Pharmaceuticals and Medical Devices Agency, Japan

ANNUAL REPORT FY 2017

April 2017 - March 2018

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 2017 (April 2017 – March 2018)

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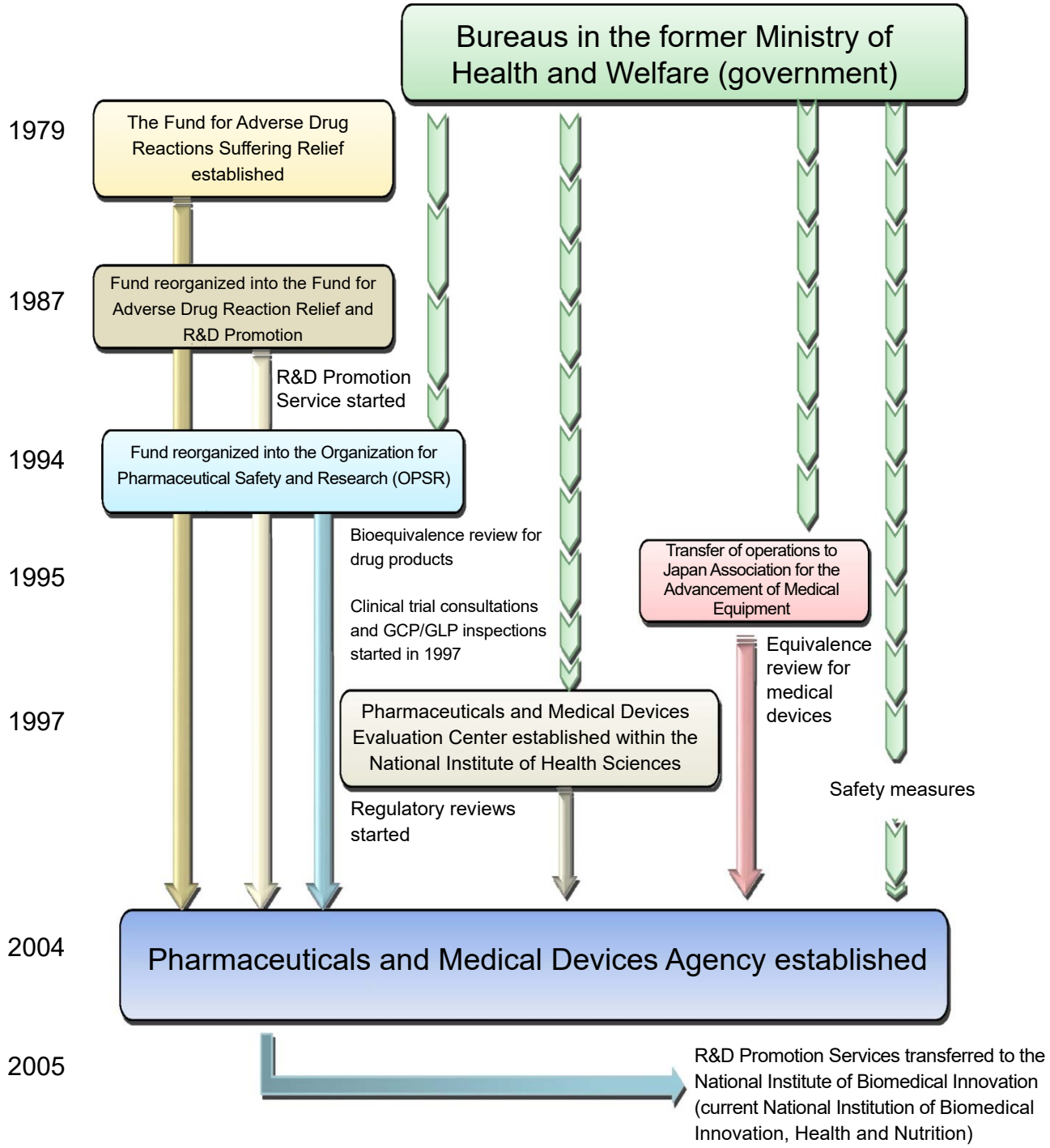
I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

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)
Bioequivalence review for drug products
1995
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 (Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D)).
- 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).

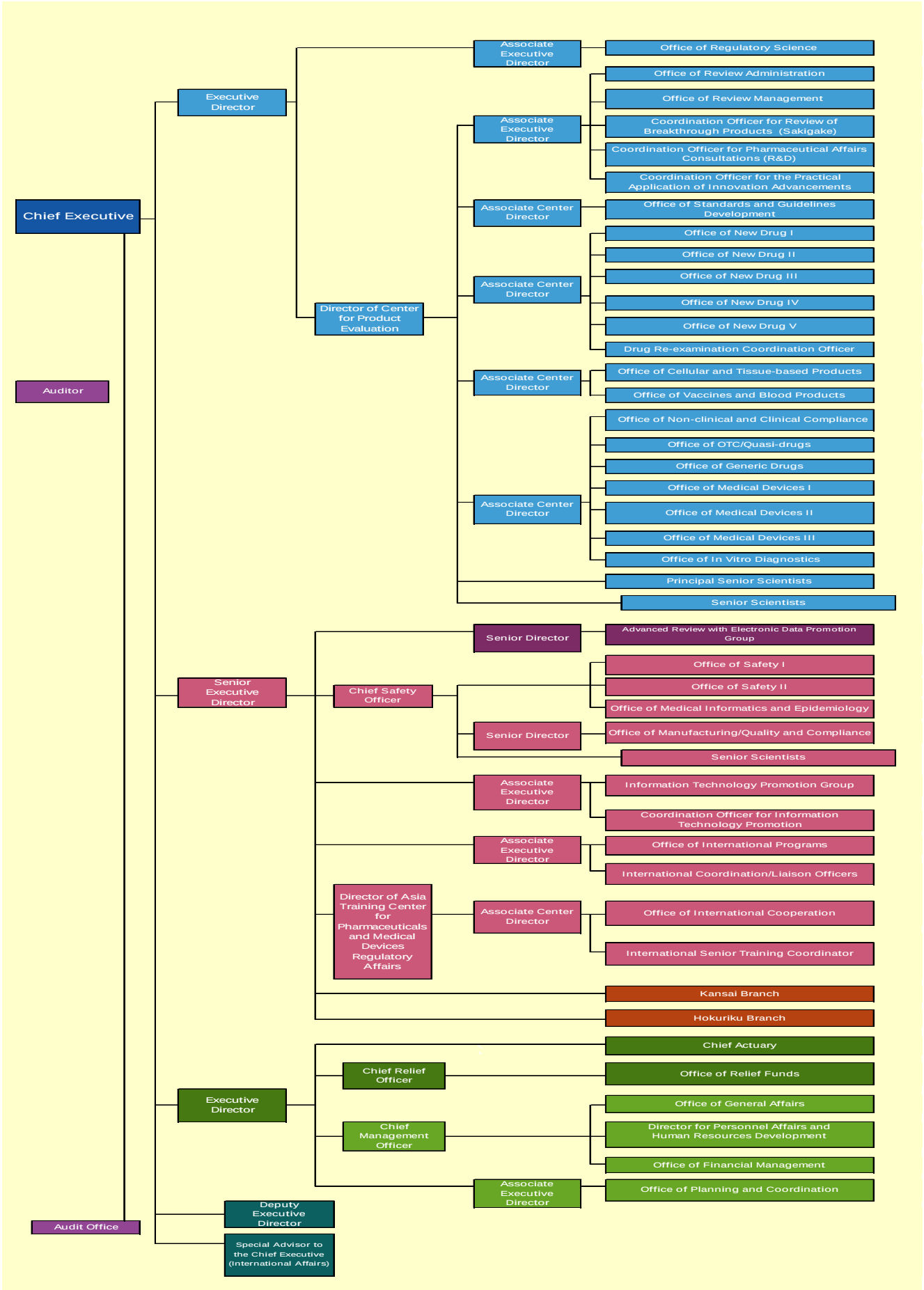
2.3. Safety Measures

- 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 developed medical information databases (MID-NET®) to promptly evaluate more detailed electronic medical records. MID-NET® was launched in April 2018.

PMDA Organizational Structure (as of March 31, 2018)



II. OPERATING PERFORMANCE FOR FY 2017 (April 2017 – March 2018)

PART 1 Development of the 2017 Fiscal Year Plan

1.1 Development and Implementation of the 2017 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 2017 Fiscal Year Plan was developed at the end of FY 2016 based on the Third Mid-term Objectives and Mid-term Plan, and the results of the evaluation of PMDA's operating performance for FY 2015 provided by the Minister of Health, Labour and Welfare, Ministry of Health, Labour and Welfare (MHLW). The FY 2017 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 2016

- 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 2016 on September 28, 2017, prepared based on expert committee interviews concerning the results of their evaluations of independent administrative agencies as of July 12, 2017. PMDA received 1 "S" rating, 3 "A" ratings, and 11 "B" ratings for 15 criteria evaluated. Among these, 1 "S" rating, 3 "A" ratings, and 3 "B" ratings were for "highly important" 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 2016 were published on the PMDA website and reported to the Advisory Council at its meeting held on November 1, 2017.

Results of the Evaluation on Operating Performance for FY 2016

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 enhancement of the Consultation System	B	B	B		
	2. Expeditious operation and systemic improvements (Relief service)	A○	B○	A○		
	3. Execution of cross-functional collaboration and health and welfare services	B	B	B		
	4. Provision of healthcare allowances for patients with SMON and patients infected with HIV through blood products	B	B	B		
	5. Expeditious operation and systemic improvements (services related to drugs)	A○	S○	S○		
	6. Expeditious operation and systemic improvements (services related to medical devices and regenerative medical products)	A○	A○	A○		
	7. Support of the initiative to facilitate development of innovative drugs, medical devices, and regenerative medical products	B○	B○	B○		
	8. Reinforcement of collecting, and systematization of organizing, assessing and analyzing information on adverse drug reactions/malfunctions	A○	B○	B○		
	9. Provision of safety information to companies/healthcare professionals and follow-up, and provision of safety information to patients and consumers	B○	B○	B○		
	10. Promotion of international activities, etc.	A○	B○	A○		
II. Increased efficiency of operations						
	11. Operation through target management and top management, ensuring transparency by establishing deliberative bodies, strengthening the consultation system, and announcement of the Agency's services.	B	B	B		
	12. Cost control efforts	A	B	B		
	13. Collection and management of contributions	B	B	B		
III. Fiscal improvement						
	14. Budget, income and expenditure plan, and financial plan	B	B	B		
IV. Others						
	15. Personnel matters and establishment of security	A○	B○	B○		
Overall assessment		A	B	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 2016 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 has a systemic approach to operational management, (e.g., strategic planning capacities concerning all operations, risk management, and inspection of operations) and an organizational system in which management decisions by the Chief Executive are promptly reflected in the 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.
- Furthermore, in light of the expanded organizational scale and functions etc., PMDA decided to start working on "PMDA Organizational Platform Proceeding Project" with the aim of overall improvement in governance under appropriate progress management, to strengthen the organizational platform that would allow PMDA to achieve its missions in the future, and to continue its efforts to become an even far more trusted organization.

How to Actually Proceed with the PMDA Organizational Platform Proceeding Project

1. Establish a decision-making process and management system that are appropriate for an organization with 1,300 employees
   (1) Strengthen the decision-making process and the business operation system
   (2) Review the rules to achieve a disciplined workplace
   (3) Strengthen the risk management
2. Secure and develop excellent human resources who can make accurate decisions from a scientific perspective and further improve the quality of operations
   (1) Systematically develop staff members by steadily operating the Career Development Program (CDP)
   (2) Review the personnel evaluation system and the annual salary system
   (3) Develop better workplace
   (4) Further enhance the quality of operations by effectively responding to inquiries and complaints
3. Strengthen financial governance
   (1) Establish financial governance that is appropriate for an organization where commissions and contributions make up a large portion of the income (expeditious improvement and operation of the decision-making system in light of the new product application trends and use of appropriate financial indices)
   (2) Establish a budget that allows stable long-term fiscal management (e.g., budget drafting by introducing an appropriate budget ceiling)
   (3) Disclose financial status periodically

- Based on the “PMDA Organizational Platform Proceeding Project”, and in accordance with the investment decision process developed in the previous fiscal year, PMDA strengthened the IT control system, by checking all (84) systems including their operation and maintenance that would be implemented within FY 2018, in detail in terms of the effects on operations, scale of investment, etc., at the Committee on Investment in Information Systems (held four times) and improved the system that allowed executives to promptly make decisions on system management.
- PMDA handles highly confidential information, including application dossiers submitted by corporations etc. and application forms for relief benefits that contain personal information. The agency held two meetings of the Headquarters of Information Systems Management, to enhance information security measures. PMDA also developed a system that allowed executives to promptly obtain information on security measures (e.g., information regarding ongoing system operations and implemented information security measures was provided every month to the Risk Management Committee at its meetings).
- In light of the severe persisting fiscal situation since the previous fiscal year, PMDA implemented a zero-based budget for FY 2018 without granting a safe-harbor exception to improve the condition of its balance sheet, and decided to make efforts to implement the FY 2018 budget as efficiently and effectively as possible while continuing to perform its operations in a stable and sustainable manner. PMDA thus introduced a conservative budget by rationalizing and streamlining operations and reducing incidental expenses.
- Specifically, budget drafting by the ceiling system was continued to further reduce the total budget for FY 2018. 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 2016. (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 2018 budget was reduced by 0.38 billion yen (-1.3%) from the FY 2017 budget. (The FY 2017 budget was reduced by 3.62 billion yen [-10.9%] from FY 2016.)

- To maintain sound fiscal performance and effective operations, the Financial Management Committee, chaired by the Chief Executive, held 16 meetings in FY 2017, to regularly monitor PMDA's financial condition. The Committee received reports on financial analyses including revenue and cash flow analysis of the user fees paid to each division each month and the declared amount of contributions, and discussed future financial prospects.

  To ensure that PMDA continues to play its roles securely during the Fourth and subsequent Mid-term Plan periods, the Committee 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 Committee have been reflected in the implementation of the budget for each fiscal year, through the Plan-Do-Check-Action (PDCA) cycle, to ensure financial soundness.

  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.

- PMDA held global strategy meetings on a regular basis to implement global measures comprehensively and strategically, and made decisions to implement necessary measures to carry out individual projects.

- To provide opportunities for communication between executives and staff members, PMDA held three "luncheon meetings for communication with executives."

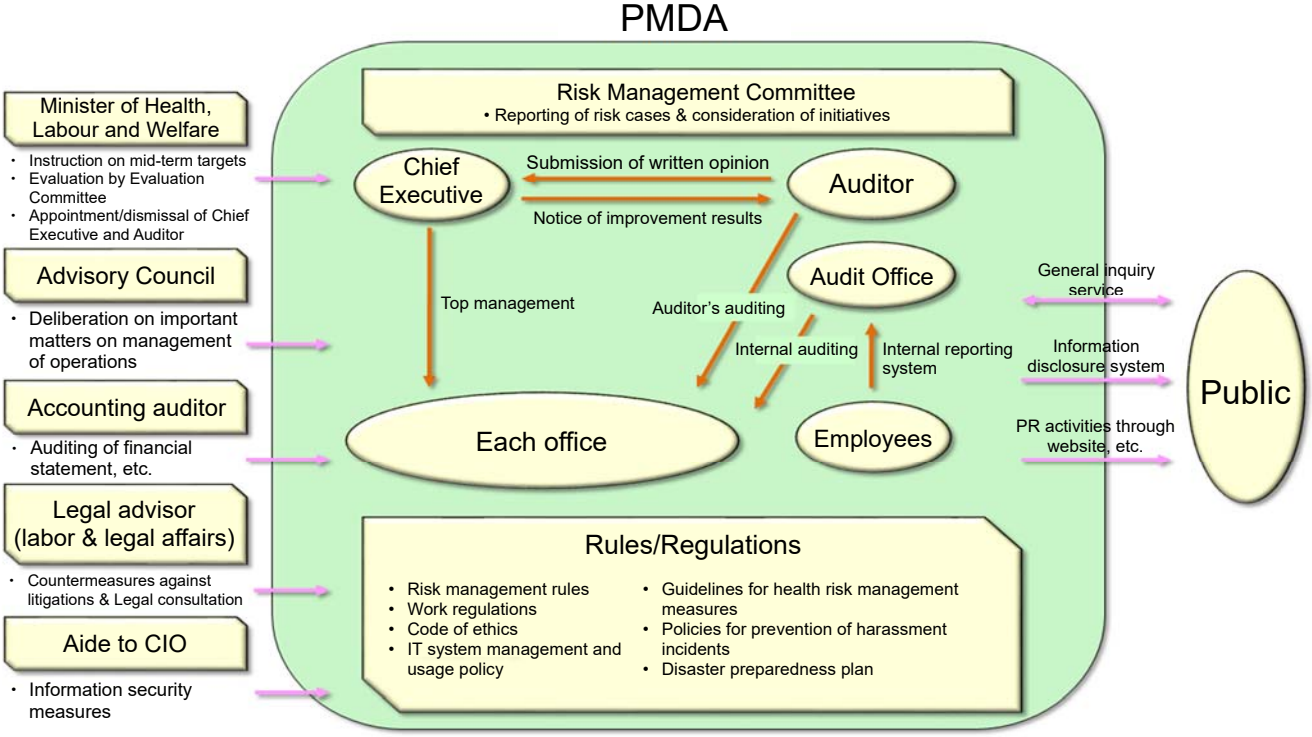
- PMDA held a joint idea exchange session on new drugs and safety measures with members of the pharmaceutical industry in December 2017.

  PMDA supported the operation of MHLW-hosted regular idea exchange sessions focusing on the approval review, safety measures, etc. of medical devices and *in vitro* diagnostics (held in August 2017).

- Operational incidents that have occurred in PMDA are reported to the Risk Management Committee, which discusses individual incidents, their potential impact, and countermeasures. The operation rules of the Committee were revised in order to clarify the causes of operational incidents to prevent recurrence. (For example, if an incident has occurred, the relevant department is required to closely investigate and analyze the causes of the incident and submit a report to the Risk Management Committee). After the revision, the Committee held 14 meetings. Preventive measures proposed at a Risk Management Committee meeting are required to be reported at the upcoming meeting of Board of Directors. The department directors are required to verbally inform all staff members about incidents and preventive measures that have been reported to the Board of Directors.

- By utilizing a new page in its intranet for the Risk Management Committee, PMDA continues its efforts to familiarize the executives and employees with risk management best practices in accordance with the risk management rules, risk management manual, and guidance on incident prevention.
- PMDA revised competence assessment items in the personnel evaluation system, and further clarified that the employees are evaluated for the stance/attitude toward “risk prevention.”
- Due to improper administrative activities, PMDA caused 5 significant operational incidents in FY 2017 and caused the concerned persons much trouble. PMDA therefore announced individual incidents as well as preventive measures (date of announcement in parentheses).
    (i) Delayed payment of healthcare allowance (monetary benefit) for patients (April 14, 2017)
    (ii) Loss of a USB memory stick containing electronic data of application filings (April 28, 2017)
    (iii) Neglect of management/supervisory roles due to frequent absence without notification (October 12, 2017)
    (iv) Loss of the original application documents and submission data of a medical device (April 17, 2018)
    (v) Incorrect payment of medical fees based on the Relief System for Sufferers from Adverse Drug Reactions (April 17, 2018)
- PMDA is seriously concerned about the fact that the agency caused these significant incidents. The Chief Executive delivered a message to all employees about the incidents and the right attitudes toward all operations. PMDA mandated all staff members to regularly participate in risk management training programs, and revised the procedures of the Risk Management Committee.
- PMDA started working on a complete overhaul of document management, including the approval, archiving, and disposal of documents.
- 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 revised its emergency contact lists as appropriate and ensured that all concerned persons are familiarized with it. PMDA also secured emergency stock in preparation for disasters, and uploaded a Manual for Handling of Emergency Stock on the website for internal use (revised in October 2017) to familiarize all staff members with it.
- To enhance the effectiveness of the safety confirmation/simultaneous transmission system in the event of a large-scale disaster, PMDA carried out drills for safety confirmation involving all staff members (once a month from January 2017 onward).
- PMDA checked the routes to the emergency assembly area in the event of a large-scale disaster and carried out a drill for emergency assembly to enhance the capability of staff members to cope with disasters (June 2017).
- The Pharmaceuticals and Medical Devices Agency’s Business Continuity Plan (BCP) to Prepare for Large-Scale Natural Disasters, specifies the range of important operations that PMDA should continue to conduct in the event of a large-scale disaster (e.g., an earthquake in the Tokyo metropolitan area). To further enhance the effectiveness of BCP, PMDA reviewed important operations that PMDA should continue to conduct in such an event, and instructed each department to create an operational manual to be used in times of disaster.

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.
- Since the establishment of the PR Committee, PMDA's operations have been further diversified and its growth has been drawing attention worldwide; and in light of these facts etc. and also in order to implement PR activities (including global PR activities) more effectively and properly, PMDA reviewed the PR Committee in March 2018.
- 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 Regulatory Science General Consultation Regulatory Science Strategy Consultation (R&D) 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. The office started to offer video conference consultations on safety measures in November 2017.

- 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. In April 2017, PMDA thus renamed the Division of Pharmaceutical Affairs Consultation as the Division of Innovation Support and Consultations on R&D Strategy, and reorganized Pharmaceutical Affairs Consultation on R&D Strategy (introductory consultations, pre-consultations, and face-to-face consultations) into Regulatory Science General Consultation (introductory consultations) and Regulatory Science Strategy Consultations (R&D) (pre-consultation consultations and face-to-face consultations). PMDA discussed and implemented measures for supporting the practical application of innovative drugs, medical devices, and regenerative medical products (e.g., the agency developed guidelines for Consultations on Cooperation for Practical Application of Innovation Advancements).
- 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 PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs provided training for the officers of 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 victims of drug and other medical product-related adverse health effects. 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 increasing 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 2017 were as follows.

Advisory Council (FY 2017)

Agenda for the 1st Meeting (June 26, 2017)

(1) Annual Report FY 2016

(2) Financial Report FY 2016

(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions.
(5) Others

Agenda for the 2nd Meeting (November 1, 2017)
(1) PMDA Organizational Platform Proceeding Project
(2) Results of evaluation of operating performance for FY 2016
(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) Condition of PMDA's financial accounts related to reviews, etc.
(7) Others

Agenda for the 3rd Meeting (March 12, 2018)
(1) FY 2018 plan (draft)
(2) Progress of PMDA Organizational Platform Proceeding Project
(3) Establishment of the Regulatory Science Center
(4) PMDA's financial condition of accounts for reviews, etc.
(5) Supplementary budget for FY 2017 and budget (draft) for FY 2018
(6) PMDA's activities in response to suggestions from the Advisory Council
(7) Employment status and extension of interim restrictions on posts of personnel from the private sector
(8) Cash contributions etc., received by external experts commissioned for Expert Discussions
(9) Others

Committee on Relief Services (FY 2017)
Agenda for the 1st Meeting (June 12, 2017)
(1) Annual Report FY 2016
(2) FY 2017 plan
(3) PR on the Relief System for Adverse Health Effects
(4) Others

Agenda for the 2nd Meeting (December 18, 2017)
(1) Results of evaluation of operating performance for FY 2016
(2) Operating performance so far in FY 2017 and current situation of recent major initiatives
(3) Collection rates of ADR and infection-related contributions from FY 2018 onward (draft)
(4) Others

Committee on Review and Safety Operations (FY 2017)
Agenda for the 1st Meeting (June 15, 2017)
(1) Annual Report FY 2016
(2) FY 2017 plan, etc.
(3) Employment status of personnel from the private sector
(4) Cash contributions etc., received by external experts commissioned for Expert Discussions.
(5) Others

Agenda for the 2nd Meeting (December 25, 2017)
(1) Results of evaluation of operating performance for FY 2016
(2) Operating performance so far in FY 2017 and initiatives to be addressed in the future
(3) Employment status of personnel from the private sector

(4) Cash contributions etc., received by external experts commissioned for Expert Discussions.
(5) Others

- The above meetings were open to the public, and the minutes and materials for the meetings of the Advisory Council and its sub-committees were published on the PMDA website (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 necessitating flexible processes, PMDA continued its 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.
  (1,395 external experts are commissioned as of March 31, 2018.)
- PMDA also has commissioned external experts to seek their opinions on the relief service for health damage caused by adverse drug reactions and infections acquired through biological products.
  (125 external experts are commissioned as of March 31, 2018.)
- 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 as advisors to handle operations that require legal 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 an outside specialist with advanced expertise in information systems as an aide to the Chief Information Officer (CIO), to ensure consistency and coordination of services across the Agency’s information systems.

2.1.(5) Standardization of operating procedures

- PMDA has continued to develop, examine, and, if necessary, revise standard operating procedures (SOPs) for its major tasks. The purpose is to implement operations properly and consistently by standardizing each operating process, and to limit the number of regular staff by effectively employing non-regular staff. Routine operations are conducted by non-regular staff.
- There were a number of errors in numeric data published in the Annual Report FY 2016 and materials submitted to the Advisory Council. Thus, the process of numeric data calculation was re-checked, and operating procedures were reviewed.

2.1.(6) Development of databases

- Since October 2016, when PMDA started to accept electronic data for new product applications transmitted through an electronic data system, no system failure that may influence operations has occurred. The application data of all approved products have been stored in a database that collects all electronic application data to be used in cross-product analyses in the future.

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

- PMDA reduced investment cost of operations and IT systems and terminated some operations and systems, to ensure that expenditures remain below the budget ceiling set in FY 2016. PMDA discussed the optimal IT system infrastructure within the ceiling.

  Elsewhere, to ensure that the individual systems are operated stably and to ascertain and classify the functions that should be further enhanced, PMDA confirmed the status of various systemic improvements as well as the details of monthly reports obtained from operational support companies. Based on this information, PMDA took actions to the extent 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 2017, PMDA enhanced the efficiency of its operations by optimizing IT systems and reducing unnecessary expenditure, as in the previous year. PMDA also made efforts to reduce procurement costs by adopting general competitive bidding, resulting in a 31.7% reduction against the FY 2014 figure, with the exception of new services starting in FY 2016 or later.

  PMDA also made efforts to effectively implement new services covered by administrative subsidies that were distributed in association with increases in newly entrusted business by the government, such as strengthening of the system for safety measures and GMP inspections, promotion of optimal uses of innovative pharmaceuticals, etc.
- PMDA outsourced arrangements for business trips within Japan on a trial basis in FY 2018. Employees are instructed to reduce operating expenses by using package tours or inexpensive

travel services exclusive to corporate employees, available on the website of the contracted travel agency.

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.
- Like the measures taken for general administrative expenses, PMDA enhanced the efficiency of its operations, such as optimization of systems, promotion of digitalization, and reduction of unnecessary expenditure in FY 2017. PMDA also made efforts to reduce procurement costs by concluding contracts through general competitive bidding, resulting in a 24.9% reduction against the FY 2014 figure, except for new services starting in FY 2016 or later.

  PMDA also made efforts to effectively implement new services covered by administrative subsidies that were distributed in association with increases in newly entrusted business by the government, such as strengthening of the system for safety measures and GMP inspections, promotion of optimal use of innovative pharmaceuticals, etc.
- Like the measures taken for general administrative expenses, PMDA outsourced arrangements for business trips within Japan on a trial basis in FY 2018. Employees are instructed to reduce operating expenses by using package tours or inexpensive travel services exclusive to corporate employees, available on the website of the contracted travel agency.

2.2.(3) Competitive bidding

- In FY 2017, the percentage of competitive contracts (including competitive requests for proposals and invitations to bid) among the total contracts decreased by 6.3% in number of bids and by 9.2% in monetary value, compared with FY 2016.

  The decreased percentage of competitive contracts in number of bids was due to the decrease in the total number of competitive contracts (i.e., a decrease of 23 compared with FY 2016).

  In FY 2017, the monetary amount of competitive contracts decreased considerably, whereas the monetary amount of optional contracts increased, for the following reasons: (a) there was an increase in services for which only optional contracts were available; (b) for some services, direct contract with licensees (i.e., optional contract) was deliberately selected because it led to a substantial price reduction.

		FY 2016	FY 2017	Change
General competitive bidding (including competitive planning competition and invitations to bids)		113 bids (81.9%) 3,041 million yen (92.1%)	90 bids (75.6%) 2,466 million yen (82.8%)	-23 bids (-6.3%) -574 million yen (-9.2%)
Non-competitive optional contracts		25 bids (18.1%) 261 million yen (7.90%)	29 bids (24.4%) 511 million yen (17.2%)	4 bids (6.3%) 250 million yen (9.2%)
	Excluding contracts in relation to office lease	21 bids (15.2%) 171 million yen (5.2%)	26 bids (21.8%) 453 million yen (15.2%)	5 bids (6.6%) -283 million yen (-10.0%)
Total		138 bids 3,302 million yen	119 bids 2,977 million yen	-19 bids -325 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 3 external experts and 2 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 2017. The Committee held 4 meetings in FY 2017 and summaries of its reviews are available on the PMDA 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 of owed contributions related to ADRs, infections, and post-marketing safety measures to be no less than 99%. In FY 2017, the collection rates achieved for ADR, infection, and post-marketing safety measure-related contributions were 99.7%, 100%, and 99.6%, respectively.
- The rate of contributions for relief of ADRs and infections was revised at the opportunity arising once every five years. PMDA drafted the future prospects based on the basic calculation rate etc., which were reviewed the previous year, proceeded with discussions, and then explained to the concerned organizations. As a consequence, PMDA decided to maintain the rate of contributions from FY 2018 onward without any changes. 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 1, 2017.

