious adverse reactions (e.g., anaphylactic reaction), PMDA sought opinions from experts regarding matters such as the appropriateness of diagnosis and causal relationships with 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 the “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 on a trial basis 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 plans to begin officially accepting reports in FY 2018.

In FY 2016, PMDA updated its SOPs in order to more smoothly obtain the information necessary to conduct efficient assessments, etc. of reported cases, while giving due consideration to the protection of personal information as appropriate.

The table below shows the number of adverse drug reaction reports from patients collected by FY 2016. PMDA has been disclosing the reported cases as they come to hand.

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Adverse drug reaction reports from patients (total number)*	154	122	91	186	50

** 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 fall under either of the following circumstances 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 conducted detailed investigations into these cases as necessary. Cases not subject to investigation by PMDA were investigated by MAHs as necessary.

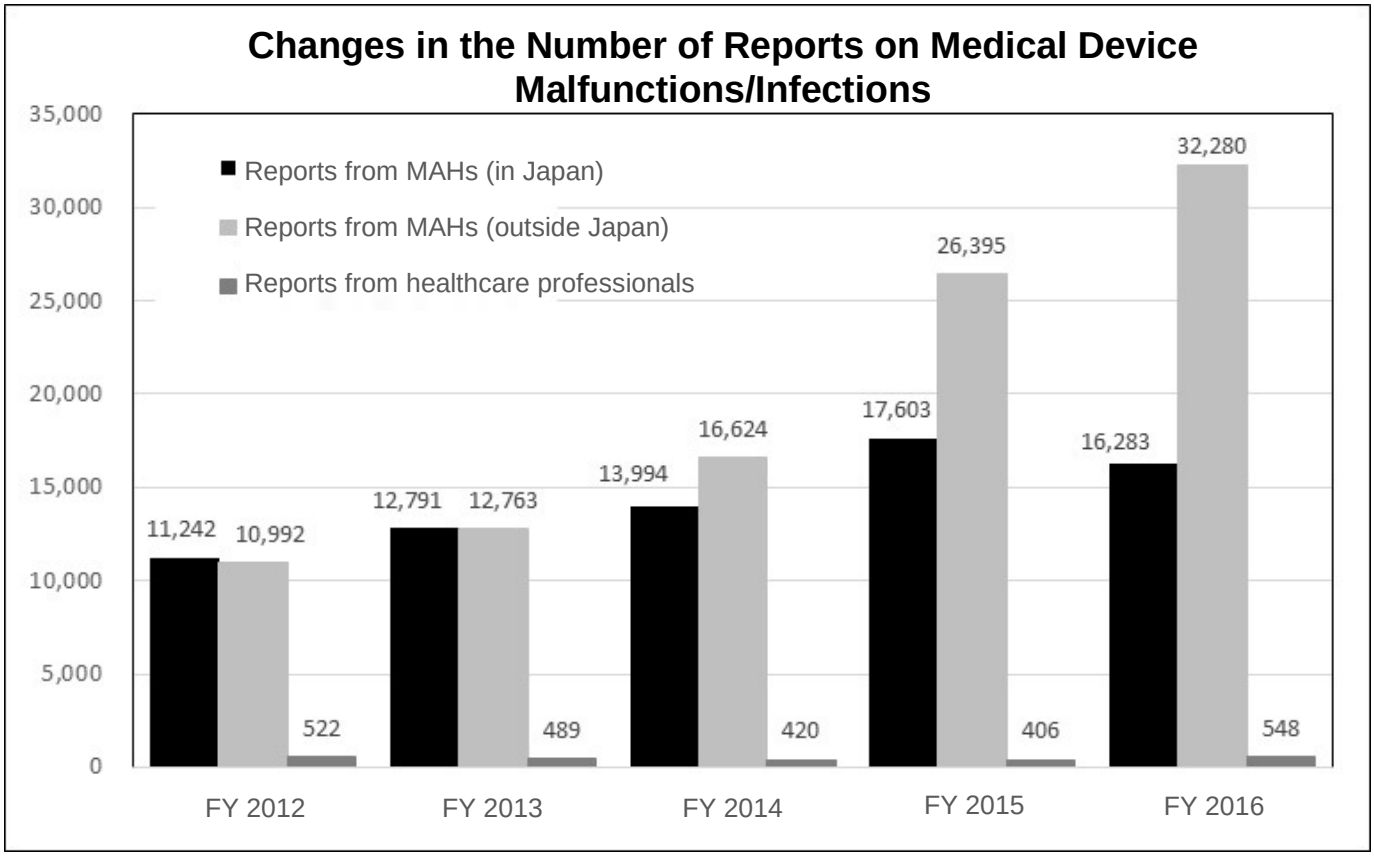
The numbers of cases investigated by PMDA in previous fiscal years are provided in the table below.

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of cases investigated by PMDA	663	862	1,067	1,100	1,132

Some case reports from medical institutions are investigated and analyzed by PMDA. Data on such case reports are provided to MAHs of suspected drugs (i.e., drugs suspected by PMDA to be the cause), via a dedicated server on the Internet.

2) Number of reports relating to medical devices

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Reports from MAHs	23,643	27,303	32,490	46,406	52,063
(medical device malfunctions, in Japan)	(11,242)	(12,791)	(13,994)	(17,603)	(16,283)
(medical device malfunctions, outside Japan)	(10,992)	(12,763)	(16,624)	(26,394)	(32,280)
(infections caused by drugs, in Japan)	(0)	(0)	(0)	(0)	(0)
(infections caused by drugs, outside Japan)	(0)	(0)	(0)	(1)	(0)
(research reports)	(3)	(5)	(20)	(598)	(1,289)
(foreign safety measure reports)	(1,337)	(1,669)	(1,779)	(1,742)	(2,144)
(periodic infection reports)	(69)	(75)	(73)	(68)	(67)
Reports from healthcare professionals	522	489	420	406	548
Total	24,165	27,792	32,910	46,812	52,611



3) Number of reports relating to regenerative medical products

	FY 2014*	FY 2015	FY 2016
Reports from MAHs	17	49	122
(medical device malfunctions, in Japan)	12	35	88
(medical device malfunctions, outside Japan)	0	0	0
(infections caused by drugs, in Japan)	0	0	0
(infections caused by drugs, outside Japan)	0	0	0
(research reports)	0	0	0
(foreign safety measure reports)	0	0	0
(periodic infection reports)	5	14	34
Reports from healthcare professionals	0	0	0
Total	17	49	122

** Number of cases after the enactment of the PMD Act on November 25, 2014.*

(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

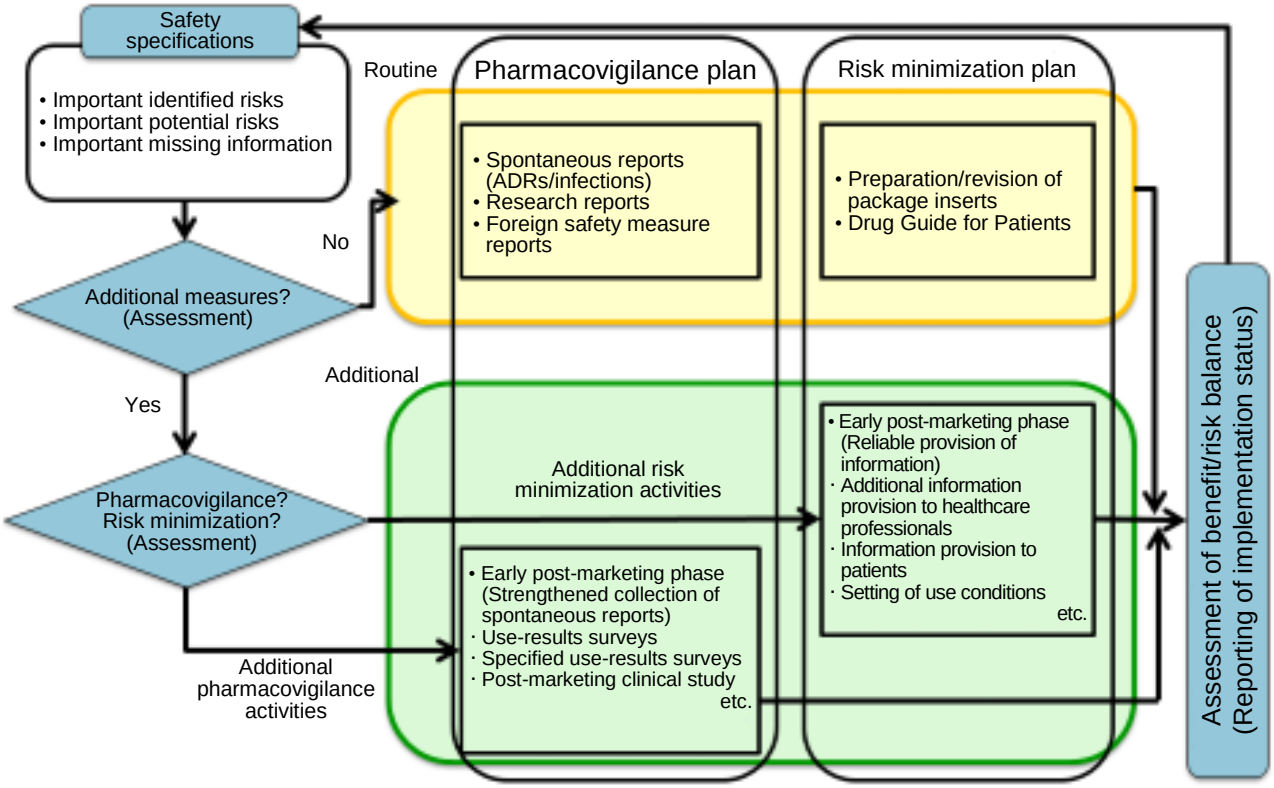
- PMDA launched a full-scale risk management system in FY 2011, and has been improving the system to consistently manage drug safety from the development phase to the post-marketing phase by having Risk Managers also work in Offices of New Drugs. The number of Risk Managers has gradually been increased. As of March 2017, 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 lifecycle of medical products, 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 became 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 May 2016, PMDA published “Summary of RMPs” (a list of contents of RMPs) and the main bodies of RMPs on the PMDA website, to promote the use of RMPs in medical practice.

  In FY 2016, new RMPs for 93 products and revised RMPs for 217 products (total) were disclosed on the PMDA website. As of the end of March 2017, RMPs for 270 products are available on the website.

Outline of Risk Management Plan

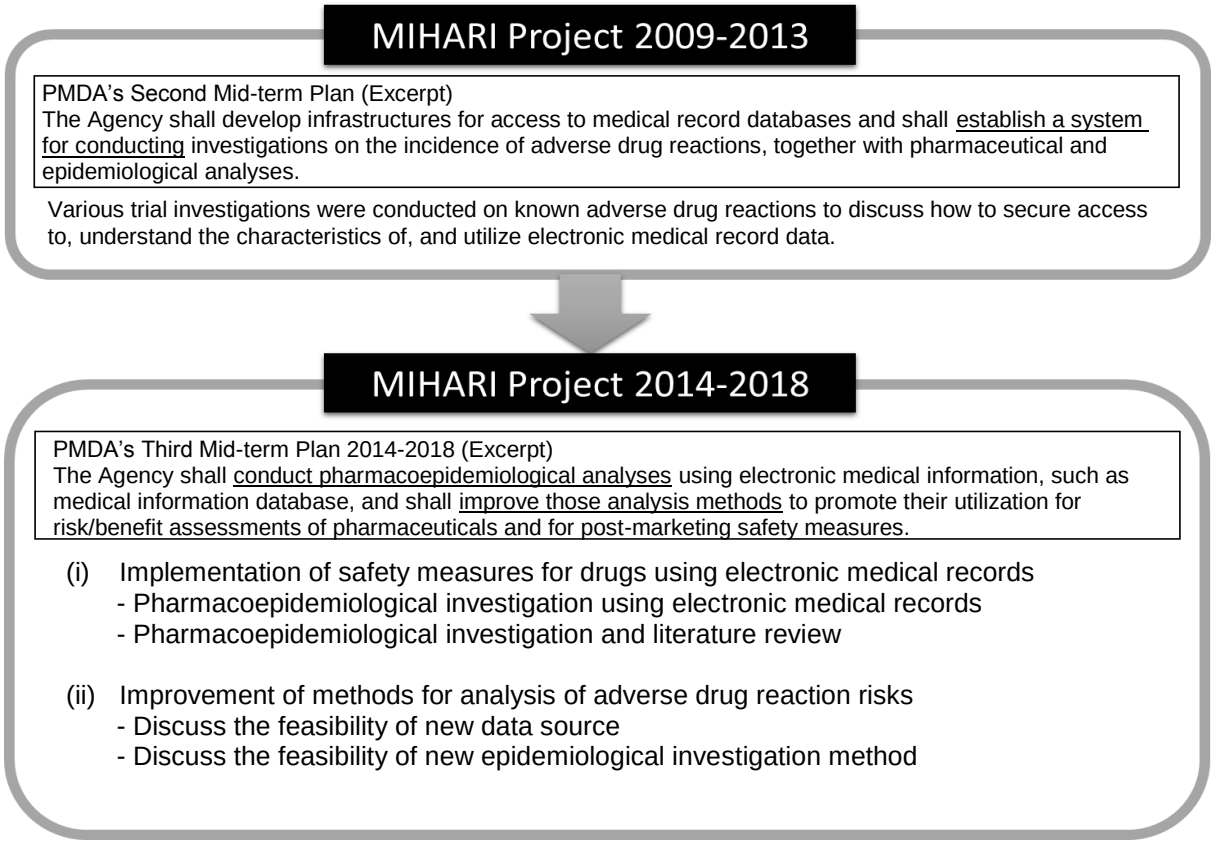


b. Use of electronic medical records etc.

- In accordance with the Third Mid-term Plan, PMDA intends to perform pharmacoepidemiological analysis using digitized medical information, such as a 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).

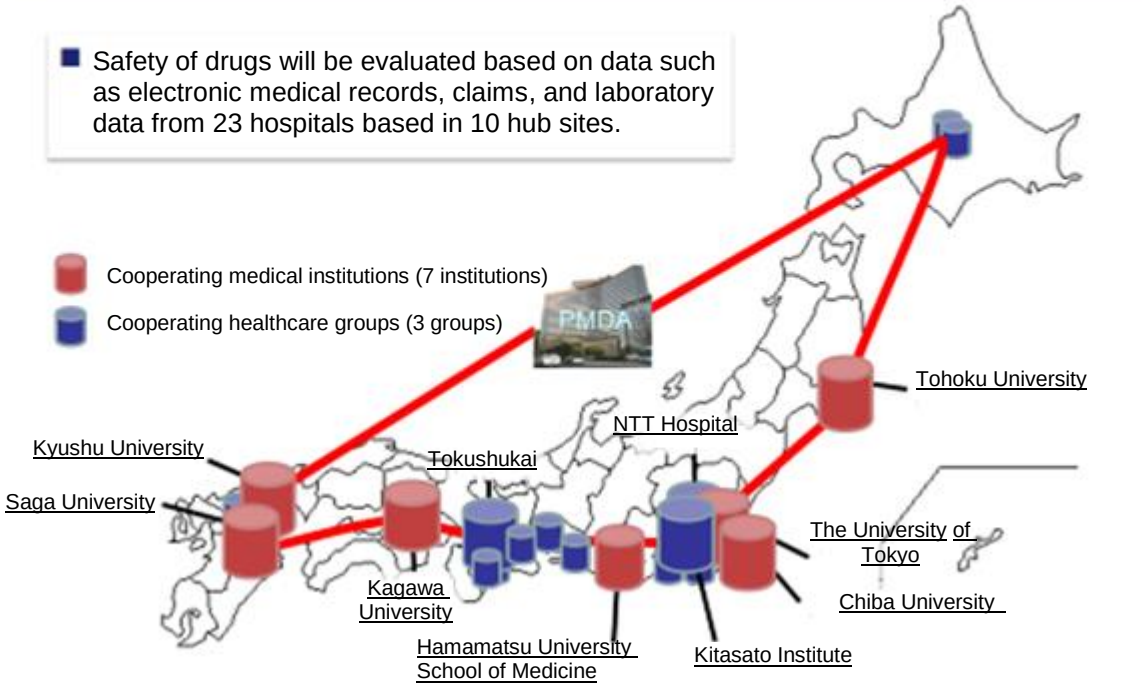
Direction of the MIHARI Project in the Third Mid-term Plan



In FY 2016, PMDA's Offices of New Drugs in its Review Division and its Offices of Safety worked together to conduct (a) reviews of post-marketing surveillance plans submitted by pharmaceutical companies and the pharmacoepidemiological research literature; and (b) a survey investigating the status of prescription drugs and associated risks by using databases (information from the survey and risk analysis is intended to be used as data to support regulatory decision-making). Also, at the request of MHLW, PMDA surveyed the use status of prescription drugs that were subject to mandatory revisions to the Precautions section of their respective package inserts by using databases. PMDA conducted a detailed analysis for "Comparison of cardiovascular risk by antidiabetic drug class" using the National Claim Data managed by the Health Insurance Bureau of MHLW as a new data source; PMDA has been making preparations for submitting a paper regarding the results of this analysis. In a working group with the pharmaceutical industry, hosted by MHLW, PMDA conducted a pilot survey on the assumption that databases may be used in post-marketing surveillance, in order to discuss the use of various medical information databases for safety measures or re-examinations. Through the survey, PMDA discussed (a) epidemiology-related issues to be addressed by the government (e.g., the launch of "epidemiological consultation" service), (b) points to note regarding items to be described in the plans for post-marketing database surveys; and (c) principles on compliance assessment. Also, PMDA discussed and reorganized the system for assessing epidemiological issues in the process of approval reviews for new drugs.

- Since FY 2011, PMDA has been developing the Medical Information Database Network (MID-NET®) system, which will serve as a key source of data for its MIHARI Project as part of MHLW's "Project for developing the MID-NET infrastructure." Specifically, PMDA is establishing a system to collect electronic medical information stored in 23 hospitals and 10 "hub" institutions, 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 the diagram below).

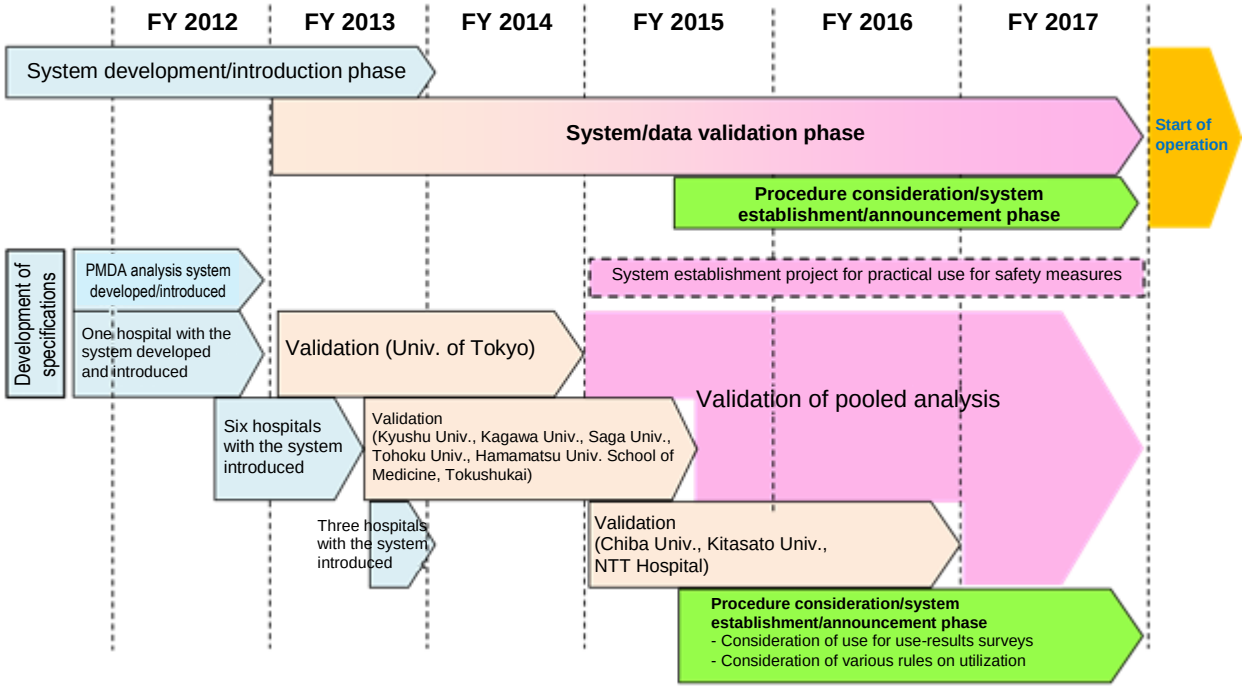
Medical Institutions Cooperating in the Medical Information Database Development Project



In FY 2016, PMDA conducted the following operations in preparation for full-scale implementation from FY 2018 onward.

- As in FY 2015, PMDA conducted validation tests to control and improve the quality of stored data in the database and made improvements as necessary for its utilization. PMDA succeeded in greatly improving the performance of the system and increased the reliability of MID-NET®.
- PMDA established system specifications at cooperating medical institutions which enabled faster analyses. These specifications were then implemented at 3 hub sites.
- As a trial survey, PMDA selected 5 topics related to safety measures for drugs and performed analyses utilizing MID-NET® in cooperation with 7 cooperating medical institutions. To create a program library, PMDA also made an analysis program that can be used in a versatile way for common research designs that are frequently used in pharmacoepidemiological surveys.
- PMDA participated in discussions at the “Workshop on Medical Information Database Operation” established by MHLW in January 2016, and considered utilization rules, expenses, etc. under the assumption of full-scale operation of the medical information database, including pharmaceutical companies’ access to the database from FY 2018.
- To advance compatibility between MID-NET® and other databases, PMDA reorganized technical problems using the pediatric and pharmaceutical information collection network of National Center for Child Health and Development as a model database.
- For the first time, PMDA revealed (1) the prescription status of codeine and the risk of codeine-induced respiratory depression in Japanese pediatric patients; and (2) the effects of safety measures against the risk of hypocalcemia due to denosumab in Japanese patients.

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 which was started in FY 2010 as a registry model project through collaboration among industries, government, and academia, 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. In FY 2016, PMDA advanced discussions on a new operation system with relevant academic societies, companies, etc. The discussions led to a decision that J-MACS Project would be managed, from FY 2017, mainly by the Japanese Association for Thoracic Surgery. As of March 31, 2017, a total 799 patients (680 for IVAD, 119 for extracorporeal VAD) have been enrolled in J-MACS at 41 medical institutions nationwide. Changes in the number of enrolled patients, survival rates, and other data have been 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 2016, PMDA continuously held the workshop on the project for the patient registration system for regenerative medical products. In the workshop, PMDA developed operational policies for the patient registration system for regenerative medical products. Three regenerative medical products have been approved to date, and a patient registration system was launched for 1 of the 3 products. (The system uses the databases of academic societies.) Further, sub-committee meetings were held to establish operational policy of patient registration system for the remaining 2 products (the

meetings were held separately for each product). As a result, the MAHs of the 2 products launched patient registration systems for the 2 products based on their own databases.

- On its website, PMDA created a web page for the “patient registration system for regenerative medical products.” The web page contains the following information:
  (a) The purpose of the patient registration system;
  (b) The operational policies for the patient registration system for regenerative medical products;
  (c) The outline of the database created by PMDA;
  (d) The roles of the workshop and sub-committees on the patient registration system for regenerative medical products and their member lists.

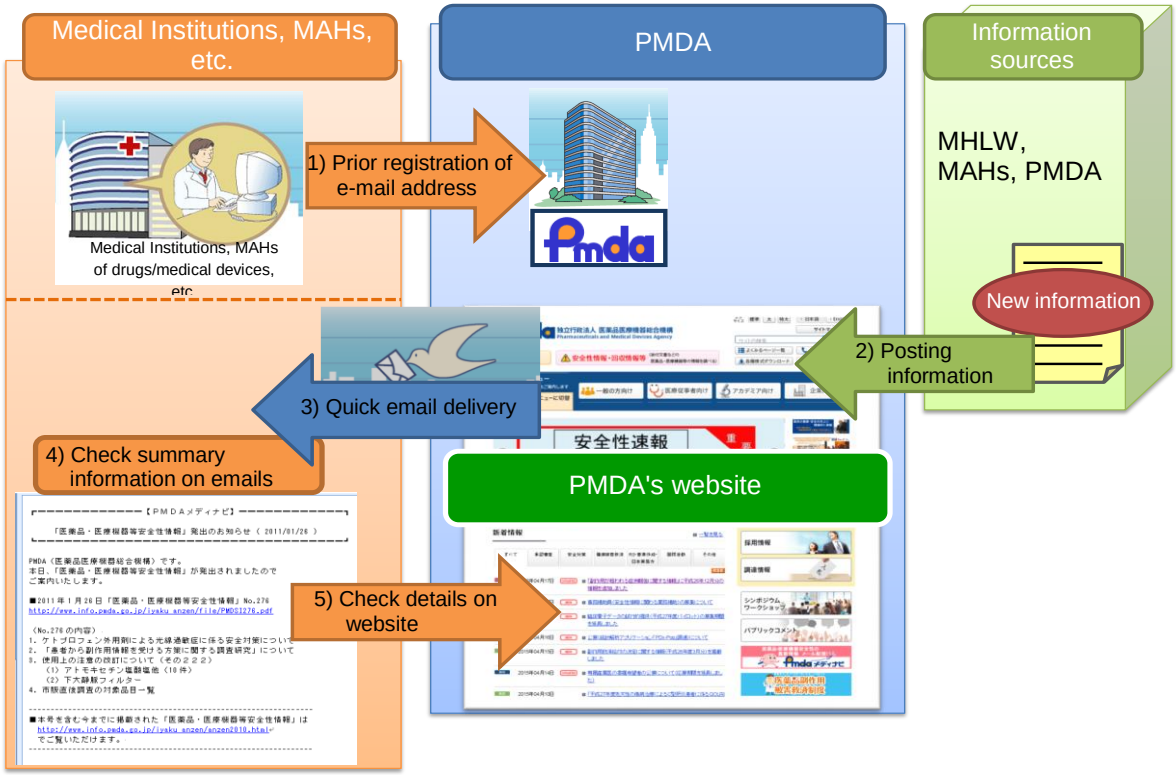
(iii) Establishment of a post-marketing safety system through information feedback

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.
- In response to comments from users of the PMDA website, PMDA made the website more user-friendly by changing the structure and display of the following web pages: “The Drug Guide for Patients,” “The list of RMPs,” and “The inquiry service on drugs/medical devices.”
- In addition, PMDA published the compilation of latest quality information of prescription drugs (commonly called the Blue Book) prepared by MHLW. PMDA publicized the Blue Book through the PMDA medi-navi service, to more effectively disseminate information regarding the quality of generic products.
- 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. At the end of FY 2015, the PMDA medi-navi service was upgraded. In FY 2016, PMDA continued to enhance its PR activities to raise the public awareness of the upgrade as well as the service itself, and to increase the number of subscribers. In addition, PMDA sent out a questionnaire to subscribers of the medi-navi service to ask how they use the information gained from the service and whether they forward the information to other people. The questionnaire results were analyzed to promote the use of the medi-navi service.
- As a result of the efforts described above, the number of subscribers to the medi-navi service was 153,596 at the end of FY 2016, showing an increase of 18,109 compared with the end of FY 2015. (This exceeded the target increase of 10,000 or more.) In FY 2016, 22,503 new subscribers were added, and 4,394 email addresses were deleted because they did not receive emails from the service as of the end FY 2016. The breakdown of subscribers is as follows:
  Approximately 45,800 hospitals or clinics (with an increase of approx. 4,600);
  Approximately 55,100 pharmacies (with an increase of approx. 8,300);
  Approximately 9,000 dental clinics or other medical facilities (with an increase of approx. 200);
  Approximately 20,200 MAHs or distributors (with an increase of approx. 2,500)

- At the end of FY 2016, there were 12,231 subscribers to the "My Drug List for Safety Update", an additional service offered by the PMDA medi-navi, with an increase of 22% (2,239) compared with FY 2015.

Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)



Breakdown of Content Distributed through the PMDA medi-navi during FY 2016

Content of e-mails	Number of e-mails	Content of e-mails	Number of e-mails
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)	0	Approval information (medical devices)	8
Product Recalls (Class I)	27	Approval information (prescription drugs)	27
Product Recalls (Class II)	313	Approval information (regenerative medical products)	1
Pharmaceuticals and Medical Devices Safety Information	10	Notifications on drugs Notifications on medical devices	36
Drug Safety Update (DSU)	12	Information on proper use of drugs	8
Revision of PRECAUTIONS of drugs	13	Information on drug risk under evaluation	12
Revision of PRECAUTIONS of medical devices	1	Information on products submitted for public knowledge-based applications, covered by national health 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)	43
Notification on self-check (medical devices)	0	Information on generic drugs	4
PMDA Medical Safety Information	3	Others	30

*Number of Information Documents Released on the PMDA's Website as of the End of FY 2016[*1]*

		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Package insert information						
	Prescription drugs	12,435	12,921	14,912	14,843	14,639
	Medical devices	17,539	19,309	20,504	22,001	23,754
	Regenerative medical products	-	-	2	3	4
	OTC drugs	10,158	10,234	11,127	11,360	11,385
	BTC drugs	-	-	20	15	16
	In vitro diagnostics	4,054	4,076	4,247	4,238	4,178
Drug Guide for Patients[*2]		1,748 (2,453 products)	2,155 (3,409 products)	2,701 (4,482 products)	3,213 (5,911 products)	3,366 (6,362 products)
Guidance for persons receiving vaccination[*2]		-	-	72 (74 products)	73 (75 products)	72 (74 products)
Safety information issued by MHLW						
	Directions for revision of package inserts (drugs)	-[*3]	257	272	284	297
	Notification of safety measures (drugs)	-[*3]	-[*3]	-[*3]	40	56
	Directions for revision of package inserts (medical devices)	45	48	50	53	54
	Notification of safety measures (medical devices)	-[*3]	-[*3]	-[*3]	83	88
	Notification on self-check	51	51	52	52	52
	Pharmaceuticals and Medical Devices Safety Information	-[*3]	168	178	188	198
	MHLW Press release	-[*3]	69	69	73[*4]	87[*4]
Dear Healthcare Professional Letters of Emergent Safety Communications (Yellow Letters)		25	27	30	24	24
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)					15[*5]	15[*5]
Risk Management Plan (RMP)		-	6[*6]	117[*6]	180	270
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])		91	101	111	121	132
Information about case reports						
	Information about case reports on suspected ADR	254,392	292,720	338,224	387,162	440,485
	Information about case reports on suspected malfunction	73,012	84,766	98,407	116,182	133,159
	Information about case reports on suspected malfunction of regenerative medical products	-	-	-	35	91
	Information about case reports on suspected malfunction in the mechanical part of combination drugs	-	-	-	6	339
Notification related to medical safety measures		87	96	108	119	130
PMDA Medical Safety Information		36	43	45	48	50
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		666 active ingredients (1,314 products)	700 active ingredients (1,416 products)	834 active ingredients (1,652 products)	[*7]	[*7]
Information on recalls[*8]						
	Drugs (including *in vitro* diagnostics)	1,907	1,913	1,817	375	351
	Quasi-drugs				49	42
	Cosmetics				229	242
	Medical devices				1,223	1,224
Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)						
	E-mails issued[*9]	207	215	234	223	557
	Subscribers	84,146	102,790	112,079	135,487	153,596

**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 The number of guidance documents and the numbers of drugs/vaccines listed in guidance.*

**3 Not totaled.*

**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 total number of files posted, including the number of revised files.*

**7 For the number of files posted, see 3.4.(4).*

**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 be 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 of contents of e-mails.*

b. Provision of information on package inserts

- At the end of FY 2016, PMDA had posted 14,639 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.
- The Guidelines for Package Inserts for Prescription Drugs is scheduled to be revised in FY 2017. To deal with the revision, in FY 2016 PMDA converted package insert information to XML and created requirement definitions for modifications of related systems.
- 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. A total of 23,754 package inserts were accessible on the PMDA website as of the end of FY 2016. Also for medical devices, PMDA has been providing links between notifications mandating revisions and the corresponding package inserts, similarly to drugs.
- For regenerative medical products, four package inserts were accessible on the website as of the end of FY 2016, following enactment of the PMD Act on November 25, 2014.
- For OTC drugs, 11,385 package inserts were accessible on the PMDA website as of the end of FY 2016.
- For BTC drugs, PMDA began providing information on package inserts upon enactment of the revised Pharmaceutical Affairs Act in June 2014. A total of 16 package inserts were accessible on the website as of the end of FY 2016.
- As of the end of FY 2016, 4,178 package inserts for in vitro diagnostic products were accessible on the PMDA website.

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 group, primary disease, height, body weight, suspected drug name (nonproprietary name and brand name), reason for use, BTC/risk category, route of administration, single-dose, start

date of administration, end date of administration, action against suspected drug, adverse drug reactions/adverse events, onset date, recurrence due to re-administration, evaluation, outcome, suspected concomitant drug name (nonproprietary name), and other concomitant drug names (nonproprietary name).

- Reports received from medical institutions that are investigated by PMDA are also published. At the end of FY 2016, PMDA had posted a total of 440,485 reports submitted by medical institutions and MAHs by November 2016.
- 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.
- The layout of line listing and the structure of JADER table were revised to meet ICH E2B (R3) standard, which was initiated in April 2016. The revised versions have been used and published since August 2016.

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 within about 4 months from the time of reporting: fiscal year reported, gender, age, outcome, term name, condition of the medical device, and adverse events experienced by patient.

  In total, 133,159 reports (submitted by November 2016) were posted by the end of FY 2016.

3) Public release of information on malfunction reports of regenerative medical products and combination drugs

- PMDA has published (a) reports submitted by MAHs concerning malfunction of regenerative medical products occurring in Japan (since July 2015) and (b) reports on malfunction of the mechanical part of combination drugs submitted by MAHs (since October 2015). In total, 91 reports on regenerative medical products (submitted by November 2016) and 339 reports on combination drugs (submitted by November 2016) were published by the end of FY 2016.

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 later determined that improper use persists or testing is being conducted improperly, the corresponding patients' claims for relief benefits for adverse reactions caused by such drugs may be rejected. 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.

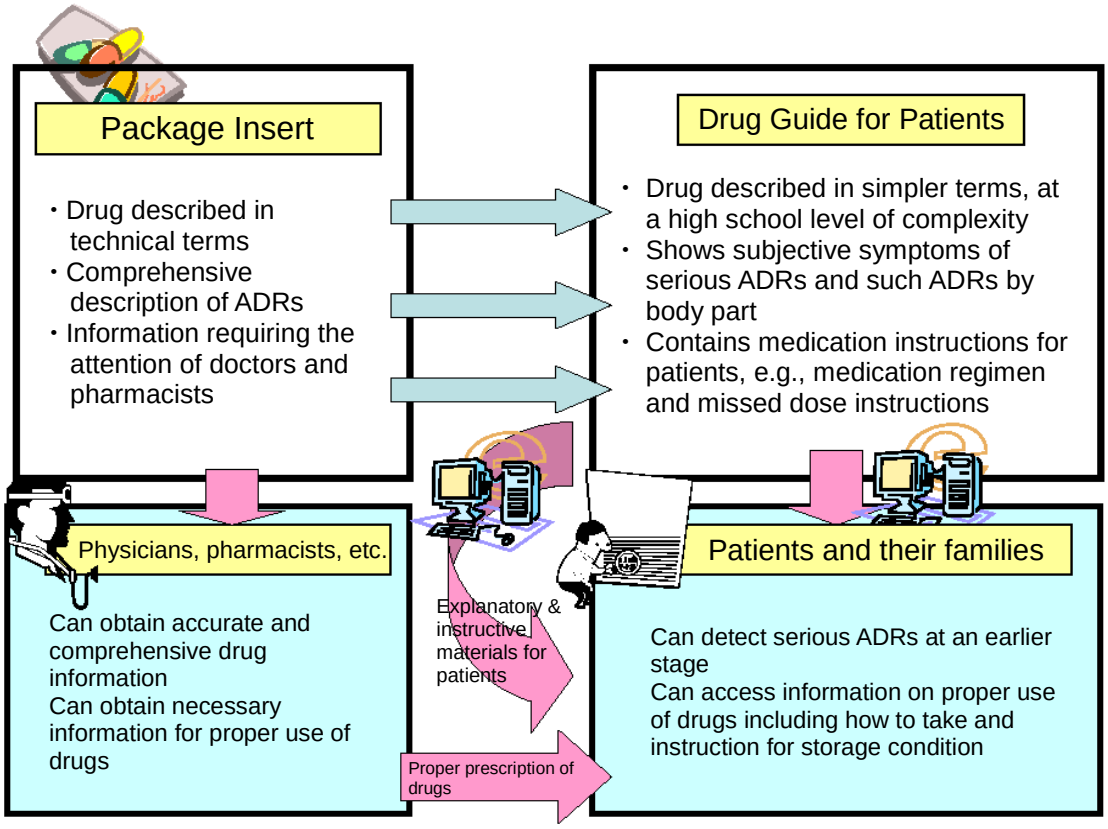
  The web page entitled, "Notices about Proper Use, etc. of Drugs from Pharmaceutical Companies," was divided into 2 separate pages: (1) a web page of information on the proper use of drugs; and (2) a web page of information on the safe use of drugs (warnings about medication mix-up). In this way, information is provided more effectively, making the web pages more accessible to users.

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 have been available on the PMDA website since January 2006. In FY 2016, 83 Drug Guides for Patients (including 11 for generic drugs) were prepared for products newly marketed or products for which the Precautions had been revised. A total of 3,366 Drug Guides for Patients (6,436 products) were posted by the end of FY 2016.

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 2016, no new products were included. A total of 72 Drug Guides for Patients (74 products) were posted by the end of FY 2016.

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.

- In FY 2016, MHLW started a project for revision of the manuals, and PMDA is supporting the project. PMDA intends to publish the manuals sequentially on its website after the 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 2016, 1,801 cases associated with drugs and 385 cases associated with medical devices were evaluated and the results were reported to MHLW. These 2,186 cases were posted on the PMDA website as shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 2,186	1,801	385
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.	23	7
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.	1,776	378

- 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 2016, the following 3 issues were posted on the web page.

No.	Posted on	PMDA Medical Safety Information titles
No.49	November 2016	Precautions against Misuse (Overdose) of Antirheumatic Methotrexate Preparations (Part 2)
No.50	March 2017	Precautions when setting syringe pumps
No.33	Revised March 2017	Accidental Burns during Surgery using a Light Source, an Electric or Laser Scalpel

g. Release of information on drug risks under evaluation

- 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. To provide healthcare professionals with faster access to potentially vital safety information, these types of information have been posted on the PMDA website before the implementation of safety measures as appropriate since July 2011 as “risk information currently under evaluation”.

h. Information provision in English

- To disseminate information on safety measures to foreign countries, PMDA translated the following documents into English and published them on the PMDA website:

  All of the PMDA Risk Communications;
  Information on revision of Precautions of drugs;
  Summaries of investigation results;
  The PMDA Medical Safety Information;
  The PMDA Request for Proper Use of Drugs;
  The Pharmaceuticals, and Medical Devices Safety Information, is issued by MHLW.

  In addition, information on revision of Precautions of medical devices (2 documents) and summaries of investigation results (2 documents) were translated into English and posted on the PMDA website.

  PMDA also provided English-language translations of notifications issued by MHLW and PMDA. In FY 2016, 6 translated notifications were newly posted on the PMDA website. In March 2017, PMDA started a project to provide package insert information (including revision information) to foreign regulatory agencies in Asian countries such as Thailand and Indonesia, and also to provide information to foreign regulatory agencies as appropriate under confidentiality agreements.

i. Responses to consultation requests from MAHs

- 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 2016 is shown below:

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs	704	776	869	991	795
Medical devices	179	95	325	772	1,597
Medical safety	80	31	72	116	78
Regenerative medical products	-	-	0*	4	3

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

- Consultations for medical safety conducted in FY 2016 were mainly in respect to 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 2016, the number of persons receiving consultations was 13,448 (15,703 calls) for drugs and 415 (463 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 Parties Receiving Consultations on Drugs/Medical Devices

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Persons receiving consultations on drugs [persons/day]	9,679 [39.5]	10,244 [42.0]	11,556 [47.4]	12,551 [51.7]	13,448 [55.3]
(of which consultations on generic drugs)	(493)	(626)	(543)	(600)	(495)
Persons receiving consultations on medical devices [persons/day]	700 [2.9]	547 [2.2]	370 [1.5]	406 [1.7]	415 [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.
- In FY 2014, PMDA conducted surveys to determine how hospitals obtain, communicate, and use safety information concerning (a) drugs (in 8,481 hospitals nationwide) and (b) medical devices (in 500 randomly-sampled general hospitals). In FY 2015, PMDA conducted a second survey to determine how medical clinics obtain, communicate, and use safety information on drugs (in 10% of general clinics nationwide providing medical services covered by national health insurance [i.e., 8,737 clinics]), and another survey to determine how pharmacies obtain, communicate, and use safety information on drugs (in 10% of health insurance pharmacies nationwide [5,664 pharmacies]). PMDA communicated the results of these surveys and issues identified, at academic conferences, lecture meetings, and other occasions in collaboration with professional organizations, in order to promote appropriate procurement, communication, and use of safety information in clinical practice.

Outline of surveys conducted to date

<table>
<tr><th>FY</th><th>Title</th><th>Target</th><th>Period</th><th>Remarks</th></tr>
<tr><td>2010</td><td>Survey on the status of communication and use of drug safety information</td><td>Hospitals nationwide
(8,679 institutions)</td><td>January 13, 2011 to
February 10, 2011</td><td>Questionnaire survey
(response rate, 41.2%)</td></tr>
<tr><td>2011</td><td>Survey on the status of communication and use of drug safety information</td><td>Hospitals nationwide
(8,640 institutions)</td><td>January 20, 2012 to
February 10, 2012</td><td>Questionnaire survey
(response rate, 25.9%)</td></tr>
<tr><td rowspan="2">2012</td><td rowspan="2">Survey on the status of procurement, communication, and use of drug safety information</td><td>Hospitals nationwide
(8,541 institutions)</td><td>January 7, 2013 to
February 28, 2013</td><td>Questionnaire survey
(response rate, 53.4%)</td></tr>
<tr><td>Half of all pharmacies nationwide
(26,915 institutions)</td><td>January 7, 2013 to
February 28, 2013</td><td>Questionnaire survey
(response rate, 64.6%)</td></tr>
<tr><td rowspan="2">2013</td><td>Survey on the status of procurement, communication, and use of good practices on drug safety information</td><td>14 hospitals and clinics/pharmacies near the hospitals in Japan</td><td>October 2013 to
February 2014</td><td>Door-to-door survey</td></tr>
<tr><td>Basic survey on the status of procurement, communication, and use of medical device safety information</td><td>9 hospitals/clinics in Japan</td><td>October 2013 to
February 2014</td><td>Door-to-door survey</td></tr>
<tr><td rowspan="4">2014</td><td rowspan="2">Survey on the status of procurement, communication, and use of drug safety information</td><td>Hospitals nationwide
(8,481 institutions)</td><td>December 15, 2014 to
March 13, 2015</td><td>Questionnaire survey
(response rate, 57.8%)</td></tr>
<tr><td colspan="3">Summary of survey results (excerpt)
1. Obtaining appropriate information based on the characteristics of the information media
2. Utilization of appropriate information when drugs are selected
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</td></tr>
<tr><td rowspan="2">Survey on the status of procurement, communication, and use of medical device safety information</td><td>500 general hospitals
(sampled randomly)</td><td>February 9, 2015 to
March 13, 2015</td><td>Questionnaire survey
(response rate, 40.0%)</td></tr>
<tr><td colspan="3">Summary of survey results (excerpt)
1. Improving the information management system and use of information according to the circumstances of 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</td></tr>
</table>

<table>
<tr><td rowspan="5">2015</td><td rowspan="5">Survey on the status of procurement, communication, and use of drug safety information</td><td>10% of general clinics
*limited to institutions providing healthcare services as stipulated by health insurance
(8,737 institutions)</td><td>October 6, 2015 to December 14, 2015</td><td>Questionnaire survey
(response rate, 53.1%)</td></tr>
<tr><td colspan="3">Summary of survey results (excerpt)
1. Utilization of the PMDA website and the PMDA medi-navi
2. Obtaining important information promptly and comprehensively
3. Obtaining information based on the characteristics of the information media
4. Sharing patient information between clinics and pharmacies</td></tr>
<tr><td>10% of health insurance pharmacies
(5,664 institutions)</td><td>October 6, 2015 to December 14, 2015</td><td>Questionnaire survey
(response rate, 68.2%)</td></tr>
<tr><td colspan="3">Summary of survey results (excerpt)
1. Utilization of electronic information including the PMDA website and the PMDA medi-navi
2. Obtaining and controlling important information promptly and comprehensively
3. Obtaining appropriate information in a timely fashion based on the characteristics of the information media
4. Sharing patient information between medical institutions and pharmacies</td></tr>
</table>

**See PMDA website for details.*

- PMDA communicated how to use safety information effectively as advice for medical institutions, mainly at the following academic conferences and workshops:

Surveys on drug safety information

- Annual Meeting of the Japanese Society of Drug Informatics
- Annual Meeting of the Japanese Society of Pharmaceutical Health Care and Sciences
- Japan Pharmaceutical Association Congress of Pharmacy & Pharmaceutical Science: PMDA Session
- Japanese Society of Hospital Pharmacists: Workshops (10 workshops a year)

Surveys on medical device safety information

- Annual Congress of Japanese Society for Quality and Safety in Healthcare
- Association of Japanese Healthcare Corporations: Medical Safety Manager Training Workshop
- Medical safety management workshop sponsored by the Tokai-Hokuriku Group of National Hospital Organization

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) Establishment of the PMDA "Rational Medicine" Initiative

- PMDA established and publicized its "Rational Medicine" Initiative and disseminated accompanying informational materials to promote regulatory science, based on which drugs, medical devices, and regenerative medical products are evaluated. PMDA also submitted an article to the DIA Global Forum (April 2017 Vol. 9 Issue 2).

(ii) Use of the Science Board

- PMDA's Science Board was formed 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 promote optimal reviews of 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 Science Board (parent committee) selected themes to be discussed during the third term starting in April 2016. The following 3 Subcommittees were set up for the respective themes. As of March 31, 2017, the parent committee has convened 6 times (including 1 document-based meeting), and the Subcommittees have been discussing the themes.
  1) Subcommittee on Clinical Evaluation of Rare Cancer (convened 3 times)
  2) Subcommittee on Facilitating R&D of Academia-Originated Pharmaceuticals (convened twice)
  3) Subcommittee on Artificial Intelligence and Its Application in Medical Field (convened twice)
- PMDA disclosed materials and meeting minutes of the Science Board and the Subcommittees (excluding confidential information) on the website.
- On August 4, 2016, PMDA held "PMDA Science Board Symposium 2016" to present the outcomes of the Science Board in the 1st and 2nd terms and to conduct a panel discussion of future prospects.
- PMDA prepared a booklet titled "Second-Term Science Board Activity Report," which includes a summary of discussions in the 5 reports prepared by the 5 subcommittees in the second term. The booklet was distributed at the above symposium, related academic conferences, etc. In this way, PMDA published the discussion results of the Science Board on various occasions as well as through its website.

(iii) 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.
- To conduct appropriate 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 the research purpose, how the research is

related to PMDA's operations, and on comments from the Regulatory Science Research Evaluation Committee. In FY 2016, 7 projects (1 new project and 6 ongoing projects) were selected as designated research, and the projects were implemented. The results of 4 of these projects were published in academic journals or lecture meetings (2 published in papers, 2 lectures) (reposted).

- For innovative products, see 3.2.(2) (i).
- PMDA conducted regulatory science research in collaboration with external organizations such as academic institutions. (28 projects used public research funds, such as AMED and Health and Labour Government-Promoted Research Project Expenditure.) In addition, 1 joint study is 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, to select new designated research projects for FY 2017 based on the relevant rules. As in last year, PMDA held a meeting where the final report on designated research was presented. Two projects that were concluded in FY 2015 were highly evaluated for a favorable outcome achieved through the provision of information in academic papers and lectures.
- PMDA developed rules, formats, etc. for regulatory science research to match actual situations. Further, the agency held meetings of the Ethics Review Committee (2 projects) based on Rules for Handling Ethical Reviews at the Pharmaceuticals and Medical Devices Agency. Subsequently, PMDA conducted expedited review for application issues (4 products) and improved the environment and systems for such research activities.
- In FY 2016, PMDA held an exhibition on the topic of regulatory science research as in FY 2015. Employees conducting designated research shared information with other employees so that they can increase their motivation for their own research.
- Since FY 2015, PMDA has allowed employees to describe their engagement in designated research projects in the personnel evaluation sheet. In FY 2016, 2 employees requested that their performance on research be recorded on the sheet.
- In the working groups (WGs) within the 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 (Companion Diagnostics WG, Pediatric Drugs WG, ICH Q12 WG, Innovative Manufacturing Technology WG, and Nanomedicine Initiative WG).
- PMDA made presentations at academic conferences regarding discussions held in the Projects Across Multi-Offices and performed PR activities (Companion Diagnostics WG [4 academic presentations/lectures], Omix WG [2 academic presentations/lectures], Pediatric Drugs WG [4 academic presentations, 2 papers, and 1 workshop], Orphan Drugs WG [1 explanatory meeting], ICH Q12 WG [14 academic conferences/lectures and 1 paper], CIN (Clinical Innovation Network) WG [3 academic conferences/lectures], Innovative Manufacturing Technology WG (6 academic conferences/lectures], Nanomedicine Initiative WG [3 academic conferences/lectures and 1 paper], and Cardiovascular Risk Evaluation WG [6 academic conferences/lectures and 2 papers]).
- The Projects Across Multi-Offices exchanged opinions about evaluation policy and other issues with drug development companies, related industry groups, academic societies, etc. (3 occasions for Companion Diagnostics WG, 1 occasion for Omix WG, 1 occasion for Pediatric Drugs WG, and 1 occasion for Orphan Drugs WG).
- Pediatric Drugs WG within the Projects Across Multi-Offices held a PMDA workshop titled "Toward promotion of pediatric drug development—what we can do now for the future of children" on

November 28, 2016. During the workshop, ideas were exchanged among the industry, academia, and government.

- Each WG within the Projects Across Multi-Offices, opinions were exchanged among the industry, academia, and government through cooperation in related AMED research projects (Companion Diagnostics WG, Pediatric Drugs WG, ICH Q12 WG, CIN WG, Innovative Manufacturing Technology WG, and Cardiovascular Risk Evaluation WG).

(iv) Enhancement of staff training

a. Lectures and guidance given by experts

- To improve the skills of its staff, PMDA provided its employees with the following training opportunities:

  (a) Special training programs including lectures on product development activities at companies, given by external experts from both Japan and other countries;

  (b) Training in respective review components with the cooperation of the National Institute of Health Sciences (NIHS) (13 sessions);

  (c) Training programs in clinical study design, to learn biostatistics (10 sessions);

  (d) Training programs in pharmacoepidemiology to learn features of pharmacoepidemiological study design (11 sessions).

  The training program of pharmacoepidemiology was enhanced by increasing the number of sessions and by offering 3 lectures by external experts. Since PMDA began to accept electronic data of clinical studies, it established and provided CDISC overview training (8 sessions) and pharmacokinetics/clinical pharmacology and modeling & simulation training (3 sessions). Joint training with AMED was also conducted (1 session; 19 participants).

- A total of 9 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 training programs were also provided (18 employees).

b. Overseas dispatch

- PMDA dispatches employees for fixed terms to provide them with opportunities to learn about review and safety-related activities of overseas regulatory authorities (1 employee).

- Based on the National Action Plan on Antimicrobial Resistance (AMR) (April 5, 2016), PMDA cooperated in the MHLW’s efforts for the early introduction of AMR therapeutic drugs/diagnostics. Also, in response to the discussion of measures against drug-resistant bacterial infections at the G7 Ise-Shima Summit (May 2016) and other conferences, PMDA held a face-to-face meeting with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in September 2016. At the meeting, the regulatory agencies shared the latest information regarding application data for approval reviews, and agreed to further cooperate with each other to discuss relevant issues.

c. On-site training

- On-site training programs such as visits to drug/medical device manufacturing facilities (4 facilities, a total of 46 employees) and IRBs of medical institutions (a total of 23 employees) were provided.

- Product hands-on training using medical devices was provided (3 facilities, a total of 37 employees). In addition, PMDA staff visited the IRB of National Cancer Center (3 employees) and the section of operations of pharmacists for outpatient cancer chemotherapy at National Cancer Center Hospital East (3 employees).
- PMDA provided radioactivity technology training, including hands-on training in radioactivity measurement, to offer opportunities for learning about technical knowledge and skills in radioactivity (2 employees).
- Four employees were dispatched to 2 hospitals for practical training under hospital pharmacists and 3 employees to 2 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, 8 employees were dispatched to 1 medical institution to observe testing procedures, treatments, etc. using medical devices.

(v) 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 and 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 2016, PMDA conducted personnel exchanges with 24 universities, etc., accepted 17 researchers as specially appointed experts (including non-regular staff), and dispatched a total 38 employees (including non-regular staff).
- Five guidelines were developed based on the outcomes of projects: guidelines on (1) durability testing methods for coronary stents, (2) durability testing methods for femoropopliteal stents, (3) in vitro thrombogenicity testing methods for blood removing tubes for left ventricular assist devices, (4) in vitro thrombogenicity testing methods for continuous hemofilters, and (5) robot navigation systems for percutaneous energy irradiation. These guidelines were published as notifications issued by the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare (as of the end of March 2016).

b. Promotion of collaboration and cooperative relationships through comprehensive partnership agreements, etc.

- Since FY 2015, PMDA has 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 Centers for Advanced and Specialized Medical Care. PMDA concluded comprehensive partnership agreements with the National Cancer Center Japan, Hiroshima University, Keio University, and University of Tsukuba in FY 2015, and with the National Center of Neurology and Psychiatry, Tohoku University, and National Center for Global Health and Medicine in FY 2016. Under the comprehensive partnership agreements, PMDA conducted human resource exchanges, lectures, study meetings, joint research, etc. as described below, and contributed to human resources development for regulatory science.

- In FY 2016, 4 individuals from the National Cancer Center Japan worked at PMDA, and 1 PMDA staff member was seconded to the Center as part of a personnel exchange program. Also, PMDA staff members participated, as research collaborators, in a Center-supported research study entitled, “Practical Application of Innovative Cancer Medicines: Research on Proper Use and Safety Assurance of Novel Anticancer Agents based on PK/PD/PGx.” The Center provided PMDA employees with 2 training programs (which allowed PMDA staff to visit the IRB and the Center’s pharmacists engaged in outpatient cancer chemotherapy). The Center and PMDA held 1 study meeting on individualized medicine, etc.
- At Hiroshima University, a PMDA executive gave 1 lecture on pharmaceutical administration and PMDA’s operations, as part of Faculty Development, to faculty members of the university. In FY 2016, 1 person from the university worked at PMDA as part of personnel exchange program.
- In FY 2016, 1 person from Keio University worked at PMDA as part of personnel exchange program.
- At University of Tsukuba, 6 PMDA officers/employees served as lecturers for the “Drugs/Medical Devices Regulatory Science Course,” a course offered by the university.
- On July 11, 2016, PMDA concluded a partnership agreement with the National Center of Neurology and Psychiatry. In FY 2016, 3 people from the Center worked at PMDA and 1 PMDA staff member at the Center, as part of personnel exchange program. A PMDA employee gave 1 lecture on pediatric epilepsy to the Center’s staff. In addition, 2 study meetings were co-held by the Center and PMDA regarding clinical evaluation, etc. of neural/muscular diseases.
- On October 31, 2016, PMDA concluded a partnership agreement with Tohoku University. In FY 2016, 3 people from the university worked at PMDA. One PMDA employee gave a lecture on PMDA’s operations, to the university’s graduate students.
- On March 14, 2017, PMDA concluded a partnership agreement with the National Center for Global Health and Medicine. PMDA Chief Executive delivered a lecture titled “Collaboration between National Center for Global Health and Medicine and PMDA.” In FY 2016, 3 individuals from the Center worked at PMDA as part of personnel exchange program.
- PMDA collaborates with the National Cancer Center Japan and the National Center of Neurology and Psychiatry, in the AMED research project, through the research group for establishment of disease registration system (patient registry).
- PMDA has the comprehensive graduate school partnership agreements with graduate schools. PMDA staff members (20 delegated and 7 non-delegated PMDA officers/employees) gave 33 lectures at the graduate schools.

3.4.(2) Actions taken for internationalization

- Based on the “PMDA International Strategic Plan 2015” and the “International Pharmaceutical Regulatory Harmonization Strategy” of MHLW (both released in June 2015), PMDA conducted the following activities:

(i) Strengthening of cooperation with the U.S., EU, Asian countries, and related international organizations

PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

- On April 2016, PMDA established the “Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (the “PMDA-ATC”).” It is the world’s first innovative attempt to provide the officers in foreign regulatory agencies with continual training not only in Japan but outside Japan.

At the same time, the Office of International Cooperation was launched to perform the Center's main practical operations and secretariat functions. PMDA-ATC systematically planned and implemented the training seminars listed in the table below (a total of 7 seminars with a total of 161 attendees from 27 countries/regions). All the seminars were highly evaluated by participants. The training seminars were successful, because individual seminars were designed specifically (e.g., lectures, case studies, group works, and visits to institutions) to achieve their own purposes. Based on the basic policies for relocation of government-related agencies (developed in March 2016), in June 2016 PMDA established its Hokuriku Branch Office in the Toyama prefectural office and the PMDA-ATC Training Institute within the Office. By utilizing this training institute, PMDA conducted a GMP training seminar as one of the above seminars.

PMDA received positive reviews of the seminars provided by the PMDA-ATC, and was therefore certified as an "APEC LSIF RHSC Training Center of Excellence for Regulatory Science: CoE" in the areas of (a) multi-regional clinical trials (MRCT)/GCP inspections and (b) pharmacovigilance (February 2017).

	Seminar content/area	Date	Venue	No. of participants (No. of countries/ regions)
1	Reviews, safety measures, etc. for drug products	July 25-29, 2016	PMDA	13 (7)
2	Reviews, safety measures, etc. for drug products	September 26-29, 2016	Thailand (Bangkok)	13 (2)
3	Reviews, safety measures, etc. for medical devices	November 7-11, 2016	PMDA	28 (13)
4	Appropriate application and review procedures for drug products	November 15-17, 2016	Taiwan (Taipei)	28 (10)
5	Drug product GMP	December 5-9, 2016	Toyama City	19 (12)
6	Multi-regional clinical trial of drugs	January 23-26, 2017	PMDA	32 (14)
7	Pharmacovigilance	February 6-9, 2017	PMDA	28 (15)

Information exchanges with regulatory authorities in Europe and the United States, etc.

- PMDA continuously exchanged information regarding consultations held with companies on clinical studies and regarding review and safety measures with the US FDA EMA, and other organizations, based on the Confidential Agreement (CA). PMDA made use of such information to ensure that review and safety measures were correctly implemented based on the latest scientific knowledge available to PMDA.

  PMDA is engaged in cluster activities as a tool for periodical information exchange with European countries and the US. PMDA strengthened its involvement in pharmacovigilance cluster to create an environment that enables exchanging information of safety measures in a closer manner, in addition to the active involvement in existing clusters such as pediatrics, biosimilars, and regenerative medical products.

- Based on the antimicrobial resistance (AMR) action plan (April 5, 2016), PMDA cooperated in the MHLW's efforts for the early introduction of AMR therapeutic drugs/diagnostics. Also, in response to the discussion of measures against drug-resistant bacterial infections at the G7 Ise-Shima Summit (May 2016) and other conferences, PMDA proposed and held a face-to-face meeting with FDA and EMA in September 2016. At the meeting, the agencies shared their policies and experiences in approval reviews, and agreed to further cooperate with each other to discuss relevant issues.

- PMDA held meetings with regulatory authorities in Europe (EMA), India (CDSCO), South Korea (MFDS), China (CFDA), Brazil (ANVISA), Taiwan (TFDA), Thailand (TFDA), and Indonesia (BPOM), to further reinforce the collaborative relationships.

  In addition, PMDA entered into a confidential agreement (CA) with WHO and further strengthened its collaborative relationship with the organization.

- The collaborative relationship between Japan and China had previously been suspended. However, in July 2016, PMDA's Chief Executive and officers of MHLW visited China to hold a meeting with senior CFDA officials. As a result, the collaborative relationship was resumed.

Dispatching liaison officers, etc.

- PMDA continued to dispatch liaison officers and PMDA staff members to the agencies in the United States and Europe (PMDA staff were sent to the review and safety divisions in the agencies) to collect information and reinforce collaboration with the agencies.

  Through the liaison officer dispatched to EMA, PMDA obtained information on EMA's scientific committees (e.g., CHMP, PRAC), detected trends in PRIME, big data, model & simulation, etc., and exchanged information and opinions with EMA. In addition, the liaison officer stationed at EMA participated in various workshops sponsored by EMA and informed EMA about the trends in Japan.

- PMDA accepted a staff member from EMA for the first time, and informed EMA with the trends in the development of pediatric drugs and other activities in Japan, and exchanged opinions with EMA.

GLP, GCP, GMP, and QMS

- PMDA conducted mutual acceptance of GLP investigation reports based on the OECD's mutual data acceptance system.

- As in FY 2015, PMDA exchanged information on GCP inspections with Taiwan. In addition to this, in FY 2016 PMDA provided on-demand training and lectures, and exchanged information on QMS inspections, thereby reinforcing the collaboration with Taiwan. PMDA exchanged GMP inspection reports with the US FDA, Health Canada, Ireland HPRA, and other agencies to improve inspection efficiency.

- PMDA exchanged opinions with FDA and EMA in the anticipation that GCP inspection reports will be exchanged between PMDA and these regulatory authorities. PMDA's participation in the EMA-FDA GCP initiative was proposed. (The initiative aims to contribute to efficient GLP/GCP/GPSP inspection and data integrity assessment.) PMDA thus made preparations for the pilot participation in the initiative

  PMDA conducted the following activities to build a relationship based on trust with the US and European regulatory agencies, in order to create an environment that promotes collaboration in GCP activities between PMDA and the agencies:

  (1) Before conducting GCP inspections outside Japan, PMDA contacted the local regulatory agencies in advance, and then conducted the inspections in the presence of representatives of the regulatory agencies, wherever possible.

  (2) PMDA accompanied, whenever possible, inspections conducted in Japan by overseas regulatory agencies, and shared information with the agencies.

  (3) PMDA dispatched its staff (members of the Office of Conformity Audit) to the US FDA and EMA. They participated in training programs, and exchanged opinions on compliance inspection methods with the agencies.