FY 2017 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.	679	679	100%	4,116
	MAHs of pharmacy-compounded drugs	4,653	4,638	99.6%	5
	Total	5,332	5,317	99.7%	4,120
Infection contributions	MAHs of approved biological products, etc.	100	100	100%	110
Post-marketing Safety measures etc., contributions	MAHs of drugs, etc.	3,156	3,146	99.6%	3,697
	MAHs of pharmacy-compounded drugs	4,653	4,639	99.6%	5
	Total	7,809	7,785	99.6%	3,701

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 the PMDA website and in relevant trade journals, and continued its efforts to raise awareness of the contribution procedure among the relevant parties obligated to make contributions by preparing and distributing a handbook. PMDA also 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 2017, the contribution rate applied to such MAHs was set at 0.27/1000 and the collected amount was 4,120 million yen.

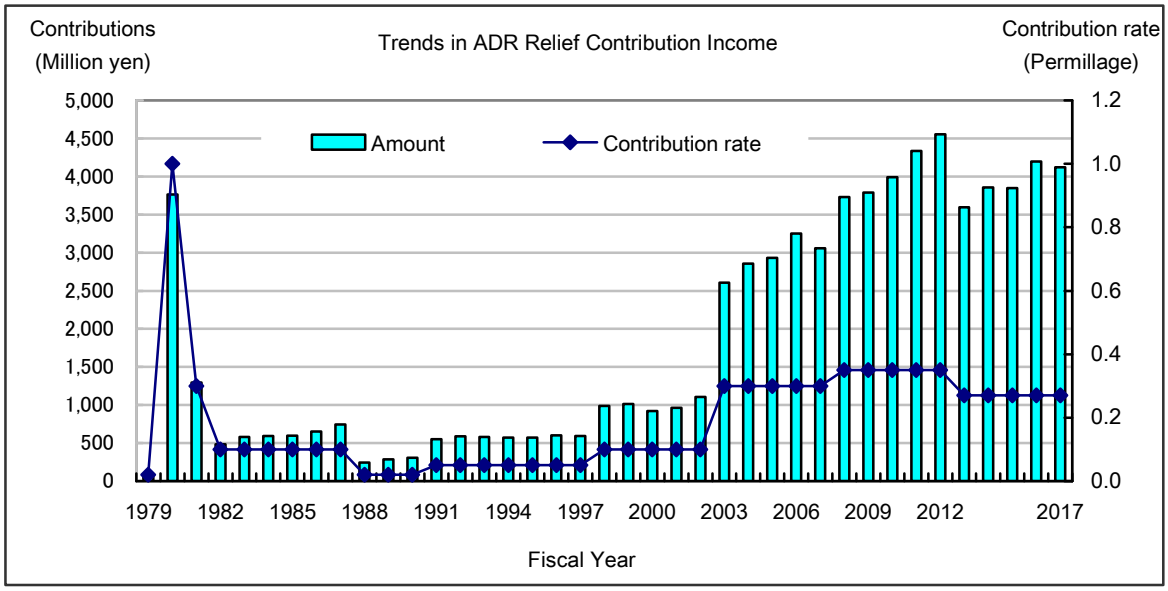
(Million yen)

Fiscal year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Contributions from MAHs of approved drugs*	3,590 [688]	3,852 [692]	3,841 [688]	4,193 [693]	4,116 [679]
Contributions from MAHs of pharmacy-compounded drugs	6 [5,866]	6 [5,658]	5 [5,439]	5 [4,974]	5 [4,638]
Total	3,596	3,857	3,847	4,198	4,120
Contribution rate	0.27/1000	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 2013 and 2014 represent the amount of contributions paid by MAHs of drug. The figures for FY 2015, 2016, and 2017 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 2017, the contribution rate applied to such MAHs was set at 0.1/1000 and the collected amount was 110 million yen.

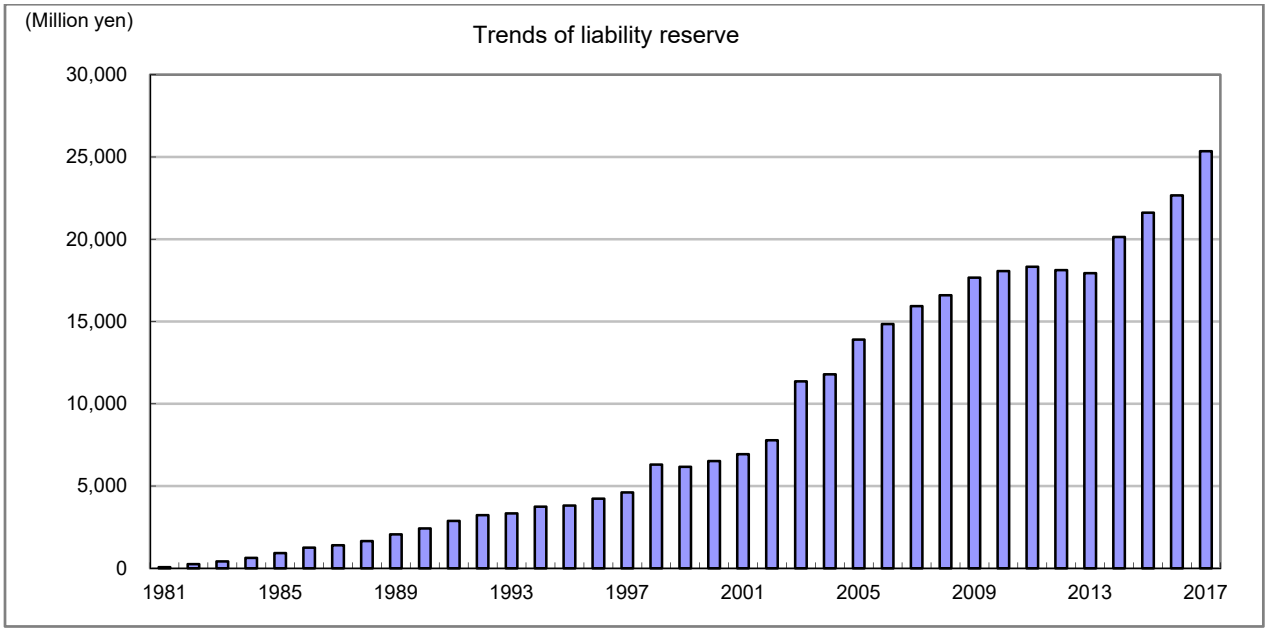
(Million yen)

Fiscal year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
MAHs of approved biological products, etc.*	869 [94]	93 [92]	93 [96]	102 [100]	110 [100]
Contribution rate	1/1000	0.1/1000	0.1/1000	0.1/1000	0.1/1000

* *The figures for FY 2013 and 2014 represent the amount of contributions paid by MAHs of approved biological products. The figures for FY 2015, 2016, and 2017 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 it should possess at the end of every fiscal year and accumulates funds accordingly. The liability reserve at the end of FY 2017 was 25,347 million yen.



(ii) Collected contributions for post-marketing safety measures

- In order to fund services for improvements in the quality, efficacy, and 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 2017, the contribution rate applied to such MAHs was 0.231/1000 for drugs, 0.127/1000 for medical devices, and 0.115/1000 for *in vitro* diagnostics and regenerative medical products; the collected amount was 3,701 million yen.

(Million yen)

Fiscal year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
MAHs of drugs, etc.*	2,810 [3,023]	2,972 [3,099]	2,952 [3,139]	3,231 [3,141]	3,697 [3,146]
MAHs of pharmacy-compounded drugs	6 [5,866]	6 [5,658]	5 [5,439]	5 [4,974]	5 [4,639]
Total	2,816	2,977	2,958	3,236	3,701
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, *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)	0.231/1000 (Drugs excluding *in vitro* diagnostics) 0.127/1000 (Medical devices) 0.115/1000 (*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 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, 2016, and 2017 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 2017, PMDA made efforts to reduce the amount of paper printed by copiers. As a result, the amount and cost of paper was reduced by 21.0% and 27.7%, respectively, over FY 2016. PMDA also thoroughly reduced unnecessary expenditures by cutting various administrative expenses based on unified management of supplies.
- Also in FY 2017, PMDA implemented budget control measures by reducing expenditures to improve its overall balance sheet. To enhance its effectiveness, PMDA strived to implement the budget efficiently without waste under strict management. Further, by standardizing this implementation process, PMDA established a budget control system and reinforced its efforts to reduce unnecessary expenditures.

  In FY 2018, PMDA will review service operations without granting a safe-harbor exception under the ceiling system as it has done in the previous fiscal year and make efforts to implement the budget efficiently without waste by further reducing the total budget.

  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 PMDA website.

- Since June 2010, PMDA has gathered input from the public (Public Voices) and has disclosed them on the PMDA website at regular intervals. The input gathered is used to improve the agencies operational management practices.
- In FY 2017, PMDA received 2,892 inquiries, of which 887 (approximately 30%) were related to applications and consultations for drugs, medical devices, etc.

	Inquiry	Complaint	Opinion/Request	Others	Total
FY 2017	2,869 (885)	8 (0)	15 (2)	0 (0)	2,892 (887)

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 2017.
- In addition, PMDA is discussing a system to sincerely respond to complaints etc. from related companies in the “PMDA Organizational Platform Proceeding Project.”

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 PMDA website in order of requests from relevant departments. Further, the PMDA 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.
- PMDA completely redesigned its official website in March 2015 so that the public, healthcare professionals, stakeholders, etc. can easily access safety and efficacy information of pharmaceuticals and medical devices, and it continues working to enforce information provision in and outside of Japan. PMDA has also improved its usability by renovating the most frequently visited pages for information search, e.g., package inserts (prescription drugs, medical devices, behind-the-counter (BTC) drugs, over-the-counter (OTC) drugs, and *in vitro* diagnostics), based on requests from users in 2016 to 2017.

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 2017, the following activities were implemented in accordance with this Plan.

- In FY 2017, on the occasion of the "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., in cooperation with pharmaceutical associations in Tokyo, Okayama, Fukuoka, Fukushima, and Gunma (5 prefectures).
- PMDA introduced its operations to researchers and healthcare professionals by making booth exhibitions at academic conferences.
- PMDA also held a press meeting in March 2018 to introduce the PMDA's roles and recent activities, including the Regulatory Science Center established in April 2018, MID-NET®, which has started full-scale operations, etc.
- 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 (21 times in Japan and 5 times overseas).

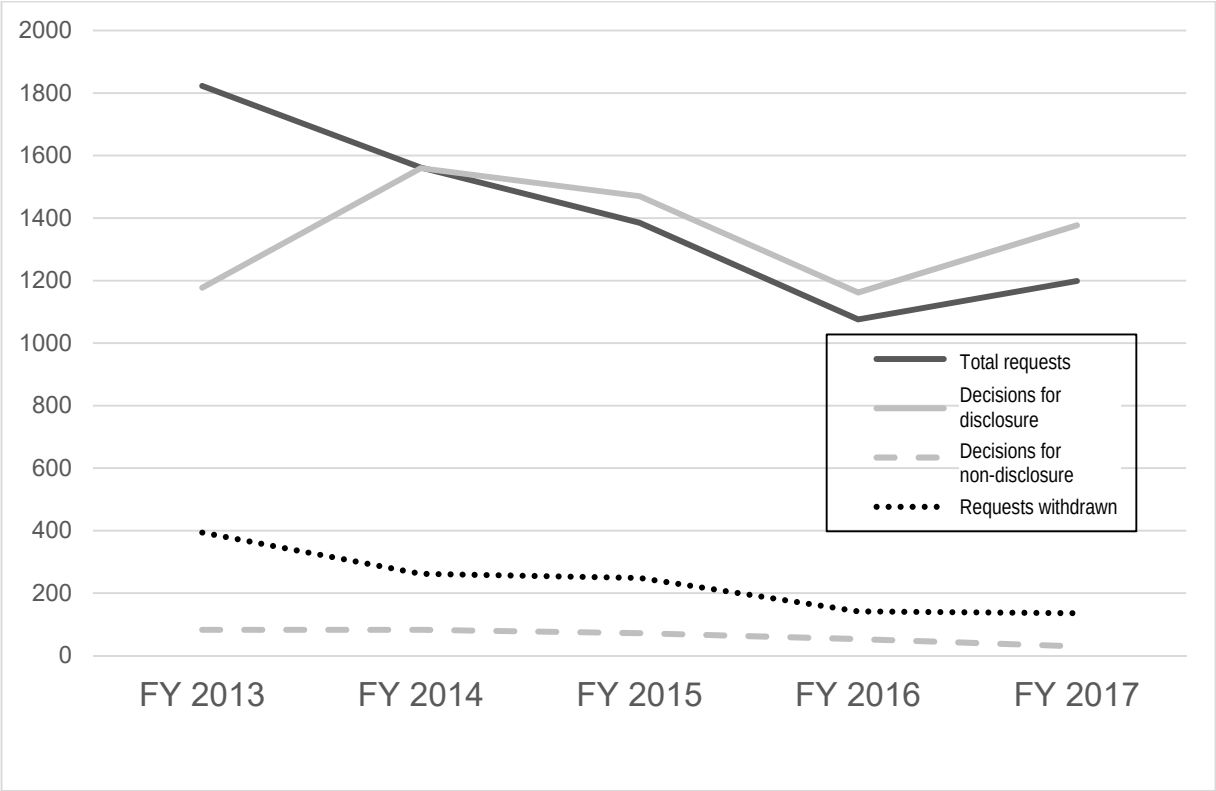
2.3.(5) Disclosure requests for internal agency documents

- 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 2017, the number of requests increased by 11.4% and the number of disclosures decided increased by 15.8% compared to FY 2016. 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 (*1)					Requests for examination
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the document exists	
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
FY 2017	1,199	136	164	1,213	4	26	0	9

**1) 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.*



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

*2) *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 2013	FY 2014	FY 2015	FY 2016	FY 2017	Examples Product application
Review	1,675	1,457	1,295	990	1,087	Marketing notification for products not subject to approval, Notification of the results of GCP inspections
Post-marketing Safety	131	97	82	70	109	ADR reports etc.
Others	17	8	8	16	3	
Total	1,823	1,562	1,385	1,076	1,199	

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					Requests for examination
			Full disclosure	Partial disclosure	Non-disclosure	Non-existing documents	Refusal to answer whether the documents exist	
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
FY 2017	3	0	2	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 2017, PMDA conducted internal audits on the status of document management, article management, cash and deposit management, PASMO card use (IC smart card used for public transportation, petty cash purchases, etc.), use of travel expenses, attendance management of all employees, funds disbursement for competitive research etc., as well as the status of compliance with rules restricting work assignments of personnel with prior work history in the private sector. The audit results were released on the PMDA website. PMDA also reported audit results on the status of compliance with rules restricting work assignments of personnel with a prior work history in the private sector to the Advisory Council etc., and released meeting materials of the Council on its website.

2.3.(8) Report on financial standing

- To ensure the transparency of expenditures, PMDA disclosed its financial standing for FY 2016 (including the utilization of user fees and contributions) in government gazettes and on the PMDA website. PMDA also released its budget for FY 2017 on the PMDA 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 2017, as was also done during FY 2016. 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 PMDA website in June 2017.

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 2016 to March 2017 in pay raises etc., as of July 2017. 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.
- 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

(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 FY 2017, PMDA prepared a training system and chart to promote easier comprehension of the role of each training program in order to encourage greater staff engagement in each training program. Regarding training of administrative staff, PMDA reviewed its training system in order to develop their management ability and necessary skills, with the expectation that these staff will support the foundation of PMDA, and clarified the persons and departments to be targeted by each training program. PMDA also developed an implementation plan for FY 2018 onward to offer more systematic training in line with the reviewed training system.

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 and Academic Degree Acquisition Support Study Committee formulated plans in view of staff need. Implemented training programs are listed below. All training programs were reviewed by collecting opinions from attendees, directors of individual departments and offices, or training proponents on later days according to the individual contents thereof. Each offering was generally highly praised with opinions that they were useful for

business operations. PMDA reflected the results of evaluation to formulate training plans for FY 2018.

1) General Training Course programs

The implementation status of major general training course programs is shown in the table on the next page. Major activities are as follows.

- As in previous years, a lecture-based training program was provided by invited lecturers from patient advocacy groups, such as those related to victims of adverse drug reactions (two sessions as part of the mental attitude training program for new staff and one session as part of the training program on adverse drug reactions).
- As for new staff training sessions, attendees were required to score all lectures in terms of lecture contents and explicitness of slides, and feedback was then provided to lecturers with scores and rankings to improve the quality of training.
- Training programs tailored to different job levels were provided. As a new endeavor, messages from senior staff were distributed at the start of follow-up training and training of mid-level staff; and as in previous years, executive directors delivered lectures to raise the staff motivation and awareness. Because prior educational training should be provided to staff who are considered to be promoted to managerial levels, PMDA designed and provided a training session before the promotion to a managerial level, primarily to reform the awareness from players to managers.
- PMDA began a training program of good practice for learning English offered by in-house staff to enhance the motivation of all employees to learn English and raise their awareness of presentations.
- PMDA provided two group training programs for risk management in addition to the existing programs to further increase all executives/employees' awareness of legal and compliance obligations, including protection of personal and/or proprietary information. PMDA also designed and provided a new training program on ethics that was attended by all staff to further reinforce the awareness of ethical concerns. PMDA also designed and provided a new training program concerning insider trading that staff can attend, as necessary, by accessing video clips uploaded on the intranet.
- A PC training program (for Microsoft Office applications) was provided not in conventional e–Learning form, but in a group training form, with the focus on items with a high demand.
- PMDA invited the director of the Office of Career Development, MHLW, as a lecturer, who gave a lecture in career design, to provide staff with an opportunity to obtain a better understanding of how to plan and optimize their careers.

2) Specialized Training Course programs

The implementation status of major specialized training course programs is shown in the table on the next page. The major activities are as follows.

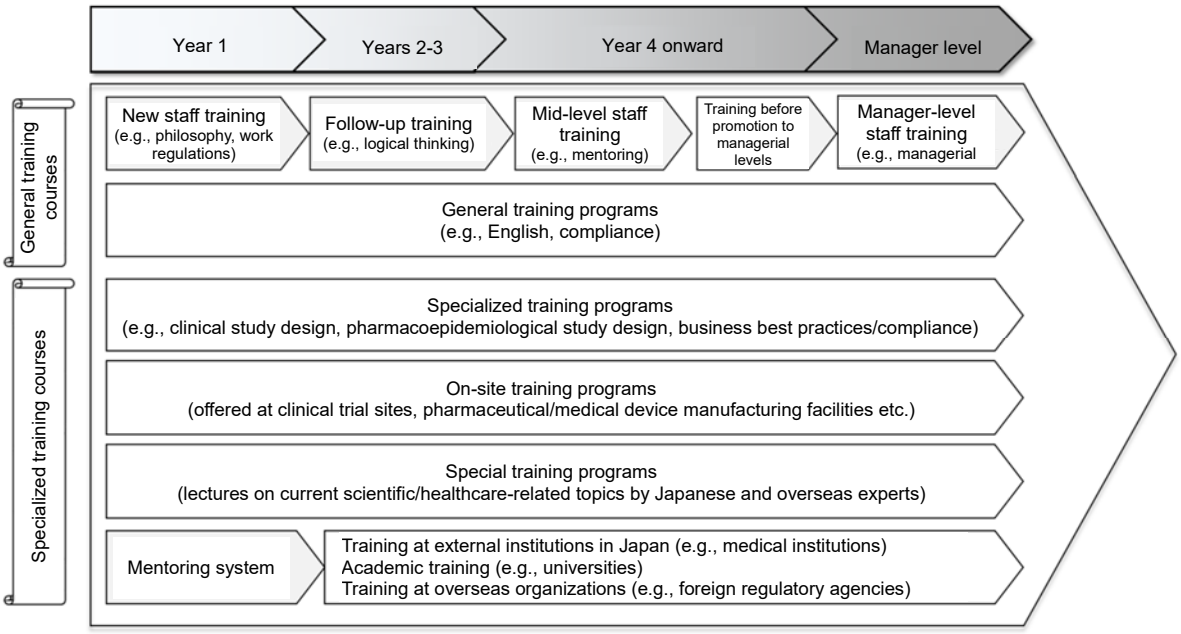
- PMDA designed and provided a pharmacometrics expert training program to employees in charge of clinical pharmacology and ADME evaluations in the new drug review process. The purpose of this program is to improve the quality of review/consultation services by ensuring that those employees enhance their expertise by acquiring pharmacometrics-related knowledge and analysis techniques.
- PMDA designed and provided a training program for research ethics in line with the revised, "Ethical Guidelines for Medical and Health Research Involving Human Subjects."

- By partially modifying on-site practical training with pharmacists, PMDA provided a visit-based training program with focus on the study of clinical study management operations.

Major Training Programs Implemented in FY 2017

Training program title, etc.			Implementation (No. of sessions[Note)] etc.)
General Training Course	Training programs tailored to different job levels	New staff training	1 session (April to May 2017)
		Follow-up training	1 session
		Mid-level staff training	1 session
		Training before promotion to managerial levels	1 session
		Manager-level staff training (i.e., labor management course, work-style reform)	1 session each
	General training programs	English language training program for employees scheduled to be dispatched overseas for a long period	3 employees
		Practical English training program for international conferences	13 employees
		English language training program (good practice for learning English etc.)	2 sessions
		Training in risk management	3 sessions (including 1 session as part of new staff training)
		Training on insider trading	1 session
		Training on adverse health effects (e.g., adverse drug reactions)	1 session
		PC training (Microsoft Office; provided in a group-training form)	3 sessions (approximately 101 employees)
		Training in career designing	1 session
Specialized Training Course	Specialized training programs	Training in clinical study design	15 sessions
		Training in pharmacoepidemiology	12 sessions
		Training in CDISC* overview * CDISC: Clinical Data Interchange Standards Consortium	2 sessions
		Training in pharmacokinetics/clinical pharmacology and modeling & simulation training	4 sessions
		Training in research ethics	2 sessions
		Training in ME technology	Type 1: 1 employee Type 2: 3 employees
		Regular course by the Pharmaceuticals Promotion Association	5 employees
		Training for accounting office workers by government-related organizations belonging to the Accounting Center of the Ministry of Finance	2 employees
		Bookkeeping training	Second grade: 1 employee Third grade: 1 employee
	On-site training programs	Visits to pharmaceutical and medical device manufacturing sites (pharmaceutical manufacturing sites, medical device manufacturing sites, and nuclear medicinal facilities)	4 sessions (approximately 57 employees)
		Visits to see institutional review board meetings of medical institutions	4 sessions (approximately 23 employees)
		Visits to see ethics committee meetings of medical institutions	1 session (4 employees)
		Visits to study cancer chemotherapy in outpatient settings and operations of pharmacists	2 sessions (4 employees)
		Training to study medical device products	2 sessions (approximately 33 employees)
	Special training programs (lecturers on the latest topics pertaining to drug development/production, medical accident investigation system)		6 sessions
	Training at external institutions in Japan	Practical training with clinical engineers	2 employees
		Visit-based training to learn clinical study management operations	1 employee
		Training in radiation technology	1 employee
		Pharmacometrics expert training program	Beginner: 2 sessions (4 employees) Intermediate: 2 sessions (4 employees) Advanced: 1 session (4 employees)
		Training in hygiene control by the National Institute of Public Health	1 employee
		Seminars on pharmacoepidemiology by the Union of Japanese Scientists and Engineers	4 employees

Note: If identical training sessions took place on several occasions, the sessions are counted as 1 session.



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

2.4.(3) Support of acquisition of an academic degree

- The Career Development Program (CDP) was established in October 2016 to strengthen the overall PMDA functions through systematic development of human resources, training provision, and personnel allocation. Based on the CDP, PMDA started the operation of a support system for technical staff to acquire a doctoral degree. In FY 2017, applicants were recruited and selected by the Training and Academic Degree Acquisition Support Study Committee, aiming at its realization in FY 2018 (6 employees for sabbatical leave etc., 3 employees for short-term dispatch training in Japan [other than medical technology acquisition]).

2.4.(4) 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.

- As part of the CDP, PMDA created a new personnel rotation policy that further focused on the expertise of employees etc., to realize optimal human resource allocation so that individual employees could use their skills and abilities more effectively. In FY 2017, personnel changes were implemented in line with this policy.

- PMDA developed a new IT system that allows unified management of necessary personnel information and information sharing between employees and their superiors, to facilitate CDP-based development of human resources. The system was launched in FY 2017. Information contained in this system was effectively used to get the right people in the right place (personnel relocation).

2.4.(5) 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 2017 by making use of its website as well as job information websites.

Employment through Open Recruitment (as of April 1, 2018)

1) Technical (specialist) employees (open recruitment conducted twice [once for those who start working on April 1, 2019])
   Number of applicants 478
   Number of persons employed 36
   (Breakdown)
   - Those who start working in April 2018 27 employees
   - Those who start working in 2017 3 employees
   - Those who start working in April 2019 (doctor's degree) 6 employees

2) Administrative regular staff members (open recruitment conduced once)
   Number of applicants 166
   Number of new hires 6
   (Breakdown)
   - Those who start working in April 2018 4 employees
   - Those who start working in 2017 2 employees

Open Recruitment of New Employees Who Start Working in April 2019 (Major Activities in 2017)

○ Information sessions on career opportunities

Technical employees: Five sessions in Tokyo and one session each in Osaka and Sendai (total 330 participants) in March 2018

Administrative employees: Two sessions in Tokyo (total 101 participants) in March 2018

○ 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

- Preparation of brochures for recruitment and 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 2019* and *Rikunavi 2019*)
- 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, 15 individuals were employed on an as-needed basis.

Numbers of Executives and Regular Staff

	FY 2004 April 1	FY 2009 April 1	FY 2014 April 1	FY 2015 April 1	FY 2016 April 1	FY 2017 April 1	FY 2018 April 1	At the end of the effective period of Third Mid-term Plan (end of FY 2018)
Total	256	521	753	820	873	906	915	1,065
Review Department	154	350	492	532	560	578	575	
Safety Department	29	82	152	165	185	190	198	
Relief Department	18	32	33	36	37	39	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, or Associate Center Directors (excluding the ones responsible for Office of Planning and Coordination, for the Information Technology Promotion Group, for Office of Research Promotion, and for Office of Manufacturing/Quality and Compliance), Office of International Programs, Office of International Cooperation, International Coordination Officers, Advanced Review with Electronic Data Promotion Group, 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, Drug Re-examination Coordination Officer, 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, Senior Director (responsible for Office of Manufacturing/Quality and Compliance), Office of Medical Informatics and Epidemiology, Offices of Safety I and II, Office of Manufacturing/Quality and Compliance, Inspection Division of Kansai Branch, and Senior Scientists.

2.4.(6) 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 by creating a staff handbook that provides a summary of related regulations, Q&A, and other information, and distributing it to executives and employees, posting the information on the PMDA intranet, and familiarizing staff members on the occasions of new staff training.
- 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 maintained 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 based on the regulations and manuals related to the prevention of harassment.

2.4.(7) Compensation policy optimization

- PMDA compared its personnel compensation system for FY 2016 against that for national government employees in order to facilitate public understanding of its compensation levels, and released the results on the PMDA website.
- Based on the recommendations of the National Personnel Authority in FY 2017, PMDA revised the overall compensation system in addition to narrowing disparities in compensation standards between PMDA and the private sector. PMDA also reduced the retirement benefits for its employees in response to the reduced payment level of retirement benefits for national government employees.

2.4.(8) Development of a better workplace

- To promote work-life balance, PMDA engaged in tasks to reduce overtime and introduce a flexible working hour system as a Work-Style Reform.
- The average monthly overtime hours per general staff were 28 hours in FY 2013, 27 hours in FY 2014, 26 hours in FY 2015, 20 hours in FY 2016, and 17 hours in FY 2017. The overtime hours have been decreasing since PMDA started the Work-Style Reform project in June 2016, and did not exceed 20 hours, indicating a considerable decrease, after reinforcing its effort in December 2016. PMDA will continue to make efforts to achieve the following targets:

  (1) To be achieved by September 2018:
  No employees (including managerial-level staff) work in the office after 22:00 for ≥10 days per month.

  To be achieved by March 2019:
  No employees work in the office after 22:00.

  (2) To be achieved in FY 2018:
  Only ≤24 employees work ≥45 hours overtime per month (monthly average).