  PMDA prepared the environment to improve collaboration and implementation for GCP.

As for the Asian region, PMDA gave lectures on Japanese regulations and standards to staff of the regulatory agencies in Taiwan, South Korea, China, etc. at their request. In this way, PMDA made efforts to disseminate information on Japanese regulations and standards, in anticipation of future collaboration with the agencies in Asia.

- PMDA supported the negotiations between Japan (MHLW) and EU for expanding the coverage of mutual recognition agreements (MRA) related to drug GMP. The countries under the MRA are recognized as having standards equivalent to the Japanese GMP requirements, and as being able to implement such standards. In addition to the 15 countries already under the MRA, in April 2016 Japan succeeded in adding the following 13 countries to the MRA: Bulgaria, Cyprus, Czechia, Croatia, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia, Slovenia.
- From November 2016, PMDA has participated in an international GMP inspection rationalization program for drug substance manufacturers conducted by EMA, the US FDA, Australia, Canada, etc., and contributed to quality assurance of drugs distributed not only in Japan but in the world by conducting activities such as sharing GMP inspection information related to overseas manufacturing sites of drug substances.

Japanese Pharmacopoeia

- In September 2016, PMDA, WHO etc. co-hosted the 7th International Meeting of World Pharmacopoeia. In collaboration with other countries, PMDA was actively engaged in drawing up the agenda for the meeting. A PMDA staff member served as the chair of the meeting and led the development of Good Pharmacopoeial Practices (GPhP). PMDA also took this opportunity to hold bilateral meetings with the staff of the British Pharmacopoeia and the Brazilian Pharmacopoeia, to promote mutual understanding and establish cooperative framework.
- Following the 7th International Meeting of World Pharmacopoeias, PMDA held an international symposium of the 130th anniversary of the Japanese Pharmacopoeia (JP), where PMDA sought to reinforce supply chains at a global level by promoting international collaboration and cooperation among Pharmacopoeias, and by promoting international understanding of the quality principles specified in the JP. Approximately 400 people from Japan and other countries participated in the symposium, including those who participated in the International Meeting of World Pharmacopoeias.
- In July 2016, PMDA exchanged opinions with the staff of the European Pharmacopoeia (EP). In September 2016, PMDA and the EP concluded a memorandum of cooperation (MOC) and a confidential agreement (CA) in the area of pharmacopoeias. In December 2016, PMDA was permitted to participate as an observer in the EP Commission. In March 2017, PMDA participated in the Commission meeting, thereby further reinforcing the collaboration with the EP and collecting information. PMDA promoted harmonization activities by taking this opportunity to hold a bilateral meeting.
- In September 2016, the United States Pharmacopeia (USP) and PMDA held a bilateral meeting and concluded memorandum of cooperation (MOC) on pharmacopoeias. To promote harmonization activities on excipients between the two parties, PMDA dispatched an employee as a liaison officer and closely exchanged information by holding teleconferences once a month.
- In October 2016, PMDA and the Brazilian National Health Surveillance Agency (ANVISA), the Brazilian regulatory authority, held a bilateral meeting and the 3rd Brazil-Japan Seminar of Regulations of Pharmaceuticals and Medical Devices. At the meeting and the seminar, PMDA and ANVISA exchanged opinions based on the “Memorandum on Cooperation in the Area of Pharmacopoeias,” which was concluded between MHLW and ANVISA in September 2015.

- In May 2016, PMDA and the Indian Central Drugs Standard Control Organization (DCSCO), the Indian regulatory authority, held a bilateral meeting and the 1st India-Japan Medical Products Regulation Symposium in India. At the meeting and the symposium, PMDA and DCSCO exchanged opinions based on the "Memorandum of Cooperation between MHLW and DCSCO on Medical Products Regulation Dialogue and Cooperation Framework," which was signed between MHLW and DCSCO in December 2015.
- In September 2016, PMDA and the Chinese Pharmacopoeia (ChP) held a bilateral meeting and concluded memorandum on cooperation (MOC) on pharmacopoeias.
- In February 2017, PMDA and Thai FDA held a bilateral meeting and the 4th Thailand-Japan Symposium. On these occasions, PMDA held training sessions as a follow-up to the last year's training in pharmacopoeia provided to the staff of Thai FDA, in order to enhance the understanding of the Japanese pharmacopoeia. This is an effort to encourage the Thai FDA to adopt the Japanese pharmacopoeia as a reference pharmacopoeia. PMDA further collaborated with Brazil, where the JP had already been adopted as a reference pharmacopoeia. For example, PMDA raised the pharmacopoeia as a topic at a meeting with ANVISA.

(ii) Strengthening of activities for international harmonization, etc.

Major actions taken in relation to drugs

- The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) held conferences in Portugal (Lisbon) in June 2016, and in Japan (Osaka) in November 2016. PMDA served as the vice chair of the ICH Assembly and as the chair or vice chair of the Management Committee and led discussions.

  As a result, several guidelines on pharmaceutical regulations (e.g. Guideline on standardizing benefit-risk information in regulatory submissions, Guideline for Good Clinical Practice, etc.) were finalized. Further, "Bioanalytical Method Validation," proposed by Japan, was adopted as a new topic for harmonization driven by ICH. ICH organizational rules and the rules on discussions were reviewed and improved so that discussions at ICH can be conducted smoothly under the leadership of Japan.

Major actions taken in relation to medical devices

- The International Medical Device Regulators Forum (IMDRF) held conferences of the management committee in Brazil (Florianopolis) in September 2016, and in Canada (Vancouver) in March 2017. At the conferences, PMDA participated in finalizing various IMDRF guidance documents (e.g. "Principles of International System of Registries Linked to Other Data Sources and Tools," "Methodological Principles in the Use of International Medical Device Registry Data," "Competence, Training, and Conduct Requirements for Regulatory Reviewers") and in formulating the direction of future activities. PMDA also actively participated in each working group. In particular, PMDA served as the chair in the Adverse Event Terminology and Coding Working Group, and succeeded in preparing the terminology for medical device defects (the first guidance document of the working group) and finalizing it at the meetings of the Management Committee.
- Harmonization by Doing (HBD) Town Hall Meetings were held within cardiology-related academic conferences in Japan and the US (in Tokyo in July 2016; in Washington DC in October 2016 and February 2017). At the meetings, PMDA sought to promote provision of information by continuously carrying forward the HBD activities by means such as widely disseminating outcomes of the HBD activities. PMDA also launched and advanced "HBD for Children" activities intended to promote Japan-US simultaneous development of pediatric medical devices.

- In addition, PMDA staff also attended various ISO working groups on the revision of ISO 14155 (GCP for medical devices) standard so that it can be adopted in Japan.

Major actions taken in other fields

- The 11th conference of the Summit of Heads of Medicines Regulatory Agencies was held in Switzerland (Interlaken) in November 2016. This annual conference brings together top officials of drug regulatory authorities in about 20 advanced countries. The Chief Executive (Tatsuya Kondo) and other officials of PMDA participated in the conference, and discussed various issues on pharmaceutical regulations.

  The 12th conference of the Summit is scheduled to be held for the first time in Japan in October 2017. PMDA and MHLW will serve as the chair of the conference. PMDA steadily made preparations for actively promoting international regulatory harmonization and international cooperation.

- In International Coalition of Medicines Regulatory Authorities (ICMRA) associated with the Summit of Heads of Medicines Regulatory Agencies, PMDA is the leading country in the capacity building activities. PMDA explored the possibility of collaboration with WHO for the capacity building activities (e.g., integrated the portal site created by PMDA with the WHO database). In addition PMDA contributed to raising the recognition of ICMRA by managing the ICMRA official website, which was created by PMDA in FY 2015 and opened in March 2016.

- The meetings of Pharmacopoeial Discussion Group (PDG) (a review committee of Japan-US-Europe Pharmacopoeias) were held in May and October 2016 in Tokyo. Through the meetings and monthly teleconferences, PMDA closely exchanged information with EP and USP. This lead to the harmonization of 1 testing method and 1 excipient and the revision of 1 testing method and 2 excipients.

  In the October meeting in Tokyo, enhancement of the efficiency of the PDG harmonization process was proposed, and subsequently 3 teleconferences were held for discussions. PMDA sought public comments in Japan for 1 excipient scheduled to be newly harmonized and 5 excipients scheduled to be revised for harmonization by PDG.

- Four consultations concerning applications for international nonproprietary names (INN) were conducted and PMDA participated in the WHO-hosted INN meetings held in April and October 2016.

- The Asia-Pacific Economic Cooperation Life Science Innovation Forum Regulatory Harmonization Steering Committee (APEC-LSIF-RHSC) convened in Peru in August 2016 and in Vietnam in February 2017. (APEC-LSIF-RHSC was established in the APEC Life Science Innovation Forum). PMDA served as a co-chair and led the discussion about the Capacity Building in the APEC region, thereby contributing to reinforcing the international collaboration.

  APEC-LSIF-RHSC has been conducting a pilot program of capacity building of regulators and relevant persons to establish the Center of Excellence (CoE) to offer such training. As part of the pilot program, PMDA-ACT provided seminars on 2 of the 6 work areas set up by APEC-LSIF-RHSC: (1) a seminar on MRCT/GCP inspections in January 2017, and (2) a seminar on pharmacovigilance and medical devices vigilance in February 2017. At the Vietnam conference of APEC-LSIF-RHSC (February 2017), PMDA was officially approved by APEC as a CoE in the 2 areas because of the seminars, and was highly regarded internationally.

- PMDA participated in the International Generic Drug Regulators Programme (IGDRP) meetings held in May and October 2016, and exchanged opinions with other regulatory authorities, particularly regarding drug substance (registration of the drug master file), quality evaluation of

generic drugs, and handling of bioequivalence. PMDA also participated in the Performance Indicator review team, which evaluates the activities of IGDRP and the review team on IPRF/IGDRP organizational integration, and exchanged opinions with other regulatory authorities regarding the future operational system and enhancement of the efficiency.

In addition, PMDA discussed various regulatory harmonization opportunities in the area of bioequivalence evaluations in Japan and overseas as part of a research project supported by Health and Labour Science Research Grants.

- PMDA participated in the 10th International Cooperation on Cosmetics Regulation (ICCR-10) meeting held in the United States in July 2016 and exchanged information on the regulations of cosmetics with regulators from the U.S., the European Union, Canada, and Brazil.
- In October 2016, PMDA hosted the 3rd meeting of the Self-Medication Collaborative ASIAN Regulator Expert Roundtable (Self-CARER) held in Nagoya, and as the chair, led discussions with regulators from Asian countries.
- PMDA contributed to 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 so that Japan can lead the international standardization of specifications and standards that originate in Japan or that reflect Japanese ideas: (a) promoted active participation in events such as ISO/IEC international conferences; (b) improved the framework for collaboration with organizations such as national mirror committees, and (c) promoted the establishment and reinforcement of trust relationships and collaboration with regulatory authorities in Asian, Europe and the US. Specifically, PMDA selected important themes (e.g., medical robots and additive manufacturing systems), for which international standardization should be promoted in a strategic manner. PMDA participated in conferences of the ISO/IEC specification review committee on such themes 121 times (26 international conferences, 80 meetings of the Japanese committee, and 15 teleconferences) to ensure that the committee incorporates opinions from Japan. Also, in the project to support the participation of academia in international conferences, in FY 2016 PMDA dispatched 3 experts in 3 areas to international conferences to participate in deliberations on specifications and collect information, and held an a study meeting that brings together academia experts who had been dispatched to international conferences, to share the trends of ISO/IEC international conference and international specifications.

  Furthermore, PMDA proposed to stakeholders the importance of establishing a framework that allows national mirror committees to share information, issues, etc. obtained through the activities described above; this proposal led to the establishment of Association of the national mirror committees in the Japan Federation of Medical Devices Associations in 2015. In FY 2015, the Association had 10 technical committees (TCs); in FY 2016, the number increased to 17 with additional 7 TCs, including ISO/TC276 (Biotechnology), ISO/TC261 (Additive manufacturing), and ISO/TC299 (Robotics). At conferences in India, South Korea, Thailand, AMDC (ASEAN Medical Device Committee), PMDA disseminated the Japanese principles on certification criteria, etc. which utilize international specifications, to promote collaborative framework for developing international specifications in the Asian region. At AMDC, PMDA proposed to hold a workshop on specifications and standards; the proposal was accepted. Through these activities, PMDA improved the infrastructure to promote the international standardization in the ASEAN region and to reinforce the collaboration between Japan and the Asian region in developing international specifications. Since IMDRF launched a standard WG in FY 2016, PMDA promoted the international harmonization for international specifications, etc. used for regulations through participation in the meetings of the WG.

- In addition to assuming the position of 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.
- 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

- PMDA negotiated with the US FDA about the new dispatch of personnel and secured the opportunity to dispatch its staff members to the fields of clinical pharmacology, pharmacovigilance, and CDISC.
- In addition to the implementation of training seminars by the PMDA-ATC, PMDA accepted trainees as needed from the regulatory authorities in the U.S., Thailand, etc. (duration, short-term to half year).
- PMDA held a bilateral joint symposium and regulators' conferences (India in May 2016, South Korea in June 2016, Brazil in October 2016, Taiwan in December 2016, and Thailand in February 2017), and promoted understanding of Japanese pharmaceutical regulations, etc. in Asian countries.

  PMDA also held regulators' conferences with other regulatory agencies (e.g., MHRA in UK, EMA, HSA in Singapore, and BPOM in Indonesia) and discussed collaborative projects while exchanging information.

(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) and Regulatory Affairs Professionals Society (RAPS) 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 provided English language training programs tailored to the degree of necessity of English in employees' operational assignments. Employees scheduled to be dispatched overseas for a long period received an English language training program specifically designed for them, to improve their practical English ability before the dispatch. Employees who give presentations in international conferences received a training program on practical English for international conferences so that they can clearly communicate PMDA's views at academic conferences. PMDA sought to improve the English skills of all employees by administering TOEIC IP tests and by providing English language training programs tailored to meet individual needs (one-on-one lessons, group lessons, and correspondence courses).

(v) Improvement and strengthening of international publicity and provision of information

Translation of review reports into English

- PMDA translated product review reports into English on drugs, medical devices, and regenerative medical products approved in Japan that may have an impact on foreign countries. The review reports were published on the PMDA website, to reveal the quality of the regulatory review process in Japan (40 reports published in FY 2016 [36 drugs, 2 medical devices, and 2 regenerative medical products]).

Providing information to foreign countries

- "PMDA Updates" were distributed monthly to stakeholders concerned with the current status of the efforts being made by PMDA regarding international conferences or bilateral relationships. PMDA Updates were also posted on the PMDA website to widely disseminate information to the general public as well as to the foreign regulatory authorities.

  In FY 2016, PMDA received 476 inquiries (by email) from foreign countries and gave 436 responses. PMDA responded to inquiries from foreign countries by explaining its policies and activities appropriately and in a timely fashion.

  PMDA continued to give booth presentations at the DIA Annual Meetings in Europe and the United States as well as in the RAPS Annual Meeting, to publicize its policies and activities.

- To promote the international harmonization of certification standards for medical devices based on the ISO/IEC specifications, PMDA translated the standards into English and published them on its website. (A total of 946 certification standards, a basic requirement conformance checklist, etc. were published until FY 2016).

  In March 2017, PMDA posted an English precautionary statement on the website to the effect that the applicability under the drug monographs of the Japanese pharmacopoeia should be determined according to provisions such as general rules and general tests. The statement is intended to prevent overseas users from mistakenly determining the applicability based solely on the provisions of the drug monographs of the Japanese pharmacopoeia.

  Through its website, PMDA disseminated information in English on the status of activities for the Projects Across Multi-offices for standards development.

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 Pediatric Drugs WG in Projects Across Multi-offices in PMDA, PMDA participated in and gathered information from the working group on orphan drugs for pediatrics from 5 countries/regions: Japan, the United States, Europe, Canada, and Australia.
- In the CIN WG in Projects Across Multi-Offices, PMDA cooperated with the AMED research group in developing patient registries for muscular dystrophy, amyotrophic lateral sclerosis (ALS), cancer/rare fractions, and brain surgical therapy.

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.

b. Releasing information related to review reports

Review reports on new drugs

- New drugs are classified into 2 categories based on the application data submitted: (1) Drugs to be deliberated on by the Drug Committees of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) (referred to as "deliberation products"); and (2) Drugs 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 2016, PMDA released 108 review reports, 88 summaries of product applications, and 48 re-examination reports.

  The percentage of review reports released within 1 month after approval was 100% in FY 2016 (100% in FY 2015). The percentage of summaries of product applications released within 3 months after approval was 100% in FY 2016 (100% in FY 2015); the median time from approval to release was 49 days, showing an achievement of 184% compared to the target time of 3 months (90 days).

  Note: The median times from approval (for re-examination reports, from notification of results) to data release were 6 days for review reports, 49 days for summary of product applications, and 6 days for re-examination reports.

Review reports on new medical devices

- In FY 2016, PMDA released 9 review reports, 10 summaries of product applications and 7 re-examination reports for new medical devices.

  The percentage of review reports released within 1 month after approval was 100% in FY 2016 (93% in FY 2015). The percentage of summaries of product applications released within 3 months after approval was 90% in FY 2016 (94% in FY 2015); the median time from approval to release was 58 days, showing an achievement of 155% compared to the target time of 3 months (90 days).

  Note: The median times from approval (for re-examination reports, from notification of results) to data release were 27 days for review reports, 58 days for summary of product applications, and 4 days for re-examination reports.

Review reports on new regenerative medical products

- In FY 2016, PMDA released 1 review report and 1 summary of product applications for new regenerative medical products.

Review reports on BTC drugs and quasi-drugs

- In FY 2016, PMDA released 1 review report and 1 summary of product application for BTC drugs, and 1 review report and 2 summaries of product applications for quasi-drugs.

Number of review reports released

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
New drugs	121	120	130	118	108
New medical devices	11	19	9	16	9
New regenerative medical products	-	-	-	2	1
BTC and OTC drugs	5	5	3	2	1
Quasi-drugs	0	0	1	3	1

3.4.(5) Ensuring the impartiality and transparency 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 November 25, 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 all 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. The information disclosed 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. The system was upgraded in order of priority in order to enable the more effective handling of necessary operations. In August 2016, PMDA began accepting advance notices of new product applications and electronic files using an electronic gateway as part of the operation of a new electronic application data system. PMDA also upgraded (a) the Adverse Drug Reaction Data Management System and (b) the Safety Measures Support System, to implement ICH-E2B (R3) (see 3.3 Safety Measure Services (i)).
- 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.
- In June 2016, at the request of the Osaka prefectural government, the Osaka Pharmaceutical Manufacturers Association, the Osaka Chamber of Commerce and Industry, and the Kansai Economic Federation, PMDA launched a teleconference-based consultation system at its Kansai

Branch in order to improve the convenience of this service for applicants based in the Kansai region. In FY 2016, PMDA conducted 41 teleconference consultations, etc.

- PMDA upgraded the application/review and the new eCTD viewer systems for managing interactions between the systems and the electronic application data system. In August 2016, PMDA started to accept electronic files via the gateway, and updated the system in response to requests from applicant companies. PMDA also created a verification environment that can be used to check the operation of the electronic application data system within PMDA. The electronic application data system was put into operation in March 2017.
- Following the progress of relevant discussions of eCTD ver.4.0 at ICH, PMDA made preparations for procurement of the system for eCTD ver.4.0 acceptance inspection. The system will be developed in or after FY 2017.

III. SUPPLEMENTARY INFORMATION

Reviews and Safety Measure Services

1. New drug application review services

Number of approved products

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Prescription drugs	3,898	4,003	3,944	3,664	3,660
BTC and OTC drugs	881	916	844	752	646
In vitro diagnostics	147	166	109	172	199
Quasi-drugs	1,968	2,028	1,779	2,495	1,924
Cosmetics	0	0	0	0	0
Total	6,894	7,113	6,676	7,083	6,429

Number of approved new drug applications

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of approved new drug applications	134	138	118	116	112
Priority review products among these new drugs	53	42	44	37	38

Reference 1 Approved new drug applications (FY 2016)

	FY 2016
Overall	
Number of approved applications	112
Total review time (months)	
Median	10.1
70th percentile	11.2
Regulatory review time (months)	
Median	4.8
70th percentile	6.3
Applicant's time (months)	
Median	4.5
70th percentile	5.6

Note: Products submitted in or after April 2004 are covered.

Reference 2 Approved new drug applications (only those with new active ingredients)

Total review time for new drugs (priority review products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	60	70
Total review time (months)	9.0	9.1	9.1	9.5	9.2
Number of approved applications	17	15	24	17	19

Reference

Regulatory review time (months)	3.3	3.4	3.8	3.8	3.8
Applicant's time (months)	4.6	5.3	5.4	6.0	5.6

Note: Figures are calculated based on the products (drugs with new active ingredients) submitted in or after FY 2004.

Total review time for new drugs (standard review products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentile	50	50	60	70	70
Total review time (months)	11.2	11.9	12.1	11.2	12.0
Number of approved applications	27	24	28	25	22

Reference

Regulatory review time (months)	5.5	6.2	6.5	5.9	7.0
Applicant's time (months)	5.6	5.4	6.5	6.7	7.3

Note 1:Figures are calculated based on the products (drugs with new active ingredients) submitted in or after FY 2004.

Note 2:The figures in "regulatory review time" and "applicant's time" represent their respective percentile values. The sum of "regulatory review time" and "applicant's time" may not equal "total review time."

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

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	Pest control agents	Total
Products submitted in FY 2016	0	0	0	0	1	6	0	5	1	7	8	33	3	595	41	700
Products approved in FY 2016	0	0	0	0	0	3	0	1	1	7	3	43	10	532	46	646

Note 1: Application categories for BTC and OTC drugs were revised on January 1, 2009. Application categories in the table are those after the revision.

Note 2: Application categories for BTC and OTC drugs:

Current 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)

Note 3: In FY 2016, there were no products approved in the former application categories (i.e., the categories before the revision.)

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)

Note 4: 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

	Current application categories								
	1	2-1	2-2	2-3	2-4	2-5	3	4	5-1
Products submitted in FY 2016	2	12	0	12	0	0	17	581	1,297
Products approved in FY 2016	0	3	0	32	0	0	6	509	1,185

	Current application categories				Former application categories			Total
	5-2	5-3	Quasi-drugs for pest control	Subtotal	1,3	2	Subtotal	
Products submitted in FY 2016	24	33	84	2,062	-	-	-	2,062
Products approved FY 2016	41	33	54	1,863	21	40	61	1,924

Note 1: The application categories for quasi-drugs were revised on November 25, 2014. The figures in "Former application categories" represent the number of products approved under the application categories before the revision.

Note 2: 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"*

Current 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 3: The numbers of "Products submitted in FY 2016" were calculated by category at the time of filing.

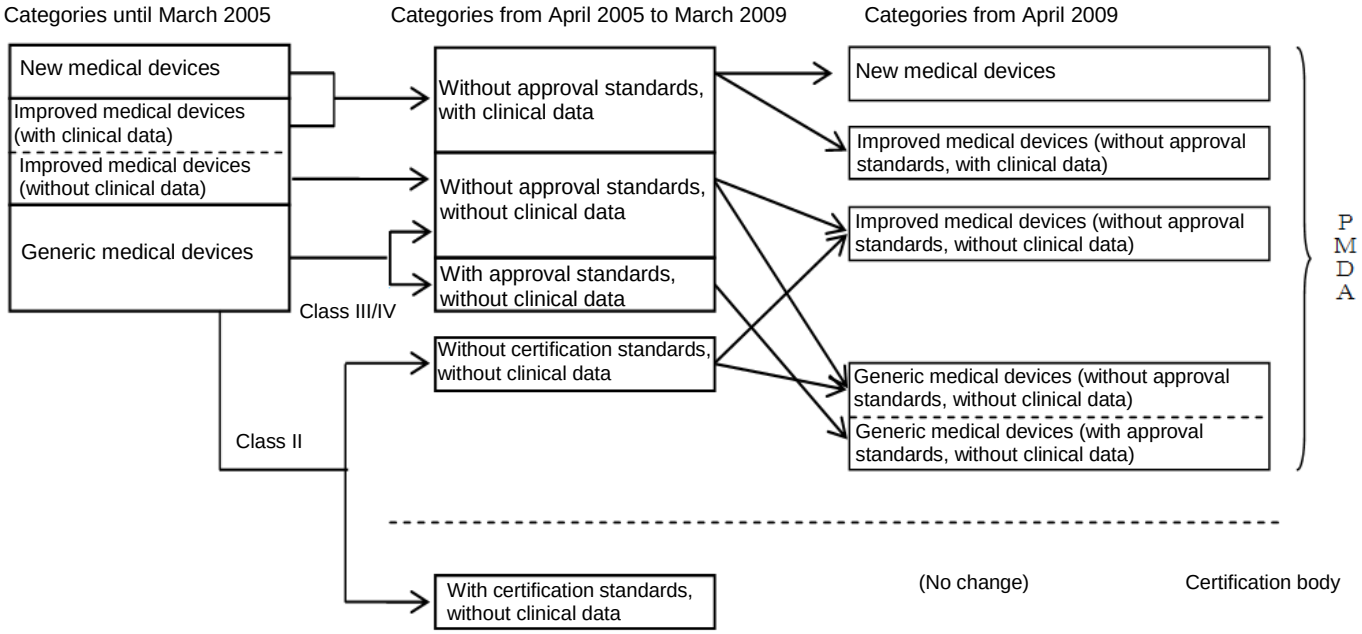
Note 4: The numbers of "Products approved in FY 2016" were calculated by category at the time of approval.

Note 5: The numbers of quasi-drugs in former application categories include pest control agents.

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 and IV medical devices as specially controlled medical devices.

Number of approved medical devices

		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Medical devices		1,535	1,347	1,235	1,217	1,120
Priority review products (included in above figures)		5	14	5	8	1*
Re-listed	New medical devices	46	94	67	56	26
	Improved medical devices (with clinical data) (From FY 2009 onward)	37	60	35	53	44
	Improved medical devices (without clinical data) (From FY 2009 onward)	218	227	213	240	225
	Generic medical devices (From FY 2009 onward)	1,191	943	917	868	825
	Without approval standards, with clinical data	7	1	0	0	0
	Without approval standards, without clinical data	30	17	3	0	0
	With approval standards, without clinical data	0	1	0	0	0
	Controlled medical devices (without approval and certification standards, without clinical data)	4	1	0	0	0
	Improved medical devices (until FY 2004)	1	3	0	0	0
	Generic medical devices (until FY 2004)	1	0	0	0	0

**One new medical device is included.*

Reference 1 Approved new medical device applications (FY 2016)

	FY 2016
Overall	
Number of approved applications	25
Total review time (months)	
Median	8.0
70th percentile	12.0
Regulatory review time (months)	
Median	4.1
70th percentile	7.6
Applicant's time (months)	
Median	2.3
70th percentile	4.7

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

Reference 2 Approved new medical device applications and their review times

	FY 2013			FY 2014		
	Total	New	Partial change	Total	New	Partial change
New medical devices (Priority and standard review products)						
Number of approved applications	94	51	43	67	24	43
Total review time (months)[Note 2]	6.7	13.5	3.3	5.6	8.9	4.3
Achievement rate	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Regulatory review time (months)[Note 2]	4.8	6.1	2.0	3.5	4.8	2.9
Achievement rate	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Priority review products						
Number of approved applications	14	11	3	5	2	3
Total review time (months)[Note 2]	9.0	9.6	5.2	8.8	8.9	5.4
Achievement rate	(86%)	(82%)	(100%)	(100%)	(100%)	(100%)
Regulatory review time (months)[Note 2]	5.1	5.5	4.6	4.0	5.6	2.8
Achievement rate	(71%)	(64%)	(100%)	(100%)	(100%)	(100%)
Standard review products						
Number of approved applications	80	40	40	62	22	40
Total review time (months)[Note 2]	6.3	13.8	3.2	5.6	9.1	4.2
Achievement rate	(79%)	(58%)	(100%)	(98%)	(96%)	(100%)
Regulatory review time (months)[Note 2]	4.0	6.4	2.0	3.5	4.8	2.9
Achievement rate	(74%)	(53%)	(95%)	(94%)	(96%)	(93%)

	FY 2015			FY 2016		
	Total	New	Partial change	Total	New	Partial change
New medical devices (Priority and standard review products)						
Number of approved applications	56	22	34	25	9	16
Total review time (months)[Note 2]	9.7	10.5	6.9	12.0	24.2	6.2
Achievement rate	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Regulatory review time (months)[Note 2]	4.8	4.8	4.8	7.6	9.5	3.7
Achievement rate	(-%)	(-%)	(-%)	(-%)	(-%)	(-%)
Priority review products						
Number of approved applications	8	6	2	1	0	1
Total review time (months)[Note 2]	7.9	8.1	7.2	8.0	-	8.0
Achievement rate	(100%)	(100%)	(100%)	(100%)	(-%)	(100%)
Regulatory review time (months)[Note 2]	4.2	4.1	4.2	3.2	-	3.2
Achievement rate	(100%)	(100%)	(100%)	(100%)	(-%)	(100%)
Standard review products						
Number of approved applications	48	16	32	24	9	15
Total review time (months)[Note 2]	10.1	11.9	6.9	12.0	24.2	5.9
Achievement rate	(88%)	(75%)	(94%)	(79%)	(44%)	(100%)
Regulatory review time (months)[Note 2]	5.0	5.4	4.9	7.8	9.5	3.9
Achievement rate	(85%)	(75%)	(91%)	(58%)	(22%)	(80%)

Note 1:Applications filed in or after April 2004 are covered.

Note 2:Median for FY 2013, the 60th percentile for FY 2014-2015, and the 70th percentile for FY 2016.

Note 3:The results in FY 2016 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 transitional period (between November 25, 2014 and February 24, 2015).

Note 4:Target review times 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 data

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of medical devices with foreign clinical trial data	26 (3)	42 (8)	30 (2)	34 (11)	35 (5)
Number of medical devices with Japanese clinical trial data	23	24	11	24	9

Note 1:The figures in parentheses indicate the number of medical devices with both Japanese and foreign clinical trial data (included in left figures).

Note 2:In FY 2016, 14 medical devices were approved based on clinical evaluation reports, in addition to the 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

Approximately 76% (152 of 199) of *in vitro* diagnostics applications approved in FY 2016 were processed within the standard administrative processing period (6 months).

Approved *in vitro* diagnostics applications and their review times

	FY 2012	Filed in or after FY 2004 (included in left figures)	FY 2013	Filed in or after FY 2004 (included in left figures)	FY 2014	Filed in or after FY 2004 (included in left figures)
Number of approved applications	147	147	166	166	109	109
Median total review time (months)	6.0	6.0	5.4	5.4	5.3	5.3
Median regulatory review time (months)	3.4	3.4	2.7	2.7	2.6	2.6
Achievement rate	(69%)	(69%)	(81%)	(81%)	(80%)	(80%)

	FY 2015	Filed in or after FY 2004 (included in left figures)	FY 2016	Filed in or after FY 2004 (included in left figures)
Number of approved applications	172	172	199	199
Median total review time (months)	7.2	7.2	6.4	6.4
Median regulatory review time (months)	3.9	3.9	3.5	3.5
Achievement rate	(71%)	(71%)	(76%)	(76%)

Note: The 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.)

(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 2016 is as follows: 134 notifications submitted, surveys on 127 notifications completed, and 4 notifications withdrawn.

(ii) In FY 2016, clinical trial notifications for drugs (excluding initial clinical trial notification) consisted of 511 n-th clinical trial notifications, 4,998 protocol change notifications, 469 trial completion notifications, 93 trial discontinuation notifications, and 111 development discontinuation notifications.

Number of clinical trial notifications for drugs

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Initial clinical trial notification	132 (13)	127 (6)	151 (20)	127 (10)	134 (10)
n-th clinical trial notification	424 (19)	474 (25)	450 (33)	530 (45)	511 (63)
Protocol change notification	4,568	4,356	4,321	4,566	4,998
Trial completion notification	495	446	498	507	469
Trial discontinuation notification	57	61	67	70	93
Development discontinuation notification	70	78	117	102	111
Total	5,746	5,542	5,604	5,902	6,316

Note 1: The figures in parentheses indicate the number of notifications of "investigator-initiated clinical trials."

(iii) The status of initial clinical trial notifications for equipment/devices in FY 2016 is as follows: 34 notifications submitted, surveys on 35 notifications completed, and 1 notification withdrawn.

(iv) In FY 2016, clinical trial notifications for equipment/devices consisted of 20 n-th clinical trial notifications, 315 protocol change notifications, 22 trial completion notifications, 2 trial discontinuation notifications, and 7 development discontinuation notifications.

Number of clinical trial notifications for equipment/devices

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Initial clinical trial notification	32 (2)	31 (4)	31 (7)	31 (8)	34 (8)
n-th clinical trial notification	11 (1)	14 (0)	6 (2)	10 (0)	20 (1)
Protocol change notification	227	253	240	283	315
Trial completion notification	21	30	33	22	22
Trial discontinuation notification	0	6	6	5	2
Development discontinuation notification	0	6	2	2	7
Total	291	340	318	353	400

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 2016 is as follows: 16 notifications submitted, surveys on 12 notifications completed, and 1 notification withdrawn.

(vi) In FY 2016, the clinical trial notifications for processed cells consisted of 5 n-th clinical trial notifications and 52 protocol change notifications, with 1 trial completion notification, 0 trial discontinuation notifications, and 0 development discontinuation notifications.

Number of clinical trial notifications for processed cells, etc.

	FY 2014	FY 2015	FY 2016
Initial clinical trial notification	3 (1)	10 (2)	16 (7)
n-th clinical trial notification	1 (1)	3 (2)	5 (0)
Protocol change notification	2	19	52
Trial completion notification	0	0	1
Trial discontinuation notification	0	0	0
Development discontinuation notification	0	0	0
Total	6	32	74

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 if necessary, requests (via MHLW) that the sponsors consider discontinuing clinical trials or taking other actions.

In FY 2016, there were 87,876 reports on adverse drug reactions from clinical trials. Of these, 1,458 were from Japanese clinical trials.

Adverse drug reaction reports from clinical trials

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of ADR reports from clinical trials	55,534	58,275	71,689	86,039	87,876
(In Japan)	891	780	910	1,339	1,458
(Outside Japan)	54,643	57,495	70,779	84,700	86,418

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 the 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 2016, there were 1,971 device malfunction reports from clinical trials.

Device malfunction reports from clinical trials

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of malfunction reports from clinical trials	1,055	1,518	2,119	2,966	1,971

Note 1: The figures represent the initial reports of case reports, research reports, safety measure 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 the actual initial reports had already been filed before the date.

In FY 2016, there were 129 processed cell-related malfunction reports from clinical trials.

Number of processed cell-related malfunction reports from clinical trials

	FY 2014	FY 2015	FY 2016
Number of malfunction reports from clinical trials	0	50	129

Note: The figures represent the initial reports of case reports, research reports, safety measure 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 submitted for DMF registration by their manufactures (since April 2005).

In FY 2016, 3,163 applications for DMF registration were filed (i.e., applications for registration, applications for registration change, minor change notifications, applications for renewal/issue of registration certificate, notifications of succession of registration, and applications for re-issue of registration). In total, 260 registrations and 189 registration changes were granted; and 2,714 other applications/notifications were filed.

Number of DMF registration applications filed and registered

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Applications for registration	1,561	1,918	2,017	2,019	3,163
Registrations granted	238	244	282	305	260
Registration change granted	103	143	161	197	189
Other applications/notifications	1,220	1,521	1,575	1,538	2,714

Note: Including carry-over applications from the previous fiscal year.

Table 1. Number of Drugs, etc. Filed and Approved (FY2012 – FY 2016)

Category		Fiscal Year	Number of products filed					Number of products approved				
			FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs, etc.	New drugs	New	157	142	115	162	124	128	160	142	109	131
		Partial change	402	326	364	350	349	377	344	362	320	337
		Total	559	468	479	512	473	505	504	504	429	468
	Generic drugs	New	1,764	1,467	1,166	905	831	1,539	1,438	1,325	635	731
		Partial change	2,313	2,424	2,286	2,595	2,329	1,882	2,066	2,122	2,600	2,461
		Total	4,077	3,891	3,452	3,500	3,160	3,421	3,504	3,447	3,235	3,192
	BTC/OTC drugs	New	784	747	671	523	513	619	657	638	589	450
		Partial change	221	266	211	195	187	262	259	206	163	196
		Total	1,005	1,013	882	718	700	881	916	844	752	646
	In vitro diagnostics	New	70	51	89	83	63	71	69	40	80	91
		Partial change	95	85	74	113	86	76	97	69	92	108
		Total	165	136	163	196	149	147	166	109	172	199
	Quasi-drugs	New	1,923	2,002	1,666	2,329	1,808	1,784	1,763	1,631	2,322	1,694
		Partial change	194	296	162	230	254	184	265	148	173	230
		Total	2,117	2,298	1,828	2,559	2,062	1,968	2,028	1,779	2,495	1,924
	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	4,698	4,409	3,707	4,002	3,339	4,141	4,087	3,776	3,735	3,097
		Partial change	3,225	3,397	3,097	3,483	3,205	2,781	3,031	2,907	3,348	3,332
		Total	7,923	7,806	6,804	7,485	6,544	6,922	7,118	6,683	7,083	6,429

Note 1: The number of product applications filed in FY 2016 and their application categories are as of April 7, 2017. 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 2012 – FY 2016)

Category \ Fiscal Year		Number of products filed					Number of products approved				
		FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
New medical devices	New	36	28	37	14	11	27	51	24	22	10
	Partial change	28	44	63	16	18	19	43	43	34	16
	Total	64	72	100	30	29	46	94	67	56	26
Improved medical devices (with clinical data) (in or after FY 2009)	New	37	36	36	23	43	32	54	27	43	38
	Partial change	5	10	9	4	6	5	6	8	10	6
	Total	42	46	45	27	49	37	60	35	53	44
Improved medical devices (without clinical data) (in or after FY 2009)	New	172	137	194	144	155	159	172	156	151	154
	Partial change	40	50	68	74	62	59	55	57	89	71
	Total	212	187	262	218	217	218	227	213	240	225
Generic medical devices (in or after FY 2009)	New	341	375	418	319	355	402	355	396	351	329
	Partial change	737	544	544	469	574	789	588	521	517	496
	Total	1,078	919	962	788	929	1,191	943	917	868	825
Medical devices (with clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	7	1	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	7	1	0	0	0
Medical devices (without approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	15	6	0	0	0
	Partial change	-	-	-	-	-	15	11	3	3	0
	Total	-	-	-	-	-	30	17	3	3	0
Medical devices (with approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	0	1	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	0	1	0	0	0
Controlled medical devices (without approval standards or certification standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	4	1	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	4	1	0	0	0
Improved medical devices (in or before FY 2004)	New	-	-	-	-	-	1	2	0	0	0
	Partial change	-	-	-	-	-	0	1	0	0	0
	Total	-	-	-	-	-	1	3	0	0	0
Improved medical devices (humans, animals, etc.) (in or before FY 2004)	New	-	-	-	-	-	0	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	0	0	0	0	0
Generic medical devices (in or before FY 2004)	New	-	-	-	-	-	1	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	1	0	0	0	0
Total	New	586	576	685	500	564	648	643	603	567	531
	Partial change	810	648	684	563	660	887	704	632	653	589
	Total	1,396	1,224	1,369	1,063	1,224	1,535	1,347	1,235	1,220	1,120

Note 1: The number of product applications filed in FY 2016 and their application categories are as of April 7, 2017. 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 2016)

Category \ Fiscal year		Number of products filed			Number of products approved		
		FY 2014	FY 2015	FY 2016	FY 2014	FY 2015	FY 2016
Regenerative Medical Products	New	2	0	0	0	2	0
	Partial change	0	3	1	0	2	1
	Total	2	3	1	0	4	1

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 2016: 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 13, 2016	1	Cellcept Capsules 250 Cellcept Powder for Oral Suspension 31.8% (Chugai Pharmaceutical Co., Ltd.) Mycophenolate Mofetil Cap. 250 mg "Teva" (Teva Pharma Japan Inc.) Mycophenolate Mofetil Capsules 250 mg [Pfizer] (Mylan Seiyaku Ltd.)	Change Change Change Change	Mycophenolate mofetil	Drugs with a new additional indication and a new dosage for the treatment of lupus nephritis. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
1	Jun. 20, 2016	2	Humira 40 mg for S.C. Injection Syringe 0.8 mL (AbbVie GK)	Change	Adalimumab (genetical recombination)	A drug with a new dosage indicated for the treatment of Crohn's disease.
1	Jul. 4, 2016	3	Epiduo Gel (Galderma S.A.)	Approval	Adapalene/Benzoyl peroxide	A new combination drug indicated for the treatment of acne vulgaris.
1	Jul. 4, 2016	4	Picoprep Combination Powder (Ferring Pharmaceuticals Co.,Ltd)	Approval	Sodium picosulfate hydrate/ Magnesium oxide/ Anhydrous citric acid	A new combination drug indicated for bowel cleansing preparation for colonoscopy or colorectal surgery.
1	Jul. 4, 2016	5	Hemangiol Syrup for Pediatric 0.375% (Maruho Co., Ltd.)	Approval	Propranolol hydrochloride	A drug with a new indication in a new dosage form indicated for the treatment of infantile hemangioma. [Orphan drug]
1	Sep. 28, 2016	6	Regroth Dental Kit 600 μg Regroth Dental Kit 1200 μg (Kaken Pharmaceutical Co., Ltd.)	Approval Approval	Trafermin (genetical recombination)	Drugs with a new route of administration indicated for the treatment of alveolar bone loss due to periodontitis.
1	Sep. 28, 2016	7	Zentacort Capsules 3 mg (Zeria Pharmaceutical Co., Ltd.)	Approval	Budesonide	A drug with a new route of administration indicated for the treatment of mild to moderately active Crohn's disease.
1	Sep. 28, 2016	8	Lialda Tab. 1200 mg (Mochida Pharmaceutical Co., Ltd.)	Approval	Mesalazine	A drug in a new dosage form indicated for the treatment of ulcerative colitis (excluding severe cases).
1	Dec. 19, 2016	9	Parsabiv Intravenous Injection for Dialysis 2.5 mg Parsabiv Intravenous Injection for Dialysis 5 mg Parsabiv Intravenous Injection for Dialysis 10 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval Approval	Etelcalcetide hydrochloride	Drugs with a new active ingredient indicated for the treatment of secondary hyperparathyroidism in patients on hemodialysis.
1	Dec. 19, 2016	10	Linzess Tablets 0.25 mg (Astellas Pharma Inc.)	Approval	Linaclotide	A drug with a new active ingredient indicated for the treatment of irritable bowel syndrome with constipation.
1	Mar. 24, 2017	11	Nobelzin Capsules 25 mg Nobelzin Capsules 50 mg Nobelzin Tablets 25 mg Nobelzin Tablets 50 mg (Nobelpharma Co., Ltd.)	Change Change Change Change	Zinc acetate dihydrate	Drugs with a new additional indication and a new dosage for the treatment of hypozincemia.
1	Mar. 30, 2017	12	Symproic Tablets 0.2 mg (Shionogi & Co., Ltd.)	Approval	Naldemedine tosilate	A drug with a new active ingredient indicated for the treatment of opioid-induced constipation.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
1	Mar. 30, 2017	13	(1) Stelara Intravenous Infusion 130 mg (2) Stelara Subcutaneous Injection 45 mg Syringe (Janssen Pharmaceutical K.K.)	Approval Change	Ustekinumab (genetical recombination)	(1) A drug with a new route of administration indicated for the induction therapy for moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatments). (2) A drug with a new indication and a new dosage for the maintenance therapy for moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatments).
1	Mar. 30, 2017	14	(1) Simponi Subcutaneous Injection 50 mg Syringe (2) Simponi Subcutaneous Injection 100 mg Syringe (Janssen Pharmaceutical K.K.)	Change Approval	Golimumab (genetical recombination)	Drugs with a new additional indication and a new dosage, in a new additional dosage form for improvement and maintenance of moderate to severe ulcerative colitis (for use only in patients who have not responded sufficiently to conventional treatments).
1	Mar. 30, 2017	15	Comclo Shampoo 0.05% (Maruho Co., Ltd.)	Approval	Clobetasol propionate	A drug in a new dosage form indicated for the treatment of psoriasis vulgaris of the scalp.
2	Jul. 4, 2016	16	Praluent 75 mg solution for injection in pre-filled pen Praluent 150 mg solution for injection in pre-filled pen Praluent 75 mg solution for injection in pre-filled syringe Praluent 150 mg solution for injection in pre-filled syringe (Sanofi K.K.)	Approval Approval Approval Approval	Alirocumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of familial hypercholesteremia 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).
2	Jul. 4, 2016	17	Duodopa Enteral Combination Solution (AbbVie GK)	Approval	Levodopa/ Carbidopa hydrate	A new combination drug indicated for the improvement of wearing-off phenomenon in the symptoms of Parkinson's disease in patients who have not responded sufficiently to conventional levodopa-containing drug therapies. [Orphan drug]
2	Sep. 28, 2016	18	Micatrio Combination Tablets (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Telmisartan/ Amlodipine besilate/ Hydrochlorothiazide	A new combination drug indicated for the treatment of hypertension.
2	Sep. 28, 2016	19	(1) Brilinta Tablets 60 mg (2) Brilinta Tablets 90 mg (AstraZeneca K.K.)	Approval Approval	Ticagrelor	Drugs with a new active ingredient indicated for the treatment of: (1) Old myocardial infarction at especially high risk of developing atherothrombosis with at least one of the following risk factors: age of 65 years or older, with diabetes mellitus requiring drug therapy, history of two or more episodes of myocardial infarction, angiography-confirmed multivessel coronary artery disease, or non-end-stage chronic renal dysfunction. (2) Acute coronary syndrome (unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction) for which percutaneous coronary intervention (PCI) is indicated. (provided that dual antiplatelet therapy including aspirin is appropriate but the administration of other antiplatelet drugs in combination with aspirin is not suitable for the patient.)
2	Sep. 28, 2016	20	Uptravi Tablets 0.2 mg Uptravi Tablets 0.4 mg (Nippon Shinyaku Co., Ltd.)	Approval Approval	Selexipag	Drugs with a new active ingredient indicated for the treatment of pulmonary arterial hypertension. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
2	Sep. 28, 2016	21	Juxtapid Capsules 5 mg Juxtapid Capsules 10 mg Juxtapid Capsules 20 mg (Aegerion Pharmaceuticals K.K.)	Approval Approval Approval	Lomitapide mesilate	Drugs with a new active ingredient indicated for the treatment of homozygous familial hypercholesterolemia. [Orphan drug]
2	Sep. 28, 2016	22	Prizbind Intravenous Solution 2.5 g (Nippon Boehringer Ingelheim Co., Ltd.)	Approval	Idarucizumab (genetical recombination)	A drug with a new active ingredient indicated for the reversal of anticoagulant effect of dabigatran under the following situations: • In life-threatening or uncontrolled bleeding • When performing emergency surgery or procedures in which serious bleeding is expected. [Priority review]
2	Sep. 28, 2016	23	Polidocasklerol 1% Inj. 2 mL Polidocasklerol 3% Inj. 2 mL (Kaigen Pharma Co., Ltd.)	Change Change	Polidocanol	Drugs with a new indication and a new dosage for the use in sclerotherapy of primary varicose veins of lower extremity.
2	Dec. 19, 2016	24	Selara Tablets 25 mg Selara Tablets 50 mg (Pfizer Japan Inc.)	Change Change	Eplerenone	Drugs with a new additional indication and a new dosage for the treatment of chronic heart failure in patients receiving basic treatment with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists, β-blockers, diuretics, etc.
2	Mar. 2, 2017	25	Epoprostenol ACT 0.5 mg Epoprostenol ACT 1.5 mg (Actelion Pharmaceuticals Japan Ltd.)	Change Change	Epoprostenol sodium	Drugs with a new additional pediatric dosage indicated for the treatment of pulmonary arterial hypertension.
3-1	May. 23, 2016	26	Botox Vista Injection 50 Units (Allergan Japan K.K.)	Change	Botulinum toxin type A	A drug with a new additional indication and a new dosage for the temporary improvement in the appearance of lateral canthal lines (crow's feet lines) in adults aged under 65 years.
3-1	Jul. 4, 2016	27	Ocnobel Tablets 150 mg Ocnobel Tablets 300 mg Ocnobel Oral Suspension 6% (Nobelpharma Co., Ltd.)	Approval Approval Approval	Oxcarbazepine	Drugs with a new active ingredient indicated for the use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Jul. 4, 2016	28	Vimpat Tablets 50 mg Vimpat Tablets 100 mg (UCB Japan Co., Ltd.)	Approval Approval	Lacosamide	Drugs with a new active ingredient indicated for the use as an adjunctive therapy with other antiepileptic drugs to treat partial seizures (including secondary generalized seizures) in patients with epilepsy who have not responded sufficiently to other antiepileptic drugs.
3-1	Sep. 28, 2016	29	Abilify Tablets 1 mg Abilify Tablets 3 mg Abilify Tablets 6 mg Abilify Tablets 12 mg Abilify OD Tablets 3 mg Abilify OD Tablets 6 mg Abilify OD Tablets 12 mg Abilify Powder 1% Abilify Oral Solution 0.1% (Otsuka Pharmaceutical Co., Ltd.)	Approval Change Change Change Change Change Change Change Change	Aripiprazole	Drugs with a new additional indication, dosage, and dosage form for the treatment of irritability associated with autism spectrum disorder in children and adolescents.
3-1	Sep. 28, 2016	30	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 Guillain-Barré syndrome (severe cases in an acute exacerbation phase with difficulty in walking).
3-1	Dec. 19, 2016	31	Tecfidera Capsules 120 mg Tecfidera Capsules 240 mg (Biogen Japan Ltd.)	Approval Approval	Dimethyl fumarate	Drugs with a new active ingredient indicated for the prevention of relapse and for delaying the accumulation of physical disability in multiple sclerosis. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
3-1	Dec. 19, 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 osteoarthritis.
3-1	Dec. 19, 2016	33	Kenketu Glovenin-I for I.V. Injection 2500 mg Kenketu Glovenin-I for I.V. Injection 500 mg Kenketu Glovenin-I for I.V. Injection 5000 mg (Nihon Pharmaceutical Co., Ltd.)	Change Change Change	Polyethylene glycol treated human normal immunoglobulin G	Drugs with a new additional indication and a new dosage for inhibiting progression of motor disability due to chronic inflammatory demyelinating polyneuropathy (including multifocal motor neuropathy) (in the cases where patients show an improvement in their acute phase treatment) [Orphan drug]
3-1	Mar. 30, 2017	34	Intuniv Tablets 1 mg Intuniv Tablets 3 mg (Shionogi & Co., Ltd.)	Approval Approval	Guanfacine hydrochloride	Drugs with a new active ingredient indicated for the treatment of pediatric attention deficit/hyperactivity disorder (AD/HD).
3-2	Aug. 26, 2016	35	Ultiva Intravenous 2 mg Ultiva Intravenous 5 mg (Janssen Pharmaceutical K.K.)	Change Change	Remifentanil hydrochloride	Drugs with a new additional indication and a new dosage for use in pediatric patients for analgesia during maintenance of general anesthesia.
3-2	Sep. 28, 2016	36	Mikeluna Combination Ophthalmic Solution (Otsuka Pharmaceutical Co., Ltd.)	Approval	Carteolol hydrochloride/ Latanoprost	A new combination drug indicated for the treatment of glaucoma and ocular hypertension.
3-2	Mar. 2, 2017	37	MaQaid Intravitreal Injection 40 mg (Wakamoto Co., Ltd.)	Change	Triamcinolone acetonide	A drug with a new route of administration indicated for alleviation of diabetic macular edema and macular edema associated with retinal vein occlusion or non-infectious uveitis.
3-2	Mar. 30, 2017	38	Narusus Tablets 2 mg Narusus Tablets 6 mg Narusus Tablets 12 mg Narusus Tablets 24 mg Narurapid Tablets 1 mg Narurapid Tablets 2 mg Narurapid Tablets 4 mg (Daiichi Sankyo Propharma Co., Ltd.)	Approval Approval Approval Approval Approval Approval Approval	Hydromorphone hydrochloride	Drugs with a new active ingredient indicated for management of moderate to severe pain in various types of cancer.
4	Aug. 26, 2016	39	Inavir Dry Powder Inhaler 20 mg (Daiichi Sankyo Company, Limited)	Change	Laninamivir octanoate hydrate	A drug with a new additional dosage and administration for the prophylaxis of influenza A or B virus infections in single inhalation doses for adults and children aged 10 years and older, and children aged under 10 years.
4	Aug. 26, 2016	40	Valixa Tablets 450 mg (Mitsubishi Tanabe Pharma Corporation)	Change	Valganciclovir hydrochloride	A drug with a new additional indication and a new dosage for the prevention of cytomegalovirus disease in organ transplant (recipients or patients) (excluding hematopoietic stem cell transplantation). [Public knowledge-based application after PAFSC's preliminary assessment]
4	Sep. 28, 2016	41	Rifxima Tablets 200 mg (Aska Pharmaceutical Co., Ltd.)	Approval	Rifaximin	A drug with a new active ingredient indicated for the improvement of hyperammonemia in patients with hepatic encephalopathy. [Orphan drug]
4	Sep. 28, 2016	42	Grazyna Tablets 50 mg (MSD K.K.)	Approval	Grazoprevir hydrate	A drug with a new active ingredient indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1). [Priority review]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
4	Sep. 28, 2016	43	Erelsa Tablets 50 mg (MSD K.K.)	Approval	Elbasvir	A drug with a new active ingredient 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	Sep. 28, 2016	44	Viekirax Combination Tablets (AbbVie GK)	Change	Ombitasvir hydrate/ Paritaprevir hydrate/ Ritonavir	A drug with a new additional indication and a new dosage for the improvement of viremia in patients with chronic hepatitis C in serogroup 2 (genotype 2).
4	Sep. 28, 2016	45	Rebetol Capsules 200 mg (MSD K.K.)	Change	Ribavirin	A drug with a new additional indication and a new dosage for the improvement of viremia in patients with chronic hepatitis C in serogroup 2 (genotype 2), for a combination use of ombitasvir hydrate, paritaprevir hydrate, and ritonavir.
4	Dec. 19, 2016	46	Ximency Combination Tablets (Bristol-Myers Squibb K.K.)	Approval	Daclatasvir hydrochloride/ Asunaprevir/ Beclabuvir hydrochloride	A new combination drug with a new active ingredient indicated for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 1 (genotype 1).
4	Dec. 19, 2016	47	Riamet Combination Tablets (Novartis Pharma K.K.)	Approval	Artemether/ Lumefantrine	A new combination drug with new active ingredients indicated for the treatment of malaria.
4	Dec. 19, 2016	48	Vemlidy Tablets 25 mg (Gilead Sciences, Inc.)	Approval	Tenofovir alafenamide fumarate	A drug with a new active ingredient indicated for the suppression of proliferation of hepatitis B virus in patients with chronic liver disease with hepatitis B virus infection in whom abnormal liver function is confirmed along with hepatitis B virus proliferation. [Priority review]
4	Mar. 2, 2017	49	Ozex Fine Granules 15% for Pediatric (Toyama Chemical Co., Ltd.)	Change	Tosufloxacin tosilate hydrate	A drug with a new additional indication for the treatment of mycoplasma pneumonia caused by *Mycoplasma pneumoniae* .
4	Mar. 24, 2017	50	Sovaldi Tablets 400 mg (Gilead Sciences, Inc.)	Change	Sofosbuvir	A drug with a new additional indication and a new dosage for the improvement of viraemia in patients with chronic hepatitis C or compensated cirrhosis type C in neither Serogroup 1 (genotype 1) nor Serogroup 2 (genotype 2). [Expedited review]
4	Mar. 24, 2017	51	Rebetol Capsules 200 mg (MSD K.K.)	Change	Ribavirin	A drug with a new additional indication for the improvement of viraemia in patients with chronic hepatitis C or compensated cirrhosis type C in neither Serogroup 1 (genotype 1) nor Serogroup 2 (genotype 2). [Expedited review]
4	Mar. 24, 2017	52	Copegus Tablet 200 mg (Chugai Pharmaceutical Co., Ltd.)	Change	Ribavirin	A drug with a new additional indication for the improvement of viraemia in patients with chronic hepatitis C or compensated cirrhosis type C in neither Serogroup 1 (genotype 1) nor Serogroup 2 (genotype 2). [Expedited review]
4	Mar. 24, 2017	53	Tamiflu Dry Syrup 3% (Chugai Pharmaceutical Co., Ltd.)	Change	Oseltamivir phosphate	A drug with a new additional dosage for newborns and infants for the treatment of influenza A or B virus infection. [Public knowledge-based application after PAFSC's preliminary assessment]
5	Jul. 4, 2016	54	Onecrinone 90mg Progesterone vaginal gel (Merck Serono 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.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
5	Jul. 4, 2016	55	Elneopa-NF No. 1 Injection Elneopa-NF No. 2 Injection (Otsuka Pharmaceutical Factory Inc.)	Approval Approval	N/A for this combination drug	Combination prescription drugs with similar formulations indicated for the supplementation of water, electrolytes, calories, amino acids, vitamins, zinc, iron, copper, manganese, and iodine in patients for whom receiving oral or enteral nutrition is impossible or insufficient and the total parenteral nutrition is the only choice.
5	Sep. 28, 2016	56	Ovidrel Syringe 250 μg (Merck Serono Co., Ltd.)	Approval	Choriogonadotropin alfa (genetical recombination)	A drug with a new active ingredient indicated for: • Induction of ovulation and luteinization in patients with anovulation or oligoovulation associated with hypothalamic-pituitary dysfunction • Induction of final follicular maturation and luteinization as part of assisted reproductive technology for infertile women.
5	Dec. 2, 2016	57	Dinagest Tablets 1 mg Dinagest OD Tablets 1 mg (Mochida Pharmaceutical Co., Ltd.)	Change Change	Dienogest	Drugs with a new additional indication for the alleviation of pain associated with uterine adenomyosis.
5	Dec. 19, 2016	58	YazFlex Combination Tablets (Bayer Yakuhin Ltd.)	Approval	Drospirenone /Ethinylestradiol betadex	A drug with new indications and a new dosage in an additional dosage form indicated for the alleviation of pain associated with endometriosis, and dysmenorrhea.
5	Mar. 30, 2017	59	D Dry 2.75S (Nikkiso Co., Ltd.)	Approval	N/A for this combination drug	A prescription drug with similar formulations to approved combination drugs used as perfusion fluids for hemodialysis in patients with chronic renal failure.
6-1	May 13, 2016	60	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new dosage indicated for plaque psoriasis, psoriatic arthritis, pustular psoriasis, and erythrodermic psoriasis in patients who have not responded sufficiently to conventional treatments.
6-1	Jul. 4, 2016	61	Taltz 80mg Syringe for SC Injection Taltz 80mg Auto-Injector for SC Injection (Eli Lilly Japan K.K.)	Approval Approval	Ixekizumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of plaque psoriasis, psoriatic arthritis, pustular psoriasis, and erythrodermic psoriasis in patients who have not responded sufficiently to conventional therapies.
6-1	Jul. 4, 2016	62	Lumicef Subcutaneous Injection 210 mg Syringe (Kyowa Hakko Kirin Co., Ltd.)	Approval	Brodalumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of plaque psoriasis, psoriatic arthritis, pustular psoriasis, and erythrodermic psoriasis in patients who have not responded sufficiently to conventional therapies.
6-1	Aug. 26, 2016	63	Spiriva 2.5 μg Respimat 60 puffs Spiriva1.25 μg Respimat 60 puffs (Nippon Boehringer Ingelheim Co., Ltd.)	Change Approval	Tiotropium bromide hydrate	Drugs with a new additional indication, dosage, and dosage form for the relief of symptoms secondary to airway obstructive disorders in mild to moderate persistent bronchial asthma.
6-1	Sep. 28, 2016	64	Desalex Tablets 5 mg (MSD K.K.)	Approval	Desloratadine	A drug with a new active ingredient indicated for the treatment of allergic rhinitis, urticaria, and itching associated with skin diseases (eczema/dermatitis, cutaneous pruritus).
6-1	Sep. 28, 2016	65	Bilanoa Tablet 20 mg (Taiho Pharmaceutical Co. Ltd.)	Approval	Bilastine	A drug with a new active ingredient indicated for the treatment of allergic rhinitis, urticaria, and itching associated with skin diseases (eczema/dermatitis, cutaneous pruritus).
6-1	Sep. 28, 2016	66	Humira 40 mg for S.C. Injection Syringe 0.8 mL Humira 40 mg for S.C. Injection Syringe 0.4 mL Humira 80 mg for S.C. Injection Syringe 0.8 mL (AbbVie GK)	Change Change Change	Adalimumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of non-infectious intermediate, posterior, and panuveitis in patients who have not responded sufficiently to conventional therapies.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-1	Sep. 28, 2016	67	Colchicine Tablets 0.5 mg "Takata" (Takata Pharmaceutical Co.,Ltd.)	Change	Colchicine	A drug with a new additional indication and a new dosage for the treatment of familial Mediterranean fever. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Dec. 2, 2016	68	Relvar 100 Ellipta 14 dose Relvar 100 Ellipta 30 dose (GlaxoSmithKline K.K.)	Change Change	Vilanterol trifenatate/ Fluticasone furoate	Drugs with a new additional indication and a new dosage for the relief of symptoms in patients with chronic obstructive pulmonary disease (chronic bronchitis, emphysema) (who require a combination therapy with an inhaled corticosteroid and a long-acting beta-2 agonist).
6-1	Dec. 19, 2016	69	Otezla Tablets 10 mg Otezla Tablets 20 mg Otezla Tablets 30 mg (Celgene K.K.)	Approval Approval Approval	Apremilast	Drugs with a new active ingredient indicated for the treatment of plaque psoriasis in patients who have not responded sufficiently to topical therapy or psoriatic arthritis.
6-1	Dec. 19, 2016	70	Ilaris for S.C. Injection 150 mg (Novartis Pharma K.K.)	Change	Canakinumab (genetical recombination)	A drug with new additional indications and a new dosage for the treatment of patients with familial Mediterranean fever who have not responded sufficiently to conventional therapies, TNF receptor-associated periodic syndrome, or hyper IgD syndrome (mevalonate kinase deficiency). [Orphan drug]
6-1	Mar. 24, 2017	71	Xolair for S.C. Injection 150 mg Xolair for S.C. Injection 75 mg (Novartis Pharma K.K.)	Change Change	Omalizumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of chronic idiopathic urticaria (for use only in patients who have not responded sufficiently to conventional therapies).
6-1	Mar. 24, 2017	72	Berinert P I.V. Injection 500 (CSL Behring K.K.)	Change	Lyophilized human C1-inactivator concentrate	A drug with a new additional indication and a new dosage for inhibiting onset of acute attacks of hereditary angioedema caused by invasive procedures. [Public knowledge-based application after PAFSC's preliminary assessment]
6-1	Mar. 30, 2017	73	Arnuity 100 µg Ellipta 14 doses Arnuity 100 µg Ellipta 30 doses Arnuity 200 µg Ellipta 14 doses Arnuity 200 µg Ellipta 30 doses (GlaxoSmithKline K.K.)	Approval Approval Approval Approval	Fluticasone furoate	Drugs with a new dosage and other characteristics indicated for the treatment of bronchial asthma.
6-2	May. 23, 2016	74	Feburic Tablets 10 mg Feburic Tablets 20 mg Feburic Tablets 40 mg (Teijin Pharma Limited)	Change Change Change	Febuxostat	Drugs with a new additional indication and a new dosage for the treatment of hyperuricemia in patients receiving cancer chemotherapy.
6-2	Sep. 28, 2016	75	Signifor LAR Kit for i.m. injection 20 mg Signifor LAR Kit for i.m. injection 40 mg Signifor LAR Kit for i.m. injection 60 mg (Novartis Pharma K.K.)	Approval Approval Approval	Pasireotide pamoate	Drugs with a new active ingredient indicated for the improvement of hypersecretion of growth hormone and IGF-I (somatomedin-C) and related symptoms in acromegaly and pituitary gigantism (when surgical therapies are not sufficiently effective or are difficult to perform).
6-2	Sep. 28, 2016	76	Inisync Combination Tablets (Takeda Pharmaceutical Company Limited)	Approval	Alogliptin benzoate/ Metformin hydrochloride	A new combination drug indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of alogliptin benzoate with metformin hydrochloride is deemed appropriate).
6-2	Sep. 28, 2016	77	Reclast for i.v. infusion 5 mg (Asahi Kasei Pharma Corporation)	Approval	Zoledronic acid hydrate	A drug with a new indication and a new dosage in an additional dosage form indicated for the treatment of osteoporosis.
6-2	Sep. 28, 2016	78	Carbaglu Dispersible Tablets 200 mg (Pola Pharma Inc.)	Approval	Carglumic acid	A drug with a new active ingredient indicated for the treatment of hyperammonemia due to N-acetylglutamate synthetase deficiency, isovaleric acidemia, methylmalonic acidemia, and propionic acidemia. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
6-2	Sep. 28, 2016	79	Tresiba Flex Touch Tresiba Penfill (Novo Nordisk Pharma Ltd.)	Change Change	Insulin degludec (genetical recombination)	Drugs with a new dosage indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
6-2	Dec. 19, 2016	80	Lyxumia 300 μg solution for injection (Sanofi K.K.)	Change	Lixisenatide	A drug with a revised indication for the treatment of type 2 diabetes mellitus.
6-2	Dec. 19, 2016	81	Humalog Cart Humalog Miriopen (Eli Lilly Japan K.K.)	Change Change	Insulin lispro (genetical recombination)	Drugs with a new dosage indicated for the treatment of diabetes mellitus in cases where insulin therapy is indicated.
In vivo diagnostics	Mar. 30, 2017	82	(1) Optiray 350 Injection 20 mL (2) Optiray 350 Injection 50 mL (3) Optiray 350 Injection 100 mL (4) Optiray 350 Injection Syringe 100 mL (5) Optiray 350 Injection Syringe 135 mL (Fuji Pharma Co., Ltd.)	Change Change Change Change Approval	Ioversol	Drugs with a new additional indication and a new dosage, and an additional dosage form used as contrast media in abdominal computed tomography.
Radio pharma ceuticals	Dec. 19, 2016	83	Amyvid Injection (Fujifilm RI Pharma Co., Ltd.)	Approval	Florbetapir (^{18}F)	A drug with a new active ingredient indicated for visualization of beta-amyloid plaques in the brain of patients with cognitive impairment suspected to be Alzheimer's disease.
Oncology drugs	May 23, 2016	84	Avastin 100 mg/4 mL Intravenous Infusion Avastin 400 mg/16 mL Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)	Change Change	Bevacizumab (genetical recombination)	Drugs with a new additional indication for the treatment of advanced or recurrent cervical cancer. [Orphan drug]
Oncology drugs	May 23, 2016	85	Cyramza Injection 100 mg Cyramza Injection 500 mg (Eli Lilly Japan K.K.)	Change Change	Ramucirumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of unresectable advanced or recurrent colorectal cancer.
Oncology drugs	Jun. 20, 2016	86	Cyramza Injection 100 mg Cyramza Injection 500 mg (Eli Lilly Japan K.K.)	Change	Ramucirumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of unresectable advanced/relapsed non-small cell lung cancer.
Oncology drugs	Jul. 4, 2016	87	Kyprolis for Intravenous Injection10 mg Kyprolis for Intravenous Injection 40 mg (Ono Pharmaceutical Co., Ltd.)	Approval Approval	Carfilzomib	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Aug. 26, 2016	88	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 for the treatment of unresectable or metastatic renal cell carcinoma. [Priority review]
Oncology drugs	Aug. 26, 2016	89	Treakisym Injection 100 mg (SymBio Pharmaceuticals Limited)	Change	Bendamustine hydrochloride	A drug with a new additional indication and a new dosage for the treatment of chronic lymphocytic leukemia. [Orphan drug]
Oncology drugs	Aug. 26, 2016	90	Afinitor Tablets 5 mg Afinitor Tablets 2.5 mg (Novartis Pharma K.K.)	Change Change	Everolimus	Drugs with a revised indication from "pancreatic neuroendocrine tumor" to "neuroendocrine tumor."
Oncology drugs	Aug. 26, 2016	91	Xeloda Tablets 300 (Chugai Pharmaceutical Co., Ltd.)	Change	Capecitabine	A drug with a new additional indication and a new dosage for adjuvant chemotherapy for rectal cancer. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	Sep. 28, 2016	92	Keytruda Injection 20 mg Keytruda Injection 100 mg (MSD K.K.)	Approval Approval	Pembrolizumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable melanoma. [Orphan drug]