- In preparation for the introduction of the “Flexible Working Hours System” (from May 1, 2018), PMDA designed the system, revised the personnel management and salary systems, provided training for employees, and implemented trial operations.
- To create a work environment that is comfortable to work in, and as part of the working style reforms, PMDA began to discuss office reform efforts to revitalize staff communications and to make business operations more efficient.
- In April 2017, PMDA resumed the activities of the “Work-Life Balance Promotion Committee” operated by committee members chosen by the in-house staff recruitment system (17 members) to discuss activities to promote the work-life balance of the employees (15 meetings held in FY 2017).

  The “Flexible Working Hours System” was proposed by the Work-Life Balance Promotion Committee in 2015. The Committee made recommendations on how to design the system, contributing to its implementation in May 2018. The Committee then started operation of an

"Opinion Box" to widely accept proposals for improving staff's business operations. This could successfully improve practical operations.

To enhance communication levels between employees, the Committee held events planned mainly by committee members, and also prepared the "Guide to e-mailing," "Guide to Meeting Arrangement and Operation/Checklist," "Checklist for Communication," "Checklist for Handover of Business Operations," etc. to ensure that all employees are familiar with these leaflets.

2.4.(9) Development of the System to Secure Diversified Human Resources

- To secure diversified human resources, PMDA established a system that allows its employees and the employees of other organizations to implement PMDA's operations and operations of other organizations as persons authorized to work in both positions (Cross-appointment System) based on agreements with these organizations.

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, to reinforce security, PMDA designated restricted floors in its office locations that cannot be accessed by elevators unless the passengers (PMDA executives and employees, etc.) have appropriate ID cards. In June 2017, PMDA introduced a system that did not allow employees to access other offices than their own on holidays.
- PMDA has taken all reasonable efforts to thoroughly inform its staff of the office access restrictions through the PMDA intranet and new staff training programming.

2.5.(2) IT security measures

- In accordance with its FY 2017 plan, PMDA has been striving to maintain and improve the security of its IT systems and is operating a security management service, introduced in FY 2016. System configurations were modified and updated in response to the results of IT audits and guidance information provided by the National Center for Incident Readiness and Cybersecurity Strategy (NISC).
- 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.
- Based on the "Common Standards for Information Security Measures for Government Agencies and Related Agencies" (2016 version) revised in 2016, PMDA revised the PMDA Information Security Policy, and implemented IT security audits and provided IT security training programs.
- 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 2017.

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

	Number of registered companies	Certificates issued
Outside PMDA	4	58
Within PMDA		94

Note: The numbers of registered companies and certificates issued as of the end of FY 2017

PART 3 Improvements in Operational Management and Quality of Services Offered by Each 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 System). These activities are detailed below.

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

3.1.(1).(i) Disclosure of information (e.g., cases concluding in disbursement) 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 PMDA 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 System for Adverse Health Effects" web page.

3.1.(1).(ii) Improvement of PR materials, etc.

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

  a) The leaflet on the Relief System features the tagline "A system that all patients 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 System in a Q&A format. This helps readers who pick up the leaflet to understand the outline of the Relief System.

  Further, the design of the leaflet was improved to highlight the name of the system by increasing its visual impact, by using a *Mincho* font 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 System 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 the PMDA website. PMDA provides instructions on how to fill out the forms of various medical certificates on the PMDA website, for the greater convenience of claimants, physicians, etc. In FY 2017, these instructions were also introduced at such events as lectures for healthcare professionals.

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

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

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

Major activities conducted in FY 2017

(i) As a PR campaign on TV, 15-second commercials were aired through 33 nationwide TV stations, including *Nippon Television network, TBS network, Fuji Television network, TV Asahi network,* and *TV Tokyo network*, to familiarize the general public with the Relief System. The commercials appeared during the “Drugs and Health Weeks” (for 2 weeks from October 14-27, 2017). Also, through 30 nationwide TV stations, 30- to 60-second publicity infomercials (spot commercials) were run.

The TV commercial videos are available on a special promotional website featuring an original mascot character “Doctor Q”.

Commercial videos for download are available on the members’ only page on the official website of the Japan Pharmaceutical Association, with its cooperation.

(ii) A 1/6 page monochrome advertisement was placed in the morning editions of 5 national newspapers (*Yomiuri Shimbun, Asahi Shimbun, Sankei Shimbun, Nikkei Shimbun,* and *Mainichi Shimbun*) on October 17, 2017.

(iii) The following PMDA advertisements have been placed on the website:

- A special article featuring the Relief System was placed on Yahoo!JAPAN for 1 month from October 17 to November 16, 2017.
- An article featuring interviews with entertainers on the Relief System was placed on the website “ORICON NEWS” for 3 months from October 17, 2017 to January 16, 2018.
- A text advertisement was placed on the home page of Yahoo!JAPAN for 1 week from October 17 to 23, 2017.
- Targeted and listing advertisements were placed by using the display networks of Yahoo!JAPAN and Google for 3 months from October 17, 2017 to January 16, 2018.
- TrueView in-stream advertisements ran on YouTube videos for 3 months from October 17, 2017 to January 16, 2018.
- Advertisements on Twitter (promotweet in timeline) and Facebook (All Facebook-Link Ad) were placed during the period when the commercial videos were broadcast on TV.
- Advertisements were placed on a job search website for healthcare professionals known as “Sphere” for 3 months from October 17, 2017 to January 16, 2018.

(iv) A 30-second commercial was shown on 938 TV monitors in 825 medical institutions/pharmacies nationwide during the period from November 1-30, 2017.

A “still image commercial” appeared on a LCD monitor beside the cash register and a 15-second narration commercial was aired as background music in 14,645 FamilyMart convenience stores nationwide for 1 week from October 17, 2017.

(v) An advertisement was placed in 6 major medical publications during the month of November 2017 (one advertisement per newspaper 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 System and to foster public awareness, PMDA actively dispatches members of its staff to serve as lecturers at employee training courses organized by medical institutions or other organizations.

In FY 2017, in response to requests from medical and related institutions, PMDA dispatched staff to 48 medical institutions and 39 related organizations, etc., to explain the Relief System and provide examples of how some institutions effectively disseminate information regarding the Systems. PMDA also sent PR materials to 122 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 System 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 System 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 3 prefectures (Tokyo, Osaka, and Fukuoka).

(iii) Academic conferences

PMDA carried out PR activities through booth exhibitions and by distributing its leaflets etc. at the Congress of the Japanese Society for Regenerative Medicine and Annual Meetings of the Pharmaceutical Society of Japan.

(iv) Requests for cooperation to governmental entities, relevant organizations, etc.

PMDA informed 21 governmental entities and other relevant organizations of the current level of awareness of the Relief System, and requested their cooperation on PR-related activities.

(v) Others

PMDA distributed leaflets on the Relief System at the 19th Forum on Eradication of Drug-induced Suffering (sponsored by the Japan Federation of Drug-Induced Sufferers Organizations).

Others

(i) PMDA maintained a promotional 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 public relations materials on the PMDA website: A poster for the Relief System to be displayed in pharmacies and a medicine envelope printed with information on the Relief System.

(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. 347 (October 2017).”

(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 (FPMAJ), PMDA published information on the Relief System 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 System was provided in a leaflet “Useful Information about Medicines” distributed during the “Drugs and Health Week.” (The leaflet is published by MHLW and the Japan Pharmaceutical Association (JPA).)

(x) PMDA asked the JPA to retain the banner ad for the Relief System on the JPA’s public-facing web page in order to raise awareness of the system.

(xi) PMDA surveyed the level of awareness of the Relief System among the general public and healthcare professionals to make PR activities more effective.

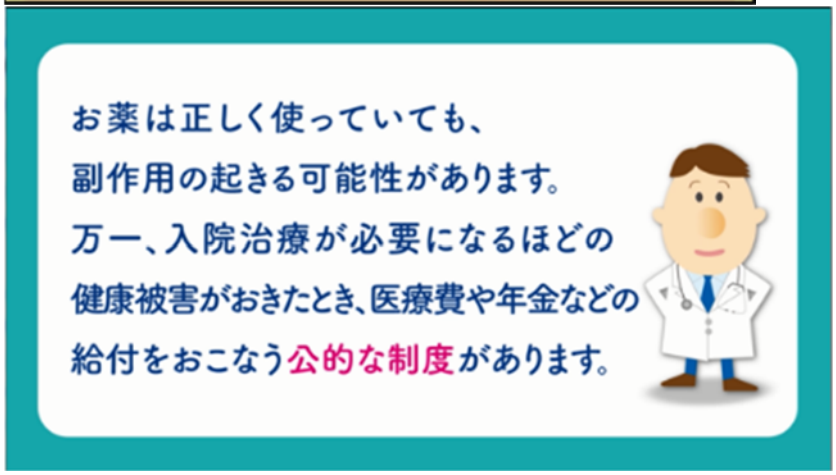
Survey period: December 21-28, 2017.

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

- 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 System, with the following options: “Physicians,” “Dentists,” “Pharmacists,” “Other medical institution staff,” “Newspaper, TV, etc.,” and “Others.” The most common answer in FY 2017 was “Physicians” (512 answers [34.0%]), followed by “Others (Internet)” (220 answers [14.6%]), “Newspaper/TV, etc.” (171 answers [11.4%]), and “Pharmacists” (136 answers [9.0%]) (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 2017, PMDA received 3,580 answers (multiple answers allowed): “The patient plans to claim benefits” (59 answers [1.6%]); “Already informed the patient of the Relief System” (164 answers [4.6%]); “The patient has no plan to claim benefits” (2,449 answers [68.4%]); “Not covered by the Relief System” (788 answers [22.0%]); and “Unknown/Others” (678 answers [18.9%]).

Home page of the promotional website

TV commercial



Newspaper Ad: 1/6 Page monochrome advertisement placed in national newspapers (*Yomiuri Shimbun, Asahi Shimbun, Sankei Shimbun, Nikkei Shimbun, Mainichi Shimbun, etc.*)

Web Advertisement (for publicity and to provide a link to the promotional website)

YAHOO! JAPAN 特別企画

提供：医薬品医療機器総合機構（PMDA）

その薬を飲む前に、知ってほしい副作用の話

最終更新：2017年10月17日（火）

病気や体調不良のとき、みなさんは薬を飲まれることがあると思います。薬を飲むとき、「副作用」という言葉は知っていても、普段、どのくらい気にされているでしょうか？
あまり気にされたことはないかもしれませんが、飲んだ薬が原因となり、ときには重い副作用を引き起こすことがあります。それは医師の処方せんが必要な薬でも、薬局・薬店で購入できる薬でも変わりません。まれではありますが、入院を必要としたり、身体に取り返しがつかない障害が残ったりすることもありますので、副作用について、ぜひ知っておいていただきたいことをご紹介します。

■薬の箱の中の説明書に書かれていること、じっくり読んだことはありますか？

写真提供：アフロ

「読んだことがない」、という方は、ぜひ一度手に取って読んでみてください。そこには、必ず副作用についての記載があると思います。また、病院で処方され渡される薬の説明書でも副作用について書かれています。

Promoting the Relief System through TV monitors placed in hospitals and pharmacies

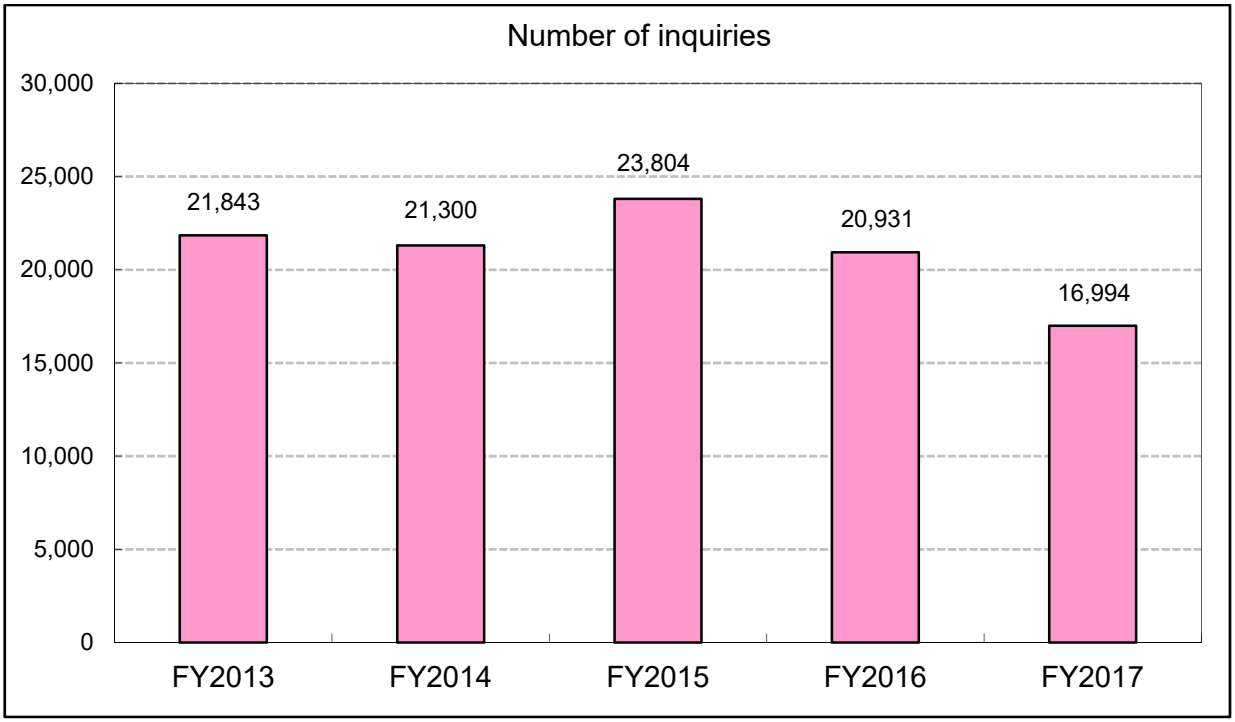
PR activities in major newspapers, magazines, and journals for healthcare professionals

◆ Double-page advertisement

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

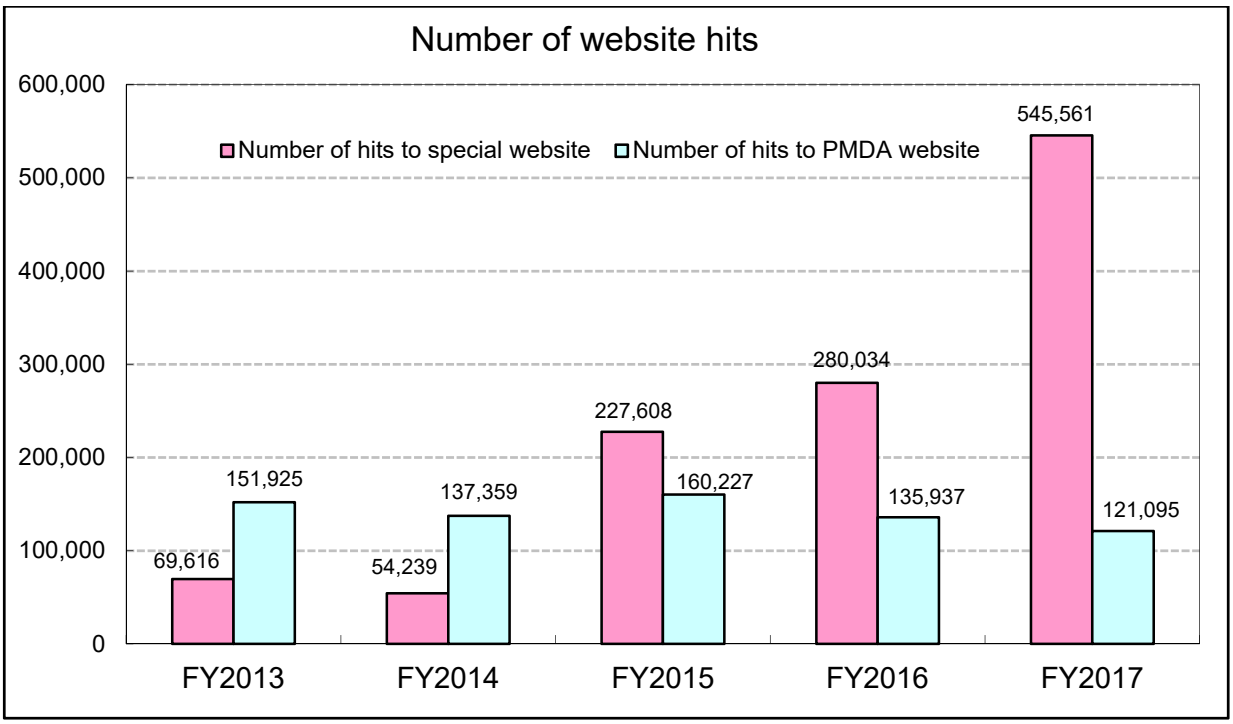
- In FY 2017, the Relief System Inquiry Service received 16,994 inquiries, which represents 81.2% versus FY 2016 (20,931 inquiries).

Fiscal year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	Versus FY 2016
Number of inquiries	21,843	21,300	23,804	20,931	16,994	81.2%



- In FY 2017, the PMDA website was accessed 121,095 times, which represents 89.1% versus FY 2016 (135,937 hits).
- The promotional website for the Relief System was accessed 545,561 times, which represents 194.8% versus FY 2016 (280,034 hits).

Fiscal year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	Versus FY 2016
Access to PMDA website	151,925	137,359	160,227	135,937	121,095	89.1%
Access to promotional website	69,616	54,239	227,608	280,034	545,561	194.8%



Relief System Inquiry Service

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

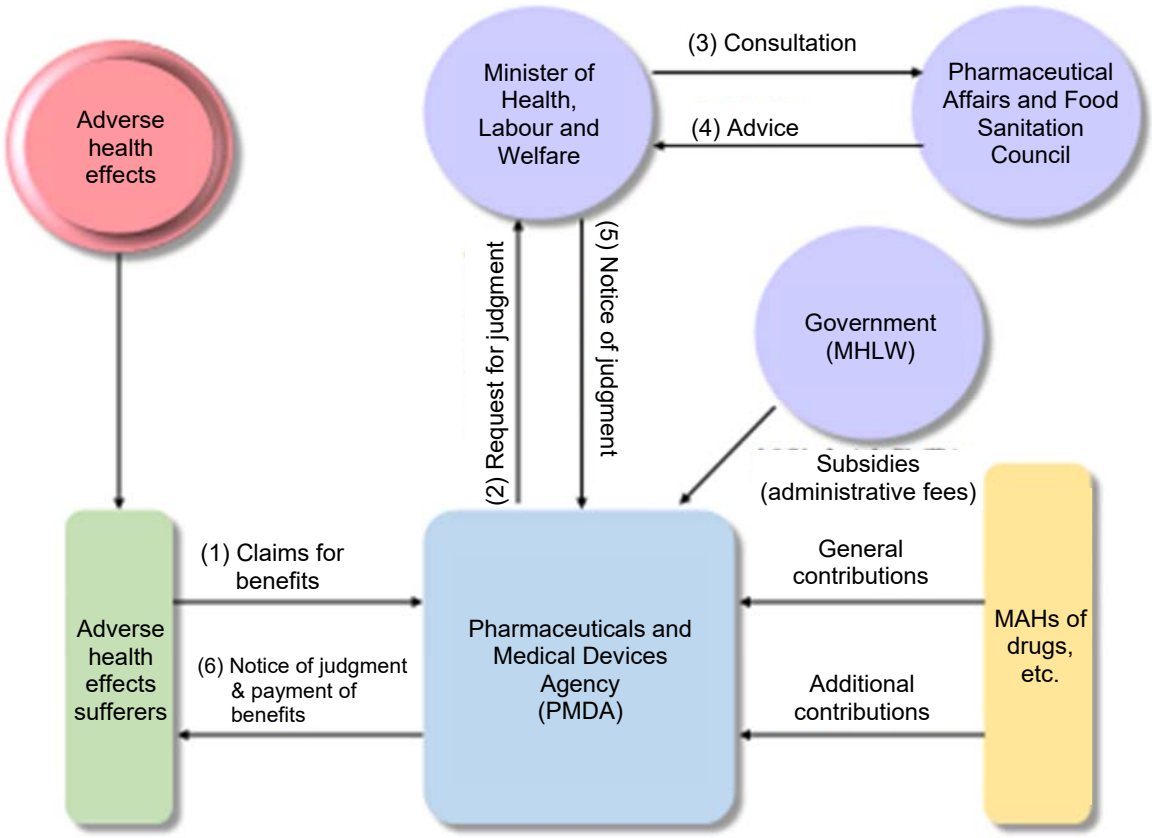
3.1.(4) Promotion of efficient database-backed services

- 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 2017, PMDA strove to process benefit claims received as quickly as possible, as in previous years.

  The number of claims submitted in FY 2017 decreased compared to the previous fiscal year, but exceeded the original prospects of the Third Mid-term Plan (FY 2014). PMDA has processed many of these claims, as in previous years. Among 1,607 claims received in FY 2017, PMDA processed 1,113 claims, accounting for 69.3%, within 6 months of filing. The achievement rate was the highest ever recorded.

  PMDA received 141 HPV-related claims in FY 2017 and processed 223 of the total claims ever received.

  The amount of benefits paid for claims reached a record high (approximately 2.352 billion yen).

HPV-associated claims

Fiscal year	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	Total
Number of claims filed	2	10	7	25	39	152	334	141	710
Number of claims judged	0	5	9	8	4	75	314	223	638

3.1.(5).(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.

3.1.(5).(i).a. Performance of the Relief Service for adverse drug reactions

The performance for FY 2017 is shown below.

Fiscal year			FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of claims filed			1,371	1,412	1,566	1,843	1,491
Number of claims judged			1,240	1,400	1,510	1,754	1,607
		Approved	1,007	1,204	1,279	1,340	1,305
		Rejected	232	192	221	411	298
		Withdrawn	1	4	10	3	4
	Within 6 months	Number of claims	754	867	915	1,182	1,113
		Achievement rate[*1]	60.8%	61.9%	60.6%	67.4%	69.3%
Claims in progress[*2]			910	922	978	1,067	951
Median processing time (months)			5.8	5.7	5.6	5.3	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.*

3.1.(5).(i).b. Number of claims by type of benefit

The numbers of claims filed in FY 2017 by type of benefit are shown below.

Fiscal year		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of claims filed		1,371	1,412	1,566	1,843	1,491
Types of benefit	Medical expenses	1,200	1,221	1,341	1,595	1,289
	Medical allowances	1,252	1,290	1,428	1,693	1,354
	Disability pensions	88	95	109	111	117
	Pensions for raising handicapped children	7	12	7	8	9
	Bereaved family pensions	49	41	37	56	46
	Lump-sum benefits for bereaved families	54	65	61	71	57
	Funeral expenses	105	103	100	128	102

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

3.1.(5).(i).c. Approval by type of benefit

The number of approved claims and amounts of benefits paid in FY 2017 by type of benefit are shown below.

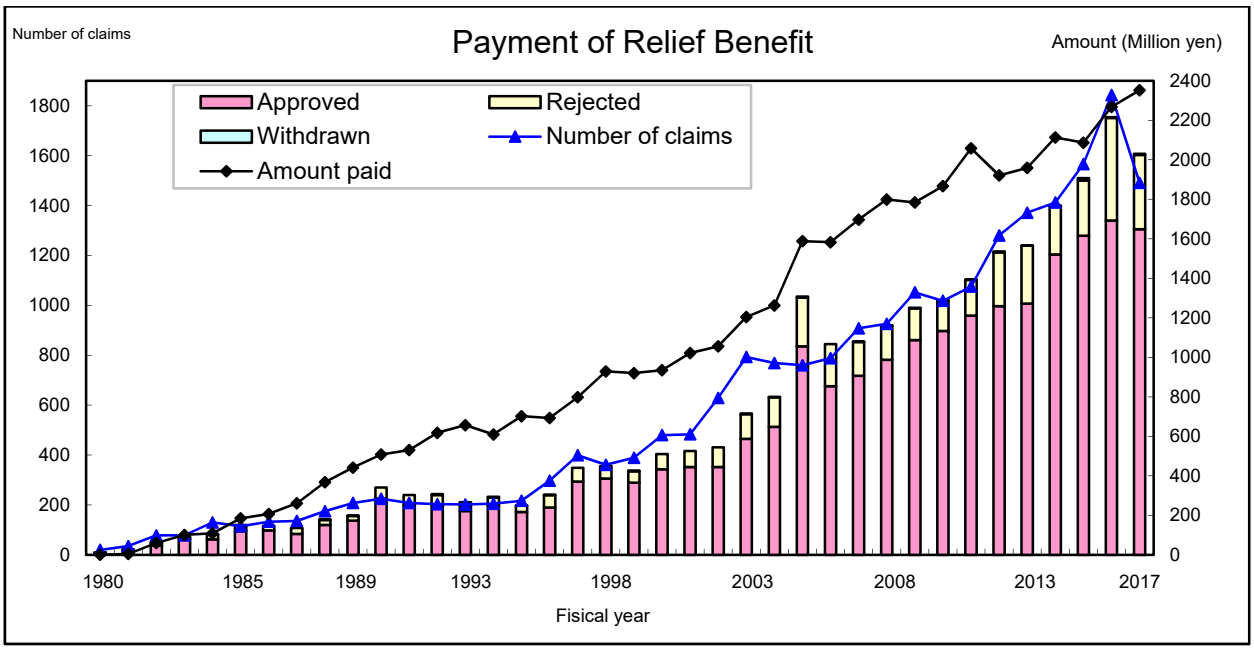
(Unit: Thousand yen)

Type	FY 2013		FY 2014		FY 2015	
	No. of claims	Amount paid	No. of claims	Amount paid	No. of claims	Amount paid
Medical expenses	886	95,025	1,108	123,987	1,146	118,235
Medical allowances	945	82,730	1,151	95,457	1,220	112,040
Disability pensions	39	905,233	37	943,939	47	1,002,305
Pensions for raising handicapped children	3	40,785	2	38,965	8	43,675
Bereaved family pensions	31	603,130	31	585,626	23	580,934
Lump-sum benefits for bereaved families	32	220,032	45	310,806	32	218,891
Funeral expenses	59	12,249	72	14,507	53	10,822
Total	1,995	1,959,184	2,446	2,113,286	2,529	2,086,902

Type	FY 2016		FY 2017	
	No. of claims	Amount paid	No. of claims	Amount paid
Medical expenses	1,190	136,997	1,178	118,173
Medical allowances	1,269	120,109	1,240	109,652
Disability pensions	53	1,082,599	45	1,156,881
Pensions for raising handicapped children	6	42,153	4	35,676
Bereaved family pensions	31	607,497	36	642,861
Lump-sum benefits for bereaved families	38	263,243	38	272,887
Funeral expenses	73	14,944	75	15,415
Total	2,660	2,267,542	2,616	2,351,545

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.



3.1.(5).(i).d. Number of current status reports from pension recipients

In FY 2017, PMDA received 624 (588) current status reports from pension recipients: 378 (343) from those receiving disability pension, 37 (36) from those receiving pensions for raising handicapped children, and 209 (209) from those receiving bereaved family pension.

* The figures in parentheses represent the number of reports received in FY 2016.

3.1.(5).(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.

3.1.(5).(ii).a. Performance of relief service for infections

The performance for FY 2017 is shown below.

Fiscal year		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of claims filed		7	3	6	1	3
Number of claims judged		4	7	2	5	2
	Approved	4	6	1	3	2
	Rejected	0	1	1	2	0
	Withdrawn	0	0	0	0	0
Claims in progress*1		5	1	5	1	2
Achievement rate*2		100.0%	42.9%	50.0%	20.0%	50.0%
Median processing time (months)		4.3	6.3	7.5	10.0	10.2

**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.*

3.1.(5).(ii).b. Number of claims by type of benefit

The numbers of claims filed in FY 2017 by type of benefit are shown below.

Fiscal year		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of claims filed		7	3	6	1	3
Types of benefit	Medical expenses	6	2	5	1	1
	Medical allowances	7	3	5	1	2
	Disability pensions	0	0	0	0	0
	Pensions for raising handicapped children	0	0	0	0	1
	Bereaved family pensions	0	1	2	0	0
	Lump-sum benefits for bereaved families	1	1	0	0	0
	Funeral expenses	1	2	2	0	0

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

3.1.(5).(ii).c. Approval by type of benefit

The number of approved claims and amounts of benefits paid in FY 2017 by type of benefit are shown below.

(Unit: Thousand yen)

Type	FY 2013		FY 2014		FY 2015		FY 2016		FY 2017	
	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	3	258	5	336	1	0	3	92	2	339
Medical allowances	4	356	6	566	1	170	3	210	2	248
Disability pensions	–	–	–	–	–	–	–	–	–	–
Pensions for raising handicapped children	–	–	–	–	–	–	–	–	–	–
Bereaved family pensions	–	2,353	–	2,338	–	2,393	–	1,005	–	–
Lump-sum benefits for bereaved families	–	–	–	–	–	–	–	–	–	–
Funeral expenses	–	–	–	–	–	–	–	–	–	–
Total	7	2,967	11	3,239	2	2,563	6	1,306	4	587

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 appropriate information communication through interoffice collaboration

- The Office of Relief Funds and the Offices of Safety conducted joint meetings approximately once a month to promote information sharing.
- The Office of Relief Funds periodically provides the following information to the Office of Safety, after taking appropriate measures to protect personal information in order to ensure that this information can be reflected in safety measures in accordance with Article 68-10 of the PMD Act: Information on diseases, disorders, and/or death of persons who filed claims for relief benefits for adverse reactions and/or infections, and information on the decision on approval/rejection of claims.
- 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 I 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.)

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

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 2017, PMDA summarized the Team's operating performance during FY 2016, prepared an investigative research report, and conducted investigative research targeting 72 individuals presenting with serious adverse health effects, including Stevens-Johnson syndrome, Reye's syndrome, and conditions 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 (72 volunteers in FY 2017).

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

3.1.(7).(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 experiencing significant restrictions to their normal activities of 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 System. 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 2017, 138 consultation sessions were held.

3.1.(7).(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 2017, PMDA issued such certificates to 749 recipients.

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

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 2017, PMDA summarized the operating performance for FY 2016, prepared an investigative research report, and conducted research in 153 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 (153 volunteers in FY 2017).

Research Team

Team Leader:	Kugahisa Teshima	Former Professor, Graduate School of Social Service, Japan College of Social Work
Team Members:	Namiki Izumi	Director, Musashino Hospital, Japanese Red Cross Society
	Midori Shima	Professor, Department of Pediatrics, Nara Medical University
	Akira Terashima	Advisor, Japanese Society for Rehabilitation of Persons with Disabilities

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.

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

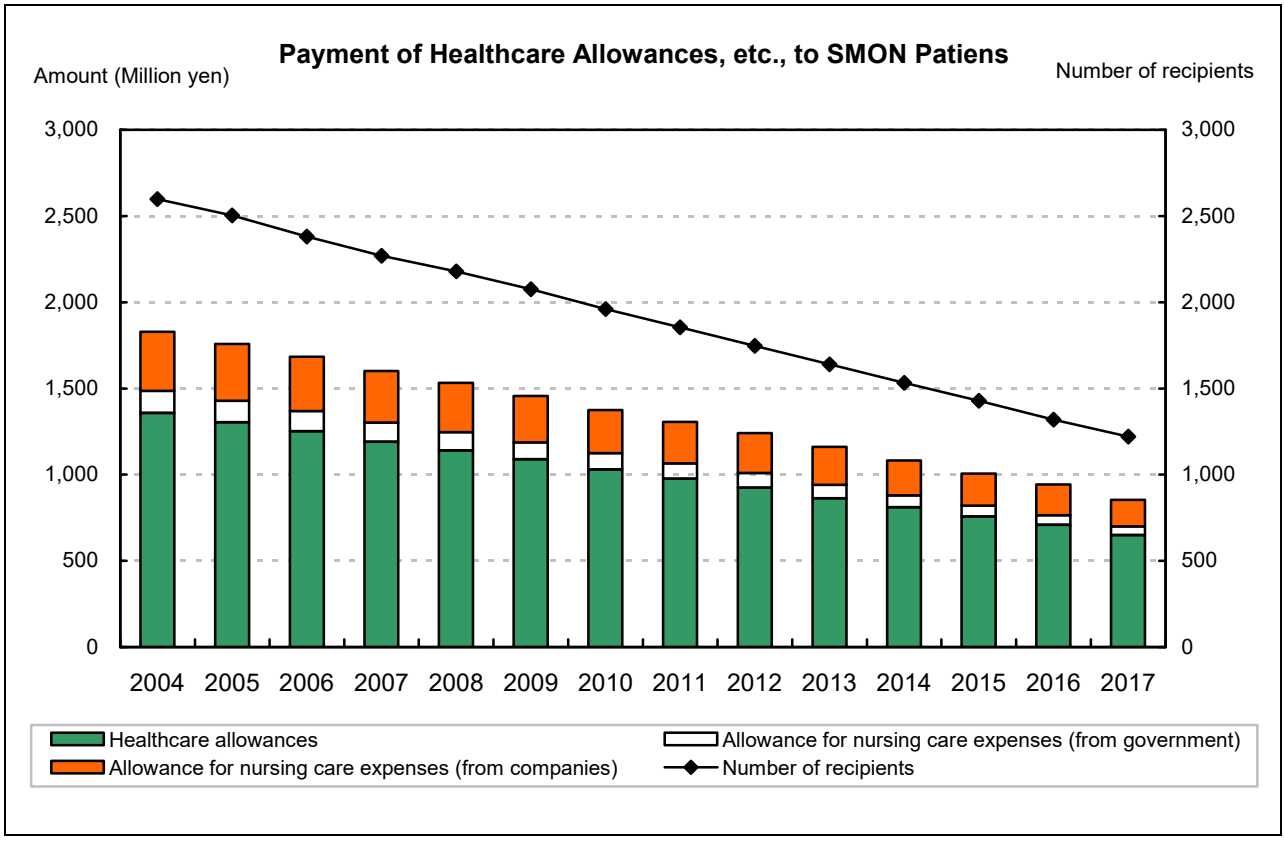
- PMDA provides healthcare allowances and nursing care expenses to patients suffering from subacute myelo-optic neuropathy (SMON) for whom an out-of-court settlement was reached. In FY 2017, a total of 855 million yen was paid to 1,221 patients.

  * SMON arising from use of quinoform products

  SMON is a disease caused by quinoform products (antiflatulents) that leads to numbness, ambulatory difficulties, visual disturbances, etc. According to a research group, approximately 10,000 individuals are estimated to have been affected by SMON.

Fiscal year		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of recipients		1,639	1,533	1,428	1,319	1,221
Amount paid (thousand yen)		1,160,944	1,082,992	1,006,135	942,828	855,351
Breakdown	Healthcare allowances	864,462	811,727	757,285	709,290	651,047
	Allowance for nursing care expenses (from companies)	219,630	201,919	185,319	176,639	154,037
	Allowance for nursing care expenses (from government)	76,902	69,346	63,532	56,899	50,267

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."



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

- PMDA provides the following three services for patients infected with HIV through blood products (services commissioned by the Yu-ai Welfare Foundation). In FY 2017, 509 HIV-positive patients received allowances under the investigative research, 119 patients with AIDS under the

healthcare support service, and 3 patients with AIDS received special allowances. In total, 631 patients received allowances under the three services (503 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

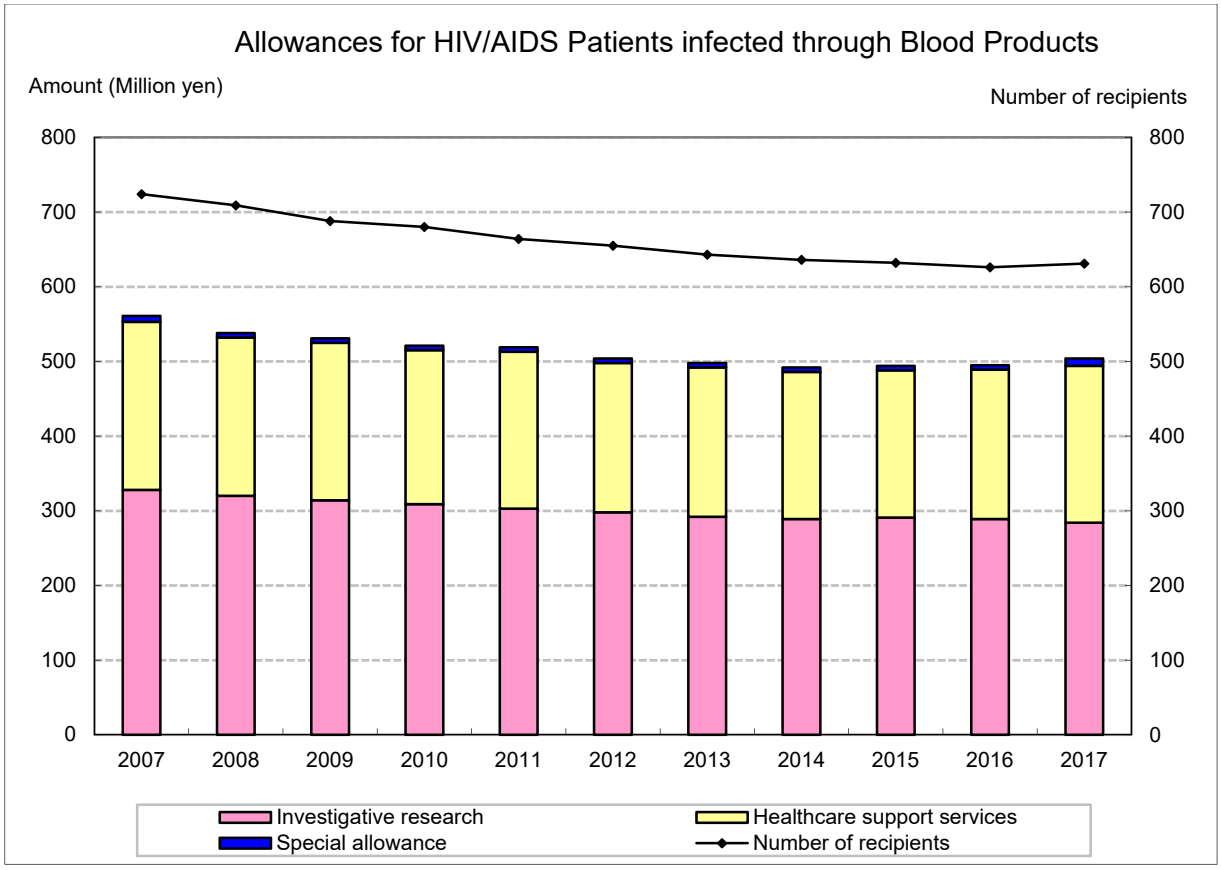
* HIV infection due to blood products

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 2013		FY 2014		FY 2015	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	529	292,349	524	288,736	520	290,935
Healthcare support services	112	199,650	110	197,400	110	197,400
Special allowance	2	6,232	2	6,190	2	6,336
Total	643	498,230	636	492,325	632	494,671

Fiscal year	FY 2016		FY 2017	
	Number of recipients	Amount paid (thousand yen)	Number of recipients	Amount paid (thousand yen)
Investigative research	513	288,703	509	283,700
Healthcare support services	111	199,650	119	209,700
Special allowance	2	6,384	3	9,565
Total	626	494,737	631	502,965

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.



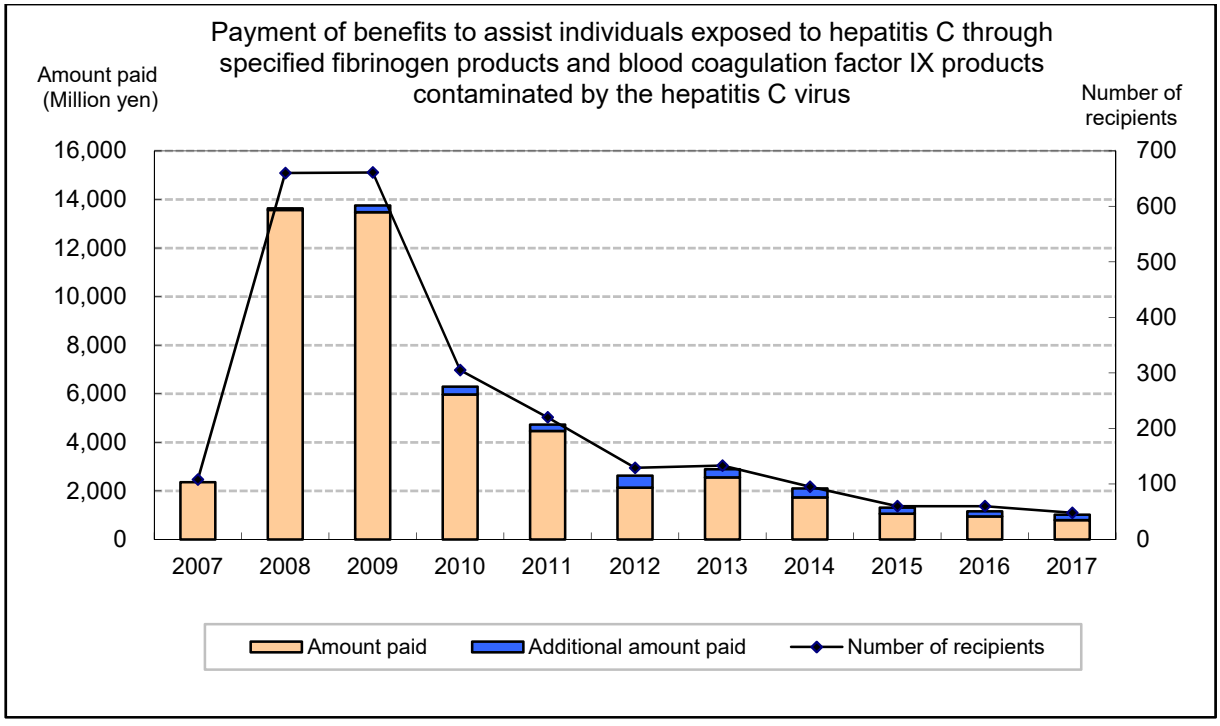
3.1.(9) Appropriate provision of benefits to individuals with hepatitis C caused by specified fibrinogen products and specified blood coagulation factor IX products

- 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 2017, 48 patients received benefits (of whom, 13 patients received additional benefits), and the total amount of benefits paid was 1.02 billion yen (of them, the amount of additional benefits was approximately 0.22 billion yen).

* A revised Act went into effect on December 15, 2017, and thereby the time frame for claiming benefits was extended by 5 years (Until January 16, 2023).

	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012
Number of recipients	660	661	305	220	129
(Number of these recipients receiving additional payment)	(4)	(22)	(20)	(20)	(28)
Amount paid (thousand yen)	13,632,000	13,748,000	6,293,000	4,732,000	2,624,000
(Amount of additional payment)	(68,000)	(272,000)	(324,000)	(268,000)	(488,000)
Number of inquiries	3,607	894	1,286	674	982

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of recipients	133	95	60	60	48
(Number of these recipients receiving additional payment)	(18)	(20)	(14)	(14)	(13)
Amount paid (thousand yen)	2,888,000	2,100,000	1,308,000	1,156,000	1,020,000
(Amount of additional payment)	(332,000)	(368,000)	(252,000)	(208,000)	(224,000)
Number of inquiries	473	660	834	1,087	2,508



3.2. Reviews and Related Services

Based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14, 2013), 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 (it is also referred to as the 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 Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D); 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 2017, 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

3.2.(1).A. 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.

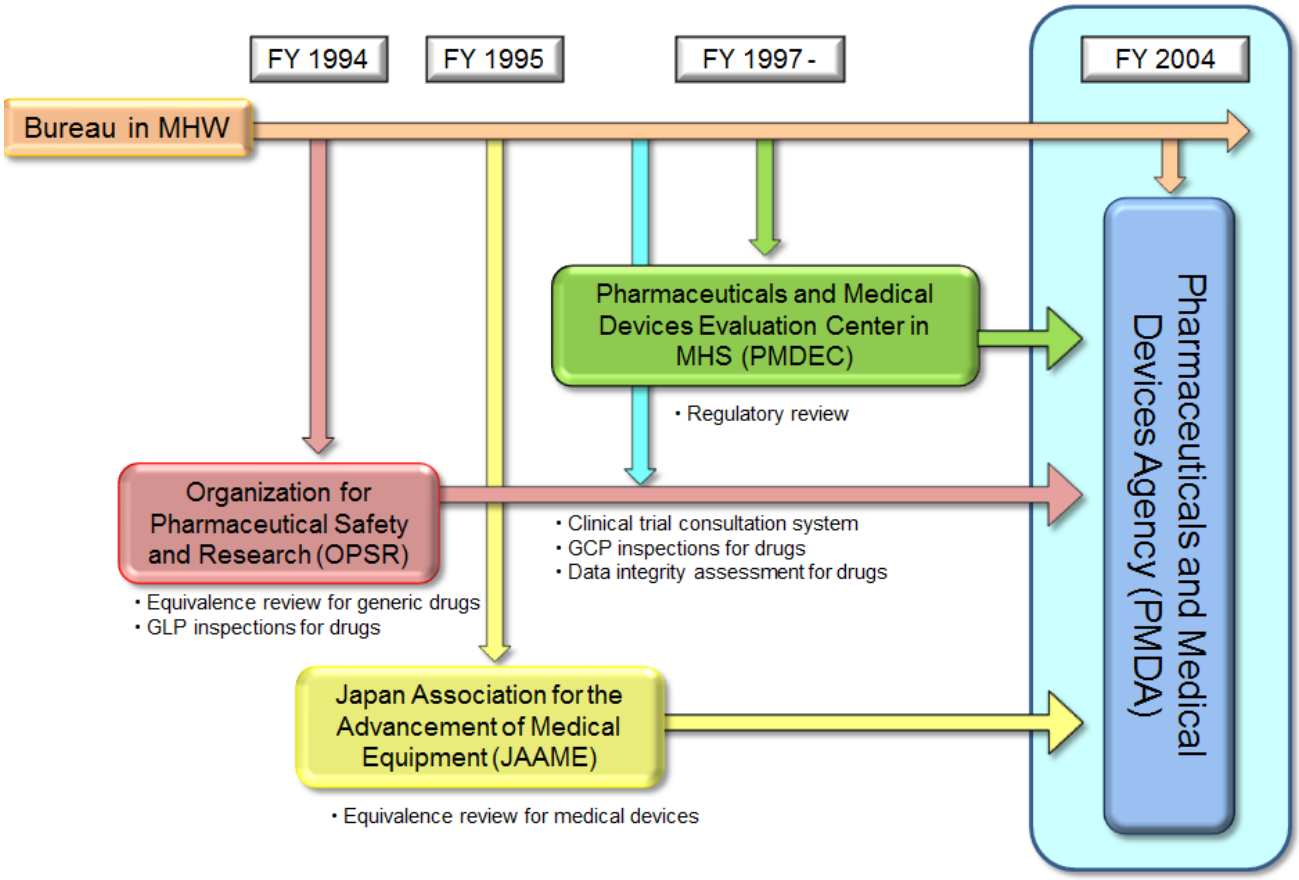
3.2.(1).A.(i) Appropriate and prompt reviews

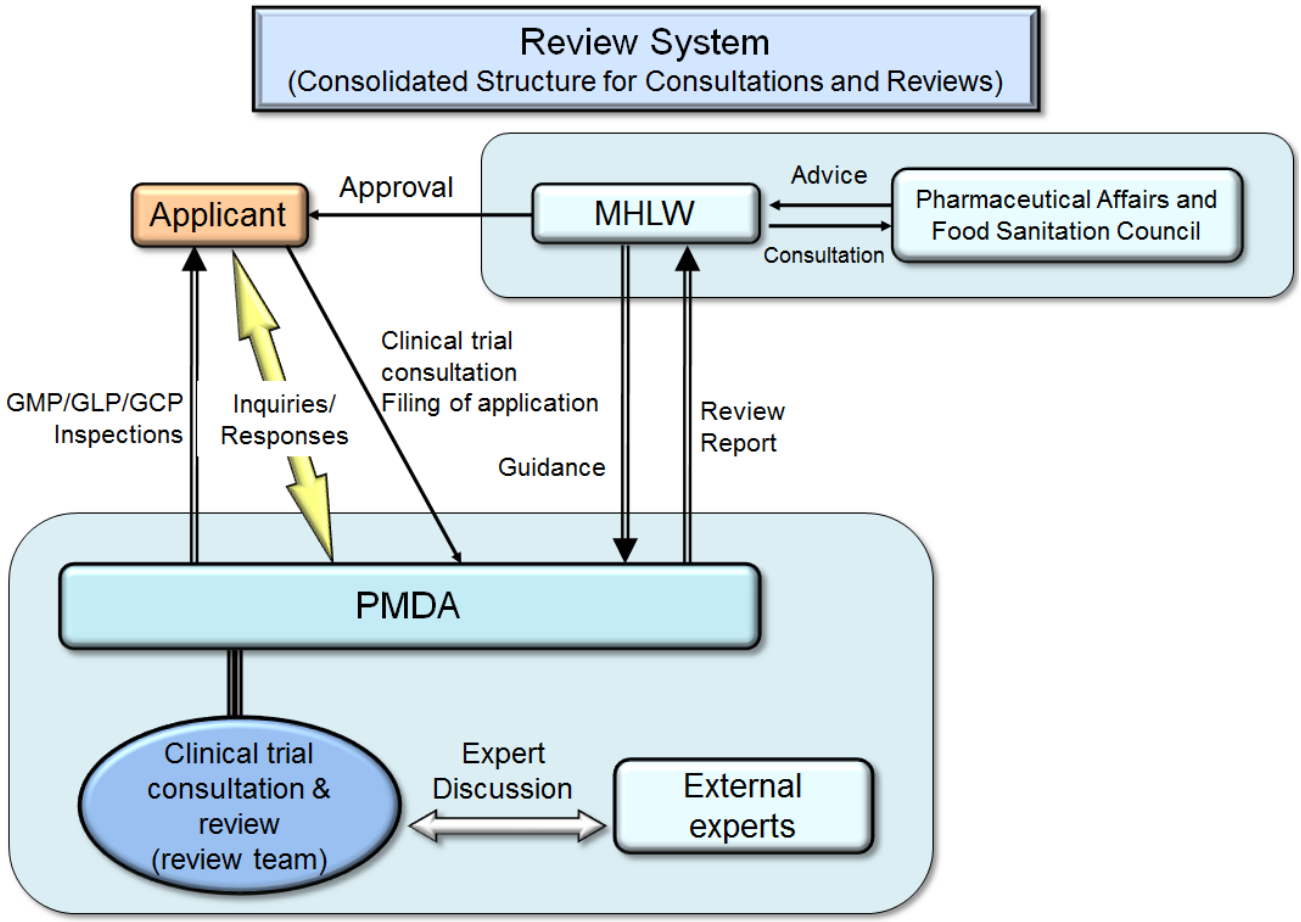
3.2.(1).A.(i).a. Structure for clinical trial consultations and reviews

- 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:

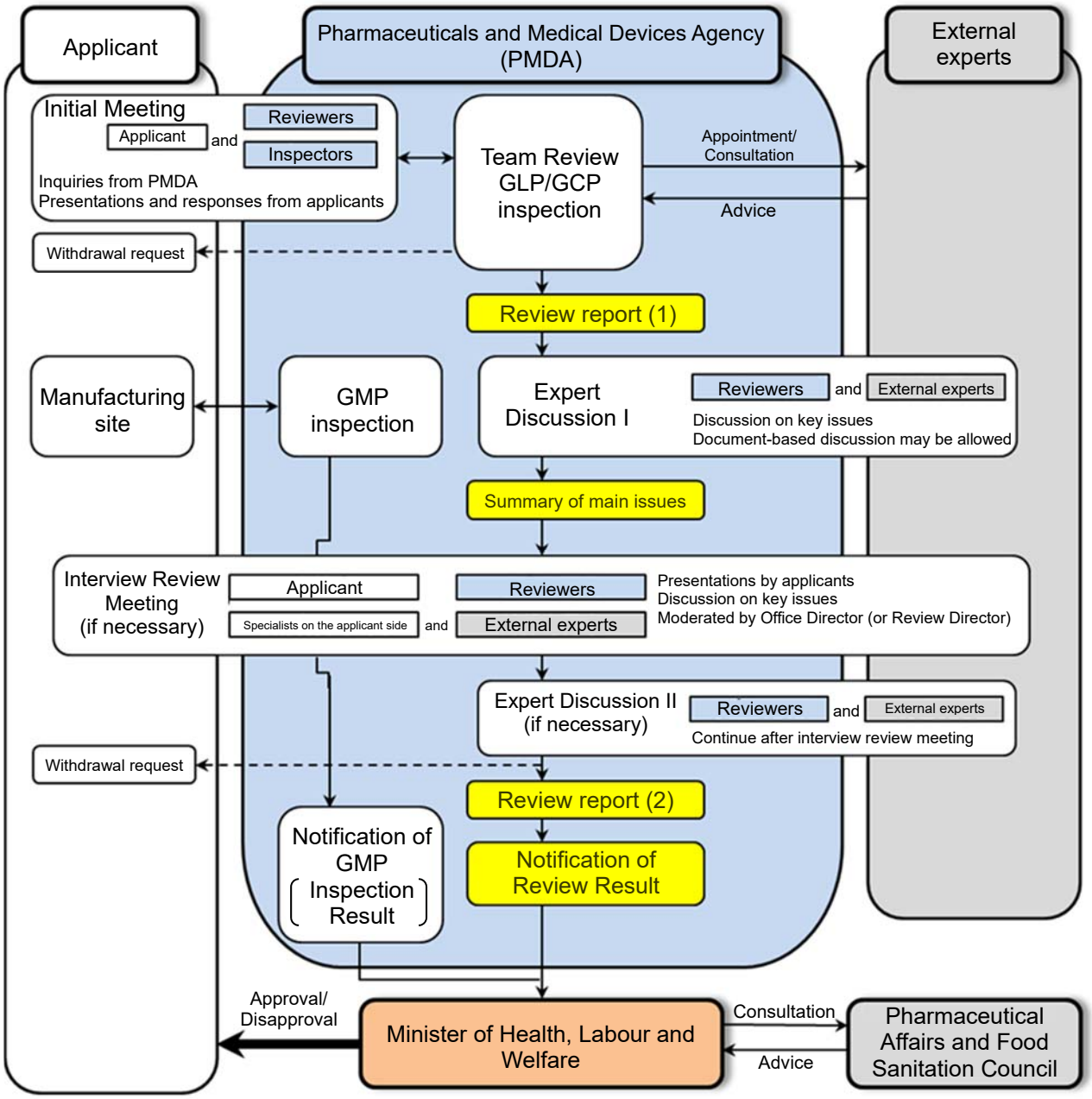
  1) In order to ensure the consistency and efficiency, the roles of three review-related agencies were thoroughly re-examined and integrated into a single "independent administrative agency, the Pharmaceuticals and Medical Devices Agency."
  2) Substantial increase in the number of staff including reviewers.
  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.
  6) Acceptance and analysis of electronic data for new drug applications.

Transition of approval review system on drugs and medical devices





Flowchart of review process

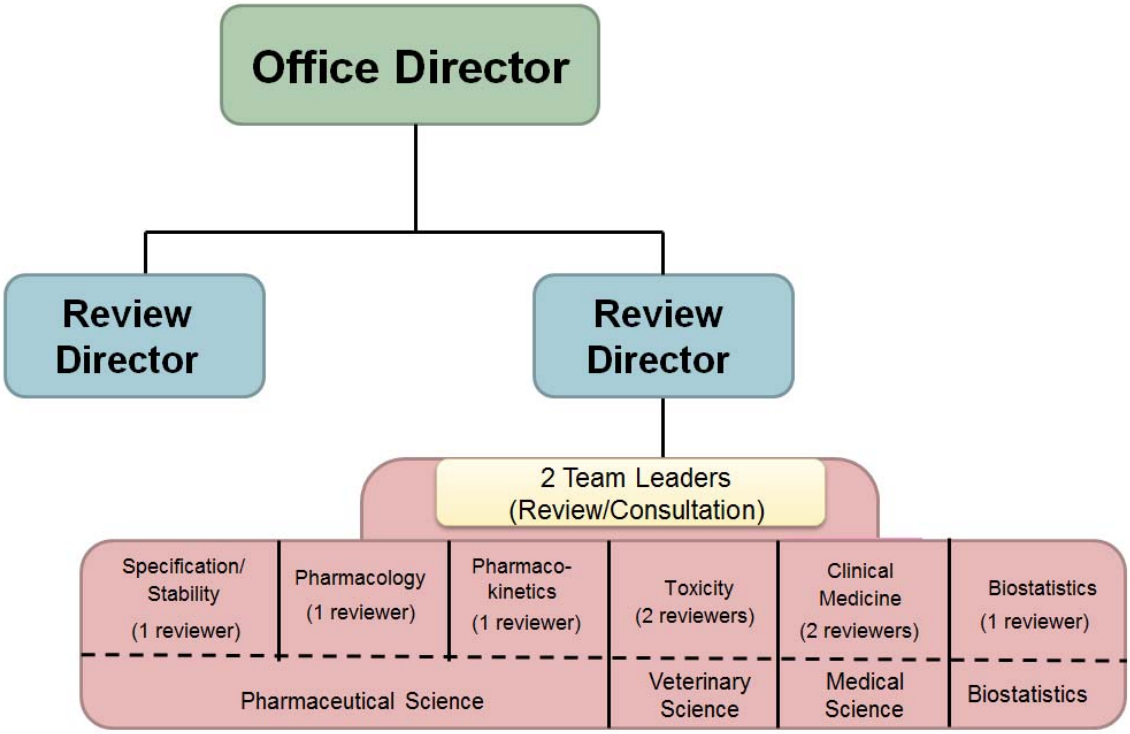


Review Performance for FY 2017 (drugs)

(1) Number of Expert Discussions conducted: 230 (192 document-based discussions, 38 meetings)
(2) Applications reviewed by the Drug Committees (under Pharmaceutical Affairs and Food Sanitation Council [PAFSC]): 67
Applications reported to the Drug Committees (under PAFSC): 38

- 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 pharmacology, 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, 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-CMCs	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 face-to-face or document-based clinical trial consultations on new drugs based on the team-reviewed guidance/advice 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.