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, 2016	93	Empliciti for I.V. Infusion 300 mg Empliciti for I.V. Infusion 400 mg (Bristol-Myers Squibb Company)	Approval Approval	Elotuzumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Sep. 28, 2016	94	Iclusig Tablets 15 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval	Ponatinib hydrochloride	A drug with a new active ingredient indicated for the treatment of chronic myelogenous leukemia with resistance or intolerance to prior drug therapies, and recurrent or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia. [Orphan drug]
Oncology drugs	Sep. 28, 2016	95	Treakisym Injection 25 mg (SymBio Pharmaceuticals Limited)	Approval	Bendamustine hydrochloride	A drug with a new additional indication, dosage, and dosage form for the treatment of chronic lymphocytic leukemia. [Orphan drug]
Oncology drugs	Dec. 2, 2016	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 for the treatment of relapsed or refractory classical Hodgkin's lymphoma. [Orphan drug]
Oncology drugs	Dec. 2, 2016	97	Imbruvica Capsules 140 mg (Janssen Pharmaceutical K.K.)	Change	Ibrutinib	A drug with a new additional indication and a new dosage for the treatment of relapsed or refractory mantle cell lymphoma. [Orphan drug]
Oncology drugs	Dec. 19, 2016	98	Erwinase for Intramuscular Injection 10000 (Ohara Pharmaceutical Co., Ltd.)	Approval	Crisantaspase	A drug with a new active ingredient indicated for the treatment of acute leukemia (including blast crisis of chronic leukemia) and malignant lymphoma (only for patients who experienced hypersensitivity to L-asparaginase preparations).
Oncology drugs	Dec. 19, 2016	99	Mozobil Injection 24 mg (Sanofi K.K.)	Approval	Plerixafor	A drug with a new active ingredient indicated for the enhancement of mobilization of hematopoietic stem cells to the peripheral blood for autologous peripheral blood stem cell transplantation. [Orphan drug]
Oncology drugs	Dec. 19, 2016	100	Treakisym Injection 100 mg Treakisym Injection 25 mg (SymBio Pharmaceuticals Ltd.)	Change Change	Bendamustine hydrochloride	Drugs with a revised indication and a new dosage for the treatment of low-grade B-cell non-Hodgkin's lymphoma and mantle cell lymphoma.
Oncology drugs	Dec. 19, 2016	101	Keytruda Injection 100 mg Keytruda Injection 20 mg (MSD K.K.)	Change Change	Pembrolizumab (genetical recombination)	Drugs with a new additional indication and a new dosage for the treatment of patients with PD-L1-positive, unresectable, recurrent or advanced non-small cell lung cancer.
Oncology drugs	Mar. 2, 2017	102	Revlimid Capsules 2.5 mg Revlimid Capsules 5 mg (Celgene K.K.)	Change Change	Lenalidomide hydrate	Drugs with a new additional indication and a new dosage for the treatment of relapsed or refractory adult T-cell leukemia/lymphoma. [Orphan drug]
Oncology drugs	Mar. 24, 2017	103	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 for the treatment of relapse or distant metastasis of head and neck cancer. [Priority review]
Oncology drugs	Mar. 30, 2017	104	Zaltrap 100 mg I.V. Infusion Zaltrap 200 mg I.V. Infusion (Sanofi K.K.)	Approval Approval	Aflibercept beta (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of unresectable advanced or recurrent colorectal cancer.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient(s) (underlined: new active ingredient)	Notes
Oncology drugs	Mar. 30, 2017	105	Mundesine Capsule 100 mg (Mundipharma K.K.)	Approval	Forodesine hydrochloride	A drug with a new active ingredient indicated for the treatment of relapsed or refractory peripheral T-cell lymphoma. [Orphan drug]
Oncology drugs	Mar. 30, 2017	106	Ninlaro Capsules 2.3 mg Ninlaro Capsules 3 mg Ninlaro Capsules 4 mg (Takeda Pharmaceutical Company Limited)	Approval Approval Approval	Ixazomib citrate	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
AIDS drugs	Jun. 17, 2016	107	Genvoya Combination Tablets (Japan Tobacco Inc.)	Approval	Elvitegravir/ Cobicistat/ Emtricitabine/ Tenofovir alafenamide fumarate	A new combination drug with a new active ingredient indicated for the treatment of HIV-1 infection. [Orphan drug]
AIDS drugs	Nov. 22, 2016	108	Prezcobix Combination Tablets (Janssen Pharmaceutical K.K.)	Approval	Darunavir ethanolate/ Cobicistat	A new combination drug with a new active ingredient indicated for the treatment of HIV infection. [Orphan drug]
AIDS drugs	Dec. 9, 2016	109	Descovy Combination Tablets LT Descovy Combination Tablets HT (Japan Tobacco Inc.)	Approval Approval	Emtricitabine/ Tenofovir alafenamide fumarate	New combination drugs indicated for the treatment of HIV-1 infection. [Orphan drug]
Vaccines	Dec. 19, 2016	110	Vaxem Hib Suspension Liquid for Injection (Takeda Pharmaceutical Company Limited)	Change	*Haemophilus influenzae* type b vaccine adsorbed (mutated diphtheria toxin CRM197 conjugate)	A drug with a new dosage indicated for the prophylaxis of *Haemophilus influenzae* type b infections.
Blood products	Sep. 28, 2016	111	Idelvion I.V. Injection 250 Idelvion I.V. Injection 500 Idelvion I.V. Injection 1000 Idelvion I.V. Injection 2000 (CSL Behring K.K.)	Approval Approval Approval Approval	Albutrepenonacog alfa (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with coagulation factor IX deficiency.
Blood products	Mar. 30, 2017	112	Kcentra for I.V. Injection 500 Kcentra for I.V. Injection 1000 (CSL Behring K.K.)	Approval Approval	Freeze-dried human prothrombin complex concentrated	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients treated with vitamin K antagonists at the time of acute serious bleeding or an emergency surgery/procedures in which serious bleeding is expected. [Orphan drug]

Table 5. Products Approved in FY 2016: 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
Robotic, ICT, and other devices (not classified as other categories)	Oct. 25, 2016 Total review time: 848 days Regulatory review time: 298 days	- Domestic clinical study results and global clinical study results	1	Neuraceq Automated Synthesizer Synthera (SCETI K.K.)	Approval	Instrument & apparatus 10 Radiopharmaceutical synthesizer	A radioactive pharmaceutical synthesizer used for the semi-automated preparation of a radioisotope labeled compound, florbetaben (^{18}F) injection, by remote control system indicated for the visualization of beta-amyloid plaques in the brain of patients with cognitive impairment suspected to be Alzheimer's disease. Results from non-clinical and global clinical studies were submitted as evaluation data on the efficacy and safety of this product and florbetaben (^{18}F) injection.
Orthopedic and Plastic Surgery	Jun. 29, 2016 Total review time: 43 days Regulatory review time: 28 days	Dec. 19, 2005 No clinical study results	2	Trabecular Metal Reverse Shoulder System (Zimmer Biomet G.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 to add the use of the product in combination with the approved product, "Comprehensive Reverse Shoulder System" (Approval No. 22700BZX00232000). (A "partial change" application submitted during the reexamination period)
Orthopedic and Plastic Surgery	Oct. 25, 2016 Total review time: 512 days Regulatory review time: 219 days	- Domestic clinical study results	3	DARTS Wrist Prosthesis (Teijin Nakashima Medical Co., Ltd.)	Approval	Medical products 4 Total wrist prosthesis	A total wrist prosthesis that functions as a substitute of a natural wrist, by replacing a severely destroyed and impaired wrist due to underlying diseases such as rheumatoid arthritis, etc. The improvement of joint function and elimination of pain can be expected by replacing the dysfunctional wrist with the device. The device is designed as a semi-constrained surface replacement type, in order to closely mimic the natural joint surface shapes, forming a structure that induces dart thrower's motion, which is more natural physiological motion of the wrist. Results from an investigator-initiated clinical study conducted in Japan were submitted to evaluate the efficacy and safety of the device.
Orthopedic and Plastic Surgery	Dec. 15, 2016 Total review time: 359 days Regulatory review time: 213 days	Dec. 26, 2013 Clinical evaluation report	4	Long-Pulsed Alexandrite Laser GentleLase Pro (Syneron Candela K.K.,)	Approval	Instrument & apparatus 31 Alexandrite laser	The device is intended to achieve long-term hair reduction by selective photothermolysis. The device is equipped with a dynamic cooling device, which sprays cryogen to prevent skin damage caused by laser irradiation. A clinical evaluation report, which summarized the results from foreign clinical studies for the previous-generation products, was submitted to evaluate the long-term efficacy of hair reduction and the risk of complications after laser treatment.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	May 11, 2016 Total review time: 57 days Regulatory review time: 24 days	- No clinical study results	5	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	Sep. 9, 2016 Total review time: 105 days Regulatory review time: 55 days	- No clinical study results	6	Revive SE Thrombectomy device (Johnson & Johnson K.K.)	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 by removing clots from blood vessels in the brain in patients with acute-phase cerebral infarction (in principle, within 8 hours of 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 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
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Oct. 14, 2016 Total review time: 114 days Regulatory review time: 66 days	ICY Catheter: Oct. 23, 2003 Quattro Catheter: Feb. 15, 2007 No clinical study results	7	Quattro・ICY IVTM Catheter (ZOLL Circulation, Inc.)	Change	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). The application was submitted for the changes in the shape and material of the luer part for connecting the catheter and start-up kit, as well as the changes in the values for specification of flow rate which are related to the performance and safety of the heat-exchange catheter. (A "partial change" application submitted during the post-market performance review period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 15, 2016 Total review time: 118 days Regulatory review time: 67 days	Jun. 12, 2015 No clinical study results	8	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 (in principle, within 8 hours of 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 was submitted for an additional size variation in the length of the stent. (A "partial change" application submitted during the reexamination period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 15, 2016 Total review time: 359 days Regulatory review time: 283 days	Oct. 5, 2015 Foreign clinical study results	9	NovoTTF-100A System (NovoCure Ltd.)	Change	Instrument & apparatus 12 Alternating electric field tumor treatment system	This non-invasive medical device delivers alternating electric fields referred to as Tumor Treating Fields (TTField) - that disrupt cancer cell division - through insulated transducer arrays (INE transducer array) placed on the scalp. The application was submitted to change the indication so that the device can be used regardless of the status of glioblastoma (indicated for both newly-diagnosed and recurrent glioblastoma). Data from a clinical study conducted to demonstrate the efficacy and safety of the device in patients with newly-diagnosed glioblastoma after receiving all possible surgeries and radiation therapies were submitted. (A "partial change" application submitted during the post-market performance review period)
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 15, 2016 Total review time: 364 days Regulatory review time: 266 days	Jul. 11, 2016 Foreign clinical study results	10	MR Guided Focused Ultrasound Surgery ExAblate 4000 (InSightec Ltd.)	Approval	Instrument & apparatus 12 Focused Ultrasound System	The device is a focused ultrasound surgery system intended for focally heating and ablating targeted brain tissues by irradiating focused ultrasound to the target in the thalamus from outside the skull. By connecting to an MR device, the device can be used to alleviate essential tremor which does not respond sufficiently to drug therapies. The cell necrosis is induced at the heated temperature of target region by focusing the ultrasound beam emitted from the transducer helmet on the central intermediate nucleus of the thalamus. Results from foreign clinical studies were submitted to evaluate the efficacy and safety of the device in patients with essential tremor who were refractory to drug therapies.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 15, 2017 Total review time: 257 days Regulatory review time: 232 days	Jul. 13, 2016 No clinical study results	11	NovoTTF-100A System (NovoCure Ltd.)	Change	Instrument & apparatus 12 Alternating electric field tumor treatment system	A non-invasive medical device delivers alternating electric fields referred to as Tumor Treating Fields (TT Field) - that disrupt cancer cell division - through insulated transducer arrays (INE transducer array) placed on the scalp. The application was submitted for an additional product type with a downsized TT Field generator. (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
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 31, 2017 Total review time: 102 days Regulatory review time: 51 days	- No clinical study results	12	Bronchial Spigot EWS (Harada Corporation)	Change	Instrument & apparatus 7 Bronchial blocker	A silicone resin bronchial spigot that is used to fill the bronchi and close fistula in patients who have refractory and inoperable secondary pneumothorax, prolonged air leak following pneumectomy or other fistula. The application was submitted to change the raw materials and manufacturing method of the bronchial spigot. (A "partial change" application submitted during the reexamination period) [Orphan device]
Gastroenterology, Genitourinary and Reproductive Medicine	Sep. 16, 2016 Total review time: 322 days Regulatory review time: 241 days	Jun. 30, 2006 Clinical evaluation report	13	InterStim II Neurostimulator for Sacral Neuromodulation (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 12 Implantable stimulator for bladder and bowel control	An implantable nerve stimulation system to be used in sacral nerve stimulation therapy for fecal incontinence and overactive bladder. The application was submitted for an additional indication of overactive bladder (A "partial change" application). A clinical evaluation report summarizing data from foreign clinical studies was submitted to demonstrate that treatment using the device improves the symptom of overactive bladder as compared to conservative treatment. (A "partial change" application submitted during the reexamination period)
Gastroenterology, Genitourinary, and Reproductive Medicine	Mar. 27, 2017 Total review time: 136 days Regulatory review time: 89 days	- No clinical study results	14	PD Laser (Meiji Seika Pharma Co., Ltd.)	Change	Instrument & apparatus 31 PDT semiconductor laser	A photodynamic therapy (PDT) semiconductor laser to be used in combination with an oncotropic photo-sensitizer, "Laserphyrin 100 mg for Injection (R)" (Approval No. 21500AMZ00509000; generic name, talaporfin sodium), for the treatment of early lung cancer that can be treated with laser irradiation, or recurrent esophageal cancer associated with local persistence after chemotherapy or radiotherapy. The application was submitted for the changes to comply with the amendments of JIS specifications on electric safety and electromagnetic compatibility of medical devices, design changes, and addition of components. (A "partial change" application submitted during the post-market performance review period)
Ophthalmology and Otorhinolaryngology	Mar. 14, 2017 Total review time: 104 days Regulatory review time: 35 days	Sep. 30, 2016 No clinical study results	15	iStent Trabecular Micro-Bypass Stent System (Glaukos Corporation)	Change	Medical products 4 Heparin using intraocular drain	A device consisting of the iStent, a titanium-alloy glaucoma implant designed to maintain a patent outflow of aqueous humor through the trabecular meshwork facilitating its drainage from anterior chamber to the Schlemm's canal and its subsequent natural outflow. This device accompanies its inserter. The surface of the iStent is coated with porcine-derived heparin. The application was submitted to change the manufacturing site. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Sep. 27, 2016 Total review time: 2007 days Regulatory review time: 641 days	May 30, 2008 Foreign clinical study results	16	Impella Circulatory Assist Pump Catheter (Abiomed, Inc.)	Approval	Instrument & apparatus 51 Implantable Pump Catheter for Ventricular Support	The catheter-based blood pump that assists systemic circulation in patients with drug resistant acute heart failure, such as cardiogenic shock, can be inserted through femoral artery and placed in the left ventricle. This device pulls blood directly from the left ventricle and expels the blood from the catheter into the ascending aorta. The catheter pump, (two models are available: Impella 2.5 and Impella 5.0), is a catheter based blood pump equipped with a small axial flow pump. The blood is unloaded from an inlet placed in the left ventricle and pumped to an outlet placed in the aorta by the pump-unit of the catheter pump. The device is used with "Impella Controller" (Approval No. 22800BZI00031000). Data from a foreign clinical studies, which demonstrated that using the device is beneficial in patients with cardiogenic shock or other acute heart failure, were submitted.

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	Sep. 27, 2016 Total review time: 2007 days Regulatory review time: 628 days	Jul. 8, 2010 Foreign clinical study results	17	Impella Controller (Abiomed, Inc.)	Approval	Instrument & apparatus 7 Controller of Implantable Pump Catheter for Ventricular Support	The device is an extermal controller for "Impella Circulatry Assist Pump Catheter" (Approval No. 22800BZI00032000) (hereinafter referred to the Catheter Pump). The device controls the performance and monitors the catheter position of the Catheter Pump, and controls the flow rate of the purge cassette, which is a component of the Catheter Pump. Data from foreign clinical studies, which demonstrated that this device is capable of controlling the Catheter Pump when used for circulatory support in patients with cardiogenic shock or other acute heart failure, were submitted.
Cardiopulmonary Circulation	Oct. 25, 2016 Total review time: 186 days Regulatory review time: 123 days	Aug. 8, 2016 No clinical study results	18	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 tachyarrhythmias. The application was submitted to add the functions of SMART Pass and AF Monitor, respectively, and to allow patients with the device to undergo MRI scans under predefined conditions. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Oct. 25, 2016 Total review time: 186 days Regulatory review time: 123 days	Aug. 8, 2016 No clinical study results	19	S-ICD Lead (Boston Scientific Japan K.K.)	Change	Instrument & apparatus 7 Implantable defibrillator /pacemaker lead	The device is a subcutaneous implantable cardioverter-defibrillator (S-ICD) lead used in patients at a high risk of sudden cardiac death caused by ventricular tachyarrhythmias. The application was submitted to allow patients with the device to undergo MRI scans under predefined conditions. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Nov. 2, 2016 Total review time: 552 days Regulatory review time: 250 days	Jul. 5, 2016 Domestic clinical study results Foreign clinical study results	20	Absorb GT1 Bioresorbable Vascular Scaffold System (Abbot Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Absorbable coronary stent	A stent system consisting of an everolimus-eluting bioresorbable scaffold used for the treatment of patients with symptomatic ischemic heart disease due to de novo native coronary artery lesions (length ≤24 mm) with a reference vessel diameter ranged from ≥2.5 mm to ≤3.75 mm, and a delivery catheter to place the stent at the site of stenosis. Results of domestic and foreign clinical studies using the previous generation model of the device were attached to show that the efficacy and safety of the device are equivalent to those of the previously approved coronary stent.
Cardiopulmonary Circulation	Nov. 8, 2016 Total review time: 288 days Regulatory review time: 161 days	Jun. 22, 2015 Foreign and domestic clinical study results	21	CoreValve Evolut R (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Transcatheter porcine pericardial valve	A prosthetic cardiac valve system used for transcatheter valve implantation in the native aortic valve for patients with symptomatic severe aortic valve stenosis attributed to sclerosis and degeneration of the cusp of the native valve, for whom surgery cannot be performed. This device has been improved in the diameter of outflow area and the length, etc. from those of the previously approved "CoreValve" (Approval No. 22700BZX00100000), for the purpose of reducing deformation caused by interference with the ascending aorta. In addition, the device includes a 23-mm-diameter size variation, which is not available in "CoreValve" system. Furthermore, the delivery system also has been improved to enhance the safety and allow the valve to be recaptured, repositioned, or retrieved, etc. Results of domestic clinical study were submitted to evaluate the efficacy and safety of the 23-mm-diameter product in Japanese patients, in addition to the results of foreign clinical studies in patients with symptomatic severe aortic valve stenosis whose risks for surgical aortic valve replacement were estimated as "High risk" or "Extreme risk."

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	Nov. 14, 2016 Total review time: 634 days Regulatory review time: 523 days	Nov. 26, 2014 Foreign clinical study results	22	HeartFlow FFR_{CT} (HeartFlow Japan G.K.)	Approval	Program 1 Circulatory dynamics analysis program	A diagnosis support program that calculates the fractional flow reserve (FFRCT) by computational fluid dynamics analysis based on the data of coronary computed-tomography angiography in clinically stable patients suspected of having coronary artery diseases. Results from foreign clinical studies were submitted to evaluate the diagnostic performance pertaining to sensitivity and specificity of FFRCT values against FFR values measured with a pressure wire.
Cardiopulmonary Circulation	Feb. 14, 2017 Total review time: 365 days Regulatory review time: 88 days	Apr. 6, 2016 Global clinical trial	23	Micra Transcatheter Pacing System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable leadless cardiac pacemaker	A single-chamber transcatheter implantable cardiac pacemaker designed to periodically deliver artificial electrical impulses to the heart of the patients with bradycardia. Results from global clinical trial including Japan were submitted to evaluate the efficacy and safety of the device in the treatment of bradyarrhythmia.
Cardiopulmonary Circulation	Feb. 17, 2017 Total review time: 241 days Regulatory review time: 97 days	- No clinical study results	24	Jarvik 2000 Implantable Ventricular Assist Device (Century Medical, Inc.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device system used to improve the blood circulation until heart transplant. The device is used for patients with severe cardiac failure who are qualified to receive heart transplant presenting continuous decompensation in spite of drug therapy or circulation assist techniques such as an external ventricular assist system and considered difficult to survive without heart transplant. This application was submitted to correct errors in the product information of the approved device. (A "partial change" application submitted during the reexamination period)
Specified partial change	Apr. 5, 2016 Total review time: 55 days Regulatory review time: 21 days	- No clinical study results	25	PD Laser (Panasonic Healthcare Co., Ltd.)	Change	Instrument & apparatus 31 PDT semiconductor laser	A photodynamic therapy (PDT) semiconductor laser to be used in combination with "Laserphyrin 100 mg for Injection" (approval No. 21500AMZ00509000; generic name, talaporfin sodium), an oncotropic photo-sensitizer, for the treatment of early lung cancer that can be treated with laser irradiation, or recurrent esophageal cancer associated with local persistence after chemotherapy or radiotherapy. This application was submitted to change the raw material used for the cover of the lateral firing tip in the lateral firing probe, 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 post-market performance review period)
Specified Partial Change	Nov. 25, 2016 Total review time: 88 days Regulatory review time: 73 days	Aug. 18, 2016 No clinical study results	26	GORE CTAG Thoracic Endoprosthesis (W. L. GORE & Associates, Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft used for intravascular treatment of thoracic aorta, consisting of the stent graft and the delivery system. The application was submitted to change the raw materials for parts of the delivery catheter. It is a partial change during the post-market performance review period, 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 post-market performance review period)

Table 6. Products Approved in FY 2016: 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
Robotic, ICT, and other devices (not classified as other categories)	May 25, 2016 Total review time: 614 days Regulatory review time: 304 days	- Foreign clinical study results	1	Freestyle Libre (Abbott Japan Co., Ltd.)	Approval	Instrument & apparatus 20 Glucose monitoring system	A glucose monitoring system to continuously measure and record glucose levels in the interstitial fluid. When the user scans the Reader over the sensor, fluctuation patterns of the interstitial fluid glucose level are displayed on the screen. In addition, the Reader also has the function of measuring blood glucose and blood ketone levels, as a glucose meter for self-testing. Results from clinical studies were submitted to compare the correlation between glucose level in blood or plasma and that in the interstitial fluid in order to evaluate the accuracy of the interstitial glucose levels measured by the product and the safety.
Robotic, ICT, and other devices (not classified as other categories)	Jun. 13, 2016 Total review time: 570 days Regulatory review time: 419 days	- Foreign clinical study results	2	Freestyle Libre Pro (Abbott Japan Co., Ltd.)	Approval	Instrument & apparatus 20 Glucose monitoring system	A glucose monitoring system for professional use to continuously measure and record glucose levels in the interstitial fluid. When the healthcare professional scans the Reader over the sensor, the fluctuation patterns of the interstitial fluid glucose level are displayed on the screen. Results from clinical studies were submitted to compare the correlation between glucose level in blood or plasma and that in the interstitial fluid in order to evaluate the accuracy of the interstitial glucose levels measured by the product and the safety.
Orthopedic and Plastic Surgery	May 9, 2016 Total review time: 1075 days Regulatory review time: 434 days	Sep. 17, 2012 Clinical evaluation report	3	KMC Kyphoplasty System (Nihon Americare Co.,Ltd.)	Approval	Instrument & apparatus 58 Single-use vertebral body restoration device	A single-use device used in balloon kyphoplasty (BKP) for restoration of fractured vertebral body. The system is used to create a cavity in the fractured vertebral body for patients in acute phase of compression fracture in one vertebral body due to primary osteoporosis, whose pain has not relieved after receiving sufficient conservative treatment. Improvements are made to enable: restoration of vertebral height using an expandable balloon; and reduction of the risk of cement leakage outside the vertebral body by creating a cavity for bone cement injection.
Orthopedic and Plastic Surgery	May 9, 2016 Total review time: 1075 days Regulatory review time: 411 days	Jun. 9, 2005 Clinical evaluation report	4	Mendec Spine Bone Cement Kit (Nihon Americare Co.,Ltd.)	Approval	Medical products 4 Orthopedic bone cement	Orthopedic bone cement for percutaneous vertebroplasty (PVP) in patients with vertebral fracture accompanying pain due to malignant vertebral tumor, or balloon kyphoplasty (BKP) in patients in acute phase of compression fracture in one vertebral body due to primary osteoporosis. Following improvements are made: enhancement of the visibility under fluoroscopy by increasing the amount of barium sulfate; and extension of the curing time as compared with that of the approved product, "KYPHON BKP Bone Cement HV-R" (Approval No. 22200BZX00119000) in order to enhance its operability.
Orthopedic and Plastic Surgery	May 25, 2016 Total review time: 299 days Regulatory review time: 253 days	- Clinical evaluation report	5	Sorbact Foam Dressing (ABIGO Medical AB)	Approval	Medical products 4 Secondary foam dressing for wound healing	A secondary foam dressing for wound healing to be used for wounds reaching subcutaneous adipose tissue (excluding third-degree burns) to protect wounds, maintain a moist wound environment, accelerate curing, and alleviate pain. The following improvement is made in the product: cellulose acetate fabric, which was made hydrophobic-by a covalent bond with dialkyl carbamoyl chloride (DACC), is used in the product surface coming into contact with the wound.
Orthopedic and Plastic Surgery	Aug. 4, 2016 Total review time: 478 days Regulatory review time: 249 days	- Domestic clinical study results	6	Renerve (Nipro Corporation)	Approval	Medical products 4 Collagen-using absorbent nerve regeneration-inducing material	An absorbent nerve regeneration-inducing material which is to be placed into the torn or deficit part of peripheral nerve, except the inside of dura mater, to induce neurotization. Pig skin collagen is used as a raw material. Japanese clinical study results were submitted to evaluate the recovery rate of sensory function after treatment with the product.