3.2.(1).A.(i).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 2017, 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. (12 meetings held in FY 2017.)

  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 "Approach to Explaining Progress in the 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.

3.2.(1).A.(i).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.

3.2.(1).A.(i).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 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 in Japan. In FY 2017, 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 US 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 US FDA or EMA in or after April 2009, 148 (US FDA) and 105 (EMA) have not been approved in Japan as of March 2018. The list of the unapproved drugs is available on the PMDA website.

3.2.(1).A.(i).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 2017.

3.2.(1).A.(i).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.
- 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 2017, re-examination result notifications were issued for 75 applications (180 products), with the median total review time being 17.8 months.

Number of Re-examinations/Re-evaluations Conducted

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Products undergoing re-examination	121	86	114	119	218

Note 1: The figures represent the number of products for which a notification of re-examination results was issued in respective fiscal year.

Note 2: Including applications submitted before FY 2014.

3.2.(1).A.(i).g. Development of the Japanese Pharmacopoeia draft

1) Development of the Japanese Pharmacopoeia draft

- In FY 2017, the Japanese Pharmacopoeia (JP) Draft Committee held 77 meetings. Subsequently, PMDA published on its website a draft of Supplement 2 to the Japanese Pharmacopoeia 17th edition to seek public comments: 112 official monographs (36 new articles, 75 amendments, 1 deletion), 20 general tests and general information (8 new tests, 12 amendments), 7 ultraviolet-visible reference spectra (7 new tests), 9 infrared reference spectra (9 new tests), and partial amendment to other general notices and general rules for preparations. Supplement 2 will be announced in the spring of 2019. PMDA also published on its website a draft of the Japanese Pharmacopoeia 18th edition to seek public comments on the revision of the general rules and the deletion of alternative names. The Japanese Pharmacopoeia 18th edition will be announced in the spring of 2021.

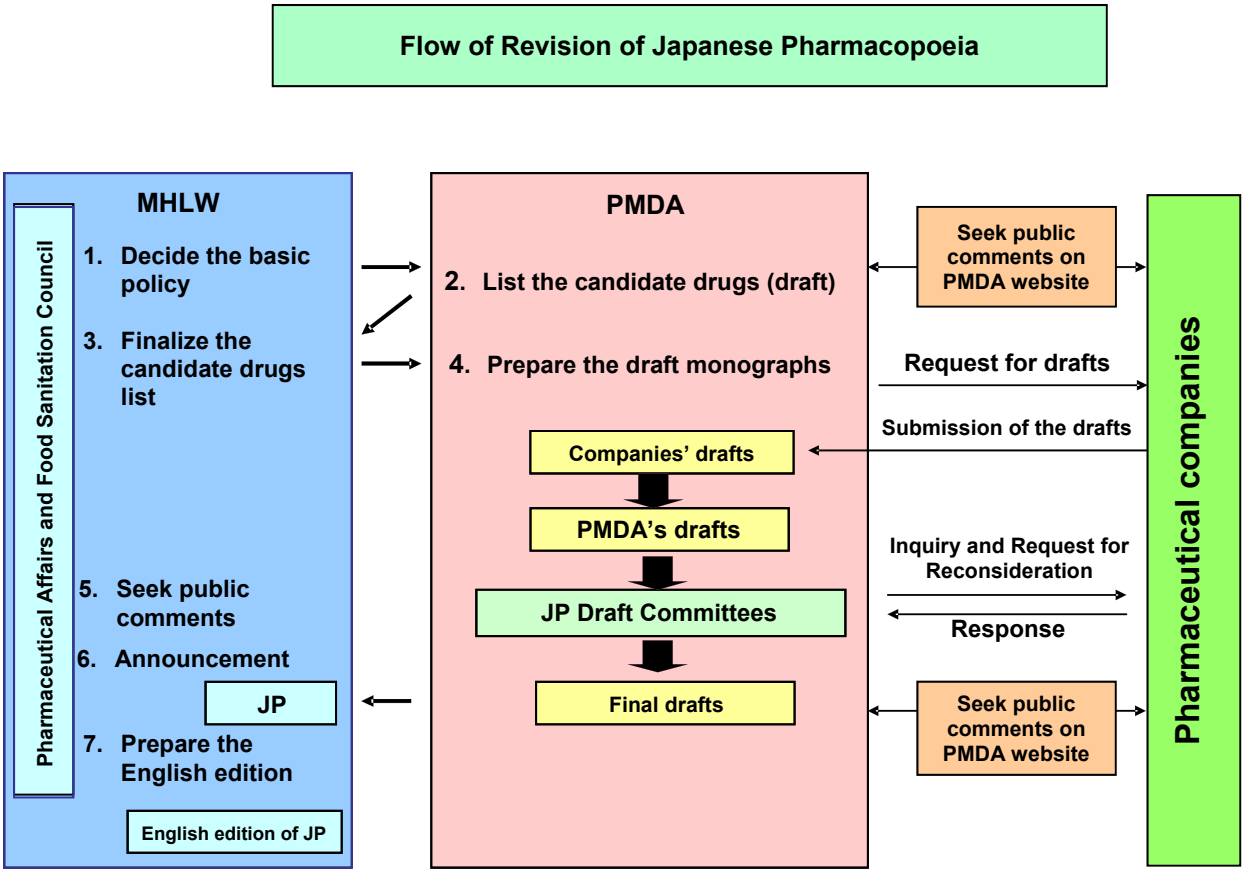
  The table below shows the number of drafts of official monographs reported to MHLW.

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

Note: In addition to drafts of the official monographs shown in this table, PMDA prepares drafts of 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 announcement of new JP. PMDA provided no drafts of General Notices etc.to MHLW in FY 2017, because no new or revised versions were announced during the year. PMDA will prepare and provide new drafts of General Notices etc. to MHLW in FY 2019 (for Supplement 2 to the 17th edition, to be announced in FY 2019).

Announcement of the Japanese Pharmacopoeia by MHLW

	16th edition	16th edition Supplement 1	Partial revision	16th edition Supplement 2	17th edition	17th edition Supplement 1
Month and year announced	FY 2011 Mar.	FY 2012 Sep.	FY 2014 May	FY 2014 Feb.	FY 2016 Mar.	FY 2017 Dec.
New monographs	106	77	0	60	76	32
Amendments	330	176	1	173	471	114
Deleted monographs	15	4	0	1	10	17
Total number of monographs	1,764	1,837	1,837	1,896	1,962	1,977



- PMDA published a draft of Supplement 2 to the 17th edition of the Japanese Pharmacopoeia to seek public comments in English on official monographs concerning all new drugs and some new general tests on the Japanese Pharmacopoeia page on the PMDA website. Supplement 2 will be announced in the spring of 2019.

2) Issuance of notifications, etc.

- PMDA developed a Q&A document regarding new drug application in response to the establishment of the Japanese Pharmacopoeia 17th edition, and reported them to MHLW. The a Q&A document was issued by MHLW (PSEHB/PED Administrative Notice, dated April 7, 2017, by the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).
- PMDA prepared a summary of Supplement 1 to the Japanese Pharmacopoeia 17th edition and a handling policy of new drug application in response to the establishment of Supplement 1, and reported them to MHLW. The summary and policy were issued by MHLW (PSEHB Notification No. 1201-3 dated December 1, 2017, by the Director General of the Pharmaceutical Safety and Environmental Health Bureau, MHLW; PSEHB/PED Notification No. 1201-3 dated December 1, 2017, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW.)

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.

- The PDG harmonized document (cover sheet) was posted on the website of the international harmonization of the Pharmacopoeia 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, Pharmaceutical Safety and Environmental Health Bureau, 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.

5) Japanese Accepted Names for Pharmaceuticals (JAN)

- PMDA held 6 meetings of Expert Discussion on drug names, thereby contributing to the establishment of 58 new Japanese Accepted Names for Pharmaceuticals (JAN).
- PMDA held 2 document-based Expert Discussions on drug names, thereby submitting comments to the World Health Organization (WHO) and revising the chemical names of already existing JANs.

Number of Applications and Notifications for new JANs and Number of new JANs established

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
(a) No. of applications and notifications for new JANs or for revisions to existing JANs	53	62	62	51	60
(b) No. of new JANs established	53	67	60	67	58
(c) No. of revisions to existing JANs	0	5	0	0	0
(d) No. of applications and notifications withdrawn	-	-	-	8	4

Note: (b), (c), and (d) include applications and notifications submitted, but not processed, in the previous fiscal years. The procedure for withdrawal (d) is based on the "Q&A for Handling of Non-proprietary Names of Drugs" (PSEHB/ELD Administrative Notice dated March 31, 2016, by the Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

3.2.(1).A.(i).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 via FAX at the request of in-country representatives and published representative cases on the PMDA website for reference purposes.

3.2.(1).A.(ii) Introduction of new review systems

3.2.(1).A.(ii).a. Implementation of prior assessment consultations

- To evaluate the quality, efficacy, and safety of drugs from the pre-application stage, PMDA has offered prior assessment consultations, as a pilot program from FY 2009 to 2010, and as a formal program since FY 2011. In FY 2017, PMDA received consultation request forms in October, and offered consultations to all requests, all in different consultation categories.

3.2.(1).A.(ii).b. Consideration toward the construction of the Advanced Review and Consultation with Electronic Data

- PMDA began to accept the electronic submission of clinical study data (hereinafter referred to as “electronic application data”) through the Electronic Application Data System on October 1, 2016, and received data for 31 products in FY 2017. The system has functions to receive electronic data submission from corporations, archive submitted electronic data at PMDA, and conduct statistical data analysis/processing. PMDA has updated configurations to solve problems associated with the operation of the system, and has revised the system manual for applicant companies on a regular basis.
- PMDA continued to exchange opinions with related industries regarding various issues on electronic submission of application data and made partial revisions 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 October 1 and 2, 2017, 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.
- PMDA began to offer “Consultations 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.

Number of consultations for electronic study data submission

	FY 2015	FY 2016	FY 2017
Number of requests	13	62	65
Conducted	11	55	70

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 held case study meetings about modeling and 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.

3.2.(1).A.(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 describe the status of reviews of new drugs in FY 2017 (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.

3.2.(1).A.(iii).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	60th	60th	70th	70th	80th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time [months] (Reference, 80th percentile) [months]	7.2 (9.1)	8.8 (9.2)	8.7 (9.5)	8.8 (9.2)	8.9 (9.0)
Number of approved applications	42	44	37	38	38

Reference

Regulatory review time [months]	3.6	4.0	4.0	4.0	4.9
Applicant's time [months]	3.8	5.0	4.9	5.3	5.4

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

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time [months] (Reference, 80th percentile) [months]	8.0 (9.9)	8.9 (9.2)	8.8 (9.8)	8.8 (9.3)	8.9 (9.0)
Regulatory review time [months]	3.4	3.8	4.0	3.9	4.8
Applicant's time [months]	4.1	5.2	5.2	5.5	5.5
Number of approved applications	31	37	33	32	33

- Priority reviews are conducted for applications for orphan drugs and other drugs that are regarded as having particularly high medical need (drugs for serious diseases and with distinctly superior efficacy or safety as compared to existing drugs or therapies). In FY 2017, 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 2017, PMDA received 5 applications for priority reviews for drugs regarded to have particularly high medical needs. During the fiscal year, 4 applications were judged to be eligible for priority review, with none judged to be ineligible. PMDA also received 2 applications for review under the conditional early approval system in FY 2017, but none were judged to be eligible or ineligible for the review system during the fiscal year.
- The priority review products accounted for 37% of products approved in FY 2017, showing an increase from 34% in FY 2016.

3.2.(1).A.(iii).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	60th	70th	70th	80th	80th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	70th	70th	80th
Total review time [months] (Reference, 80th percentile) [months]	11.3 (12.3)	11.9 (12.3)	11.3 (11.7)	11.6 (12.0)	11.8
Number of approved applications	96	73	79	74	66

Reference

Regulatory review time [months]	6.7	6.8	7.3	7.3	7.7
Applicant's time [months]	4.6	5.4	5.8	6.0	7.0

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."

- In total, 85 applications were under review at the end of FY 2017 (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	119 (1)	0	4	0 [-1]
FY 2014	128	118	0	9	1
FY 2015	125	119 (4)	0	5 (1)	1 [-5]
FY 2016	101	94 (70)	0	3 (2)	4 [-72]
FY 2017	110	29 (29)	0	4 (4)	77
Total	1,638	1,419 (104)	1	133 (7)	85 [-2]

Note 1: The figures in parentheses in "Approved" and "Withdrawn" represent the number of applications processed in FY 2017 (included in figures to the left).

Note 2: The figures in brackets represent differences from the status reported in FY 2016.

3.2.(1).A.(iv) Promotion of global clinical trials

- In order to mitigate 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 No. 0928010 dated September 28, 2007, issued by the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW), “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 principles and best practices when conducting global clinical trials.

Number of Clinical Trial Notifications of Global Clinical Trials

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of notifications	173	181	276	240	323

- PMDA intends to take an active approach to global clinical trials. In FY 2017, PMDA received requests for consultation on global clinical trials of drugs with new active ingredients, and conducted consultations for all the requests.

Number of Consultations on Global Clinical Trials with New Active Ingredients

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of consultations	59	67	66	73	74

- To promote global clinical trials in the Asian region, PMDA acted as a leader (Champion) in the area of global clinical trials/GCP inspections of the APEC Life Sciences Innovation Forum (LSIF) Regulatory Harmonization Steering Committee (RHSC), which was established as a sectoral association to harmonize regulatory affairs. PMDA also held the PMDA-ATC MRCT Seminar 2018 (January 2018) as an APEC Training Center of Excellence (CoE) for Regulatory Science. PMDA reported this achievement at the APEC-LSIF-RHSC meeting in Singapore (February 2018), which was internationally highly appreciated.

3.2.(1).A.(v) Efficient conduct of clinical trial consultations

3.2.(1).A.(v).a. Conduct of priority consultations

- In accordance with the start of the SAKIGAKE designation system, in FY 2015 priority consultation service began to cover SAKIGAKE designation drugs, in addition to orphan drugs. In FY 2017, PMDA handled those drugs in a similar manner (4 priority face-to-face consultations for SAKIGAKE designation drugs were conducted in FY 2017).

3.2.(1).A.(v).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.

3.2.(1).A.(v).c. Implementation of clinical trial consultations and improvement of the consultation service

Number of Consultations

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	354	411	371	422	395
Withdrawn	30	38	33	61	34

Number of Prior Assessment Consultations for Drugs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	32	32	1	7	0
Withdrawn	0	0	0	0	0

Number of Consultations on Drug Product Eligibility for Priority Review

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	10	6	7	5	4
Withdrawn	0	0	0	0	0

Number of Consultations on Drug Product Eligibility for Conditional Early Approval

	FY 2017
Conducted (face-to-face)	2
Withdrawn	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. Consultations on drug product eligibility for conditional early approval have been conducted since FY 2017. The numbers of all types of consultations were counted on the basis of the dates of delivery 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).

- 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 2017, PMDA provided 389 consultations (34 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 2017, the target was achieved in 384 of 390 consultations (98.5%).
- 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 2017

Review category	Results												Total
	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
Category 1 (Gastrointestinal drugs etc.)	8	4	2	5	5	3	3	2	9	7	3	4	55
Category 6-2 (Hormone drugs)	7	0	4	5	1	3	3	1	2	2	6	2	36
Category 2 (Cardiovascular drugs)	2	3	5	1	1	2	4	3	3	1	2	3	30
Category 5 (Drugs for the urogenital system etc.)	0	2	1	2	0	0	0	1	2	1	2	2	13
Radiopharmaceuticals	0	0	0	1	0	0	0	0	0	0	1	0	2
In vivo diagnostics	0	0	0	0	0	0	0	0	0	0	0	0	0
Category 3-1 (Central nervous system drugs etc.)	4	3	1	2	3	2	5	3	3	2	1	4	33
Category 3-2 (Anesthetic drugs etc.)	1	2	1	1	1	0	1	4	1	3	2	0	17
Category 4 (Antibacterial agents etc.)	1	1	2	2	1	3	1	1	1	0	2	1	16
Category 6-1 (Respiratory tract drugs etc.)	2	1	2	2	1	1	5	3	3	1	3	3	27
AIDS drugs	0	0	0	1	0	0	0	0	0	0	0	0	1
Oncology drugs	1	6	12	8	6	9	11	10	13	4	10	8	98
Bio-CMC	1	3	0	1	1	2	0	2	5	1	2	1	19
Vaccines	2	1	1	1	0	3	1	5	1	2	3	2	22
Blood products	1	1	2	3	3	3	3	0	0	1	1	0	18
Generic drugs	0	1	0	1	1	0	1	1	0	1	2	0	8
[Re-listed] Prior assessment	0	0	0	0	0	0	0	0	0	0	0	0	0
[Re-listed] Drug product eligibility for priority review	0	0	0	1	0	0	0	0	1	0	0	2	4
[Re-listed] Drug product eligibility for conditional early approval	0	0	0	0	0	0	0	1	0	1	0	0	2
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	30	28	33	36	24	31	38	36	43	26	40	30	395
Withdrawn	5	1	2	1	6	0	5	0	5	5	2	2	34
Total	35	29	35	37	30	31	43	36	48	31	42	32	429

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, consultations on drug product eligibility for priority review, and consultations on drug product eligibility for conditional early approval were counted on the basis of on the date of delivery 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.

3.2.(1).A.(v).d. Reclassification of consultation categories and their uses

- PMDA exchanged opinions with MHLW and related industries on clinical trial consultation services. As a result, PMDA began to offer the following consultations:

  Launched in November 2017:

  (a) Consultation on epidemiological surveys of drugs
  This consultation provides guidance and advice based on post-marketing information on the design of use-results comparison surveys or post-marketing database surveys, conducted to submit application for re-examination/re-evaluation of drugs or to carry out post-marketing surveillance of biosimilars.

  (b) Consultation on drug product eligibility for conditional early approval
  This consultation is conducted to determine the eligibility for review under the "Conditional Early Approval System for Drugs" prior to application.

  Launched in January 2018:

  (c) Consultation on revision of package inserts of drugs
  When an applicant proposes revisions (deletions, additions, or modifications) to the information given in the package insert for a drug (e.g., precautions for indications or dosage and administration, clinical data) based on new data from post-marketing clinical trials, this consultation is conducted to assess whether the proposed revisions should be carried out after evaluating the efficacy and safety. A report on the consultation results is prepared.

  (d) Consultation on Compliance Assessment Concerning Data Supporting Revisions to Package Inserts for Drugs
  This consultation provides guidance and advice on the reliability of clinical study data supporting revision to the package insert of the drug, according to the data integrity standards.

  PMDA also began to offer Post-Approval Change Management Protocol (PACMP) consultation, which provides guidance and advice on changes to approved product information using PACMP in April 2018.

3.2.(1).A.(vi) Promotion of evaluation of new technologies

3.2.(1).A.(vi).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, 2018, the number of commissioned experts was 1,395 including external experts commissioned for issues relating to safety measures)

- In FY 2017, 230 Expert Discussions were conducted (192 through document-based discussions; 38 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 (US 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 has accumulated the current knowledge by joining the following research groups:

  (a) As a study collaborator, PMDA joined a research group that conducted "Research on Development of Next-Generation Toxicity/Safety Evaluation Test System for Drugs Using Human iPS Cell Differentiation Technology and International Standardization." This research is part of a project called "Research on Regulatory Science of Pharmaceuticals and Medical Devices" implemented by the Japan Agency for Medical Research and Development (AMED).

  (b) As an external collaborator, PMDA joined research groups that conducted "Research on Development of *in vitro* Test System for Prediction/Evaluation of Hepatotoxicity of Drugs Using Human iPS Cell-derived Hepatocytes" and "Research on Development of an *in vitro* Safety Pharmacology Evaluation System Using Human iPS Cell-derived Neurons to Predict the Risk of Drug-Induced Seizures in Humans." These researches are part of a project called "Research on Practical Application of Regenerative Medical Products" implemented by 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.

3.2.(1).A.(vi).b. Support for the development of national guidelines

- PMDA supported the development of evaluation guidelines through the activities of working groups (WG) involved in the Projects Across Multi-offices to Develop Standards etc. (hereinafter referred to as "Projects Across Multi-offices"). In FY 2017, individual working groups collaborated with MHLW in preparing the following notifications:

  (a) Pediatric Drug WG
  "Annex to the Guidance on Clinical Studies for the Development of Drugs in Pediatric Populations" (PSEHB/PED Notification No. 1227-5 dated December 27, 2017, issued by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

  (b) Omics WG
  The "Guidelines for Collection of Genomic Specimens and Handling of Genomic Data" (PSEHB/PED Notification No. 0118-1 dated January 18, 2018, issued by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

  (c) ICH Q12 WG
  "Handling of Changes to Approved Product Information Pertaining to the Quality of Drugs" (PSEHB/PED Notification No. 0309-1 and PSEHB/CND Notification No. 0309-1 dated March 9, 2018, jointly issued by the Director of the Pharmaceutical Evaluation Division and the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

- In addition to the above, MHLW issued 9 notifications etc. in FY 2017 with the cooperation of relevant review categories or offices in PMDA.

3.2.(1).A.(vi).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 2013	FY 2014	FY 2015	FY 2016	FY 2017
No. of preliminary reviews for Type 1 Use	0	3	2	3	1
Median review time [months]	-	0.8	0.9	2.9	2.9
No. of preliminary reviews for Type 2 Use	24	25	21	23	14
Median review time [months]	0.9	1.3	1.0	1.3	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.

3.2.(1).A.(vi).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 PMDA provided in FY 2017 is shown in the table below. (Pharmaceutical Affairs Consultation on R&D Strategy was reorganized into Regulatory Science [RS] General Consultation and Regulatory Science [RS] Strategy Consultation (R&D).)
- In FY 2017, PMDA provided 55 on-site consultations in various prefectures throughout Japan, including Miyagi, Fukushima, Saitama, Aichi, Okayama, Fukuoka, and Okinawa prefectures.
- PMDA contributed to the promotion of healthcare-related innovation by making use of the Kansai Branch Office, established in October 2013, which provided 57 RS General Consultations (including Kobe) and RS Strategy Consultations (R&D) (62 pre-consultations [which also included pre-consultations for medical devices in special zones] and 11 face-to-face consultations [through video conference system]) in FY 2017.
- 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 response to the “Japan Revitalization Strategy” revised in 2015 (approved by the Cabinet on June 30, 2015), PMDA launched Pharmaceutical Affairs Consultation on R&D Strategy for Medical Devices in Special Zones (renamed “RS Strategy Consultation for Medical Devices in Special Zones” in April 2017) in October 2015. The PMDA consultation service offers advice on the development of innovative medical devices in core hospitals for clinical research in 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 2017, PMDA conducted 5 Pre-consultations in Special Zones.

Number of RS Strategy Consultations (R&D) and RS General Consultations

Consultation Category	Up to FY 2013[1]	FY 2014	FY 2015	FY 2016	FY 2017	Total
RS General Consultation[2] (Number of consultations conducted at the Kansai branch[4])	657 (20)	271 (63)	221 (56)	190 (63)	231 (57)	1,570 (259)
RS Strategy Consultation (R&D): Pre-consultations[3] (Number of consultations conducted at the Kansai branch[4])	753 (26)	325 (57)	411 (60)	388 (52)	336 (61)	2,213 (256)
RS Strategy Consultation (R&D): Pre-consultations for medical devices in special zones[5] (Number of consultations conducted at the Kansai branch)	-	-	1 (0)	9 (1)	5 (1)	15 (2)

RS Strategy Consultation (R&D): Face-to-face consultations on[3]:	Up to FY 2013[1]	FY 2014	FY 2015	FY 2016	FY 2017	Total
Drugs	114	48	58	40	61	321
Medical devices	49	16	16	20	24	125
Regenerative medical products[6]	-	2	11	14	13	40
Quality and safety of regenerative medical products[7]	31 [52]	18 [44]	29 [55]	26 [64]	29 [71]	133 [286]
Development plannning[8]	-	1	0	0	0	1
Total	194 [215]	85 [111]	114 [140]	100 [138]	127 [169]	620 [773]

Note 1: The service for RS Strategy Consultations (former, Pharmaceutical Affairs Consultations on R&D Strategy) was launched on July 1, 2011.

Note 2: These consultations were provided as introductory consultations of Pharmaceutical Affairs Consultations on R&D Strategy until March 31, 2017.

Note 3: These consultations were provided as Pharmaceutical Affairs Consultations on R&D Strategy until March 31, 2017.

Note 4: This consultation category was introduced on October 1, 2013.

Note 5: This consultation category was introduced on November 20, 2015.

Note 6: 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 7: This consultation category includes Pharmaceutical Affairs Consultations on R&D Strategy for drugs before November 24, 2014. Some consultations were divided into multiple sessions over several days to confirm the quality and safety of the relevant products before submission of clinical trial notifications. The figures in brackets indicate the total number of these sessions.

Note 8: This consultation category was introduced on November 25, 2014. (It was provided as a Pharmaceutical Affairs Consultation on R&D Strategy for pharmaceutical development plans until March 31, 2017.)

3.2.(1).A.(vii) Handling of Changes to Approved Product Information Pertaining to the Quality of Drugs

- MHLW issued a notification, “Strict Compliance with the Marketing Approval Documents of Drugs” on June 1, 2016 (PSEHB/ELD Notification No. 0601-3 and PSEHB/CND Notification No. 0601-2 dated June 1, 2016, jointly issued by the Director of the Evaluation and Licensing Division and the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In response to the notification, PMDA exchanged opinions with MHLW and related industries, to ensure that approved product information is revised appropriately after change in the manufacturing process of a drug, and that manufacturing processes can be changed efficiently. PMDA established detailed procedures for trial operation of the product approval information revision system, which uses the Post-Approval Change Management

Protocol (PACMP). (Trial operations began in April 2018.) As a result, MHLW issued a notification, “Handling of Changes to Approved Product Information Pertaining to the Quality of Drugs” (PSEHB/ELD Notification No. 0309-1 and PSEHB/CND Notification No. 0309-1, dated March 9, 2018, jointly issued by the Director of the Evaluation and Licensing Division and the Director of Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

3.2.(1).A.(viii) Cooperation in the development of proper use guidelines

- PMDA provided assistance to MHLW in developing the Optimal Clinical Use Guidelines of innovative drugs (developed on a trial basis) published by MHLW.

FY 2017

Drug name	Indication	Date of issue
Opdivo Intravenous Infusion 20 mg Opdivo Intravenous Infusion 100 mg	Unresectable advanced or recurrent gastric cancer that has progressed after cancer chemotherapy	Sep. 22, 2017
Bavencio Injection 200 mg	Unresectable Merkel cell carcinoma	Nov. 21, 2017
Keytruda Injection 20 mg Keytruda Injection 100 mg	Relapsed or refractory classical Hodgkin lymphoma	Nov. 30, 2017
	Unresectable urothelial carcinoma that has progressed after cancer chemotherapy	Dec. 25, 2017
Repatha SC Injection 140 mg Syringe Repatha SC Injection 140 mg Pen Repatha SC Injection 420 mg Auto mini-doser	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.	Dec. 15, 2017 (revised)
Tecentriq Intravenous Infusion 1200 mg	Unresectable advanced or recurrent non-small cell lung cancer	Apr. 17, 2018
Dupixent 300 mg Syringe for S.C. Injection	Atopic dermatitis in patients who have not responded sufficiently to conventional treatments	Apr. 17, 2018

FY 2016

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

3.2.(1).A.(ix) Establishment and Operation of the Conditional Early Approval System

- MHLW had been planning to introduce the conditional early approval system. PMDA supported MHLW in launching the system by joining discussions between MHLW and related industries, and by introducing a new consultation category (i.e., consultation on drug product eligibility for conditional early approval, which determines eligibility for conditional early approval prior to application). PMDA provided 2 consultations on drug product eligibility for conditional early approval in FY 2017.

3.2.(1).B. Generic drugs, etc.

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

3.2.(1).B.(i) Appropriate and prompt reviews

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

3.2.(1).B.(i).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.

3.2.(1).B.(i).b. Development of the Japanese Pharmacopoeia draft

- See Section 3.2.(1).A.(i).g.

3.2.(1).B.(i).c. Implementation of the master file workshop

- See Section 3.2.(1).A.(i).h.

3.2.(1).B.(i).d. Ensuring more efficient and transparent reviews

- PMDA prepared and released 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. In FY 2016, PMDA began to accept a trial version of the CTD for new applications from companies able to prepare CTD. PMDA provided companies submitting the trial version with individual feedback on areas for improvement in CTD preparation. On March 11, 2016, MHLW issued a notification titled "Handling of Materials That Should be Attached to Application Dossiers for Prescription Drugs" (PSEHB/ELD Notification No. 0311-3, issued by the Director of the Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In accordance with the notification, companies have, in principle, been required to submit application data compiled in CTD format for new products submitted after March 1, 2017. In FY 2017, in collaboration with various industry associations, PMDA prepared a Q & A document that contains answers to questions about CTD preparation, in order to promote submission of CTD for new generic drug applications. The Q&A document was published in August 2017 and February 2018.
- 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 2017, and published review reports concerning 2 products produced by 1 company.
- 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 ophthalmic solutions and dry powder inhalers. As a result, MHLW issued the following administrative notices: "Basic Principles on Bioequivalence Evaluation of Generic Dry Powder Inhalers" (PSEHB/ELD Administrative Notice, dated March 11, 2016, issued by the Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau,

MHLW) and "Basic Principles concerning Bioequivalence Evaluation of Generic Aqueous Ophthalmic Solutions" (PSEHB/ELD Administrative Notice, dated March 11, 2016, issued by the Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In FY 2017, PMDA discussed other dosage forms, such as suspension-type ophthalmic solutions and nasal solutions.

3.2.(1).B.(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.

  MHLW and PMDA discussed the handling of approval applications and the total review period to increase the predictability of approval of generic drugs etc. As a result, MHLW issued a notification, "Policy for Handling Approval Applications and Total Review Period to Increase the Predictability of Approval of Generic Drugs etc." (PSEHB/PED Notification No. 0223-1, dated February 23, 2018, issued by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

- 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 2017 is as follows:

3.2.(1).B.(ii).a. Review time for new application for generic drugs

Targets

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	FY 2017
Approved products	1,325	635	731	805
Median regulatory review time [months]	6.1	8.2	8.2	8.9

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

3.2.(1).B.(ii).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	FY 2017
Approved products	586	701	537	559
Median total review time [months]	15.5	13.0	11.7	11.7

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

3.2.(1).B.(ii).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	FY 2017
Change of test methods, etc.	Approved products	1,367	1,594	1,676	1,495
	Median total review time [months]	7.3	6.9	7.0	7.3
Expedited review	Approved products	168	305	248	237
	Median total review time [months]	4.0	4.8	4.3	3.3

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 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	3,163	3,192	254	3,099
FY 2017	2,151	3,096	311	1,843

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

Document-based Compliance Assessments for Generic Drugs by Fiscal Year

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Generic drugs	1,086	1,080	1,045	870	883

- PMDA conducted 883 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.

3.2.(1).B.(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 concerning generic drug bioequivalence." The applications for these consultation types have been increasing alongside growing awareness 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	17	24	48	56	79
Withdrawn	1	1	8	4	12

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

Number of Consultations for Generic Drugs by Consultation Category in FY 2017

Consultation category	Conducted	Withdrawn
Consultations on bioequivalence of generic drugs	68	9
Quality consultations for generic drugs	11	3
Total	79	12

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

- See Section 3.2.(1).A.(vii)

3.2.(1).C. Behind-the-counter (BTC) drugs, over-the-counter (OTC) drugs, and quasi-drugs

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

3.2.(1).C.(i) Appropriate and prompt reviews

3.2.(1).C.(i).a. Enhancement 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 FY 2016, PMDA issued the "Procedures for Conducting Document-based Compliance Inspections Related to Approval Application for Behind-the-counter (BTC) Drugs and Over-the-counter (OTC) Drugs" (PMDA Notification No. 0306053, dated March 6, 2017, by the Chief Executive of the Pharmaceuticals and Medical Devices Agency). The Office of OTC/Quasi-drugs took the lead in handling document-based compliance assessments based on this notification, and made efforts to promote post-marketing surveillance in response to the establishment of BTC drugs category.

  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 Section 3.2.(1).A.(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.

- PMDA supported MHLW in preparing (a) the Guidance on Measuring Consumers' Level of Understanding of Package Inserts of BTC Drugs and (b) notifications related to Chinese herbal products and crude products. As a result, MHLW the following notifications in FY 2017.

- "Q&A on the Guidance on Measuring Consumers' Level of Understanding of Package Inserts of BTC Drugs" (PSEHB/PED Administrative Notice dated May 19, 2017, by the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

- "Q&A on Handling of Administrative Operations for Marketing Approval of Chinese Herbal Products Approved by Prefectural Governors" (PSEHB/PED Administrative Notice, dated June 20, 2017, by the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

- "Standards for Marketing Approval of OTC Crude Drugs" (PSEHB Notification No. 1221-4, dated December 21, 2017, by the Director General of the Pharmaceutical Safety and Environmental Health Bureau, MHLW)

- "Handling of Administrative Operations for Marketing Approval of Crude Drugs Approved by Prefectural Governors" (PSEHB/PED Notification No. 0329-19, dated March 29, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

- "Partial Revision of 'Descriptions in the Application Form and Handling of Submission Data for OTC Drugs for Which Standards for Approval Have Been Specified'" (PSEHB/PED Notification No.

0329-21, dated March 29, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

- "Q&A on Handling of Administrative Operations for Marketing Approval of Crude Drugs Approved by Prefectural Governors" (PSEHB/PED Administrative Notice, dated March 29, 2018, by the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

3.2.(1).C.(i).b. Reinforcement of the review system for quasi-drugs

- To improve the efficiency of review, PMDA made efforts to familiarize applicants with the "Checklist for Application Data for Marketing Approval of Quasi-drugs, etc.," and encouraged them to use the checklist for products filed for approval in FY 2017.
- 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 also 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). In addition, MHLW issued the following notifications in FY 2017.
- "Guidance on Evaluation Systems with Combined Alternative Testing Methods for Skin Sensitization for Safety Evaluation of Quasi-drugs and Cosmetics" (PSEHB/PED Notification No. 0111-1, dated January 11, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- "Partial Revision of the 'Japanese Standards of Quasi-drug Ingredients 2006'"(PSEHB Notification No. 0329-4, dated March 29, 2018, by the Director General of the Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- "Handling of Marketing Approval Application for Quasi-drugs Associated with Partial Revision of 'Japanese Standards of Quasi-drug Ingredients 2006'" (PSEHB/PED Notification No. 0329-4, dated March 29, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- "Insecticide Standards 2018" (PSEHB Notification No. 0329-7, dated March 29, 2018, by the Director General of the Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- "Handling of Marketing Approval Application for Drugs etc. Associated with Partial Revision of 'Insecticide Standards 2018'" (PSEHB/PED Notification No. 0329-7, dated March 29, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- "Instructions on Insecticide Effectiveness Tests" (PSEHB/PED Notification No. 0329-10, dated March 29, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)
- 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.

3.2.(1).C.(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; the 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 describing the degree of realization of the target review times were collected periodically 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 had a discussion about 1 OTC ingredient. The BTC/OTC Drug Committee discussed 1 new active ingredient in 1 product (a BTC [OTC] drug with a new active ingredient) and 1 new active ingredient in 2 products (2 BTC [OTC] drugs with new indications).
- 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 2 new quasi-drugs.
- The approval status of BTC drugs, OTC drugs, and quasi-drugs in FY 2017 is as follows:

3.2.(1).C.(ii).a. Review time for BTC drugs and OTC drugs

Targets

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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Approved products	916	844	752	646	537
Median regulatory review time [months]	4.9	6.3	5.5	4.3	4.6

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.

3.2.(1).C.(ii).b. Review time for quasi-drugs

Targets

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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Approved products	2,028	1,779	2,495	1,924	1,891
Median regulatory review time [months]	4.9	4.9	4.7	4.4	4.4

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.

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 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
	FY 2017	624	537	115	1,597
Quasi-drugs	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
	FY 2017	1,824	1,891	187	1,936

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

3.2.(1).C.(iii) Efficient conduct of consultations

3.2.(1).C.(iii).a. Improvement of pre-application consultations for BTC drugs and OTC drugs

- PMDA began offering pre-development and pre-application consultations related to OTC drugs in FY 2010 based on opinions from 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. While exchanging opinions with related industries, PMDA also began holding discussions on the establishment of a new consultation service to respond to the "Review Committee Meetings on Prescription to BTC/OTC switch" held in MHLW.

Consultations for OTC Drugs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	21	21	15	23	35
Withdrawn	0	0	1	0	0

Number of Pre-development and Pre-application Consultations for OTC Drugs by Consultation Category in FY 2017

Consultation category	Conducted	Withdrawn
Pre-application consultation for OTC switch drugs	3	0
Consultation on key points of clinical trial protocols for OTC drugs	3	0
Consultation on appropriateness of development of new OTC drugs	29	0
Total	35	0

3.2.(1).C.(iii).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 launched, on a trial basis, new types of consultations on the development of quasi-drugs (i.e., “human study plan confirmation consultation,” “new excipient development consultations”).

Number of Pre-application Consultations for Quasi-drugs by Consultation Category in FY 2017

Consultation category	Conducted
Human study plan confirmation consultation	1
New excipient development consultation	1
Total	2

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

- See Section 3.2.(1).A.(vii)

3.2.(1).D. Medical devices

- Various measures were implemented or considered to accelerate reviews of new medical devices in accordance with the "Collaboration 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," the "Healthcare and Medical Strategy," and the "Growth Strategy Council."

3.2.(1).D.(i) Appropriate and prompt reviews

3.2.(1).D.(i).a. Clinical trial consultations 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.

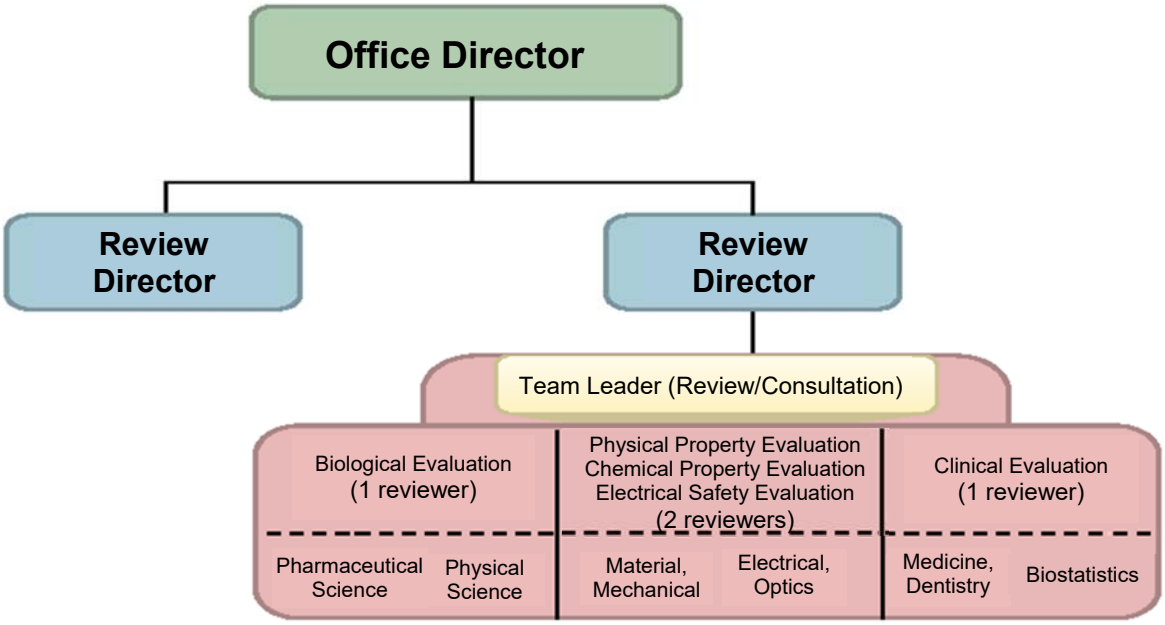
Note:

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 (as defined 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. (as defined 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 (as defined under the PMD Act)*
- *Medical devices that are regarded as substantially equivalent to existing approved medical devices in terms of structure, usage, indications, performance, etc. (as defined under the PMD Act)*

Organization for New or 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.

  PMDA has been making efforts to share information, to standardize the level of reviews, and to increase information flow between the new/improved device review teams and the generic device review team through the restructuring of review categories. 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, PMDA's review teams were able to handle a sudden increase in applications/consultations, leading to a reduction in the review time as compared with previous years.

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

Office	Review Areas	
Office of Medical Devices I	Robotic, ICT, and other devices	Primarily innovative medical devices utilizing robotics and advanced ICT technologies, multicategory medical devices, and other uncategorized medical devices
	Orthopedic and Plastic Surgery	• Primarily medical devices targeting the hips, knees, upper extremities, hands, and digits, etc. among orthopedic devices • Primarily 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	Primarily gastrointestinal and urinary systems, obstetrics and gynecology-related products
	Dentistry and Oral Medicine	Primarily dentistry-related products
Office of Medical Devices III	Ophthalmology and Otorhinolaryngology	Primarily ophthalmology and otorhinolaryngology-related products
	Cardiopulmonary and cardiovascular areas	• Primarily cardiology-related materials used in medical devices pertaining to the circulatory system • Primarily 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) AI and 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 2017 (medical devices and in vitro diagnostics)

(1) Number of Expert Discussions conducted: 81 (57 document-based discussions, 24 meetings)
(2) Applications deliberated at the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 14
Applications reported to the Committee on Medical Devices and *in vitro* Diagnostics (under PAFSC): 207 (183 medical devices, 24 *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.

3.2.(1).D.(i).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 2017, PMDA promoted the system based on the experiences in previous fiscal years.

3.2.(1).D.(i).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" (PFSB/ELD/OMDE Notification No. 1120-1 dated November 20, 2013, by the Director of Office of Medical Device Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW), "On the Standard Review Timeline for Improved Medical Device Applications (with Clinical Data)" (PFSB/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" (PFSB/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" (PMDA Notification No. 0530001 dated May 30, 2014, by the Chief Executive of the Pharmaceuticals and Medical Devices Agency), 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.

3.2.(1).D.(i).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.

3.2.(1).D.(i).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 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 2017, the Study Group convened twice and the working group convened twice. 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 7 medical devices in FY 2017. 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.

3.2.(1).D.(i).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 between consultations and actual review processes is maintained and teams are flexibly organized as necessary.

3.2.(1).D.(i).g. Efficient operation and implementation of the use-results evaluation system

- With the enactment of the PMD Act, PMDA strove to further improve the efficiency of its operations and to implement its use-results evaluation system for medical devices (introduced on November 25, 2014), in accordance with the "Basic Principles on Products Subject to Use-results Evaluation at the Time of Approval" was deliberated and approved at the 6th meeting of the Committee on Medical Devices and In Vitro Diagnostics, the Pharmaceutical Affairs and Food Sanitation Council in MHLW in FY 2014.

  Based on this principle, 14 medical devices (including 11 medical devices selected for use-results survey) were approved in FY 2017.

- 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, 15 medical devices subject to re-examination were processed in FY 2017.

3.2.(1).D.(ii) Introduction of new review systems

3.2.(1).D.(ii).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 33 of 36 products approved in FY 2017 was not more than 2 months, excluding the period for GCP/GLP inspections.

3.2.(1).D.(ii).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 4 meetings in FY 2017.

  The table below shows the number of approval or certification standards reported to MHLW in FY 2017 to be established or revised.

FY (for reporting)	Up to FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	Total
Approval standards	37	4	0	3	2	8	54
Certification standards (designated controlled medical devices)	609	82	129	99	156	34	1109
Certification standards (designated specially controlled medical devices)	-	-	3	7	1	0	11
Review guidelines	9	0	0	0	1	0	10

The following table shows the number of standards established by MHLW in FY 2017 based on the reports from PMDA.

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

FY (for establishment)	Up to FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	Total
Approval standards	41	4	0	-1[*1]	0	1	45
Certification standards (designated controlled medical devices)	824	3	109	0	-1[*2]	0	935
Certification standards (designated specially controlled medical devices)	-	-	3	7	1	0	11
Review guidelines	8	0	0	0	0	1	9

**1 In FY 2015, one established approval standards was switched to certification standards, resulting in a negative number.*

**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 2017)

Established: Certification standards,0; Approval standards,1; Review guidelines, 1	
Date of issue	Name of standards
PSEHB Notification No. 0602-7 dated June 2, 2017, by the Pharmaceutical Safety and Environmental Health Bureau, MHLW	Approval Standards for Long-term Enteral Feeding Kits etc.
PSEHB/MDED Notification No. 0803-1 dated August 3, 2017, by the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW	Review Guidelines for Superficial Femoral Artery Stents

- 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. The information on the web page is updated, 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). MHLW issued a notification, “Handling of Procedures for Minor Changes Associated with Partial Changes for Medical Devices” (PSEHB/MDED Notification No. 0731-5 dated July 31, 2017, by the Director of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In response to the notification, PMDA established a consultation category, “simple consultation prior to submission of change notifications for medical devices.” This type of consultation serves to provide advice to Marketing Authorization Holders (MAHs) who plan to submit a medical device change notification that is likely to fall under “minor change notification” but may possibly fall under “partial change application,” to determine which category applies in advance. The establishment of this consultation category contributed to a reduction in the operational burdens of both MAHs and regulatory agencies.
- 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.
- Based on the accumulated knowledge concerning irradiation sterilization, PMDA supported MHLW in preparing the following notifications that provide guidance on the handling of approval (certification) of sterile medical devices:

  “Partial Revision of ‘Points to Consider in Preparing Summary Technical Documentation (STED) for Medical Devices’” (PSEHB/MDED Notification No. 0228-7 dated February 28, 2018, by the Director of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

  “Handling of Sterilization in the Application for Marketing Approval (Certification) of Sterile Medical Devices” (PSEHB/MDED Notification No. 0228-10 dated February 28, 2018, by the Director of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

  “Q&A on Handling of Sterilization in the Application for Approval of Sterile Medical Devices” (PSEHB/MDED Administrative Notice dated February 28, 2018, by the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

PMDA appropriately conducted approval reviews and consultations for individual medical devices.

- 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 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, 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).

3.2.(1).D.(ii).c. Equivalence review of generic medical devices

- PMDA conducted equivalence reviews for generic medical devices filed in FY 2017 based on a notification titled "Points to Consider in Preparing Summary Technical Documentation (STED) 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 3 meetings with related industry associations and strove to identify and summarize problems that needed to be resolved.

3.2.(1).D.(iii) Efforts to realize “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 implemented “team-based 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 between review teams and to ensure prompt and appropriate medical device reviews, PMDA developed standard operating procedures (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.

- PMDA contributed to the activities of Harmonization by Doing (HBD), which is a cooperative effort by industry, government, and academia in Japan and the US, as shown below.
  - PMDA facilitated active discussions on the conduct of global clinical trials, development support, and post-marketing data utilization by 164 attendees from industry, government, and academia in Japan and the US at the HBD East 2017 Think Tank Meeting held in the National Center for Global Health and Medicine on December 7, 2017.
  - As part of the HBD activities for children, PMDA participated in regular teleconferences and HBD sessions at the meeting of TCT (Transcatheter Cardiovascular Therapeutics, October 2017, Denver). PMDA held face-to-face consultations with concerned persons to discuss tangible measures for global development of pediatric medical devices, and reached an agreement on the conduct of the first global clinical trial in the area of pediatric medical devices.
  - As part of the HBD activities, PMDA participated in scientific sessions held at the following academic conferences. At these conferences, PMDA conducted publicity activities concerning HBD activities and discussed issues and countermeasures in the development of individual new medical devices, and the utilization of post-marketing data, etc. by representatives of industry, government, and academia.

    Major scientific sessions:

    - CVIT (July 2017, Kyoto)
    - VIVA (Vascular InterVentional Advances; September 2017, Las Vegas)
    - CRT (Cardiovascular Research Technologies, March 2018, Washington, D.C.)
    - Annual Scientific Meeting of the Japanese Circulation Society (March 2018, Osaka)
- PMDA worked to achieve its target total review times through these measures. The status of reviews for medical devices in FY 2017 was as follows:

3.2.(1).D.(iii).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	60th	60th	70th	70th	80th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time [months] (Reference, 80th percentile) [months]	9.0 (10.0)	8.8 (8.9)	7.9 (8.2)	8.0 (8.0)	8.3[Note] (9.6)
Number of cases	14	5	8	1	3

Note: In FY 2017, the total review time of 10 months was achieved for 2 of 3 products, with an achievement rate of 66.7%; the target for the total review time was achieved from the standpoint of the percentiles of products, but was not achieved from the standpoint of the achievement rate.

Reference

Regulatory review time [months]	5.1	4.0	4.2	3.2	5.5
Applicant's time [months]	3.5	3.3	3.8	4.8	3.0

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."

- In FY 2017, PMDA conducted priority reviews of applications for orphan medical devices and other devices with particularly high medical needs (medical devices for serious diseases; or medical devices exhibiting clearly superior efficacy or safety in comparison with existing medical devices or therapies). As a result, several priority review products were approved.
- The approval results of priority review products in FY 2017 substantially exceeded the target.

3.2.(1).D.(iii).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	60th	60th	70th	70th	80th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time [months] (Reference, 80th percentile) [months]	6.3 (14.8)	5.6 (10.6)	10.1 (11.9)	12.0 (14.0)	11.9 (12.0)
Number of cases	80	62	48	24	24

Reference

Regulatory review time [months]	4.0	3.5	5.0	7.8	6.0
Applicant's time [months]	1.6	2.2	4.3	4.3	6.5

Note 1: Applications submitted for approval in or after April 2004 are covered.
Note 2: The results in FY 2016 and FY 2017 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."

- The approval results of new medical devices (standard review products) in FY 2017 exceeded the target.

Review Status of New Medical Devices by Fiscal Year of Submission

New medical devices (FY of submission)	Applied	Approved	Withdrawn	Under review
Up to FY 2003 (i.e., until 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	0
FY 2011	42	40	2	0
FY 2012	64	63	1	0
FY 2013	72	72	0	0
FY 2014	99	95 (2)	4	0 [-2]
FY 2015	30	28	0	2
FY 2016	30	28 (17)	1	1 [-17]
FY 2017	37	11 (11)	1 (1)	25
Total	713	559 (30)	126 (1)	28 [+6]

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 2017 (included in values to the left).
Note 4: The figures in brackets indicate differences from FY 2016.

3.2.(1).D.(iii).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	52th	54th	56th	58th	60th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	52th	54th	56th	58th
Total review time [months] (Reference, 60th percentile) [months]	11.6 (13.2)	9.9 (10.5)	11.0 (11.6)	10.0 (11.6)	8.8 (8.8)
Number of approved applications	63	35	53	43	42

Reference

Regulatory review time [months]	5.7	5.0	5.3	6.3	4.7
Applicant's time [months]	5.5	5.0	4.8	4.7	4.0

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 and FY 2017 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."
Note 5: The number of applications was counted by initial review category selected on the receipt date of submission data.

- The approval results of improved medical devices (with clinical data) in FY 2017 substantially exceeded the target. The number of approvals in FY 2017 was nearly equal to that in previous 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	0
FY 2013	46	42	4	0
FY 2014	45	41 (1)	4	0 [-1]
FY 2015	27	24	3 (1)	0 [-1]
FY 2016	50	44 (27)	2 (2)	4 [-29]
FY 2017	60	14 (14)	1 (1)	45
Total	364	291 (42)	24 (4)	49 [14]

Note 1: The figures in "Approved" include the number of approved products includes those approved under other application categories for medical devices.

Note 2: The figures in parentheses indicate applications processed in FY 2017 (included in values to the left).

Note 3: The figures in brackets indicate differences from FY 2016.

Note 4: Applications submitted in FY 2017 include those for new and re-manufactured single-use medical devices (based on the fee categories [Article 33, Paragraph 1, Item 1 (a)] 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).

Note 5: The number of applications could change due to a change in the initial application categories or withdrawal of applications.

3.2.(1).D.(iii).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	52th	54th	56th	58th	60th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	52th	54th	56th	58th
Total review time [months] (Reference, 60th percentile) [months]	7.5 (9.2)	6.0 (7.4)	6.0 (7.0)	5.8 (5.9)	5.8 (5.8)
Number of approved applications	231	213	233	218	205

Reference

Regulatory review time [months]	3.7	3.3	3.9	3.4	3.4
Applicant's time [months]	3.7	3.4	2.6	2.6	2.1

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 to FY 2017 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."
Note 5: The number of applications was counted by initial review category selected on the receipt date of submission data.

- The approval results of improved medical devices (without clinical data) in FY 2017 achieved the target. The number of approved applications in FY 2017 was nearly equal to that in previous 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	12 (1)	0 [-1]
FY 2013	190	177	12	1
FY 2014	255	226 (11)	4	25 [-11]
FY 2015	219	202 (1)	11 (2)	6 [-3]
FY 2016	216	201 (104)	8 (5)	7 [-109]
FY 2017	166	88 (88)	2 (2)	76
Total	1,734	1,515 (204)	104 (10)	115 [-48]

Note 1: The figures in "Approved" include the number of applications approved under other medical device categories.
Note 2: The figures in parentheses indicate applications processed in FY 2017 (included in values to the left).
Note 3: The figures in brackets indicate differences from FY 2016.
Note 4: The number of applications could change due to a change in the initial application categories or withdrawal of applications.

3.2.(1).D.(iii).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	52th	54th	56th	58th	60th

Results

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	52th	54th	56th	58th
Total review time [months] (Reference, 60th percentile) [months]	3.9 (5.3)	3.9 (4.5)	4.4 (5.0)	3.5 (3.6)	3.6 (3.7)
Number of approved applications	958	920	868	825	869

Reference

Regulatory review time [months]	1.8	1.9	2.0	1.9	2.2
Applicant's time [months]	2.1	1.8	2.3	1.4	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."
Note 4: The number of applications was counted by initial review category selected on the receipt date of submission data.

- The approval results of generic medical devices in FY 2017 exceeded 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	100	1
FY 2011	995	931	64	0
FY 2012	1,075	1,031	43	1
FY 2013	921	889 (10)	29 (5)	8 [-15]
FY 2014	946	897 (2)	47 (3)	2 [-5]
FY 2015	785	762 (11)	21 (1)	2 [-12]
FY 2016	925	894 (266)	16 (8)	15 [-274]
FY 2017	865	587 (587)	4 (4)	274
Total	8,658	7,948 (876)	412 (21)	298 [-32]

Note 1: The figures in "Approved" include the number of applications approved under other medical device categories.
Note 2: The figures in parentheses indicate applications processed in FY 2017 (included in values to the left).
Note 3: The figures in brackets indicate differences from FY 2016.
Note 4: The number of applications could change due to a change in the initial application categories or withdrawal of applications.

3.2.(1).D.(iv) Efficient conduct of clinical trial consultations

3.2.(1).D.(iv).a. Conduct of priority consultations

- During FY 2017, there were no requests for priority consultation designation or consultations related to GLP/GCP compliance for priority medical device products.

3.2.(1).D.(iv).b. Implementation of clinical trial consultations and improvements to consultation service offerings

Number of Consultations

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	162	196	203	276	263
Withdrawn	11	11	4	7	16

Number of Prior Assessment Consultations for Medical Devices

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

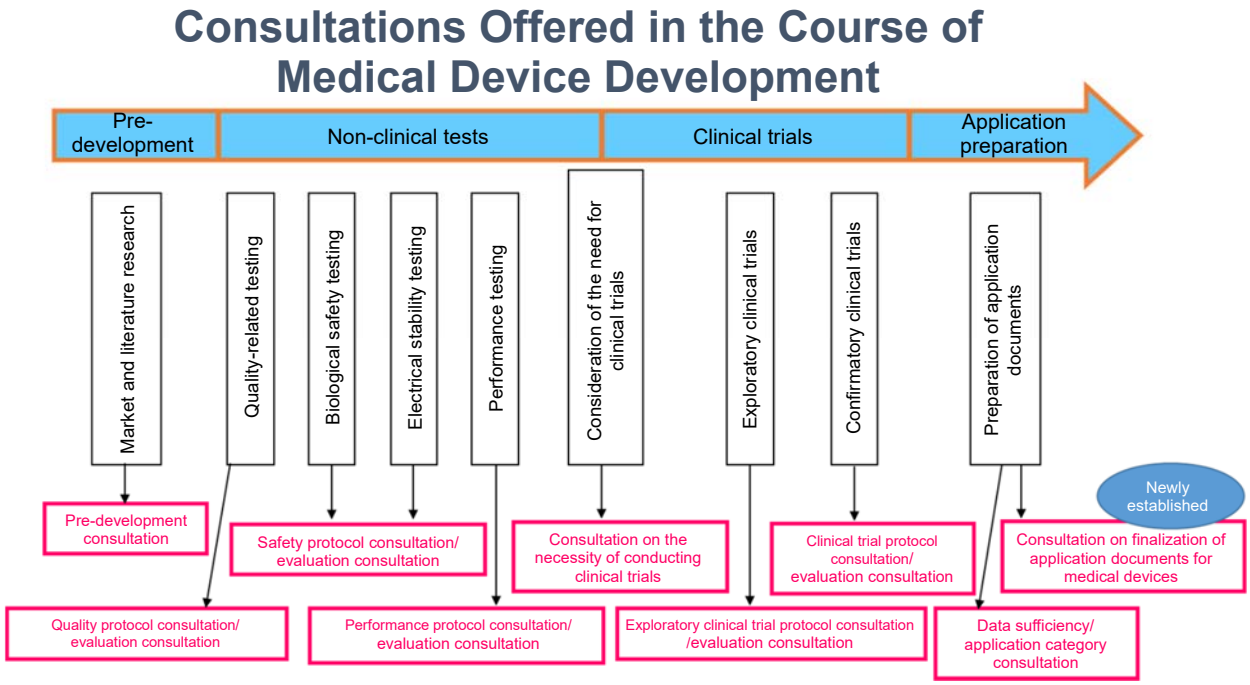
Note 1: Prior assessment consultations for medical devices were abolished in association with the revision of the consultation framework as of November 25, 2014.