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	Sep. 9, 2016 Total review time: 260 days Regulatory review time: 78 days	Oct. 22, 2013 Foreign clinical study results	7	Juvederm Vista Voluma XC (Allergan Japan K.K.)	Approval	Medical products 4 Injectable material to a soft tissue using hyaluronic acid	An injectable material to soft-tissue using hyaluronic acid injected into a subcutaneous or a supraperiosteal deep tissue to correct volume loss in the midface, chin or temple in adults. The product contains 0.3 wt% of lidocaine hydrochloride to alleviate pain at the time of injection. Results from foreign clinical studies were submitted to evaluate the effect of volume correction in the midface.
Orthopedic and Plastic Surgery	Oct. 19, 2016 Total review time: 807 days Regulatory review time: 81 days	Jul. 18, 1997 Clinical evaluation report	8	Titanium Elastic Nail (Sterilized) (Johnson & Johnson K.K.)	Approval	Medical products 4 Intramedullary nail for internal fixation of femoral fracture	An intramedullary nail made of titanium alloy used for fracture fixation of the femur, tibia, humerus, radius, and ulna in pediatric patients, and the humerus, radius, and ulna in adult patients. The nailing system is used for the elastic stable intramedullary nailing technique, which allows fixation in the medullary cavity without damaging the epiphyseal line, for diaphyseal fractures in pediatric patients. A clinical evaluation report summarizing foreign clinical study results on the device was submitted to verify that fracture healing can be achieved without any serious complication.
Orthopedic and Plastic Surgery	Dec. 22, 2016 Total review time: 155 days Regulatory review time: 37 days	Jan. 3, 2007 Clinical evaluation report	9	Smart Curette (Medical U&A, Inc.)	Approval	Instrument & apparatus 12 Ultrasonic surgical instrument	The device is an ultrasonic surgical instrument used for wound debridement. It sprays physiological saline from the tipping of the probe and dissects necrotic tissue, etc. by vibrating the probe tip. A clinical evaluation report summarizing results from domestic and foreign clinical studies on the device and similar products was submitted to demonstrate that debridement by ultrasonic surgical instruments is effective in wound therapy.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	May 31, 2016 Total review time: 407 days Regulatory review time: 238 days	Feb. 13, 2009 Foreign clinical study results Domestic clinical study results Clinical evaluation report	10	Lifestent Solo Vascular Stent System (Medicon, Inc.)	Approval	Instrument & apparatus 7 Stent for blood vessel	A self-expanding vascular stent used for the treatment of symptomatic arterial disease with a lesion length up to 200 mm in the region from native superficial femoral artery (SFA) to proximal popliteal artery with reference vessel diameter of 4.0-6.5mm, and for the treatment of acute or impending occlusion in the aforementioned sites following the failure of interventional treatment. The following data was submitted: results from the foreign pivotal study to evaluate the performance of the product in lesion lengths up to 150 mm and a domestic study conducted to investigate whether the data can be extrapolated to Japanese population; a clinical evaluation report compiling the data from a foreign clinical study conducted to evaluate the performance of the product in lesion lengths up to 200 mm and literature reports on the results of surgical and endovascular treatments for lesions up to 200 mm in length.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Nov. 2, 2016 Total review time: 267 days Regulatory review time: 148 days	- Domestic clinical study results	11	DURAWAVE (GUNZE LIMITED)	Approval	Medical products 4 Synthetic artificial dura mater	The device is an artificial dura mater, primarily composed of polyglycolic acid, and identical to the previously approved product "NEOVEIL" (Approval No. 20400BZZ00322000). This application was submitted to newly obtain the indication of prosthetic dura mater, which is listed as a contraindication in the package insert for the already approved product. With the use of biological tissue adhesive, suturing is not necessary and the functioning as a prosthesis for dura mater deficit is easily and successfully achieved. Clinical study results on the device examining the sealing capability as well as effectiveness in prevention of cerebrospinal fluid leakage and subcutaneous cerebrospinal fluid retention were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Nov. 17, 2016 Total review time: 266 days Regulatory review time: 151 days	Feb. 29, 2016 Foreign clinical study results	12	Gore Excluder AAA Endoprosthesis (W. L. GORE & Associates, Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	The device consists of a stent graft and delivery system used for endovascular treatment of abdominal aortic aneurysm and aortic aneurysms extending from the abdominal aorta to the iliac artery (hereinafter referred to as "aortoiliac aneurysms"). The application was submitted to add an iliac branch endoprosthesis used for common iliac artery aneurysms (aortoiliac aneurysms and isolated common iliac artery aneurysms) (A "partial change" application). Results of foreign clinical studies were submitted to evaluate the performance of the device in the treatment of common iliac artery aneurysms.

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. 13, 2016 Total review time: 300 days Regulatory review time: 178 days	Jul. 30, 1993 Clinical evaluation report	13	Mini-BAL Sampling Catheter (Halyard Healthcare, Inc.)	Approval	Instrument & apparatus 51 Bronchoalveolar lavage (BAL) catheter	A single-use catheter used to collect specimens by bronchoalveolar lavage (BAL) without bronchoscope to diagnose pneumonia. The device is used in adult patients with an artificial airway created by procedures such as tracheal intubation or tracheotomy. Although the catheter is inserted without visualization, the tip of the catheter is curved so that the catheter can be smoothly inserted into the right and left bronchi. In addition, the area of catheter tip coming in contact with the bronchial wall is round-shaped. A clinical evaluation report based on the information collected from the literatures on the device and the similar products was submitted as the clinical evaluation data.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 27, 2016 Total review time: 641 days Regulatory review time: 425 days	Apr. 16, 2014 Foreign clinical study results	14	TruePath Chronic Total Occlusion (CTO) Device (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 51 Oscillating peripheral artery recanalization catheter system	The device is used for chronic total occlusion that is difficult to be penetrated with a guidewire during percutaneous transluminal angioplasty. Using mechanical rotation, the device penetrates the lesion to secure the passage for a guidewire. Results of foreign clinical study using this device were submitted to verify the status of penetration through lesions in peripheral vessels and the presence or absence of blood vessel perforation after the procedure.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 27, 2016 Total review time: 224 days Regulatory review time: 156 days	May 15, 2013 Foreign clinical study results	15	Denali IVC Filter (Medicon, Inc.)	Approval	Instrument & apparatus 51 Inferior vena cava filter	The device, consisting of an inferior vena cava filter and the delivery system, is used to prevent pulmonary embolism. The device was developed based on the concept of risk reduction for blood vessel penetration, enhancement of resistance to migration and fracture, and secure retrieval of the devices after a long-term implantation, etc., and characterized by addition of an anchor and penetration limiter to the legs and the one-piece body by laser cutting. Data of foreign clinical studies conducted to evaluate the success rates of placement and retrieval of the devices were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 9, 2017 Total review time: 232 days Regulatory review time: 202 days	May 4, 2015 Clinical evaluation report	16	ERBE CRYO2 (Amco Inc.)	Approval	Instrument & apparatus 31 Versatile cryosurgical unit	A cryosurgery unit used for tissue biopsy or removal of foreign matters by cooling/freezing the bronchus, bronchial peripheral tissue, or foreign matters in the bronchus by touching with the probe tip cooled by high pressure carbon dioxide. It was judged that clinical evaluation was necessary because its indications differ from those of existing cryosurgery equipment.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 9, 2017 Total review time: 178 days Regulatory review time: 132 days	- Foreign clinical study results Domestic clinical study results	17	Misago 3 (Terumo Corporation)	Approval	Instrument & apparatus 7 Stent for blood vessel	A stent system consisting of a self-expanding nickel-titanium alloy stent and a delivery system to deliver the stent to the lesion site, used for the treatment of symptomatic artery diseases with reference vessel diameters of 4-7 mm and target lesion length of 40-150 mm in the superficial femoral artery region by dilatation of the artery and maintenance of the lumen, and for the treatment of acute or impending occlusions associated with unsuccessful intervention treatments in the same lesion. The system uses the same stent as the company's approved product, "Misago" (Approval No. 22400BZX00463000), but differs from the approved product in that its delivery system is specialized in placing the stent to the target lesion by the ipsilateral approach. The results of clinical studies using the original product "Misago" were provided as clinical evaluation material and the rationale for its extrapolation was explained.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 23, 2017 Total review time: 226 days Regulatory review time: 186 days	Oct. 3, 2016 Foreign clinical study results	18	Prodigy MRI Dual 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 12 Implantable stimulator for pain relief	An implantable stimulator that generates electrical stimulation and its accessories used in spinal stimulation therapy for patients with chronic refractory pain in the trunk and extremities who are not sufficiently responsive to pain relief therapy with drugs or nerve block. Results of foreign clinical studies using this product were submitted to demonstrate that efficacy and safety of the new stimulation mode not included in conventional products were not inferior to those of the conventional stimulation mode.

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Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 29, 2017 Total review time: 300 days Regulatory review time: 238 days	May 29, 2015 Foreign clinical study results	19	Vagus Nerve Stimulation Device Aspire SR (Cyberonics, Inc.)	Approval	Instrument & apparatus 12 Vagus nerve stimulation device with anti-seizure effects	An electrical stimulation device to stimulate vagus nerve as an adjuvant therapy to reduce the frequency of seizures for patients with drug-resistant epilepsy who have refractory epileptic seizures (excluding those responding to craniotomy procedure). This device was developed based on the "Vagus Nerve Stimulation Device VNS System" (Approval No. 22600BZI00008000) and equipped with an additional automatic stimulation mode to automatically deliver electrical stimulation triggered by the sudden increase in heart rate before and after epilepsy seizure. Results from foreign clinical studies were submitted to evaluate the efficacy and safety of the automatic stimulation mode.
Gastroenterology, Genitourinary, and Reproductive Medicine	Jun. 21, 2016 Total review time: 365 days Regulatory review time: 268 days	- Domestic clinical study results	20	AdSpray (Terumo Corporation)	Approval	Medical products 4 Bioresorbable adhesion barrier	An adhesion barrier applied to the surgical wound to prevent surgical adhesions after surgery of abdomen or pelvic cavity. A spray style was adopted to improve the workability and to enable the use in areas of complex structures. When sprayed, gel is formed in the applied area and works as a physical barrier to prevent adhesion. The results of a pharmacokinetics study in humans demonstrate that gel remains for about 24 hours, and subsequently undergoes breakdown and absorption. Results from a Japanese clinical trial were submitted, in which the product was applied right under a midline incision following laparoscopic surgery, to evaluate the product's effects to reduce the incidence rate, size, and the severity of adhesion.
Gastroenterology, Genitourinary and Reproductive Medicine	Oct. 14, 2016 Total review time: 198 days Regulatory review time: 156 days	- Domestic clinical study results	21	Toraylight HDF (Toray Medical Co., Ltd.)	Approval	Instrument & apparatus 7 Hemodiafilter	A hemodiafilter used to remove fluid and uremic substances stored in the body due to uremia in patients with extremely impaired renal function caused by chronic or acute kidney failure. Based on the previously approved "Toraylight NV" (Approval No. 22200BZX00871000), a light-weight, hollow-fiber dialyzer without filling fluid, this device was developed to improve the operability in hemodiafiltration with increased surface area of the membrane. Results from a domestic clinical study were submitted to evaluate safety and efficacy of the device, in accordance with the PFSB Notification No. 0301-5 dated March 1, 2013.
Gastroenterology, Genitourinary, and Reproductive Medicine	Feb. 13, 2017 Total review time: 250 days Regulatory review time: 188 days	- Domestic clinical study results	22	Asahi Hollow Fiber Hemodiafilter ABH-PA (Asahi Kasei Medical Co., Ltd.)	Approval	Instrument & apparatus 7 Hemodiafilter	A hemodiafilter used to remove fluid and uremic substances stored in the body due to uremia. This device is indicated for patients with extremely impaired renal function caused by chronic or acute kidney failure. The device differs in the composition of hollow fiber polymer from that of the approved "Asahi Hollow Fiber Hemodiafilter" (Approval No. 22200BZX00577000), using a wavy hollow fiber to reduce transmembrane pressure difference during hemodiafiltration.
Gastroenterology, Genitourinary, and Reproductive Medicine	Feb. 23, 2017 Total review time: 265 days Regulatory review time: 137 days	- Domestic clinical study results	23	IRIS Monitor (Atom Medical Corporation)	Approval	Instrument & apparatus 21 Heart rate monitor	A heart rate monitor designed to non-invasively measure, display, and save fetal heart rate through the mother's abdomen. Unlike the approved similar medical devices using the ultrasonic or direct induction method, this device detects bioelectric signals via the electrode placed on the mother's abdominal wall and thereby determing the fetal heart rate based on the extracted signals.
Ophthalmology and Otorhinolaryngology	Apr. 25, 2016 Total review time: 1060 days Regulatory review time: 789 days	Jun. 13, 2002 Domestic clinical study results	24	Paragon Ortho-K (Eyemed Co., Ltd.)	Approval	Instrument & apparatus 72 Orthokeratology contact lens	Orthokeratology contact lens with a specially shaped inner surface intended to reshape the corneal surface by wearing it during sleep and to correct and maintain the unaided vision during daytime after removal of the lens. A domestic clinical study was conducted to evaluate the efficacy such as how precisely the eyesight is corrected, etc. and the safety such as harm to the cornea, etc.

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
Ophthalmology and Otorhinolaryngology	Jun. 13, 2016 Total review time: 593 days Regulatory review time: 79 days	Sep. 11, 2013 Foreign clinical study results	25	Bausch + Lomb Aqualox (B.L.J. Company, Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Reusable tint-colored contact lenses with vision correction which may be worn whole day for maximum two weeks. The lens is made of samfilcon A, a silicone hydrogel material with a water content of 46% and an oxygen permeability (Dk) of 114. Because of the novelty in the raw materials, a clinical study was conducted to confirm the efficacy and safety in wearing the lenses to correct visual acuity.
Ophthalmology and Otorhinolaryngology	Jan. 10, 2017 Total review time: 218 days Regulatory review time: 166 days	- Foreign clinical study results	26	Tecnis Symfony VB (AMO Japan K.K.)	Approval	Instrument & Multifocal posterior chamber lens	A multifocal posterior chamber lens to be inserted as a substitute for a crystalline lens to correct near, intermediate and far vision in patients with aphakia. The raw material and basic structure of this device are identical to those of the company's approved product, "Tecnis 1-Piece VB" (Approval No. 22400BZX00172000), but with the same diffractive multifocal function as "Tecnis Symfony" (Approval No. 22900BZX00006000) at the posterior optic zone. Results of foreign clinical studies using "Tecnis Symfony" (Approval No. 22900BZX00006000) to evaluate clinical efficacy and fundamental safety, including visual function as a multifocal posterior chamber lens, were submitted, and the rationale for its extrapolation was explained.
Ophthalmology and Otorhinolaryngology	Jan. 10, 2017 Total review time: 263 days Regulatory review time: 175 days	Jul. 15, 2016 Foreign clinical study results	27	Tecnis Symfony (AMO Japan K.K.)	Approval	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, intermediate and far vision in patients with aphakia. The raw material and basic structure of this device are identical to those of the company's approved product "Tecnis Multifocal 1-Piece" (Approval No., 22300BZX00277000), but this device differs in light distribution, focused mainly from far to intermediate distance by improving the diffractive multifocal function such as the number of diffractive rings and step heights. Results of foreign clinical studies using an approved monofocal posterior lens as a control to evaluate the clinical efficacy and fundamental safety, including visual function as a multifocal posterior lens, were submitted.
Cardiopulmonary Circulation	Apr. 26, 2016 Total review time: 403 days Regulatory review time: 223 days	- Clinical evaluation report	28	Optisure Single Screw-In (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead that is connected to an automatic implantable cardioverter-defibrillator, a dual-chamber automatic implantable cardioverter-defibrillator, or an implantable biventricular pacing pulse generator with defibrillator function used for the treatment of ventricular tachycardia and other condition. The application was submitted to allow patients to undergo an MRI scan under predefined conditions (A "partial change" application). To evaluate the safety of the device under MRI scans, a clinical evaluation report summarizing the results from foreign clinical studies relating to the product was submitted.
Cardiopulmonary Circulation	Apr. 26, 2016 Total review time: 403 days Regulatory review time: 223 days	- Clinical evaluation report	29	Optisure Dual Screw-In (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	The device is an implantable defibrillator/pacemaker lead that is connected to an automatic implantable cardioverter-defibrillator, a dual-chamber automatic implantable cardioverter-defibrillator, or an implantable biventricular pacing pulse generator with defibrillator function used for the treatment of ventricular tachycardia and other condition. The application was submitted to allow patients to undergo an MRI scan under predefined conditions (A "partial change" application). To evaluate the safety of the device under MRI scans, a clinical evaluation report summarizing the results from foreign clinical studies relating to the product was submitted.
Cardiopulmonary Circulation	Apr. 26, 2016 Total review time: 362 days Regulatory review time: 191 days	- Clinical evaluation report	30	Fortify Assura (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Automatic implantable defibrillator	The device is an automatic implantable defibrillator used in patients at a high risk of sudden death due to ventricular tachyarrhythmia. The application was submitted to allow patients to undergo an MRI scan under predefined conditions (A "partial change" application). To evaluate the safety of the device under MRI scans, a clinical evaluation report summarizing the results from foreign clinical studies relating to the product was 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
Cardiopulmonary Circulation	Jun. 8, 2016 Total review time: 229 days Regulatory review time: 112 days	- Global clinical trial results	31	Ultimaster (Terumo Corporation)	Change	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 application was submitted for an additional stent size of 4.0 mm in diameter (A "partial change" application). To expand the size variation from the range of 2.5-3.5 mm to 2.5-4.0 mm of vessel diameter, the results from the global clinical trials conducted to evaluate the efficacy and safety of the product were submitted.
Cardiopulmonary Circulation	Jun. 24, 2016 Total review time: 84 days Regulatory review time: 64 days	Aug. 11, 2016 Foreign clinical study results	32	Thermocool Smarttouch SF (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An ablation catheter to be used for conducting cardiac ablation with high-frequency current and cardiac electrophysiologic technique for the treatment of patients with drug refractory symptomatic paroxysmal or persistent atrial fibrillation, atrial flutter, and patients with ventricular tachycardia who have not responded to other therapies. This product is an ablation catheter with the irrigation function of "Navistar Thermocool SF" (Approved No. 22300BZX00453000) with additional contact force-sensing function of the "Thermocool Smarttouch" (Approval No. 22400BZX00163000). The results of SMART-AF study, conducted outside Japan were submitted as clinical evaluation data, in order to demonstrate the safety and efficacy of "Thermocool Smarttouch," as an irrigation catheter with contact force-sensing function, in the treatment of patients with drug refractory symptomatic paroxysmal atrial fibrillation.
Cardiopulmonary Circulation	Aug. 22, 2016 Total review time: 280 days Regulatory review time: 208 days	Dec. 17, 2011 Clinical evaluation report	33	Kodama Catheter (ACIST Medical Systems)	Approval	Instrument & apparatus 51 Central circulation system intravascular ultrasound catheter	An intravascular ultrasound catheter for imaging of the vascular lumen and wall of the central circulatory system using ultrasound. The device is connected to the previously certified device "HD-IVUS System" (Certification No. 226ADBZX00178000) to irradiate the observation target site with ultrasonic wave from the sensor in the tip, and display images by processing the reflected signals. Majority of approved intravascular ultrasound catheters can be set at 40 MHz of ultrasonic frequency only; in contrast, the device can be set at either 40 or 60 MHz to improve the distance resolution and azimuth resolution. A clinical evaluation report summarizing foreign clinical studies was submitted to evaluate the ability to distinguish vascular lesions.
Cardiopulmonary Circulation	Oct. 25, 2016 Total review time: 403 days Regulatory review time: 222 days	Dec. 4, 2015 Foreign clinical study results	34	Stingray System (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 51 Coronary recanalization catheter	A coronary recanalization catheter used to treat coronary chronic total occlusion (CTO) during percutaneous transluminal coronary angioplasty (PTCA). The device is used in the difficult cases to pass the guidewire through a lesion, assisting the guidewire inserted into the subintimal space to re-enter into the true lumen and securing the passage. The catheter and the guidewire with a projected tip allow the guidewire to re-enter into the true lumen. Results from foreign clinical studies, which confirmed that the guidewire of this system was able to be placed in the true lumen crossing the CTO in patients unsuccessfully treated with the existing guidewire, were submitted.
Cardiopulmonary Circulation	Oct. 27, 2016 Total review time: 706 days Regulatory review time: 291 days	Oct. 24, 2014 Foreign clinical study results	35	TactiCath Quartz Ablation System (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A device consisting of an electrode catheter and the dedicated system components. The device system is intended to treat drug treatment resistant, symptomatic paroxysmal atrial fibrillation and common atrial flutter, and is capable of percutaneous transluminal myocardial ablation with a high-frequency current as well as cardiac electrophysiological study. The device also allows real-time monitoring of the contact force. Data related to foreign clinical study were submitted to show the efficacy and safety of the device used in the treatment of paroxysmal atrial fibrillation.

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. 27, 2016 Total review time: 80 days Regulatory review time: 64 days	Oct. 24, 2014 Foreign clinical study results	36	TactiCath Quartz Ablation System N (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A device consisting of an electrode catheter and the dedicated system components. The device system is intended to treat drug treatment resistant, symptomatic paroxysmal atrial fibrillation and common atrial flutter, and is capable of percutaneous transluminal myocardial ablation with a high-frequency current as well as cardiac electrophysiological study. This device was developed based on the approved "TactiCath Quartz Ablation System" (Approval No. 22800BZX00394000), with modifications of the adhesive at the tip of the catheter and image sensor. Data related to foreign clinical study were submitted to show the efficacy and safety of the device used in the treatment of paroxysmal atrial fibrillation.
Cardiopulmonary Circulation	Nov. 29, 2016 Total review time: 343 days Regulatory review time: 124 days	May 10, 2011 Foreign clinical study results	37	CrossBoss Coronary CTO Crossing Catheter (Boston Scientific Japan K.K.)	Approval	Instrument & apparatus 51 Coronary recanalization catheter	A coronary recanalization catheter used to treat coronary chronic total occlusion (CTO) during percutaneous transluminal angioplasty (PTCA). The device is used in the difficult cases to pass the guidewire through the lesion for the purpose of securing the passage. The device may be moved toward the target lesion along the guidewire or precede the guidewire. Results from foreign clinical studies, which confirmed that the guidewire was able to be placed in the true lumen crossing the CTO in patients unsuccessfully treated with the existing guidewire, were submitted.
Cardiopulmonary Circulation	Nov. 29, 2016 Total review time: 152 days Regulatory review time: 128 days	- Domestic clinical study results	38	Ultimaster (Terumo Corporation)	Change	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 application was submitted for an additional stent size of 2.25 mm in diameter (A "partial change" application). To expand the size variation from the range of 2.5-4.0 mm to 2.25-4.0 mm of vessel diameter, the results from the domestic clinical study conducted to evaluate the efficacy and safety of the product were submitted.
Cardiopulmonary Circulation	Dec. 15, 2016 Total review time: 244 days Regulatory review time: 112 days	- Foreign clinical study results	39	FlexAbility SE Irrigated Catheter (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An ablation catheter intended to treat common atrial flutter, diagnosing arrhythmia by pacing and mapping during percutaneous transluminal myocardial ablation. The device was developed based on "FlexAbility Irrigated Catheter" (Approval No. 22500BZX00096000). The approval application was submitted for the major changes such as additions of a magnetic sensor to acquire position information and an indication for paroxysmal atrial fibrillation, and a change in raw materials. To demonstrate the efficacy and safety of the device in the treatment of paroxysmal atrial fibrillation, data from foreign clinical studies using the devices different from this product was submitted. However, the results of the study could not be extrapolated for the examination of this device. Therefore, paroxysmal atrial fibrillation was removed from the indication.
Cardiopulmonary Circulation	Feb. 14, 2017 Total review time: 365 days Regulatory review time: 115 days	Sep. 27, 2013 Global clinical trial	40	Micra Introducer (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiac catheter introducer kit	A kit composed of an introducer sheath and dilator used to transdermally insert the treatment or diagnostic device including the "Micra Transcatheter Pacing System" (Approval No. 22900BZX00047000) into a vein. The results of global clinical studies including Japan conducted to evaluate the efficacy and safety when using the Micra Transcatheter Pacing System with this product in the treatment of bradyarrhythmia 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
Cardiopulmonary Circulation	Feb. 17, 2017 Total review time: 262 days Regulatory review time: 129 days	- Foreign clinical study results	41	INSPIRIS RESILIA Aortic Valve (Edwards Lifesciences Limited)	Approval	Instrument & Bovine pericardial valve	A bovine pericardial valve intended to function as a substitute for a malfunctioning cardiac valve. The product structure is based on the approved product "Carpenter-Edwards Bovine Pericardial Biological Valve Magna EASE ThermaFix Process" (Approval No. 22300BZX00320000) and it has a specially-processed leaflet tissue to enhance anticalcification and enable storage without glutaraldehyde solution. The results of US and EU clinical studies were submitted to evaluate the efficacy and safety of this product in patients with aortic valve disease requiring aortic valve replacement.
Cardiopulmonary Circulation	Mar. 3, 2017 Total review time: 403 days Regulatory review time: 230 days	Feb. 12, 2016 Foreign clinical study results	42	Quadra Assura MP (St. Jude Medical Japan Co., Ltd.)	Approval	Instrument & Implantable biventricular pacing pulse generator with defibrillator function	An implantable biventricular pacing pulse generator with a defibrillator function (CRT-D) for cardiac resynchronization therapy (CRT). A multi-point pacing (MPP) function of this product allows the user to choose 2 electrodes as the left ventricular pacing positions while similar CRT-Ds can provide only one out of 4 electrodes (hereinafter referred to as BiV pacing). The MPP function is used in patients who do not respond to BiV pacing. Results from a non-clinical study ensuring the required function for CRT and safety in MRI and foreign clinical study evaluating the efficacy and safety of the MPP function were submitted.
Cardiopulmonary Circulation	Mar. 21, 2017 Total review time: 264 days Regulatory review time: 93 days	Mar. 19, 2017 Global clinical trial and foreign clinical study results	43	Diamondback 360 Coronary Orbital Atherectomy System Micro Crown (Cardiovascular Systems, Inc.)	Approval	Instrument & apparatus 51 Angioplasty catheter for ablation atherectomy	An atherectomy device used to remove calcified plaques in severely calcified lesions of new stenotic lesions caused by coronary arteriosclerosis using high speed rotation of diamond coated crown and diamond coated tip at end of shaft thereby facilitating postoperative coronary intervention. The product controls the eccentricity of the crown by the speed of rotations and therefore can be used for large or small lumen diameter vessels without changing the size of the product in contrast to approved similar products whose size must be changed to the larger size depending on the diameter of the target lumen. The results of non-clinical studies demonstrating the ability of this device to cut calcified plaques in the coronary artery as an atherectomy device and those of foreign clinical studies and Japan-US global clinical trial performed to evaluate the efficacy and safety of the adjuvant therapy for stent placement using the product for severely calcified lesions were submitted.
Cardiopulmonary Circulation	Mar. 27, 2017 Total review time: 234 days Regulatory review time: 155 days	Feb. 24, 2016, Jul. 7, 2016, Mar. 2, 2017 Foreign clinical study results	44	BSC OI Ablation Catheter (Boston Scientific Japan K. K.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	A catheter for the treatment of arrhythmia. It is designed to be inserted percutaneously to the heart through a blood vessel to apply a radiofrequency current to the target site of arrhythmia identified electrophysiologically, in order to treat persistent or recurrent type I atrial flutter. The improvement from the company's approved product is an irrigation function of this product to deliver saline from the irrigation holes at the electrode tip. Results from foreign clinical studies that evaluated the efficacy and safety of the irrigation function were submitted.

Table 7. Products Approved in FY 2016: Regenerative Medical Products

Review Category	Approval Date	Brand Name (Applicant Company, Corporate No.)	New Approval/ Partial Change	Classification	Non-proprietary Name	Notes
Regenerative Medical Products	Sep. 29, 2016	JACE (Japan Tissue Engineering Co., Ltd.)	Change	Human somatic cell-processed product	Human (autologous) epidermis-derived cell sheet	A product consisting of human (autologous) epidermis-derived cell sheet, which is produced using Green's technique, packaged in a primary container (main component), and a container (filled with tissue transport fluid) for transporting the patient's skin tissue to the manufacturing site (sub-component). To prepare the cell sheet, epidermal cells derived from a postage-stamp-sized piece of skin taken from the patient's own healthy skin tissue are co-cultured with mouse embryo-derived 3T3-J2 feeder cells and formed into a sheet. The cell sheet is released in the state of being immersed in preservative liquid. The product has already been approved for an indication for cases of serious and extensive burns where sufficient donor skin sites for autologous skin grafts are not available, and at the same time, where the total area of deep dermal and full-thickness burns accounts for 30% or more of the total body surface area (Approval No. 21900BZZ00039000). The application was submitted for an additional indication for the treatment of "giant congenital melanocytic nevus" (A "partial change" application). The results from domestic clinical studies in which the product was grafted to cover the site of excised melanocytic nevus were submitted to evaluate the efficacy and safety of the product.

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 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	1,099
FY 2015	51,103	345,253	4,891	1,238	402,485	1,219
FY 2016	56,478	394,951	4,960	1,091	457,480	1,117

* *The figures in FY 2012 represent the total number of reports of suspected 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 suspected 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 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
FY 2016	16,283	32,280	548	49,111	1,289

(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
FY 2016	88	0	0	88	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 2016

○ Revisions to PRECAUTIONS for drugs, etc. and other information implemented by MHLW based on PMDA reports in FY 2016

	Drugs	Medical devices
Directions concerning revisions to PRECAUTIONS in product package insert[*1]	152	6
Information published as Pharmaceuticals and Medical Devices Safety Information	32	0

**Note 1: Including the issuance of notifications concerning self-checks for medical devices, etc.*

○ Revisions to PRECAUTIONS for Drugs, as Directed by MHLW during FY 2016

Date	Drug name
Apr. 21, 2016	01. Gabapentin (Tablets) Gabapentin (Syrup) 02. Levodopa (Tablets) Levodopa (Capsules, Powders) Levodopa (Injections) Levodopa/Benserazide hydrochloride combination product Levodopa/Carbidopa hydrate combination product Levodopa/Carbidopa hydrate/Entacapone combination product 03. Gabapentin enacarbil 04. Edoxaban tosilate hydrate 05. Rivaroxaban (Tablets) Rivaroxaban (Fine granules) 06. Sitagliptin phosphate hydrate Vildagliptin Vildagliptin/Metformin hydrochloride combination product 07. Afatinib maleate 08. Trabectedin 09. Fexofenadine hydrochloride/Pseudoephedrine hydrochloride combination product 10. Oseltamivir phosphate (Capsules) Oseltamivir phosphate (Dry syrup) 11. Peramivir hydrate 12. Sodium chloride/Potassium chloride/Sodium sulfate anhydrous/Macrogol 4000/Ascorbic acid/Sodium L-ascorbate combination product 13. Products containing pseudoephedrine hydrochloride (OTC drugs) Products containing pseudoephedrine sulfate (OTC drugs)
May 18, 2016	01. Asunaprevir Simeprevir Sodium Telaprevir Vaniprevir 02. Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir Sofosbuvir Daclatasvir hydrochloride Ledipasvir acetonate/ Sofosbuvir
May 31, 2016	01. Levetiracetam (Tablets) Levetiracetam (Dry syrup) Levetiracetam (Injection) 02. Alendronate sodium hydrate (Tablets) Alendronate sodium hydrate (Tablets) Alendronate sodium hydrate (Oral jelly) Alendronate sodium hydrate (Injection) Alendronate sodium hydrate (Injection) Ibandronate sodium hydrate (Tablets) Ibandronate sodium hydrate (Injection) Etidronate disodium

Date	Drug name
	Zoledronic acid hydrate Zoledronic acid hydrate Pamidronate disodium hydrate Minodronic acid hydrate Minodronic acid hydrate Risedronate sodium hydrate Risedronate sodium hydrate Risedronate sodium hydrate
Jul. 5, 2016	01. Diclofenac sodium (Oral tablets) Diclofenac sodium (Suppositories) Diclofenac sodium (Capsules) Diclofenac sodium (Enema ointment) 02. Oxytocin 03. Benzoyl peroxide 04. Clindamycin phosphate hydrate/Benzoyl peroxide 05. Apixaban 06. Nintedanib ethanesulfonate 07. Fingolimod hydrochloride 08. Carmustine 09. Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir 10. Sofosbuvir 11. Ribavirin 12. Ledipasvir acetonate/ Sofosbuvir
Aug. 4, 2016	01. Olanzapine (Tablets) Olanzapine (Tablets) Olanzapine (Fine granules) Olanzapine (Injection) 02. Azosemide 03. Imatinib mesilate Imatinib mesilate 04. Dasatinib hydrate 05. Nilotinib hydrochloride hydrate 06. Bosutinib hydrate 07. Sitafloxacin hydrate
Sep. 13, 2016	01. Natalizumab (genetical recombination) 02. Nartograstim (genetical recombination) Filgrastim (genetical recombination) Filgrastim (genetical recombination) [filgrastim biosimilar 1] Filgrastim (genetical recombination) [filgrastim biosimilar 2] Filgrastim (genetical recombination) [filgrastim biosimilar 3] Lenograstim (genetical recombination) 03. Pegfilgrastim (genetical recombination) 04. Eltrombopag olamine 05. Afatinib maleate 06. Corticorelin (human)

Date	Drug name
Oct. 18, 2016	01. Atorvastatin calcium hydrate Atorvastatin calcium hydrate Simvastatin Simvastatin Pitavastatin calcium hydrate Pitavastatin calcium hydrate Pravastatin sodium Fluvastatin sodium Rosuvastatin calcium 02. Amlodipine besilate/Atorvastatin calcium hydrate 03. Warfarin potassium (Tablets) Warfarin potassium (Granules) Warfarin potassium (Fine granules) 04. Miconazole (Oral gel) Miconazole (Injection) 05. Voriconazole (Tablets) Voriconazole (Dry syrup) Voriconazole (Injection) Itraconazole (Capsules) Itraconazole (Tablets) Itraconazole (Oral solution) Itraconazole (Injection) Fluconazole (Capsules) Fluconazole (Dry syrup) Fluconazole (Injections) Fluconazole (Injections) Fluconazole (Injections) Fosfluconazole 06. Ustekinumab (genetical recombination) 07. Nivolumab (genetical recombination) 08. Daptomycin 09. Peramivir hydrate
Nov. 22, 2016	01. Polaprezinc (Granules) Polaprezinc (Tablets) 02. Formalin 03. Formalin/Cresol Cresol/Formalin/Clove oil/Zinc oxide mix Formalin/Guaiacol 04. Allopurinol Allopurinol Allopurinol 05. Alogliptin benzoate Alogliptin benzoate/Pioglitazone hydrochloride Linagliptin Teneligliptin hydrobromide hydrate Alogliptin benzoate/Metformin hydrochloride

Date	Drug name
	06. Zoledronic acid hydrate Zoledronic acid hydrate Zoledronic acid hydrate Zoledronic acid hydrate 07. Famciclovir
Nov. 25, 2016	01. Duloxetine hydrochloride Venlafaxine hydrochloride Milnacipran hydrochloride
Jan. 10, 2017	01. Iguratimod 02. Lenalidomide hydrate 03. Interferon beta-1b (genetical recombination)
Feb. 14, 2017	01. Hydroxyzine hydrochloride (Injection) Hydroxyzine hydrochloride (Tablets) Hydroxyzine pamoate (Powders) Hydroxyzine pamoate (Capsules/Dry syrup) Hydroxyzine pamoate (Syrup) Hydroxyzine pamoate (Tablets) 02. Vemurafenib
Mar. 21, 2017	01. Lamotrigine 02. Aluminum potassium sulfate hydrate, Tannic acid Aluminum potassium sulfate hydrate, Tannic acid 03. Amobarbital 04. Alprazolam Ethyl loflazepate (Fine granules) Ethyl loflazepate (Tablets) 05. Eszopiclone 06. Estazolam (Tablets) Estazolam (Powder) 07. Oxazolam (Tablets/Powder) Oxazolam (Fine granules) 08. Quazepam 09. Cloxazolam 10. Clorazepate dipotassium 11. Chlordiazepoxide (Tablets) Chlordiazepoxide (Powder) Diazepam (Powder) Diazepam (Tablets) Diazepam (Syrup) Diazepam (Injection) Diazepam (Injection) 12. Secobarbital Sodium 13. Zopiclone 14. Zolpidem tartrate (Tablets) Zolpidem tartrate (Tablets)

Date	Drug name
	Zolpidem tartrate (Oral solution) 15. Triazolam (Tablets) 16. Triclofos sodium Bromovalerylurea 17. Nitrazepam (Powder) Nitrazepam (Fine granules) Nitrazepam (Tablets) 18. Nimetazepam 19. Haloxazolam Clotiazepam (Granules) Clotiazepam (Tablets) 20. Phenobarbital (Oral dosage form) Phenobarbital sodium (Suppository) Phenobarbital sodium (Suppository) 21. Phenobarbital (Injection) Phenytoin/Phenobarbital Phenytoin/Phenobarbital/Caffeine and sodium benzoate Phenobarbital sodium (Injection) 22. Fludiazepam 23. Flutazolam 24. Flutoprazepam 25. Flunitrazepam (Tablets) Bromazepam (Tablets/Fine granules) 26. Flurazepam hydrochloride 27. Brotizolam (Tablets) Brotizolam (Tablets) 28. Pentobarbital Calcium 29. Chloral hydrate (Suppository) Chloral hydrate (Enemas) 30. Mexazolam 31. Medazepam 32. Rilmazafone hydrochloride hydrate 33. Lorazepam Lormetazepam 34. Clonazepam 35. Clobazam 36. Diazepam (Suppository) 37. Primidone 38. Midazolam (products with an indication to treat status epilepticus) 39. Etizolam (Fine granules) Etizolam (Tablets) Etizolam (Tablets)

**Note: More detailed information is available on the PMDA website.*

Table 10. Revisions to PRECAUTIONS for Medical Devices and Other Information, as Directed by MHLW Based on Reports from PMDA during FY 2016

Date	Title
December 27, 2016	Notification: "Handling of Powdered Medical Gloves"(6 term names)

**Note: More detailed information is available on the PMDA website.*

Table 11. FY 2016 Pharmaceuticals and Medical Devices Safety Information (No.332-341)

Date	No.	Table of Contents
April 19, 2016	332	1. Notification Regarding Fulminant Type 1 Diabetes Mellitus During Use of Nivolumab (genetical recombination) 2. Change in Report Forms for "Drugs and Medical Devices Safety Information Reporting System" 3. Important Safety Information (1) Furosemide 4. Revision of Precautions (No. 273) Flunitrazepam (Injections) (and 7 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
May 24, 2016	333	1. Use of "PMDA Medi-navi" and "My Drug List for Safety Updates" 2. Precautions Concerning Recurrent and Similar Incidents of Medical Accidents 3. Important Safety Information (1) Sodium chloride/potassium chloride/sodium sulfate anhydrous/Macrogol 4000/Ascorbic acid/sodium L-ascorbate (2) Vildagliptin, Vildagliptin/Metformin hydrochloride, Sitagliptin phosphate hydrate (3) Fexofenadine hydrochloride/pseudoephedrine hydrochloride combination product (4) Peramivir hydrate (5) Levodopa, Levodopa/Benserazide hydrochloride, Levodopa/Carbidopa hydrate, Levodopa/Carbidopa hydrate/Entacapone 4. Revision of Precautions (No. 274) Gabapentin (and 7 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
June 28, 2016	334	1. Risk Management Plans (RMPs) Outline Sheets 2. Surveillance on Access to, Dissemination, and Utilization of Drug Safety Information in Clinics and Pharmacies 3. Important Safety Information (1) Telaprevir, Simeprevir Sodium, Daclatasvir hydrochloride, Asunaprevir, Vaniprevir, Sofosbuvir, Ledipasvir acetone adduct/Sofosbuvir, Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir (2) Levetiracetam 4. Revision of Precautions (No. 275) Alendronate sodium hydrate, Ibandronate sodium hydrate, Etidronate disodium, Zoledronic acid hydrate, Pamidronate disodium hydrate, Minodronic acid hydrate, Risedronate sodium hydrate 5. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
August 2, 2016	335	1. Precautions Relating to the Teratogenicity of Mycophenolate Mofetil Preparations 2. Important Safety Information (1) Nintedanib ethanesulfonate (2) Ombitasvir hydrate/Paritaprevir hydrate/Ritonavir (3) Sofosbuvir, Ribavirin (4) Ledipasvir acetonate/Sofosbuvir 3. Revision of Precautions (No. 276) Diclofenac sodium (oral, suppository, enema ointment) (and 6 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
September 6, 2016	336	1. Precautions Relating to Interstitial Lung Disease During Administration of Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors 2. Genome Research Relating to Drug-induced Serious Skin Disorders 3. Important Safety Information (1) Olanzapine (2) Azosemide 4. Revision of Precautions (No. 277) (1) Imatinib mesilate, (2) Dasatinib hydrate (and 3 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
October 11, 2016	337	1. Summary of the Relief System for Adverse Drug Reaction and Request of Cooperation for the System 2. Amendment of Procedures for Bar Code Labeling on Prescription Drugs 3. Important Safety Information (1) Imatinib mesilate, Dasatinib hydrate, Nilotinib hydrochloride hydrate, Bosutinib hydrate (2) Afatinib maleate (3) Corticorelin (human) 4. Revision of Precautions (No. 278) Natalizumab (genetical recombination) (and 3 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
November 15, 2016	338	1. Interactions in Co-administration of Miconazole and Warfarin Potassium 2. Safety Measures against Bladder Cancer Associated with Diabetes Medication "Pioglitazone Hydrochloride-Containing Products" 3. Project of the Japan Drug Information Institute in Pregnancy 4. Important Safety Information (1) Atorvastatin calcium hydrate, Simvastatin, Pitavastatin calcium hydrate, Pravastatin sodium, Fluvastatin sodium, Rosuvastatin calcium, Amlodipine besilate/Atorvastatin calcium hydrate (2) Ustekinumab (genetical recombination) (3) Nivolumab (genetical recombination) 5. Revision of Precautions (No. 279) Warfarin potassium (and 4 others) 6. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
December 20, 2016	339	1. Precautions for Driving, etc. under the Treatment with Milnacipran Hydrochloride, Duloxetine Hydrochloride, or Venlafaxine Hydrochloride 2. Suspected Adverse Reactions to Influenza Vaccines in the 2015 Season 3. Safety of Influenza Antiviral Drugs 4. Important Safety Information (1) Polaprezinc (2) Allopurinol (3) Alogliptin benzoate, Alogliptin benzoate/Pioglitazone hydrochloride, Alogliptin benzoate/Metformin hydrochloride, Teneligliptin hydrobromide hydrate, Linagliptin 5. Revision of Precautions (No. 280) Formalin (and 4 others) 6. List of Products Subject to Early Post-marketing Phase Vigilance
		1. Precautions Concerning Recurrent and Similar Medical Accidents 2. Revision of Precautions (No. 281) Iguratimod (and 2 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Precautions Regarding Handling of Fire During Long-term Oxygen Therapy (LOT)
March 14, 2017	341	1. Revisions of Proper Control Procedures for Revlimid/Pomalyst (RevMate) 2. Research on Actual Status in Drugs and Medical Devices Safety Information Reporting System 3. Revision of Precautions (No. 282) (1) Hydroxyzine hydrochloride, (2) Hydroxyzine pamoate, (3) Vemurafenib 4. List of Products Subject to Early Post-marketing Phase Vigilance Reference: Terminology of "Acute Kidney Injury"

**Note: More detailed information is available on the PMDA website.*

Table 12. FY 2016 PMDA Medical Safety Information

No.	Month and year published	Title
49	November 2016	Precautions against Misuse (Overdose) of Antirheumatic Methotrexate Preparations (Part 2)
50	March 2017	Precautions when Setting Syringe Pumps
33	Revised in March 2017	Accidental Burns during Surgery using a Light Source, an Electric or Laser Scalpel

**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	6,747,000 + overseas travel expenses	30,535,100 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(1)	Article 32, Paragraph 2, Item 1 (a) and Paragraph 3	
		Line extension products		2,464,000	1,686,600 + overseas travel expenses	4,150,600 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(3)	Article 32, Paragraph 2, Item 1 (c) and Paragraph 3	
New drugs (No. 1) (orphan drugs)		First application products		19,934,100	3,379,900 + overseas travel expenses	23,314,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(2)	Article 32, Paragraph 2, Item 1 (b) and Paragraph 3	
		Line extension products		2,061,500	841,500 + overseas travel expenses	2,903,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(4)	Article 32, Paragraph 2, Item 1 (d) and Paragraph 3	
New drugs (No. 2) (non-orphan drugs)		First application products		11,353,100	2,533,600 + overseas travel expenses	13,886,700 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(5)	Article 32, Paragraph 2, Item 1 (e) and Paragraph 3	
		Line extension products		1,174,300	633,600 + overseas travel expenses	1,807,900 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(7)	Article 32, Paragraph 2, Item 1 (g) and Paragraph 3	
New drugs (No. 2) (orphan drugs)		First application products		9,345,700	1,267,700 + overseas travel expenses	10,613,400 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(6)	Article 32, Paragraph 2, Item 1 (f) and Paragraph 3	
		Line extension products		1,004,100	319,000 + overseas travel expenses	1,323,100 + overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(8)	Article 32, Paragraph 2, Item 1 (h) and Paragraph 3	
Generic drugs	with inspections			618,200	330,200 +overseas travel expenses	948,400 +overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(9)	Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	
	without inspection			618,200		618,200
				Article 32, Paragraph 1, Item 1 (a)-(9)		
BTC/OTC drugs	Switch to OTC status, etc.	First application products	with inspections	1,291,600	330,200 +overseas travel expenses	1,621,800 +overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(10)	Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	
			without inspection	1,291,600		1,291,600
				Article 32, Paragraph 1, Item 1 (a)-(10)		
		Line extension products	with inspections	1,291,600	330,200 +overseas travel expenses	1,621,800 +overseas travel expenses
				Article 32, Paragraph 1, Item 1 (a)-(10)	Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	
			without inspection	1,291,600		1,291,600
				Article 32, Paragraph 1, Item 1 (a)-(10)		
	Others		with inspections	110,300	330,200 +overseas travel expenses	**440,500 +overseas travel expenses**
				Article 32, Paragraph 1, Item 1 (a)-(11)	Article 32, Paragraph 2, Item 1 (i) and Paragraph 3	
			without inspection	110,300		110,300
				Article 32, Paragraph 1, Item 1 (a)-(11)		
Quasi-drugs		New active ingredients		2,981,100		2,981,100
				Article 32, Paragraph 1, Item 1 (b)-(1)		
		New dosage, etc.		246,600		246,600
				Article 32, Paragraph 1, Item 1 (b)-(2)		
		Others		63,500		63,500
				Article 32, Paragraph 1, Item 1 (b)-(6)		

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)						
	Pest control agents		New active ingredients	4,987,900		4,987,900
				Article 32, Paragraph 1, Item 1 (a)- (12) and (b)-(3)		
			New dosage, etc.	392,200		392,200
				Article 32, Paragraph 1, Item 1 (a)- (13) and (b)-(4)		
			Others	95,500		95,500
				Article 32, Paragraph 1, Item 1 (a)- (14) and (b)-(5)		
	Cosmetics			63,500		63,500
				Article 32, Paragraph 1, Item 1 (c)		
	New application for change or replacement of brand name			35,600		35,600
				Article 32, Paragraph 1, Item 1 (d)		
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	2,533,600 + overseas travel expenses	12,724,100 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	
			Line extension products	1,057,400	633,600 + overseas travel expenses	1,691,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	
		Others		205,100	124,200 + overseas travel expenses	329,300 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(3)	Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	
	New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300	1,267,700 + overseas travel expenses	9,702,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(4)	Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	
			Line extension products	875,600	319,000 + overseas travel expenses	1,194,600 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(5)	Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	
		Others		132,700	112,900 + overseas travel expenses	245,600 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(6)	Article 32, Paragraph 2, Item 2 (f) and Paragraph 3	
	New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products	10,190,500	2,533,600 + overseas travel expenses	12,724,100 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	
			Line extension products	1,057,400	633,600 + overseas travel expenses	1,691,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	
		Others		205,100	124,200 + overseas travel expenses	329,300 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(3)	Article 32, Paragraph 2, Item 2 (c) and Paragraph 3	
	New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products	8,434,300	1,267,700 + overseas travel expenses	9,702,000 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(4)	Article 32, Paragraph 2, Item 2 (d) and Paragraph 3	
			Line extension products	875,600	319,000 + overseas travel expenses	1,194,600 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(5)	Article 32, Paragraph 2, Item 2 (e) and Paragraph 3	
		Others		132,700	112,900 + overseas travel expenses	245,600 + overseas travel expenses
				Article 32, Paragraph 1, Item 2 (a)-(6)	Article 32, Paragraph 2, Item 2 (f) 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
Review for approval of drugs (approval for partial changes to approved matters)							
	Generic drugs	Changes in indications, etc.	First application products		10,190,500	2,533,600 + overseas travel expenses	12,724,100 + overseas travel expenses
					Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (a) and Paragraph 3	
			Line extension products		1,057,400	633,600 + overseas travel expenses	1,691,000 + overseas travel expenses
					Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (b) and Paragraph 3	
		Changes based on guidelines, etc.			53,400		53,400
					Article 32, Paragraph 1, Item 2 (a)-(7)		
		Others			307,700	186,200 +overseas travel expenses	493,900 +overseas travel expenses
					Article 32, Paragraph 1, Item 2 (a)-(8)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
	BTC/OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	10,190,500	186,200 +overseas travel expenses	10,376,700 +overseas travel expenses
				with inspections	Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
				without inspection	10,190,500		10,190,500
					Article 32, Paragraph 1, Item 2 (a)-(1)		
				Line extension products	1,057,400	186,200 +overseas travel expenses	1,243,600 +overseas travel expenses
				with inspections	Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
				without inspection	1,057,400		1,057,400
					Article 32, Paragraph 1, Item 2 (a)-(2)		
			Others		56,400	186,200 +overseas travel expenses	242,600 +overseas travel expenses
				with inspections	Article 32, Paragraph 1, Item 2 (a)-(9)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
				without inspection	56,400		56,400
					Article 32, Paragraph 1, Item 2 (a)-(9)		
		Changes based on guidelines, etc.			35,600	186,200 +overseas travel expenses	221,800 +overseas travel expenses
				with inspections	Article 32, Paragraph 1, Item 2 (a)-(10)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
				without inspection	35,600		35,600
					Article 32, Paragraph 1, Item 2 (a)-(10)		
		Others			56,400	186,200 +overseas travel expenses	242,600 +overseas travel expenses
				with inspections	Article 32, Paragraph 1, Item 2 (a)-(9)	Article 32, Paragraph 2, Item 2 (g) and Paragraph 3	
				without inspection	56,400		56,400
					Article 32, Paragraph 1, Item 2 (a)-(9)		
	Quasi-drugs/cosmetics				35,600		35,600
					Article 32, Paragraph 1, Item 2 (b)-(1) and (c)		
	Pest control agents				48,400		48,400
					Article 32, Paragraph 1, Item 2 (a)-(11) and (b)-(2)		

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
		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

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
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
GCP inspection of drugs						
	New GCP	First application products	In Japan		2,801,000 Article 32, Paragraph 4, Item 2 (a)-(1) and (b)-(1)	2,801,000
			Overseas		3,098,000 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(2) and (b)-(2)	3,098,000 + overseas travel expenses
		Line extension products	In Japan		741,400 Article 32, Paragraph 4, Item 2 (a)-(3) and (b)-(3)	741,400
			Overseas		773,300 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(4) and (b)-(4)	773,300 + overseas travel expenses
	GCP inspection of generic drugs		In Japan		663,600 Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	663,600
			Overseas		977,400 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	977,400 + overseas travel expenses
	GCP inspection of BTC /OTC drugs		In Japan		663,600 Article 32, Paragraph 4, Item 2 (a)-(5) and (b)-(5)	663,600
			Overseas		977,400 +overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6) and (b)-(6)	977,400 +overseas travel expenses
Re-examination of drugs						
	Re-examination	First application products		806,600 Article 32, Paragraph 9, Item 1	2,750,100 + overseas travel expenses Article 32, Paragraph 10, Item 1 (a) and Paragraph 11	3,556,700 + overseas travel expenses
		Line extension products		271,500 Article 32, Paragraph 9, Item 2	917,600 + overseas travel expenses Article 32, Paragraph 10, Item 1 (b) and Paragraph 11	1,189,100 + overseas travel expenses
	GPSP	First application products	In Japan		2,256,000 Article 32, Paragraph 10, Item 2 (b)-(1)	2,256,000
			Overseas		2,478,500 + overseas travel expenses Article 32, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	2,478,500 + overseas travel expenses
		Line extension products	In Japan		774,100 Article 32, Paragraph 10, Item 2 (b)-(3)	774,100
			Overseas		794,400 + overseas travel expenses	794,400 + overseas travel expenses

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 Article 33, Paragraph 1, Item 1 (a)-(1)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	11,736,000 + overseas travel expenses
New medical devices (Class II/III)			7,766,200 Article 33, Paragraph 1, Item 1 (a)-(3)	854,300 + overseas travel expenses Article 33, Paragraph 2, Item 1 (a) and Paragraph 3	8,620,500 + overseas travel expenses
Improved medical devices with clinical data (Class IV)			6,213,000 Article 33, Paragraph 1, Item 1 (a)-(2)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	6,896,500 + overseas travel expenses
Improved medical devices with clinical data (Class II/III)			3,721,200 Article 33, Paragraph 1, Item 1 (a)-(4)	683,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (b) and Paragraph 3	4,404,700 + overseas travel expenses
Improved medical devices without clinical data, without approval standards (Class IV)			2,355,400 Article 33, Paragraph 1, Item 1 (a)-(7)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	2,425,900 + overseas travel expenses
Generic medical devices without clinical data, without approval standards (Class IV)			1,767,700 Article 33, Paragraph 1, Item 1 (a)-(8)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	1,838,200 + overseas travel expenses
Improved/generic medical devices without clinical data, without approval standards (Class II/III)			1,409,900 Article 33, Paragraph 1, Item 1 (a)-(9)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	1,480,400 + overseas travel expenses
Generic medical devices with approval standards (Class IV)			429,200 Article 33, Paragraph 1, Item 1 (a)-(5)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	499,700 + overseas travel expenses
Generic medical devices with approval standards (Class II/III)			344,100 Article 33, Paragraph 1, Item 1 (a)-(6)	70,500 + overseas travel expenses Article 33, Paragraph 2, Item 1 (c) and Paragraph 3	414,600 + overseas travel expenses
In vitro diagnostics	New products		2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
	Out of scope of approval standards		2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
	Nonconformity with approval standards	With clinical data	2,147,500 Article 33, Paragraph 1, Item 1 (b)-(2)		2,147,500
		Without clinical data	996,900 Article 33, Paragraph 1, Item 1 (b)-(4)		996,900
	Conformity with approval standards	Without clinical data	362,000 Article 33, Paragraph 1, Item 1 (b)-(3)		362,000
	Addition of series		60,300 Article 33, Paragraph 1, Item 1 (b)-(1)		60,300
Change of brand name			35,600 Article 33, Paragraph 1, Item 1 (c)		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 medical devices and *in vitro* diagnostics (approval for 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	

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
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)	
Use-results evaluation of medical devices and *in vitro* diagnostics					
	Target medical devices and *in vitro* diagnostics		502,600	642,400 + overseas travel expenses	1,145,000 + overseas travel expenses
			Article 33, Paragraph 12, Item 1 (a) and Item 2	Article 33, Paragraph 13, Item 1 and Paragraph 14	
	Child items with multiple brand names of the target medical device		35,600		35,600
			Article 33, Paragraph 12, Item 1 (b)		
	GPSP	In Japan		628,200	628,200
				Article 33, Paragraph 13, Item 2 (b)-(1)	
		Overseas		976,100 + overseas travel expenses	976,100 + overseas travel expenses
				Article 33, Paragraph 13, Item 2 (b)-(2) and Paragraph 14	

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

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 regenerative medical products					
	GCP	In Japan		653,400	653,400
				Article 35, Paragraph 4, Item 2 (a)	
		Overseas		944,700 +overseas travel expenses	944,700 +overseas travel expenses
				Article 35, Paragraph 4, Item 2 (b)	
GPSP inspection of regenerative medical products					
	GPSP	In Japan		628,500	628,500
				Article 35, Paragraph 4, Item 3 (a)	
		Overseas		976,100 +overseas travel expenses	976,100 +overseas travel expenses
				Article 35, Paragraph 4, Item 3 (b)	
Re-examination of regenerative medical products					
	Regenerative medical products		504,400	642,400 +overseas travel expenses	1,146,800 +overseas travel expenses
			Article 35, Paragraph 9	Article 35, Paragraph 10, Item 1 and Paragraph 11	
	GPSP	In Japan		628,500	628,500
				Article 35, Paragraph 10, Item 2 (b)-(1)	
		Overseas		976,100 +overseas travel expenses	976,100 +overseas travel expenses
				Article 35, Paragraph 10, Item 2 (b)-(2) and Paragraph 11	

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. Classification of user fees, etc.

Attached Table (related to Article 4)

Revised August 26, 2016

(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	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation on re-examination compliance for drugs	per consultation	1,497,700		+ overseas travel	
	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 consultations 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	(Conducted at the Kansai branch)** +280,000 yen		

Attached Table (related to Article 4)

Revised August 26, 2016

(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
	Consultation before the start of expanded clinical trials for medical devices		per consultation	249,000		
	Pre-development consultation for medical devices		per consultation	294,100		
	Pre-development consultation for medical devices (preliminary consultation completed)		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 (preliminary consultation completed)		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.) (preliminary consultation completed)		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

Attached Table (related to Article 4)

Revised August 26, 2016

(Yen)

			User fees				Timing of payment
Consultations							
Medical devices	Evaluation consultation for medical devices	Safety (2 tests)	per consultation	196,000	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
		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			
		Exploratory clinical trial	per consultation	980,300			
		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			

Attached Table (related to Article 4)

Revised August 26, 2016

(Yen)

			User fees			Timing of payment
Consultations						
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 (preliminary consultation completed)		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 (preliminary consultation completed)		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 studies	per consultation 490,200			
		Clinical performance study (after the preparatory interview)	per consultation 458,700			
		Clinical performance study (additional consultation)	per consultation 245,100	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
		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			
	Consultation on evaluation for *in vitro* diagnostics	Quality	per consultation 98,000			
		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			

Attached Table (related to Article 4)

Revised August 26, 2016

(Yen)

			User fees				Timing of payment
Consultations							
In vitro diagnostics	Consultation on evaluation for *in vitro* diagnostics	Correlation	per consultation	196,000	(Conducted at the Kansai branch)** +280,000 yen		
		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 studies	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			
Regenerative medical products	Procedural consultation for regenerative medical products		per consultation	134,800	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	Consultation before the start of expanded clinical trials for regenerative medical products		per consultation	249,000			
	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 on qualification of materials for regenerative medical products		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			
	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)		per consultation	2,398,600			
	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			

Attached Table (related to Article 4)

Revised August 26, 2016

(Yen)

		User fees				Timing of payment
Consultations						
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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-consultation for regenerative medical products (with recording)	per consultation	94,500			
	Post-consultation for regenerative medical products (with recording)	per consultation	94,500			
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			
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000		+ overseas travel	
	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	(Conducted at the Kansai branch)** +280,000 yen	+ overseas travel	
	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	
	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	
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	(Conducted at the Kansai branch)** +280,000 yen		
	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 for regenerative medical products (universities/research institutions and venture companies meeting 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 requirements specified separately*)	per consultation	87,400			
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600			

Attached Table (related to Article 4)

Revised August 26, 2016

(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	
	New drugs			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	
GLP inspection of test facilities						
All test items	Basic fee		With animal-rearing facility	per facility	1,299,600	Request to PMDA after advanced payment
			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

**** When a teleconference consultation is conducted at the Kansai branch, a usage fee of 280,000 yen is required uniformly.**
(excluding post-consultations for drugs [with recording], pre-interviews for regenerative medical products [with recording], post-consultations for regenerative medical products [with recording], and simple consultations)

On and After August 26, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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
	Consultation before the start of expanded clinical trials for regenerative medical products	per consultation	249,000		
	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 on qualification of materials for regenerative medical products	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		
	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	(Conducted at the Kansai branch)** +280,000 yen	
	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		
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500		Payment by the date of consultation application after arrangement of the consultation date
	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	(Conducted at the Kansai branch)** +280,000 yen	
	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 pro	per consultation	399,700		
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products (additional consultation)	per consultation	197,900		
	Pre-consultation for regenerative medical products (with recording)	per consultation	94,500		
	Post-consultation for regenerative medical products (with recording)	per consultation	94,500		

Before August 26, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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
	Consultation before the start of expanded clinical trials for regenerative medical products	per consultation	249,000		
	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		
	(New consultation categories)				
	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		
	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	(Conducted at the Kansai branch)** +280,000 yen	
	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		
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,098,500		Payment by the date of consultation application after arrangement of the consultation date
	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	(Conducted at the Kansai branch)** +280,000 yen	
	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 pro	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 June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700			
	Consultation on re-examination compliance for drugs	**per consultation**	**1,497,700**		**+ overseas travel**	
	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 consultations 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			
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400			
	Consultation before the start of expanded clinical trials for medical devices	**per consultation**	**249,000**			
	Pre-development consultation for medical devices	per consultation	294,100	(Conducted at the Kansai branch)** +280,000 yen		
	Pre-development consultation for medical devices (preliminary consultation completed)	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 (preliminary consultatio	per consultation	950,600			

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700			
	(New consultation categories)					
	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 consultations 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			
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400			
	(New consultation categories)					
	Pre-development consultation for medical devices	per consultation	294,100	(Conducted at the Kansai branch)** +280,000 yen		
	Pre-development consultation for medical devices (preliminary consultation completed)	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 (preliminary consultation completed)	per consultation	950,600			

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)	per consultation	490,200	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)	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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)	per consultation	490,200	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)	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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700			
	Consultation on re-examination compliance for drugs	**per consultation**	**1,497,700**		**+ overseas travel**	
	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 consultations 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			
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400			
	Consultation before the start of expanded clinical trials for medical devices	**per consultation**	**249,000**			
	Pre-development consultation for medical devices	per consultation	294,100	(Conducted at the Kansai branch)** +280,000 yen		
	Pre-development consultation for medical devices (preliminary consultation completed)	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 (preliminary consultation completed)	per consultation	950,600			