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.

3.2.(1).D.(iv).c. Review of consultation categories

- To better accommodate the diverse range of needs for clinical trial consultations for medical devices arising in the industry, PMDA provided guidance and advice on data for products that had undergone assessment consultations for medical devices, to ensure that such data meet the requirements for application documents. PMDA also established a new consultation category, “Consultation on finalization of application dossiers for medical devices” (enforced as of January 4, 2018). This consultation service assesses the sufficiency of data contained in draft application documents for medical devices (by consultation category, e.g., data describing safety, quality, and performance).
- 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.*

3.2.(1).D.(v) Promotion of evaluation of new technologies

3.2.(1).D.(v).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, 2018, there were 8 commissioned experts in safety measures.)
- The number of Expert Discussions conducted in FY 2017 was 81 (57 document-based discussions, 24 meetings).
- In order to appropriately conduct operations related to medical device products employing the latest scientific technologies such as AI, 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.”

3.2.(1).D.(v).b. Support for the development of national guidelines

- PMDA supported the project for development of guidance for the approval process of new-generation medical products and regenerative medicine products to accelerate development and facilitate regulatory review of next-generation medical devices utilizing new technologies. More specifically, PMDA participated in the working groups that prepare guidance documents for “boron neutron capture therapy (BNCT)” and for “artificial intelligence areas,” for which substantial discussions are under way, and discussed the guidance contents.

3.2.(1).D.(v).c. Preliminary reviews under Cartagena Act

- See Section 3.2.(1).A.(vi).c.

3.2.(1).D.(v).d. Implementation of Pharmaceutical Affairs Consultations on R&D Strategy

- See Section 3.2.(1).A.(vi).d.

3.2.(1).D.(v).e. Support project for promoting consultations/applications for innovative medical devices

- PMDA advanced the “support project to promote consultations/applications for innovative medical devices etc.,” to prevent delays in practical application of innovative medical devices or regenerative medical products (hereinafter, “medical devices etc.”) due to financial difficulties at small and medium-sized enterprises (SMEs) and venture companies that discovered promising seed-stage technologies. The purpose of the project is to provide a subsidy to SMEs and venture companies that meet certain requirements for the purpose of reducing their financial burdens for consultations/applications for regulatory approval. This scheme reimburses 50% of the consultation or application fee for innovative medical devices after the fee is paid by the relevant company. PMDA provided fee subsidies to 2 consultations conducted in FY 2017.

3.2.(1).E. *In vitro* diagnostics

3.2.(1).E.(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.
- On the backdrop of recent advancements in personalized medicine, PMDA has been promoting approval review of companion diagnostics and diagnostic agents used in tests recommended by the optimal use promotion guidelines. In FY 2017, PMDA received 4 applications for diagnostics, including partial change applications for addition of cancer or specimen types. PMDA contributed to the review of 1 companion diagnostic system approved as a medical device.

Review Status of In Vitro Diagnostics

In vitro diagnostics (FY of submission)	Applied	Approved	Withdrawn	Under review
Up to FY 2003 (i.e., until Mar. 31, 2004)	327	223	76	28
FY 2004	615	596	19	0
FY 2005	69	65	4	0
FY 2006	180	173	7	0
FY 2007	197	189	8	0
FY 2008	170	160	10	0
FY 2009	183	173	10	0
FY 2010	164	157	7	0
FY 2011	177	170	7	0
FY 2012	165	155	10	0
FY 2013	136	123	13	0
FY 2014	163	153 (1)	9 (2)	1 [-3]
FY 2015	196	185 (10)	6 (1)	5 [-11]
FY 2016	149	137 (62)	7 (4)	5 [-66]
FY 2017	196	114 (114)	1 (1)	81
Total	3,087	2,773 (187)	194 (8)	120 [+1]

Note 1: The figures in parentheses indicate applications processed in FY 2017(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).

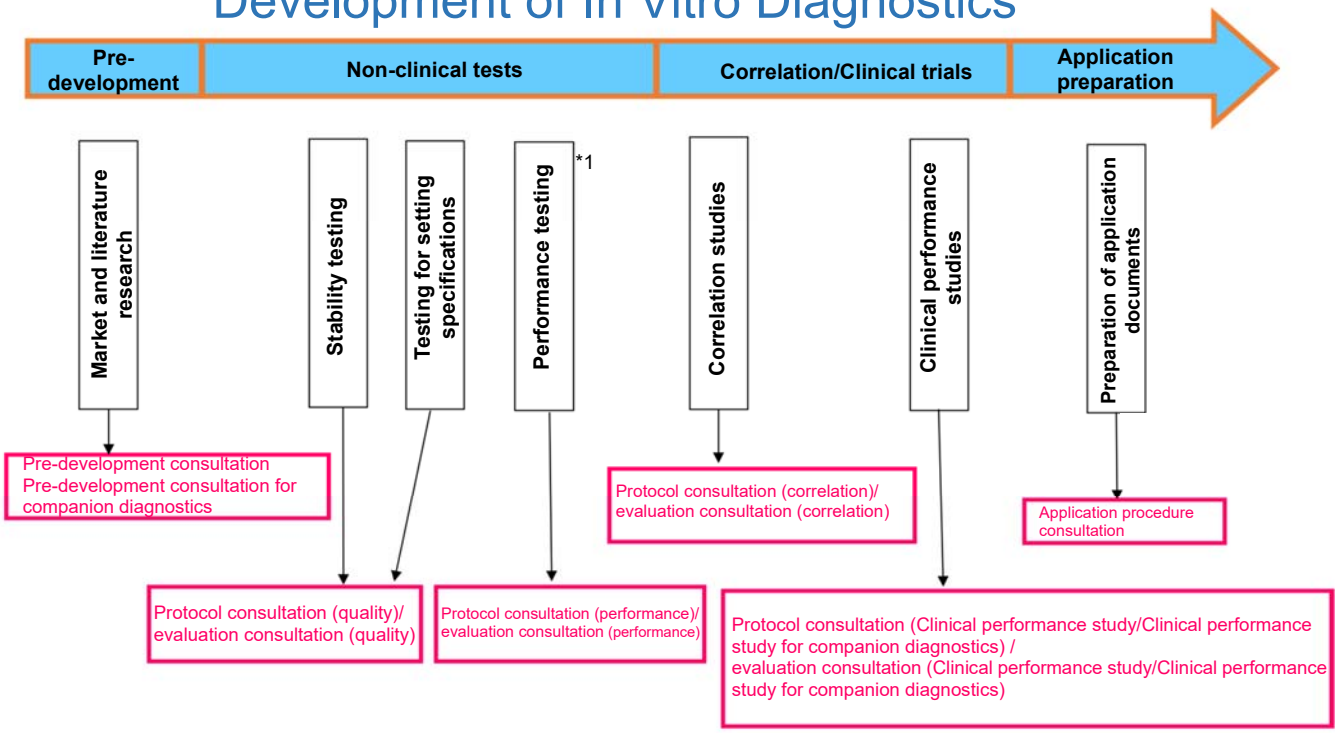
3.2.(1).E.(ii) Expansion of consultation services

- PMDA revised its clinical trial consultation offerings related to *in vitro* diagnostics in 2014, in order to provide more efficient and effective consultations. In FY 2017, PMDA began to offer face-to-face consultation sessions in response to applicant demand.

Number of Consultations

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	7	25	45	43	36
Withdrawn	1	0	0	1	1

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.*

3.2.(1).F. Regenerative medical products

3.2.(1).F.(i) New review systems and appropriate and prompt reviews

- With the enactment of the PMD Act in November 2014, PMDA has conducted consistent and efficient review and consultation activities by maintaining communications between consultation teams and review teams, in order to ensure appropriate implementation of a new conditional time-limited authorization system for regenerative medical products.

3.2.(1).F.(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 2017 was 9 months; product reviews were carried out in consideration of this target. In FY 2017, no regenerative medical products were granted marketing approval.

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	FY 2017
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	0

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

3.2.(1).F.(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 for Regenerative Medicine, and industry associations, and encouraged these organizations to take advantage of consultations offered by PMDA. In consideration of the unique characteristics of regenerative medical products, PMDA provides consultation services designed to clearly explain the requirements of its review procedures with respect to the appropriateness of ingredients, product quality and safety, clinical study plans, etc., as well as the SAKIGAKE designation system.
- The pre-trial notification (confirmation) application scheme for gene therapy products was abolished and incorporated into the purview of RS Strategy Consultations (R&D) 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 RS Strategy Consultations (R&D) for Development Plan. 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	FY 2017
Conducted	6	18	28	38
Withdrawn	0	1	2	4

Number of Prior Assessment Consultations regarding Regenerative Medical Products

	FY 2014	FY 2015	FY 2016	FY 2017
Conducted	0	1	0	0
Withdrawn	0	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)

3.2.(1).F.(iv) Promotion of evaluation of new technologies

3.2.(1).F.(iv).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 Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D) based on viewpoints presented in the following reports:
    - "Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products" dated August 14, 2015 (Cell Processing Center 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 (Cellular and Tissue-based Products Subcommittee).

  PMDA exchanged opinions about future international regulations on regenerative medical products and information on products under development with experts of regulatory authorities in the EU and the US at international academic conferences and through teleconferences on a regular basis.

3.2.(1).F.(iv).b. Knowledge accumulation

- PMDA has dispatched staff to Japanese academic conferences held by scientific societies including the Japanese Society for Regenerative Medicines, the Japan Society of Gene and Cell Therapy, and to international academic conferences held by the International Society for Cellular Therapy (ISCT), the Asian Cellular Therapy Organization (ACTO), and other meetings. Through these dispatch activities, PMDA endeavors to deepen its understanding of the needs of medical institutions engaged in the development of regenerative medical products and to collect information regarding their practical application.

3.2.(1).F.(iv).c. Support for the development of national guidelines

- PMDA collaborated with MHLW in the development of guidelines for the evaluation of products developed using state-of-the-art technologies, such as regenerative medical products.
- To proceed with the project on the development of guidance on the review of next-generation medical devices and regenerative medical products, PMDA participated as an observer in group

meetings regarding the regeneration of human (autologous) epidermis (skin) (entrustee, Rumi Sawada; chairperson, Hajime Matsumura [Chief Professor, Department of Plastic Surgery, Tokyo Medical University]) in FY 2017. PMDA thus supported the development of guidance on this matter.

- To proceed with the initiative to foster development of innovative drugs, medical devices, and regenerative medical products, PMDA supported research conducted at research institutions for the development of seed-stage resources. PMDA also supported study groups to evaluate regenerative medical products through the development of their guidelines, and the handling of public comments on draft guidelines for the following evaluations in FY 2017.
  - Cell-based products: 4 topics (Kyoto University [iPS platelets], Osaka University [cardiac failure, corneal epithelium disease], Mie University [cancer immunotherapy])
  - Gene therapy products: 1 topic (National Center for Child Health and Development [virotherapy for WAS])
  - Other products: 1 topic (Chiba University [central nervous system disorders])

3.2.(1).F.(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 RS Strategy Consultation (R&D). PMDA has promoted the use of RS Strategy Consultation (R&D) 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, PMDA received 42 initial clinical trial notifications, including those for investigator-initiated trials of regenerative medical products, between November 2014 and the end of FY 2017. PMDA has thus supported and promoted the execution of clinical trials [for the results of RS Strategy Consultations (R&D), see Section 3.2.(1).A.(vi).d.].
- For preliminary reviews under the Cartagena Act, see Section 3.2.(1).A.(vi).c.

3.2.(1).G. Promotion of GLP/GCP/GPSP compliance assessments and clinical trials, etc.

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

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

- PMDA discussed the potential use of electronic application data to select sites subject to on-site GCP inspections.
- 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 US FDA and EMA in the anticipation that GCP inspection reports will be exchanged between PMDA and these regulatory authorities. PMDA began participation in the EMA-US FDA GCP initiative on a pilot basis in June 2017 (until December 2018), with the aim of contributing to more efficient GLP/GCP/GPSP inspections and data integrity assessments.
- PMDA discussed how to conduct inspections of clinical trials that adopt CDISC standards. As a result, PMDA began to use electronic application data, if submitted, in a complementary manner before the conduct of inspections of clinical studies.

3.2.(1).G.(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 2017, PMDA conducted on-site GCP inspections of the manufacturer of 1 new medical device and 5 improved medical devices under the proper procedures and systems.
- PMDA participated in working-level meetings with respect to the "Cooperation Plan to Accelerate Reviews of Medical Devices" to exchange opinions with industry on specific requirements for compliance inspections to expedite reviews of medical devices. As a result, PMDA established a working group on increased reliability to discuss the above matters from a technical standpoint.
- PMDA agreed with industry on the content of the "Points to consider for implementation of document-based conformity inspection for medical devices (non-clinical studies)," prepared based on the "Cooperation Plan to Accelerate Reviews of Medical Devices." This guidance was posted on the PMDA website and issued as an administrative notice by the Office of Non-clinical and Clinical Compliance to prefectural governors and medical device-related organizations.

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

- In FY 2017, PMDA made preparations for conduct of inspections of regenerative medical products in accordance with the inspection procedure for drugs.

3.2.(1).G.(iv) Efficient GLP inspections and data integrity assessments

- Until the end of FY 2017, a staff member of the Office of Non-clinical and Clinical Compliance served 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.
- PMDA participated in the GLP working group of the OECD (a staff member of PMDA served as the chairperson until the end of FY 2017) and dispatched 1 staff member to the OECD office, thereby introducing PMDA's knowledge and know-how into international GLP-related activities.

3.2.(1).G.(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 2017.
- 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.) Based on this discussion, MHLW issued "Points to Consider for Reliability Assurance of Post-marketing Database Surveys of Drugs" (PSEHB/PED Notification No. 0221-1 dated February 21, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).
- PMDA completed a pilot survey of safety information control sheets. Companies participating in the pilot survey were required to submit relevant data by filling out the sheet. In September 2017, submitting some part of the data was made mandatory and other part of the data optional.
- In response to mandatory submission of some data in the safety information control sheet, PMDA revised the notification "Partial Revision of the 'Procedure for Document-based Compliance Assessment and On-site GPSP Inspections on Application Data for Re-examination/Re-evaluation of Drugs" (PMDA Notification No. 1128005 dated November 28, 2017, by the Chief Executive of the Pharmaceuticals and Medical Devices Agency).
- Office of Non-clinical and Clinical Compliance and Office of Medical Devices shared information regarding the progress of the inspection into re-examination of medical devices.
- PMDA participated in working-level meetings (the working group on increased reliability) on the "Cooperation Plan to Accelerate Reviews of Medical Devices," to exchange opinions with industry on specific requirements for compliance inspections to expedite reviews of medical devices.
- PMDA provided 15 re-examination compliance inspection consultations for drugs.

3.2.(1).G.(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, on-site GCP 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.

PMDA provided information regarding GLP/GCP/GPSP compliance assessments (e.g., points to consider), such as document-based compliance inspections, on-site GCP inspections, and post-marketing surveillance of medical devices, at briefing sessions hosted by the medical device-related organizations in October and November in 2017, and February in 2018.

Number of Participants in GCP/GPSP Workshops

Venue	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Tokyo	1,189	1,242	1,140	1,043	1,122
Osaka	404	448	352	368	385
Total	1,593	1,690	1,492	1,411	1,507

- As a sub-investigator, PMDA participated in a study group for Health and Labour Sciences Research, and conducted research on operation of GCP, to contribute to the efficient implementation of clinical trials. To introduce the ICH-E6 (R2) guidelines in Japan, PMDA prepared a draft revision of the guidance on the “Ministerial Ordinance on Good Clinical Practice for Drugs” and its draft notification.
- In FY 2014, PMDA launched new consultation categories concerning GCP/GLP/GPSP compliance assessments. PMDA provided 63 consultations for drugs, 39 for medical devices, and 3 for regenerative medical products in FY 2017.
- PMDA accepted any invitation to give lectures concerning GCP/GLP/GPSP, etc., to the extent scheduling and resources permitted, in order to foster greater understanding of GCP/GLP/GPSP compliance assessment procedures and requirements.

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

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Document-based assessments	2,610	2,396	2,332	2,066	2,118
New drugs	364	370	389	381	394
Generic drugs	1,086	1,080	1,045	870	883
Medical devices	1,160	946	894	812	840
Regenerative medical products	-	0	4	3	1
On-site GCP inspections	242	236	201	204	207
New drugs	222	221	191	191	192
Generic drugs	15	10	7	11	9
Medical devices	5	5	1	1	6
Regenerative medical products	-	0	2	1	0
Document-based assessments for re-examination	80	81	136	230	137
New drugs	71	74	120	176	106
New medical devices	9	7	16	54	31
On-site GPSP inspections for re-examination	71	74	120	176	107
New drugs	71	74	120	176	106
New medical devices	0	0	0	0	1
Document-based assessments for re-evaluation	0	0	19	0	0
On-site GPSP inspections for re-evaluation	0	0	19	0	0
GLP inspections	21	40	36	24	45
Drugs	18	27	22	17	22
Medical devices	3	13	9	4	14
Regenerative medical products	-	0	5	3	9

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," "on-site GCP 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.

3.2.(1).H. Promotion of GMP/GCTP/QMS inspections

3.2.(1).H.(i) Efficient GMP/GCTP/QMS inspections

3.2.(1).H.(i).a. Implementation of GMP/GCTP/QMS inspections

- In accordance with the amended Pharmaceutical Affairs Act, which came into effect in 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 associated 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.
- PMDA has begun to discuss a revision to the GMP Ordinance, revised in 2005, to harmonize the evolving international GMP regulations.
- In 2015, a MAH was found to have manufactured blood products for many years using processes diverging from those prescribed 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 (“Thorough Implementation of For-cause Inspections of Drugs,” PSEHB/CND Notification No. 0115-3 dated January 15, 2016, by the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In FY 2017, PMDA conducted 40 unannounced on-site inspections.

- PMDA issued “Confirmation of the Status of Pre-approval GMP Compliance Inspection for New Drugs” (Administrative Notice dated September 19, 2017, by the Office of Manufacturing/Quality and Compliance), in order to set a timeline for standard administrative procedures, to ensure expeditious and effective reviews. PMDA also issued “Submission Documents for Application of Drug Compliance Inspection” (Administrative Notice dated September 15, 2017, by the Office of Manufacturing/Quality and Compliance), to ensure that manufacturers submit appropriate application documents for GMP Inspections.
- As in previous years, PMDA joined the activities of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S), to promote international harmonization of GMP in Japan. PMDA also participated in the working group for the development of 4 PIC/S guidelines and 3 training programs.
- PMDA joined the international GMP inspection rationalization program for drug substance manufacturers, launched in FY 2016. Within the scope of the program, PMDA held a meeting to exchange information on GMP inspection plans and results etc., and conducted a joint inspection, thereby promoting international cooperation.
- 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 Practices)
  Note 2: QMS (Quality Management System)
  Note 3: GCTP (Good Gene, Cellular, and Tissue-based Product Manufacturing Practices)

3.2.(1).H.(i).b. Establishment of the inspection system

- PMDA had 60 GMP/GCTP/QMS inspectors (including inspectors in the Kansai Branch) at the end of FY 2017.

  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 Inspection Division of the Kansai Branch efficiently utilized the overall quality supervision system and conducted inspections mainly in the Western region of Japan, the Asian region.

- The processing status of GMP/GCTP/QMS inspections in FY 2017 is shown below. PMDA completed 15 QMS compliance inspections by using the Medical Device Single Audit Program (MDSAP) in FY 2017.

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

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

	FY 2014				FY 2015			
	Applied	Completed	Withdrawn	In progress	Applied	Completed	Withdrawn	In progress
Drugs*	1,877	1,672 (163)	51	1,030 (0)	1,719	1,647 (165)	67	1,039
In vitro diagnostics	65	38 (1)	0	27 (0)	1 179	1 (0) 146 (33)	0 1	0 50
Quasi-drugs	5	6 (0)	0	2 (0)	2	2 (0)	0	2
Medical devices	755	512 (42)	18	225 (86)	70 2,333	178 (25) 1,854 (326)	7 38	1 436
Regenerative medical products	0	0 (0)	0	0 (0)	9	8 (3)	1	0
Total	2,702	2,228 (206)	69	1,284 (86)	4,313	3,836 (552)	114	1,528

	FY 2016				FY 2017			
	Applied	Completed	Withdrawn	In progress	Applied	Completed	Withdrawn	In progress
Drugs*	1,818	1,783 (171)	122	959	1,753	1,796 (237)	119	796
In vitro diagnostics	0 54	0 (0) 83 (44)	1 1	0 20	0 61	0 (0) 49 (18)	0 3	0 29 (11)
Quasi-drugs	1	3 (0)	0	0	2	1 (0)	0	1
Medical devices	0 739	1 (0) 951 (251)	10 11	0 210	0 693	0 (0) 577 (142)	0 13	0 (0) 313 (115)
Regenerative medical products	1	0 (0)	0	1	0	1 (0)	0	0
Total	2,613	2,821 (466)	145	1,190	2,509	2,423 (397)	135	1,138 (126)

**) 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 to FY 2017 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 2017 are shown below:

Median Processing Time of GMP/GCTP/QMS Inspections

	FY 2012		FY 2013		FY 2014	
	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*	147	77	118	71	172	76
In vitro diagnostics	83	38	106	66	147	102
Quasi-drugs	-	-	272	71	166	96
Medical devices	113	21	106	56	118	74
Regenerative medical products	-	-	-	-	-	-
	FY 2015		FY 2016		FY 2017	
	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	81	163	84	149	59
In vitro diagnostics	160/120	38/72	772/128	30/57	-/118	-/70
Quasi-drugs	422	158	141	74	100	63
Medical devices	114/140	60/85	601/105	35/49	-/112	-/72
Regenerative medical products	84	54	-	-	128	47

** 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 2017 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs*	9 (4)	25 (11)	26 (18)	19 (11)	16 (6)
In vitro diagnostics	3 (3)	0 (0)	-	-	-
Medical devices	0 (0)	2 (2)	-	-	-
Regenerative medical products	-	1 (1)	1 (1)	-	3 (2)
Total	12 (7)	28 (14)	27 (19)	19 (11)	19 (8)

** 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 2017 is shown below:

Number of For-cause Inspections (Manufacturers in Japan)

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs*	6	5	7	15	31
In vitro diagnostics	1	0	0	0	0
Medical devices	0	0	0	0	0
Regenerative medical products	-	0	0	3	0
Total	7	5	7	18	31

** Excluding in vitro diagnostics.*

- PMDA conducts simple consultations concerning GMP/GCTP/QMS inspections. The number of such consultations conducted in FY 2017 is shown below.

Number of Simple Consultations Conducted for GMP/QMS Inspections

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs*	44	32	33	36	26
In vitro diagnostics	0	0	4	0	0
Quasi-drugs	0	0	0	0	0
Medical devices	3	51	64	34	11
Regenerative medical products	-	-	3	0	0
Total	47	83	104	70	37

** Excluding in vitro diagnostics.*

3.2.(1).H.(i).c. Promotion of on-site inspections of foreign manufacturing sites

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

On-site Inspections of Foreign Drug Manufacturing Sites by Region

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
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
FY 2017	9	7	89	0	105

Note: Breakdown of FY 2017:
Europe: Spain, Italy, Austria, Finland, and Romania
North, Central, and South America: the United States, Mexico, and Argentina
Asia/Oceania: China, India, South Korea, Taiwan, Singapore, Vietnam, Malaysia, and Macau

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

	Europe	North, Central, and South America	Asia/Oceania	Africa	Total
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	12	0	12
FY 2016	0	0	3	0	3
FY 2017	6	15	10	0	31

Note 1) Breakdown of FY 2017:
Asia, Oceania: China, South Korea, Thailand, and Taiwan
North, Central, and South America: the United States and Mexico
Europe: UK, Spain, and Germany

Note 2) The following number of inspections was corrected due to a change in the counting method.
The number of inspections in Asia and Oceania in FY 2015 was corrected from "9" to "12," resulting in a correction of the total number of inspections to "12."
The number of inspections in Asia and Oceania in FY 2016 was corrected from "2" to "3," resulting in a correction of the total number of inspections to "3."

- The table below shows the number of inspections of buildings and facilities in foreign manufacturing sites conducted in FY 2017 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs*	383	384	356	686	510
In vitro diagnostics	79	23	-	-	-
Quasi-drugs	58	58	33	69	54
Medical devices	1,453	722	-	-	-
Regenerative medical products	-	0	0	0	2
Total	1,973	1,187	389	755	566

** 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 2017 is shown below:

Number of For-cause Inspections at Foreign Manufacturing Sites

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs*	2	1	0	0	9
In vitro diagnostics	0	0	0	0	0
Medical devices	1	0	0	0	0
Regenerative medical products	-	0	0	0	0
Total	3	1	0	0	9

** Excluding in vitro diagnostics.*

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

Region	Country	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Europe	France	6	1	3	2	1	3	0	1	0
	Denmark	2	0	0	0	2	0	0	0	0
	Ireland	3	2	0	1	1	0	0	0	0
	UK	3	0	0	1	1	0	0	0	0
	Netherlands	5	0	0	2	0	0	0	0	0
	Spain	1	0	0	0	0	1	0	0	2
	Italy	3	2	0	1	2	3	0	1	3
	Belgium	4	3	1	0	2	3	0	1	0
	Austria	2	0	1	2	0	1	0	2	2
	Finland	2	0	0	1	0	0	0	0	1
	Germany	7	0	3	1	0	1	0	0	0
	Sweden	0	0	0	0	1	0	0	0	0
	Romania	0	0	0	0	1	0	0	0	1
	Czech Rep.	0	0	0	1	0	0	0	0	0
	Ukraine	0	0	0	1	0	0	0	0	0
	Lithuania	0	0	0	1	0	0	0	0	0
	Slovenia	1	0	0	0	0	0	0	0	0
	Portugal	0	3	0	0	0	0	0	0	0
	Greece	0	0	1	0	0	0	0	0	0
	Turkey	0	1	0	0	0	1	0	0	0
	Iceland	0	0	0	0	1	0	0	0	0
	Hungary	0	0	0	0	0	3	0	1	0
	Cyprus	0	0	0	0	0	1	0	0	0
	Latvia	0	0	0	0	0	2	0	0	0
	Slovakia	0	0	0	0	0	1	0	0	0
	Subtotal	39	12	9	14	12	20	0	6	9
North, Central, and South America	USA	18	23	6	14	8	3	2	6	2
	Canada	2	1	0	0	1	0	0	0	0
	Mexico	0	0	1	0	0	0	0	0	2
	Argentina	0	0	0	0	0	0	0	0	3
	Brazil	0	0	0	0	1	0	0	0	0
	Subtotal	20	24	7	14	10	3	2	6	7
Asia/Oceania	China	25	10	20	16	18	23	27	30	28
	India	4	7	4	4	3	4	19	18	30
	Singapore	0	0	0	0	2	0	0	1	1
	South Korea	9	10	18	14	11	13	10	11	19
	Indonesia	0	0	0	1	0	0	3	0	0
	Taiwan	6	1	1	2	6	6	2	6	8
	Thailand	2	0	1	0	2	1	0	1	0
	Vietnam	0	1	1	0	0	3	0	0	1
	Israel	0	0	0	1	0	0	0	0	0
	New Zealand	1	0	0	0	0	0	0	0	0
	Malaysia	0	0	0	0	0	1	0	0	1
	Macau	0	0	0	0	0	0	0	0	1
Subtotal		47	29	45	38	42	51	61	67	89
Grand Total		106	65	61	66	64	74	63	79	105

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 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Europe	Ireland	0	4	1	3	0	1	0	0	0
	UK	0	0	1	0	1	2	0	0	2
	Italy	0	2	1	1	0	1	0	0	0
	Netherlands	0	1	0	0	0	0	0	0	0
	Switzerland	1	0	0	0	1	0	0	0	0
	Spain	0	0	0	1	0	0	0	0	1
	France	1	1	1	4	0	0	0	0	0
	Denmark	1	0	0	0	0	0	0	0	0
	Austria	0	0	0	1	0	0	0	0	0
	Belgium	0	0	0	1	0	0	0	0	0
	Turkey	0	0	0	0	1	0	0	0	0
	Germany	0	0	0	0	0	0	0	0	3
	Subtotal	3	8	4	11	3	4	0	0	6
North, Central, and South America	USA	27	19	12	21	8	4	0	0	12
	Mexico	0	0	1	0	0	1	0	0	3
	Brazil	1	0	0	0	0	0	0	0	0
	Canada	0	0	1	1	4	0	0	0	0
	Costa Rica	0	0	1	0	0	0	0	0	0
	Subtotal	28	19	15	22	12	5	0	0	15
Asia	China	3	0	0	1	1	6	0	0	2
	South Korea	0	1	0	0	5	8	7	2	6
	Thailand	0	0	0	1	0	0	0	0	1
	Singapore	2	0	0	0	2	1	1	1	0
	Philippines	0	0	0	2	0	0	0	0	0
	Israel	0	0	1	0	1	0	0	0	0
	Taiwan	0	0	0	0	1	3	3	0	1
	UAE	0	0	0	0	1	0	0	0	0
	Malaysia	0	0	0	0	0	1	1	0	0
	India	0	0	0	0	0	1	0	0	0
	Subtotal	5	1	1	4	11	20	12	3	10
Grand Total		36	28	20	37	26	29	12	3	31

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: Due to a change in the method of counting the number of inspections at foreign manufacturing sites by country, the number in Korea in FY 2015 was corrected from "4" to "7," resulting in a correction of the subtotal in Asia and the grand total from 9" to "12" for both. The number in Korea in FY 2016 was also corrected from "1" to "2," resulting in a correction of the subtotal in Asia and the grand total from "2" to "3" for both.