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	(Conducted at the Kansai branch)** +280,000 yen	
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	2,957,700		
	(New consultation categories)				
	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		
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	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 consultations for generic drugs	per consultation	505,800		
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	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		
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400		
	(New consultation categories)				
	Pre-development consultation for medical devices	per consultation	294,100	(Conducted at the Kansai branch)** +280,000 yen	
	Pre-development consultation for medical devices (preliminary consultation completed)	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 (preliminary consultation completed)	per consultation	950,600		

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200		Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
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		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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200		Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
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		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		
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		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		
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	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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Evaluation consultation for medical devices	Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400		Payment by the date of consultation application after arrangement of the consultation date
		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
		Exploratory clinical trial	per consultation	980,300		
		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		

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Evaluation consultation for medical devices	Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400		Payment by the date of consultation application after arrangement of the consultation date
		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
		Exploratory clinical trial	per consultation	980,300		
		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		

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
In vitro diagnostics		Preparatory interview of consultations for *in vitro* diagnostics	per consultation	29,400		Payment by the date of consultation application after arrangement of the consultation date
		Pre-development consultation for *in vitro* diagnostics	per consultation	196,000		
		Pre-development consultation for *in vitro* diagnostics (preliminary consultation completed)	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 (preliminary consultation completed)	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 studies	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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
	Consultation on evaluation for *in vitro* diagnostics	Quality	per consultation	98,000		
		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		

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
In vitro diagnostics		Preparatory interview of consultations for *in vitro* diagnostics	per consultation	29,400		Payment by the date of consultation application after arrangement of the consultation date
		Pre-development consultation for *in vitro* diagnostics	per consultation	196,000		
		Pre-development consultation for *in vitro* diagnostics (preliminary consultation completed)	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 (preliminary consultation completed)	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 studies	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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
	Consultation on evaluation for *in vitro* diagnostics	Quality	per consultation	98,000		
		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		

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees				Timing of payment
Consultations							
In vitro diagnostics	Consultation on evaluation for *in vitro* diagnostics	Correlation	per consultation	196,000			Payment by the date of consultation application after arrangement of the consultation date
		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 studies	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) (preliminary consultation completed)	per consultation	779,600			
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	220,600			
Regenerative medical products		Procedural consultation for regenerative medical products	per consultation	134,800			
		Consultation before the start of expanded clinical trials for regenerative medical products	**per consultation**	**249,000**			
		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	(Conducted at the Kansai branch)** +280,000 yen		
		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			
		Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600			
		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			

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees				Timing of payment
Consultations							
In vitro diagnostics	Consultation on evaluation for *in vitro* diagnostics	Correlation	per consultation	196,000			Payment by the date of consultation application after arrangement of the consultation date
		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 studies	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			
Regenerative medical products		Procedural consultation for regenerative medical products	per consultation	134,800			
		(New consultation categories)					
		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	(Conducted at the Kansai branch)** +280,000 yen		
		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			
		Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600			
		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			

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees				Timing of payment
Consultations						
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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			
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			
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000		+ overseas travel	
	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	
	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	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (quality)	per consultation	1,499,700	(Conducted at the Kansai branch)** +280,000 yen		
	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	
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 for regenerative medical products (universities/research institutions and venture companies meeting 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 requirements specified separately*)	per consultation	87,400			
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600			

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees				Timing of payment
Consultations						
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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			
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			
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000		+ overseas travel	
	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	
	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	
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (quality)	per consultation	1,499,700	(Conducted at the Kansai branch)** +280,000 yen		
	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	
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 for regenerative medical products (universities/research institutions and venture companies meeting 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 requirements specified separately*)	per consultation	87,400			
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600			

On and after June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	
	New drugs			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	
GLP inspection of test facilities						
All test items	Basic fee		With animal-rearing facility	per facility	1,299,600	Request to PMDA after advanced payment
			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

**** When a teleconference consultation is conducted at the Kansai branch, a usage fee of 280,000 yen is required uniformly.**
(excluding post-consultations for drugs [with recording], pre-interviews for regenerative medical products [with recording], post-consultations for regenerative medical products [with recording], and simple consultations)

Before June 20, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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 **pesticides/rodenticides**)			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	
GLP						
All test items	Basic fee		With animal-rearing facility	per facility	1,299,600	Request to PMDA after advanced payment
			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 April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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	**(Conducted at the Kansai branch)** +280,000 yen		
	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 consultations 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			
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400			
	Pre-development consultation for medical devices	per consultation	294,100			
	Pre-development consultation for medical devices (preliminary consultation completed)	per consultation	264,700	**(Conducted at the Kansai branch)** +280,000 yen		
	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 (preliminary consultation completed)	per consultation	950,600			

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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 consultations 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	
Medical devices	Preparatory interview of consultations for medical devices	per consultation	29,400	
	Pre-development consultation for medical devices	per consultation	294,100	
	Pre-development consultation for medical devices (preliminary consultation completed)	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 (preliminary consultation completed)	per consultation	950,600	

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200		Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)		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	**(Conducted at the Kansai branch)** **+280,000 yen**	
		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		
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000		
		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		

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Consultation on necessity of clinical trials for medical devices (additional consultation)		per consultation	490,200	Payment by the date of consultation application after arrangement of the consultation date
	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.) (preliminary consultation completed)		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	
	Evaluation consultation for medical devices	Safety (1 test)	per consultation	98,000	
		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	

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
Medical devices	Evaluation consultation for medical devices	Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400		Payment by the date of consultation application after arrangement of the consultation date
		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	**(Conducted at the Kansai branch)** +280,000 yen**	
		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		
		Exploratory clinical trial	per consultation	980,300		
		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		

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
Medical devices	Evaluation consultation for medical devices	Safety (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	264,400	Payment by the date of consultation application after arrangement of the consultation date
		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	
		Exploratory clinical trial	per consultation	980,300	
		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	

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics		per consultation 29,400			Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for in vitro diagnostics		per consultation 196,000			
	Pre-development consultation for in vitro diagnostics (preliminary consultation completed)		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 (preliminary consultation completed)		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 studies	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	**(Conducted at the Kansai branch)** **+280,000 yen**		
		Clinical performance study for companion diagnostics (additional consultation)	per consultation 367,600			
	Application procedure consultation for in vitro diagnostics		per consultation 78,300			
	Consultation on evaluation for in vitro diagnostics	Quality	per consultation 98,000			
		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			

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Preparatory interview of consultations for in vitro diagnostics		per consultation 29,400		Payment by the date of consultation application after arrangement of the consultation date
	Pre-development consultation for in vitro diagnostics		per consultation 196,000		
	Pre-development consultation for in vitro diagnostics (preliminary consultation completed)		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 (preliminary consultation completed)		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 studies	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		
	Consultation on evaluation for in vitro diagnostics	Quality	per consultation 98,000		
		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		

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees			Timing of payment
Consultations						
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Correlation	per consultation	196,000		Payment by the date of consultation application after arrangement of the consultation date
		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 studies	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	(Conducted at the Kansai branch)** +280,000 yen	
		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		
Regenerative medical products		Procedural consultation for regenerative medical products	per consultation	134,800		
		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		
		Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600		
		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	(Conducted at the Kansai branch)** +280,000 yen	
		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		

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

			User fees		Timing of payment
Consultations					
In vitro diagnostics	Consultation on evaluation for in vitro diagnostics	Correlation	per consultation	196,000	Payment by the date of consultation application after arrangement of the consultation date
		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 studies	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	
Regenerative medical products		Procedural consultation for regenerative medical products	per consultation	134,800	
		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	
		Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)	per consultation	2,398,600	
		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	

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees				Timing of payment
Consultations						
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
	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**			
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			
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000		+ overseas travel	
	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	(Conducted at the Kansai branch)** +280,000 yen	+ overseas travel	
	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	
	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	
Pharmaceutical affairs consultation on R&D strategy	Consultation on R&D strategy for drugs	per consultation	1,541,600	(Conducted at the Kansai branch)** +280,000 yen		
	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 for regenerative medical products (universities/research institutions and venture companies meeting 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 requirements specified separately*)	per consultation	87,400			
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600			

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(Yen)

		User fees			Timing of payment
Consultations					
Regenerative medical products	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	824,500		Payment by the date of consultation application after arrangement of the consultation date
	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		
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		
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	2,989,000	+ overseas travel	
	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	
	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	
	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	
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 for regenerative medical products (universities/research institutions and venture companies meeting 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 requirements specified separately*)	per consultation	87,400		
	Consultation on R&D strategy for pharmaceutical development plans, etc.	per consultation	73,600		

On and after April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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 pesticides/rodenticides)		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	
GLP inspection of test facilities					
All test items	Basic fee	With animal-rearing facility	per facility	1,299,600	Request to PMDA after advanced payment
		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

**** When a teleconference consultation is conducted at the Kansai branch, a usage fee of 280,000 yen is required uniformly.**
(excluding post-consultations for drugs [with recording], pre-interviews for regenerative medical products [with recording], post-consultations for regenerative medical products [with recording], and simple consultations)

Before April 1, 2016

Attached Table (related to Article 4)

Classification of user fees, etc.

(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 pesticides/rodenticides)		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	
GLP inspection of test facilities					
All test items	Basic fee	With animal-rearing facility	per facility	1,299,600	Request to PMDA after advanced payment
		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

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.
- 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.
   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.
   c) Calculate administrative subsidies
      - 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.

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.

Attachment 2

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.

Attachment 3

Cash Flows Plan

Cash Flows 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 2016)

(Unit: million yen)

Classification	Amount								
			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			569	872	1,441				1,441
Governmental subsidies	178	121	337	222	559				859
Contributions	3,594	92		3,072	3,072	4,722			11,481
User fees			10,538		10,538				10,538
Commissioned operations			248		248		1,034	645	1,928
Management income	347	68	4	1	5				421
Miscellaneous income	2	0	93	9	102	0	1	1	106
Total	4,121	282	11,789	4,176	15,966	4,723	1,035	646	26,773
Expenditure									
Operating expenses	2,912	217	12,519	4,796	17,315	7,598	1,024	639	29,705
Personnel expenses	239	27	5,779	1,379	7,158	18	38	18	7,499
Administrative expenses	2,673	190	6,740	3,417	10,157	7,580	986	621	22,206
General administrative expenses	138	21	2,669	623	3,292	4	12	7	3,474
Personnel expenses	68		745	150	895				964
Non-personnel expenses	69	21	1,924	473	2,397	4	12	7	2,510
Total	3,050	238	15,188	5,419	20,607	7,602	1,035	646	33,179

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

Income and Expenditure Plan for Fiscal Year Plan (FY 2016)

(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	4,655	343	15,389	5,102	-58	20,433	7,603	1,038	640	34,712
Relief benefits	2,159	36								2,195
Operating expenses for health and welfare	33	104								137
Operating expenses for reviews			3,929			3,929				3,929
Operating expenses for safety measures				1,772		1,772				1,772
Specified relief benefits							7,560			7,560
Benefits (healthcare allowances, etc.)								970		970
Benefits (special allowances, etc.)									247	247
Operating expenses for research and study									350	350
Provision for liability reserve	1,566	101								1,667
Other administrative expenses	763	81	8,866	2,745		11,612	40	55	36	12,586
Personnel expenses	223	25	5,241	1,270		6,510	17	35	17	6,828
Depreciation expenses	67	7	1,252	832		2,083	2	1	0	2,161
Retirement benefit expenses	8	1	232	54		287	0	1	1	298
Provision for accrued bonuses	7	1	333	50		382	1	2	1	393
Other expenses	459	47	1,809	540		2,349	20	15	17	2,905
General administrative expenses	133	21	2,592	584	-58	3,118	4	12	7	3,294
Personnel expenses	64		674	137		811				876
Depreciation expenses	0		282	0		282				282
Retirement benefit expenses	2		28	4		32				34
Provision for accrued bonuses	2		42	8		50				52
Other expenses	65	21	1,565	435	-58	1,942	4	12	7	2,050
Financial expenses	0		1	0		1				1
Miscellaneous losses	1	1		1		1		1	1	5
Ordinary income	4,089	282	11,878	4,266	-58	16,086	7,603	1,035	646	29,742
Governmental subsidies	178	121	341	194		535				834
Administrative subsidies			569	831		1,400				1,400
Other governmental grants							42			42
Contributions	3,594	92		3,072		3,072				6,758
User fees			10,538			10,538				10,538
Gain on reversal of specified relief fund deposit received							7,560			7,560
Commissioned operations			248			248		1,034	645	1,928
Reversal of asset offset subsidies			44	145		188	2			190
Reversal of asset offset administrative subsidies			0	23		23				23
Reversal of asset offset gifts received			0			0				0
Financial income (no operating income)	317	69	4	1		5				391
Miscellaneous income			134	0	-58	76		1	1	78
Ordinary net income (△ net loss)	-566	-61	-3,511	-836		-4,347	0	-3	7	-4,970
Current net income before tax (△ net loss)	-566	-61	-3,511	-836		-4,347	0	-3	7	-4,970
Current net income (△ net loss)	-566	-61	-3,511	-836		-4,347	0	-3	7	-4,970
Reversal of appropriated surplus	-	-	1,398	994		2,392	-	-	-	2,392
Current gross income (△ gross loss)	-566	-61	-2,113	158		-1,955	0	-3	7	-2,577

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

Cash Flow Plan for Fiscal Year Plan (FY 2016)

(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	3,058	259	14,573	5,414	-45	19,942	7,611	1,060	643	32,572
Relief benefits	2,157	35								2,192
Operating expenses for health and welfare	33	104								137
Operating expenses for reviews			6,100			6,100				6,100
Operating expenses for safety measures				3,190		3,190				3,190
Administrative expenses	501	59					29	15	17	621
Specified relief benefits							7,560			7,560
Benefits (healthcare allowances, etc.)								982		982
Benefits (special allowances, etc.)									247	247
Operating expenses for research and study									350	350
General administrative expenses	57	32	1,598	397		1,996	3	9	6	2,103
Personnel expenses	297	26	6,240	1,463		7,703	18	37	18	8,098
Repayment money	1	1		1		1		1	1	5
Other cash outflow from operating activities	11	2	635	362	-45	952	1	16	4	987
Cash outflow from investing activities	4,021	603	1,318	1,101		2,418			7	7,049
Amount carried forward to next fiscal year	2,623	379	6,190	1,333		7,523	263	35	132	10,956
Total	9,701	1,240	22,082	7,847	-45	29,884	7,874	1,095	782	50,577
Cash Inflows										
Cash inflows from operating activities	4,124	282	12,219	4,183	-45	16,358	4,714	1,042	647	27,166
Contributions	3,594	92		3,072		3,072	4,714			11,472
Administrative subsidies			569	872		1,441				1,441
Governmental subsidies	178	121	397	222		619				919
User fees			10,824			10,824				10,824
Commissioned operations			228			228		1,040	645	1,914
Amount of interests received	347	68	4	1		5				421
Other incomes	4	0	197	16	-45	168	0	1	1	175
Cash inflows from investing activities	2,705	500								3,205
Amount carried forward from preceding fiscal year	2,872	458	9,862	3,663		13,526	3,160	54	135	20,205
Total	9,701	1,240	22,082	7,847	-45	29,884	7,874	1,095	782	50,577

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

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, 2017)

(Unit: yen)

Account item	Amount		Account item	Amount	
Assets			Liabilities		
I Current assets			I Current liabilities		
Cash and deposits		20,144,512,922	Administrative subsidies obligations		20,170,000
Securities		3,200,504,512	Accrued benefits		327,227,796
Expenses for work-in-process reviews, etc.		1,373,196,885	Accounts payable		2,094,595,926
Prepaid expenses		4,747,232	Advances received		7,889,288,207
Accounts due		477,798,514	Deposits received		134,634,626
Accrued income		43,859,442	Lease obligations		31,441,685
Other current assets		3,625,475	Allowance		
			Accrued bonuses	577,394,698	577,394,698
Total of current assets		25,248,244,982	Total of current liabilities		11,074,752,938
			II Fixed liabilities		
II Fixed assets			Per contra liabilities for property acquisition		
Tangible fixed assets			Administrative subsidies for assets as per contra	65,222,425	
Tools, equipment and fixtures	4,013,420,147		Governmental subsidies, etc. for assets as per contra	384,799,875	
Cumulative total of depreciation	-1,980,480,061	2,032,940,086	Contributions for assets as per contra	31,594,042	
Building and accompanying facilities	46,475,917		Amount of received goods for assets as per contra	722,342	482,338,684
Cumulative total of depreciation	-2,500,672	43,975,245	Deposits of specific relief funds		
			Long-term deposit subsidy, etc.	127,304,620	
			Deposit contribution	3,726,636,642	3,853,941,262
Total of tangible fixed assets		2,076,915,331	Allowances		
			Allowances for retirement benefits	2,365,625,332	2,365,625,332
Intangible fixed assets			Liability reserve		22,666,139,830
Software		4,115,639,496	Total of fixed liabilities		29,368,045,108
Software in progress		282,279,600	Total of liabilities		40,442,798,046
Telephone subscription right		286,000	Net assets		
Total of intangible fixed assets		4,398,205,096	I Capital funds		
Investments and other assets			Government investment		1,179,844,924
Investment securities		35,954,862,079	Total of capital funds		1,179,844,924
Rental deposit		13,272,360	II Capital surplus		
Total of investments and other assets		35,968,134,439	Capital reserves		4,670,640
			Cumulative total of depreciation that are not recorded as expenses (-)		-681,217,617
Total of fixed assets		42,443,254,866	Loss on retirement or sale of fixed assets that are not recorded as expenses (-)		-98,706,116
			Total of capital surplus		-775,253,093
			III Retained earnings		26,844,109,971
			Total of net assets		27,248,701,802
Total of assets		67,691,499,848	Total of liabilities and net assets		67,691,499,848

Profit and Loss Statement (Corporate basis)

(From April 1, 2016 to March 31, 2017)

(Unit: yen)

Account item	Amount		
Ordinary expenses			
Adverse reaction relief benefits		2,267,542,134	
Infection relief benefits		1,306,200	
Operating expenses for health and welfare		123,704,271	
Operating expenses for reviews		3,590,458,053	
Operating expenses for safety measures etc.		1,707,932,923	
Specific relief benefits		1,156,000,000	
Benefits for healthcare allowances, etc.		942,870,886	
Benefits for special allowances, etc.		206,034,000	
Investigative research		288,703,100	
Provision of liability reserves		1,049,856,785	
Other operating expenses			
Personnel expenses	6,327,505,867		
Depreciation expenses	2,079,753,775		
Retirement benefit expenses	629,843,420		
Provision for accrued bonuses	385,102,989		
Estate rental fees	1,505,125,173		
Other expenses	520,686,243	11,448,017,467	
General administrative expenses			
Personnel expenses	852,061,307		
Depreciation expenses	232,458,821		
Retirement benefit expenses	82,019,979		
Provision for accrued bonuses	66,129,321		
Estate rental fees	257,078,028		
Other expenses	1,307,072,473	2,796,819,929	
Financial expenses			
Interest paid		1,227,011	
Miscellaneous losses		33,027,106	
Total of ordinary expenses			25,613,499,865
Ordinary revenues			
Administrative subsidies		1,410,921,723	
Reversal of provision for deposits of specific relief funds			
Revenues from contributions		1,156,000,000	
User fees		11,097,097,268	
Contributions		7,529,410,800	
Revenue from governmental subsidies		788,963,918	
Revenue from contributions		12,127,375	
Commissioned operations for government		57,495,281	
Commissioned operations for others		1,751,482,670	
Return of administrative subsidies for assets as per contra		22,572,064	
Return of subsidies, etc. for assets as per contra		175,604,850	
Return of contributions for assets as per contra		3,774,626	
Return of amount of received goods for assets as per contra		265,098	
Return of liability reserves		1,040,938	
Financial revenue			
Interest received	970,957		
Interest on securities	369,807,514	370,778,471	
Miscellaneous gains		19,172,088	
Total of ordinary revenues			24,396,707,170
Ordinary losses			-1,216,792,695
Extraordinary losses			
Loss on disposal of fixed assets		19,763	
Loss from prior period adjustment		2,375,288	2,395,051
Extraordinary revenues			
Profit from prior period adjustment		57,290,336	57,290,336
Current net losses			-1,161,897,410
Reversal of reserve carried forward from the previous Mid-term target period			2,613,483,732
Current gross profit			1,451,586,322

Cash Flow Statement (Corporate basis)

(From April 1, 2016 to March 31, 2017)

(Unit: yen)

Account item	Amount
I. Cash flow from operating activities	
Expenditure for adverse reaction relief benefits	-2,272,026,064
Expenditure for infection relief benefits	-1,505,600
Expenditure for operating expenses for health and welfare	-124,226,812
Expenditure for operating expenses for reviews	-3,905,897,787
Expenditure for operating expenses for safety measures	-2,089,019,507
Expenditure for specific relief benefits	-1,156,000,000
Expenditure for benefits for healthcare allowances, etc.	-952,665,845
Expenditure for benefits for special allowances, etc.	-206,330,000
Expenditure for expenses for investigative research	-289,393,100
Expenditure for personnel expenses	-7,637,151,720
Expenditure for money refunded for settlement of subsidies, etc.	-109,001,445
Other operating expenditures	-3,983,749,475
Income from administrative subsidies	1,440,780,000
Income from governmental subsidies	713,593,000
Income from contributions	8,705,403,800
Income from user fees	10,405,463,136
Income from commissioned operations for government	57,495,281
Income from commissioned operations for others	1,820,317,503
Other incomes	137,269,888
Income from subsidies	47,496,043
Income from contributions	47,496,043
Subtotal	648,347,339
Interest paid	-1,227,011
Interest received	407,603,155
Cash flow from operating activities	1,054,723,483
II. Cash flow from investing activities	
Expenditure for acquisition of investment securities	-4,527,649,000
Income from redemption of investment securities at maturity	3,200,000,000
Expenditure for acquisition of tangible fixed assets	-931,986,049
Expenditure for acquisition of intangible fixed assets	-394,311,871
Cash flow from investing activities	-2,653,946,920
III. Cash flow from financing activities	
Expenditure for repayment of finance lease obligations	-30,650,989
Cash flow from financing activities	-30,650,989
IV. Increase in funds	-1,629,874,426
V. Beginning-of-term balance of funds	21,774,387,348
VI. End-of-term balance of funds	20,144,512,922

Government Service Implementation Cost Statement (Corporate basis)

(From April 1, 2016 to March 31, 2017)

(Unit: yen)

Account item	Amount		
I. Operating expenses			
(1) Expenses in the profit and loss statement			
Adverse reaction relief benefits	2,267,542,134		
Infection relief benefits	1,306,200		
Operating expenses for health and welfare services	123,704,271		
Operating expenses for reviews	3,590,458,053		
Operating expenses for safety measures	1,707,932,923		
Specific relief benefits	1,156,000,000		
Benefits for healthcare allowances, etc.	942,870,886		
Benefits for special allowances, etc.	206,034,000		
Expenses for investigative research	288,703,100		
Provision of liability reserves	1,049,856,785		
Other operating expenses	11,448,017,467		
General administrative expenses	2,796,819,929		
Financial expenses	1,227,011		
Miscellaneous losses	33,027,106		
Extraordinary losses	2,395,051	25,615,894,916	
(2) (Exemption) Self-generated income, etc.			
Income from contributions	-8,685,410,800		
Income from user fees	-11,097,097,268		
Income from commissioned operations for government	-57,495,281		
Income from commissioned operations for others	-1,751,482,670		
Return of liability reserves	-1,040,938		
Financial revenue	-370,778,471		
Miscellaneous gains	-19,172,088		
Extraordinary revenues	-57,290,336	-22,039,767,852	
Total of operating expenses			3,576,127,064
II. Amount equivalent to depreciation that are not recorded as expenses			10,761,702
III. Estimated amount of non-allowance bonuses			13,017,126
IV. Estimated increased amount of non-allowance retirement benefits			186,345,373
V. Opportunity costs			
Opportunity costs of investments by the government or local governments, etc.			330,641
VI. Government service implementation costs			3,786,581,906

Notes

I. Important Accounting Policies

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.

1. Criteria for allocation of revenue from administrative subsidies

The percentage-of-completion method is employed.

Change of accounting policies

The percentage-of-expense method had been employed as criteria for allocation of revenue from administrative subsidies until FY 2015, but was replaced by the percentage-of-completion method in FY 2016 in accordance with the Amendments. The percentage-of-period method is employed to deal with all administrative activities, except those where progress is clearly correlated with administrative subsidies.

These changes would have a negligible impact on financial statements.

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 - 22 years
Building and accompanying facilities	8 - 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.

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

Rate for opportunity costs from government and local government

The opportunity cost was calculated at a rate of 0.065%, by reference to the 10-year Japanese government bond yield at the end of March 2017.

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	20,144,512,922	20,144,512,922	0
B. Securities and investment securities	39,155,366,591	40,321,820,000	1,166,453,409
C. Accounts payable	(2,094,595,926)	(2,094,595,926)	0

The figures in parenthesis are recorded as liabilities.

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	35,590,479,080	36,774,580,000	1,184,100,920
Bonds with current prices not exceeding balance sheet amount	3,564,887,511	3,547,240,000	-17,647,511
Total	39,155,366,591	40,321,820,000	1,166,453,409

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	7,400,000,000	3,000,000,000	0
Government-guaranteed bonds	0	6,500,000,000	9,000,000,000	0
Local government bonds	0	0	700,000,000	0
Corporate bonds	400,000,000	800,000,000	7,300,000,000	0
FILP agency bonds	2,800,000,000	0	1,100,000,000	0
Total	3,200,000,000	14,700,000,000	21,100,000,000	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: 95,992,480 yen

(3) Estimated amount of non-allowance retirement benefits

Estimated amount of retirement benefits to be covered by the administrative subsidies: 189,521,858 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: 20,144,512,922 yen

End-of-term balance of funds: 20,144,512,922 yen

4. Notes for government service implementation cost statements

The estimated increased amount of non-allowance retirement benefits includes 69,851,900 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, 2016 - March 31, 2017
[1] Beginning-of-term retirement benefit obligations	2,189,895,025
[2] Service expenses	282,050,021
[3] Interest expenses	4,016,686
[4] Actuarial difference of the current term	380,312,827
[5] Retirement benefits paid	-110,336,400
[6] End-of-term retirement benefit obligations ([1] + [2] + [3] + [4] + [5])	2,745,938,159

(3) Reconciliation of retirement obligation and allowances for retirement benefits reported on the balance sheet

(Unit: yen)

Classification	As of March 31, 2017
[1] Retirement benefit obligations	2,745,938,159
[2] Unrecognized actuarial difference	-380,312,827
[3] Allowance for retirement benefits ([1] + [2])	2,365,625,332

(4) Profit and Loss of retirement benefit

Classification	April 1, 2016 - March 31, 2017
[1] Service expenses	283,964,951
[2] Interest expenses	4,082,209
[3] Amortization expenses for actuarial difference	423,539,039
[4] Retirement benefit funded from the administrative subsidies	277,200
[5] Retirement benefits expenses ([1] + [2] + [3] + [4])	711,863,399

Note: Retirement benefit expenses for workers temporally transferred from other institutions are included: [1] 1,914,930 yen for service expenses; and [2] 65,523 yen for interest expenses.

(5) Items related to basic calculation of actuarial

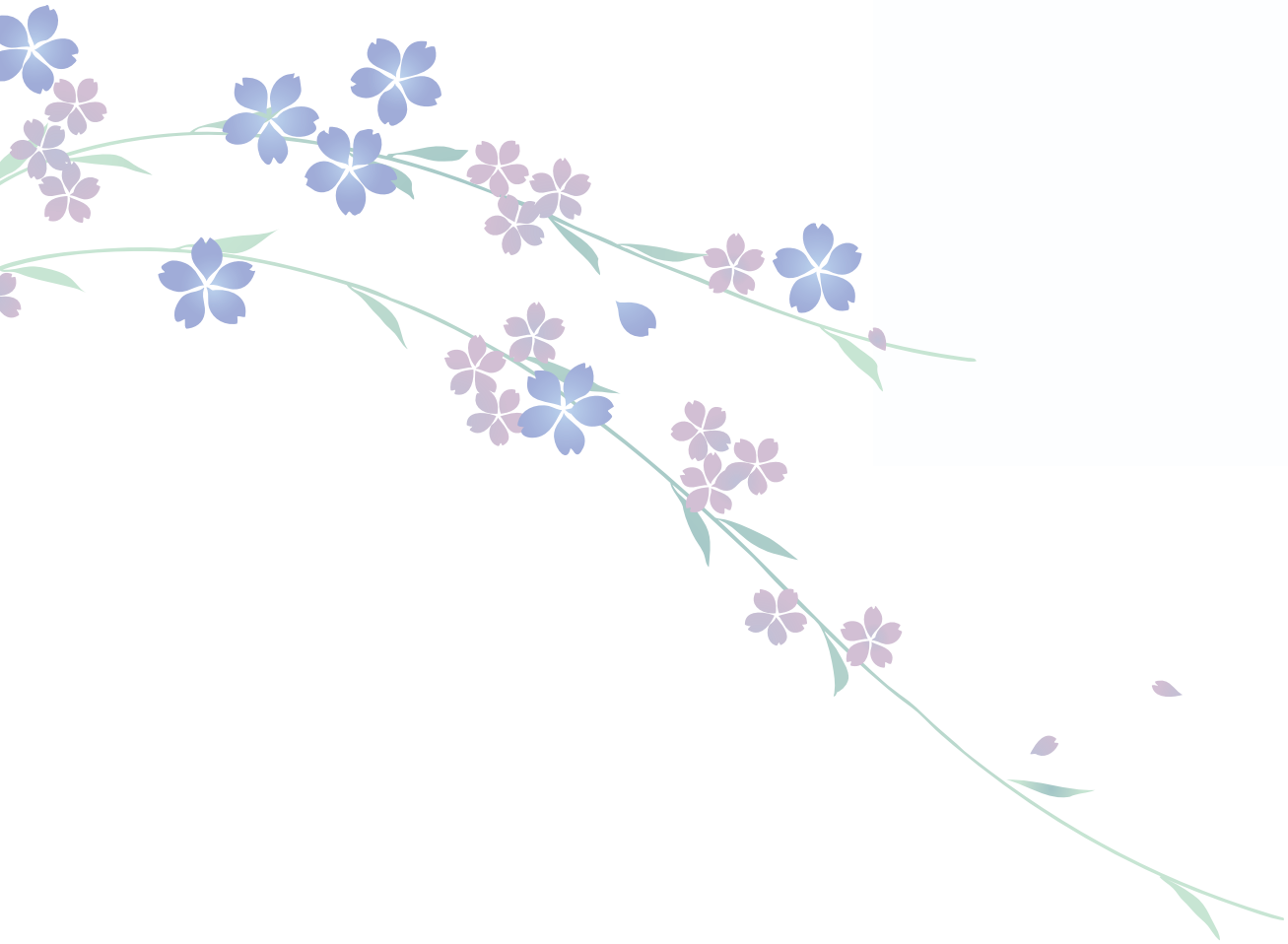
Classification	As of March 31, 2017
Discount rate	0.39%
Method of periodic allocation of estimated amounts of retirement benefits	Straight-line attribution
Amortized period of actuarial difference	1 year Actuarial differences are to be collectively amortized in the next fiscal year after the occurrence.

III. Important Acts of Bearing Obligation

There are no corresponding events.

IV. Important Subsequent Events

There are no corresponding events.



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