3.2.(1).H.(i).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.

3.2.(1).H.(i).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 2017, PMDA conducted inspections of Japanese certification bodies: 12 periodic for-cause inspections.

3.2.(1).H.(i).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 (13 inspections conducted in FY 2017).

Note: The Medical Device Single Audit Program (MDSAP) permits auditing organizations jointly certified by participating regulatory authorities (Japan, USA, Canada, Australia, and Brazil) to conduct a single QMS inspection of a medical device manufacturer. The inspection results are shared and utilized by the regulatory authorities within the range of individual regulations.

3.2.(1).H.(ii) Building of the inspection system based on the Act on Safety of Regenerative Medicine

3.2.(1).H.(ii).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.

  PMDA is also required to conduct for-cause inspections according to instructions from the Health Policy Bureau of MHLW. In FY 2017, PMDA conducted one for-cause inspection at the request of MHLW.

  As in previous years, PMDA provided training on inspection methods to inspectors in the Office of Manufacturing/Quality and Compliance, to enhance their inspection proficiency. PMDA is also making efforts to secure the necessary number of inspectors to handle all applications submitted.

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
Applications for manufacturing licensure (in Japan)	19	0	0	19	43	37 (36)	2	4	13	7 (7)	1	5
Applications for manufacturing licensure (outside Japan)	0	0	0	0	4	1 (1)	1	2	2	1 (1)	0	1
For-cause Inspections	0	0 (0)	0	0	0	0 (0)	0	0	0	0 (0)	0	0
Total	19	0	0	19	47	38 (37)	3	6	15	8 (8)	1	6

	FY 2017			
	Application	Completed	Withdrawn	In progress
Applications for manufacturing licensure (in Japan)	9	7 (7)	0	2
Applications for manufacturing licensure (outside Japan)	1	0 (0)	0	1
For-cause Inspections	0	1 (1)	0	0
Total	10	8 (8)	0	3

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		FY 2017	
	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)	Median total processing time (days)	Median PMDA processing time (days)
Applications for manufacturing licensure (in Japan)	-	-	134	83	142	64	127	80
Applications for manufacturing licensure (outside Japan)	-	-	166	136	133	114	-	-

Number of For-cause Inspections Conducted by PMDA

Region	FY 2014	FY 2015	FY 2016	FY 2017
Japan	0	0	0	1
Outside Japan	0	0	0	0
Total	0	0	0	1

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
FY 2017	0	0	1	0	1

Number of On-Site Inspections of Foreign Facilities by Region

Region	Country	FY 2014	FY 2015	FY 2016	FY 2017	Total
Europe	-	-	-	-	-	-
	Subtotal	-	0	0	0	0
North, Central, and South America	-	-	-	-	-	-
	Subtotal	-	0	0	0	0
Asia	South Korea	-	2	2	0	4
	Taiwan	-	0	0	1	1
	Subtotal	-	2	2	1	5
Grand Total		-	2	2	1	5

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

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

- The Science Board was established in May 2012 as a forum where PMDA reviewers exchange opinions with leading researchers in Japan regarding methods of evaluating new and advanced sciences and technologies. PMDA continued to hold Science Board meetings in FY 2017. For details regarding the “Use of the Science Board” during its third term (April 2016 to March 2018), see Section 3.4.
- The initiative to foster development of innovative drugs, medical devices, and regenerative medical products, was completed in FY 2016. The guidelines (Guidelines for Evaluation of Non-contact Power Feeding System for Implantable Medical Devices) developed based on the outcomes of the initiative were issued by MHLW (PSEHB/MDED Notification No. 0809-7 dated August 9, 2017, by the Director of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).
- To ensure the proper execution of reviews, safety measures, and relief services for adverse health effects, and to enhance the quality of these operations, 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 2017, 8 projects (4 new project and 4 ongoing projects) were selected as designated research and the results of 5 of these projects were published in academic journals or lecture meetings (3 published in papers, 2 lectures).
- PMDA completed preparations for the establishment of the Regulatory Science Center by the end of FY 2017, and launched the Center as planned in April 2018.
- 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, “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 2017, individual working groups collaborated with MHLW to issue the following notifications:

  Pediatric Drugs WG:
  “Addendum to ICH E11: Clinical Investigation of Medicinal Products in the Pediatric Population” (PSEHB/PED Notification No.1227-5, dated December 27, 2017, by the Director of the

Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

Omics WG:
"Guideline on Genomic Sampling and Management of Genomic Data" (PSEHB/PED Notification No. 0118-1, dated January 18, 2018, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW)

ICH Q12 WG:
"Treatment of Changes to Approved Product Information related to Drug Product Quality" (PSEHB/PED Notification No. 0309-1 and PSEHB/CND Notification No. 0309-1, dated March 9, 2018, jointly issued by the Directors of the Pharmaceutical Evaluation Division and the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

- The Companion Diagnostics WG for Projects Across Multi-Offices exchanged opinions with related industry organizations about a draft administrative notice for companion diagnostics.
- The Pediatric Drugs WG for Projects Across Multi-Offices had teleconferences with US FDA and EMA experts on a regular basis to share issues to solve and discuss countermeasures. The Pediatric Drugs WG also participated as an observer in the study group for practical application of pediatric drugs, led by the Japan Agency for Medical Research and Development (AMED).
- The Innovative Manufacturing Technology WG for Projects Across Multi-Offices produced a document, "PMDA Views on the Application of Continuous Manufacturing to Pharmaceutical Products for Industry (provisional draft)," which was posted on the PMDA website.
- The ICH Q12 WG for Projects Across Multi-Offices exchanged opinions about the draft ICH Q12 Guidelines with related industry organizations and held a briefing session for the industry to seek public comments on the draft guidelines.
- The Pediatric Drugs WG, Omics WG, Nanomedicine Initiative WG, ICH Q12 WG, Cardiovascular Risk Evaluation WG, and Innovative Manufacturing Technology WG for Projects Across Multi-Offices exchanged opinions with US FDA, EMA, and other foreign regulatory authorities.
- The ICH Q12 WG, Clinical Innovation Network WG, Innovative Manufacturing Technology WG, and Cardiovascular Risk Evaluation WG for Projects Across Multi-Offices facilitated the exchange of opinions between the industry, government, and academia by cooperating with the AMED Research Project. The Clinical Innovation Network WG and the AMED Research Project Group also co-hosted a symposium titled "Policy for Data Reliability to Utilize Patient Registries Under the Regulatory Framework."

3.2.(2).(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 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 the report, PMDA discussed measures to support the practical application of innovative drugs, medical devices, and regenerative medical products, and took the following actions in April 2017:

(a) The Division of Pharmaceutical Affairs Consultation was renamed the Division of Innovation Support and Consultations on R&D Strategy.

(b) Pharmaceutical Affairs Consultation on R&D Strategy (introductory consultation, pre-consultation, and face-to-face consultations) was reorganized into RS General Consultation (introductory consultations) and RS Strategy Consultation (R&D) (pre-consultation consultation and face-to-face consultations).

(c) Development of Procedures for Consultation on Cooperation for Practical Application of Innovation Advancements.

- To promote the use of PMDA's Kansai Branch Office, PMDA posted on its website a guide to the "video conference system," which allows applicants to receive RS General Consultations and RS Strategy Consultations (R&D) without visiting the PMDA head office in Tokyo. The Kansai Branch Office prepared leaflets stating that these consultations are available at the Kansai Branch Office, and distributed them to academic institutions, etc. based in the Kansai region. The Kansai Branch Office also organized lecture activities and observational tours to familiarize interested parties with its consultation services.

  The video conference system has been available also for consultations on safety measures since November 2017. A total of 59 consultations, including 11 RS Strategy Consultations (R&D), used the video conference system in FY 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 that research projects adopted by AMED that have advanced to the stage of practical application should in principle undergo RS Strategy Consultation (R&D). PMDA held discussions, as appropriate, with AMED about the timing and content of RS Strategy Consultations (R&D) for research projects.

3.2.(2).(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 RS Strategy Consultations (R&D), and provided relevant information at academic conferences and similar events, and thus promoted the use of the system.

3.2.(2).(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, PMDA's review offices conducted pre-evaluations of products submitted to be considered for SAKIGAKE designation. Based on the results of the pre-evaluations, MHLW designated 17 drugs, 7 medical device products, 1 *in vitro* diagnostic product, and 9 regenerative medical products as SAKIGAKE-designated products in FY 2017. The progress of regulatory review process for these designation products was managed by review partners on a per product basis. (Designation for 1 drug and 1 medical device was cancelled by the end of FY 2017). The

standard review period for SAKIGAKE-designated products is 6 months. In FY 2017, 1 medical device (application date: June 30, 2017) was approved on December 15, 2017; this was the first product to be approved within the standard review period of 6 months. In addition to this product, 2 other drugs were approved under the SAKIGAKE designation system. A current list of SAKIGAKE-designated products and a summary of their characteristics are both available on the PMDA website.

3.3 Safety Measure Services

3.3.(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 encourage patients and healthcare professionals to use these products as safely as possible, PMDA works to efficiently collect and examine product safety information, process this information, devise appropriate corrective and preventative measures, and rapidly disseminate the details of these measures with easy-to-understand safety information, in order to integrate the risk management aspects of both PMDA's reviews and pharmacovigilance activities.
- Every year, PMDA receives various types of case reports from industry: approximately 486,000 reports on serious adverse reactions and infections attributable to drugs (from Japanese and foreign companies); approximately 51,000 reports on medical device malfunctions and infections attributable to medical devices (from Japanese and foreign companies); approximately 110 reports on regenerative medical product malfunctions and infections attributable to such products; approximately 4,000 case reports on suspected malfunctions, etc. of equipment components from combination products (from Japanese and foreign companies); and 216 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 US 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 and Safety offices, and between the relief office and safety offices.
- Based on the 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs	160	100	87[*2]	152	219[*3]
Medical devices	14	4	28	6	0
Regenerative medical products	-	0[*1]	0	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 drugs and 3 reports concerning in vitro diagnostics.*

**3 A total of 218 reports concerning drugs and 1 report concerning quasi-drugs*

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

		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs	Directions for revision to precautions in package insert	160	100	87[*1]	152	219[*2]
	Releasing PMDSI reports	40	29	28[*3]	32	32
Medical devices	Directions for revision to precautions in package insert or issuance of self-check notifications[*4]	11 (3)	4 (2)	28 (3)	6 (1)	0 (0)
	Releasing PMDSI reports	4	1	1	0	0
Regenerative medical products	Directions for revision to precautions in package insert or issuance of self-check notifications	-	0[*5]	0	0	0
	Releasing PMDSI reports	-	0[*5]	0	0	0

**1 A total of 84 reports concerning drugs and 3 reports concerning in vitro diagnostics.*
**2 A total of 218 reports concerning drugs and 1 report concerning quasi-drugs*
**3 A total of 27 reports concerning drugs and 1 report concerning in vitro diagnostics.*
**4 Figures in parentheses indicate the number of notifications, etc.*
**5 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 codeine and tramadol were revised to add the statement, “this product should not be used in children under the age of 12 years” etc.
- The precautions concerning anaphylaxis in the package inserts for chlorhexidine gluconate and chlorhexidine hydrochloride were revised.
- The precautions in the package inserts for gadolinium-based contrast agents were revised to include the statement, “the necessity of performing MRI scans using gadolinium-based contrast agents should be determined carefully,” since it is known to remain in the brain.
- The precautions in the package inserts for propofol were revised to delete the contraindication in pregnant and parturient women.
- The precautions in the package inserts for adrenergics and antipsychotics with α-blocking activity were revised to delete the contraindication of concomitant use of these drugs.
- As collaborative activities with its 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 together with 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. In accordance with the PMD Act, PMDA has organized information and conducted a survey of applications for relief benefits in collaboration with Office of the Relief Fund. 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 evaluated post-marketing safety data regarding drugs approved on the condition that MAHs conduct post-marketing surveillance covering all patients treated. PMDA also held consultations with such MAHs and provided instruction as necessary to distribute information materials to patients and healthcare professionals who use the drugs.

  When the approval conditions of a drug were lifted, PMDA notified the public and medical information-related parties by releasing the risk management plan (RMP) and package inserts.

- As for collaboration with overseas regulatory authorities, PMDA officially started participating as an observer in US FDA-EMA pharmacovigilance cluster in FY 2016. Up to date, PMDA has participated in 7 teleconferences. Through these activities, PMDA endeavors to participate in the global exchange and early stage consideration of safety information.

- 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 2017 PMDA carried out the following actions:

  a. In FY 2016, PMDA launched an electronic reporting system for adverse drug reactions in accordance with the ICH-E2B (R3) guideline. The agency has conducted operations for the system without delay. (Paper reporting will be completely replaced by electronic reporting in April 2019).

  b. PMDA upgraded the malfunction data management system so that the agency can receive malfunction case reports more efficiently.

  c. In April 2018, PMDA upgraded the system for receiving disease reports in line with enforcement of the Clinical Research Act.

  d. There are 2 systems used to manage ADR reports received from medical institutions: the receipt management system and the progress management system. These systems were integrated to enhance usability.

  e. PMDA began to deliver lectures to healthcare professionals, in order to familiarize them with adverse reaction reporting, to increase adverse reaction reports from medical institutions. PMDA also supported the project (regulatory harmonization research initiative) implemented by the Japan Agency for Medical Research and Development (AMED) to promote reporting of adverse drug reactions.

Collection of adverse reaction reports etc.

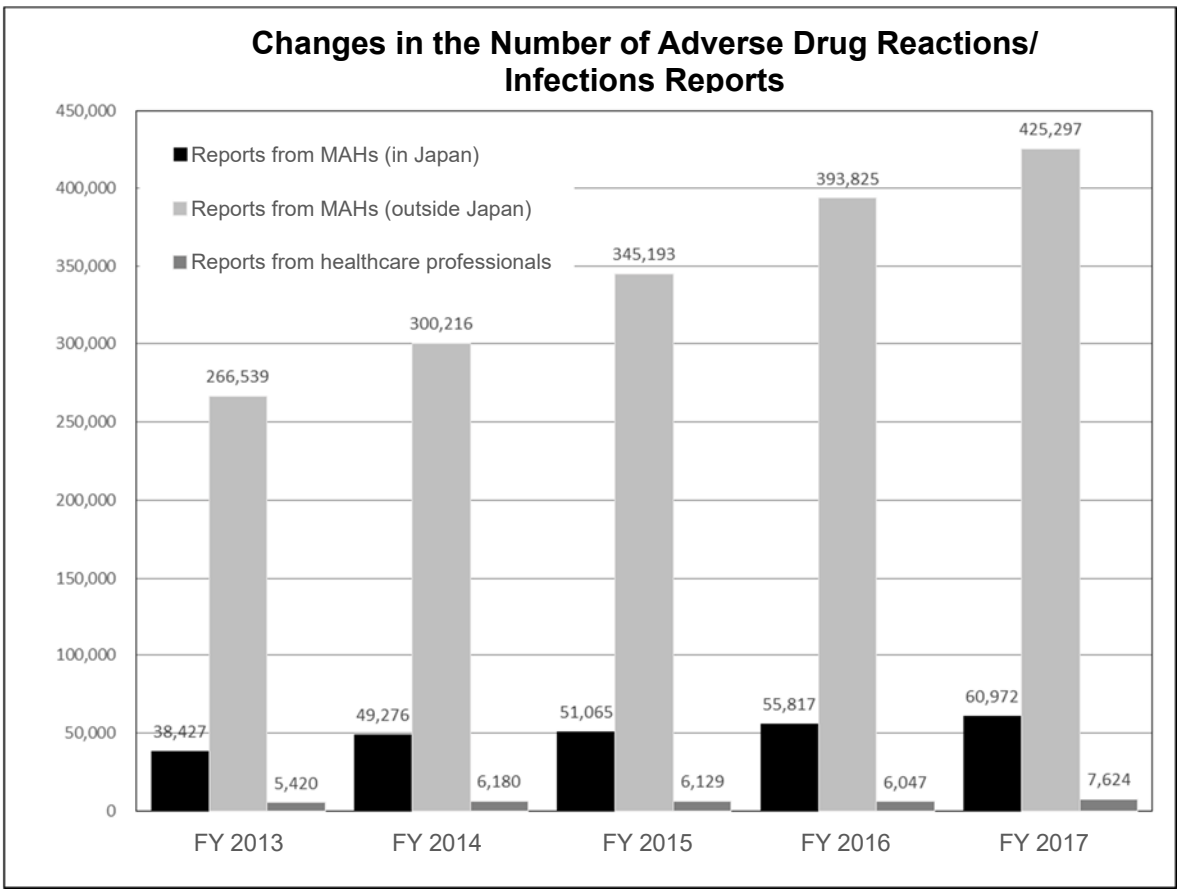
1-1) Number of reports relating to drugs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Reports from MAHs	308,383	352,908	399,852	453,296	490,019
(adverse drug reactions, in Japan)	(38,329)	(49,198)	(50,977)	(55,728)	(60,872)
(infections caused by drugs, in Japan)	(98)	(78)	(88)	(89)	(100)
(adverse drug reactions, outside Japan)	(266,506)	(300,191)	(345,161)	(393,767)	(425,251)
(infections caused by drugs, outside Japan)	(33)	(25)	(32)	(58)	(46)
(research reports)	(962)	(1,099)	(1,219)	(1,117)	(1,206)
(foreign safety measure reports)	(1,317)	(1,219)	(1,273)	(1,397)	(1,492)
(periodic infection reports)	(1,138)	(1,098)	(1,102)	(1,140)	(1,052)
Reports from healthcare professionals	5,420	6,180	6,129	6,047	7,624
([1] Safety information reporting system)	(4,067)	(4,782)	(4,891)	(4,956)	(6,606)
([2] Vaccines)	(1,353)	(1,398)	(1,238)	(1,091)	(1,018)
Total	313,803	359,088	405,981	459,343	497,643

		FY 2014	FY 2015	FY 2016	FY 2017
Cases of malfunctions of combination drugs (in Japan)	Reports from MAHs	0	38	661	1,120
	Reports from healthcare professionals	-	-	4	12
Cases of malfunctions of combination drugs (outside Japan)	Reports from MAHs	0	60	1,126	2,951

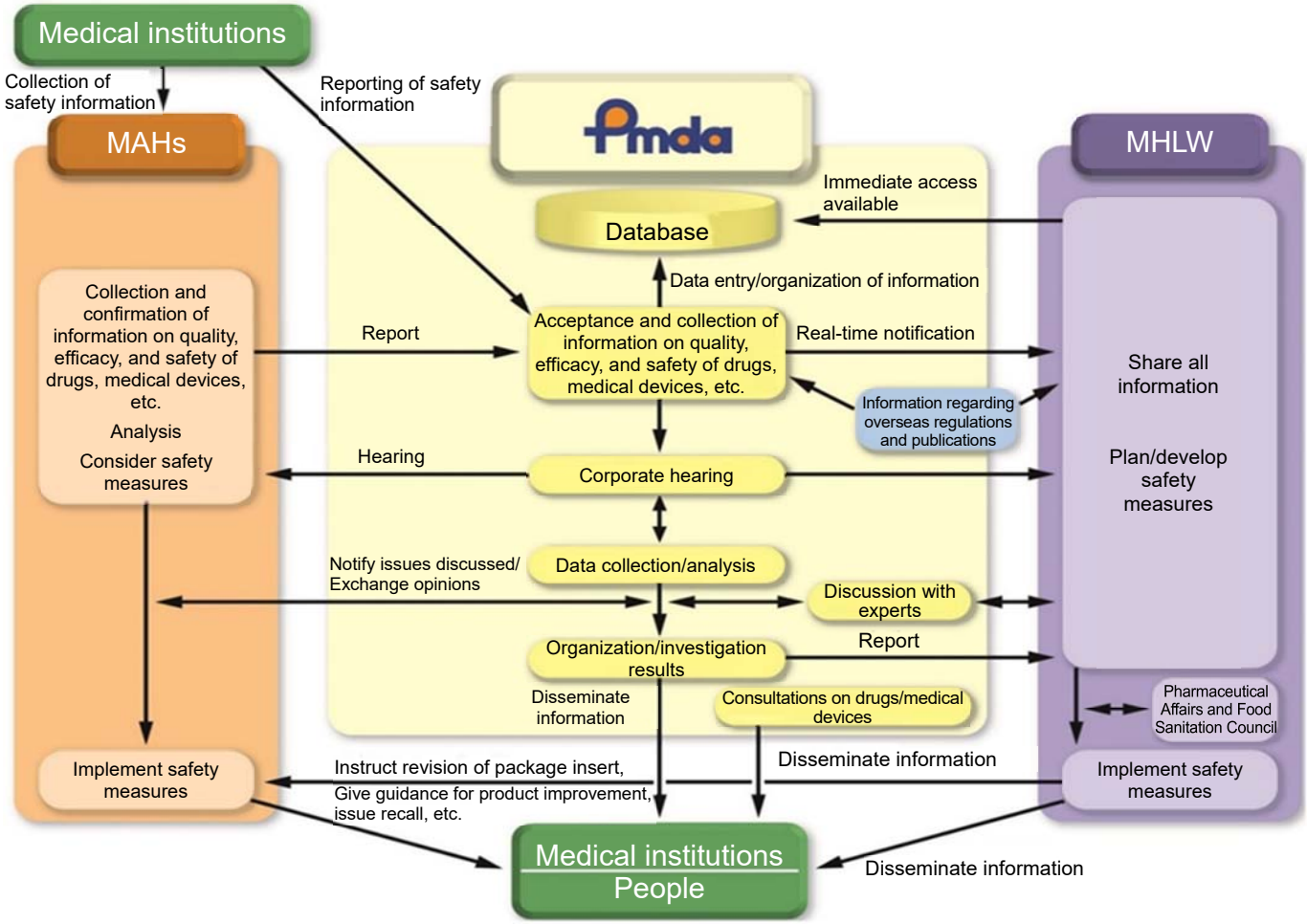
Note: The transitional period (during which reporting was not mandatory) was from November 25, 2014 to November 24, 2016. Reporting was made mandatory on November 25, 2016. The number of reports in FY 2014 is the number of reports after enactment of the PMD Act on November 25, 2014.

	FY 2014	FY 2015	FY 2016	FY 2017
Quasi-drugs	561	323	146	119
Cosmetics	116	114	71	97



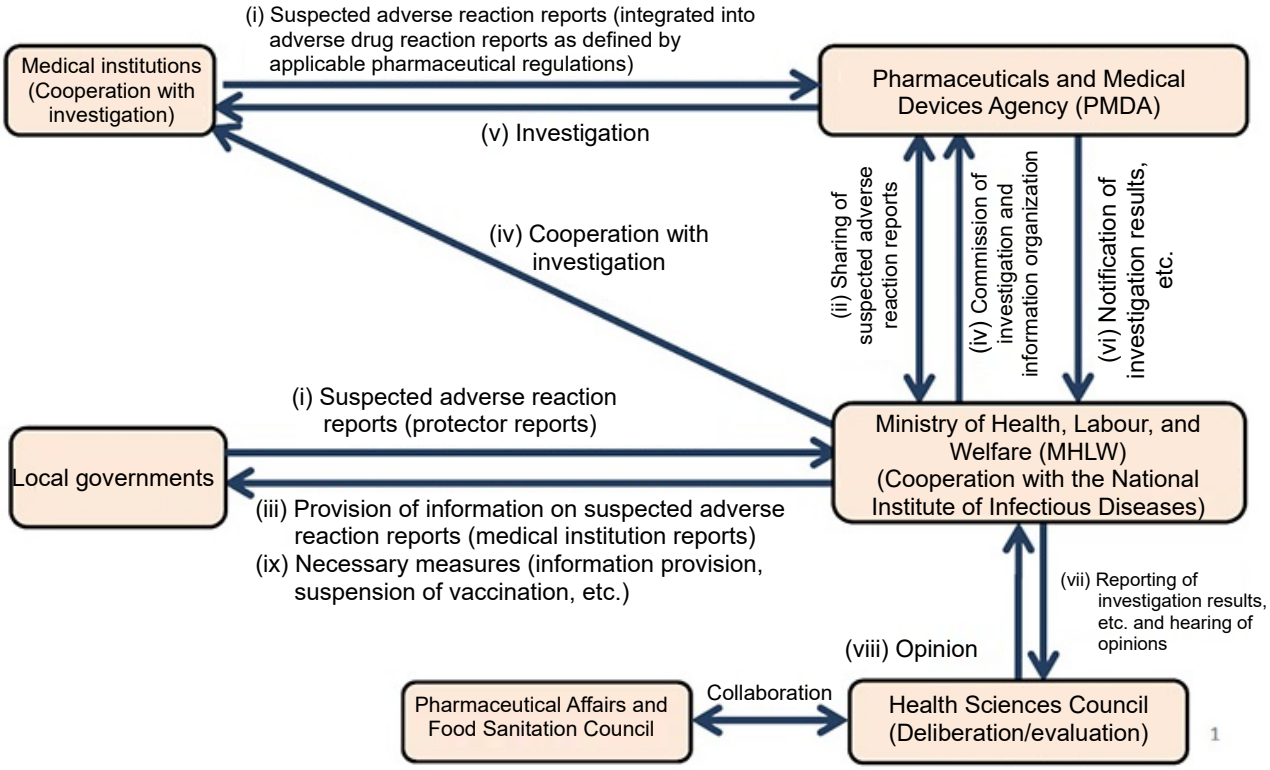
- MAHs submit to PMDA adverse drug reaction/infectious disease reports originally made by healthcare professionals and other sources. Among the reports submitted by MAHs in Japan in FY 2017, 88.9% had been collected from healthcare professionals (physicians, 67.2%; pharmacists, 14.5%; other healthcare professionals, 7.2%) and 11.1% from non-healthcare professionals (attorneys, 0.0%; consumers or other non-healthcare professionals, 7.1%; unknown, 4.0%).
- In total, 98.6% of adverse drug reaction/infection reports from MAHs in Japan, were submitted electronically (online reporting),[1] and 34.3% of adverse drug reaction reports from healthcare professionals were submitted electronically (by email).[2]

[1, 2] Including reports exempted from reporting requirements (e.g., follow-up reports).


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.” As of November 25, 2014, suspected adverse reaction reports have to be submitted to PMDA in accordance with the revised Preventive Vaccination Act and the Ministerial Ordinance for Enactment thereof (see diagram below). In FY 2017, PMDA received 1,018 suspected adverse reactions reports. After receiving suspected adverse reaction reports, PMDA provides the information to the MAHs of the suspect vaccines, and instructs medical institutions etc. to properly handle such events in accordance with the regulations set forth in 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 experiencing adverse drug 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 by the end of FY 2018.

In FY 2017, PMDA (1) confirmed the reports collected from patients; (2) implemented, on a trial basis, the procedures for efficiently collecting data needed to evaluate reported cases (the procedures established in FY 2016); and (3) continued preparatory work for the full-scale operation of the patient reporting system.

The table below shows the number of adverse drug reaction reports from patients collected by FY 2017. PMDA has been disclosing the reported cases as they come to hand.

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Patient-submitted adverse drug reaction reports (total number)*	122	91	186	50	84

* *The figures indicate the numbers of reports at the end of each fiscal year. Reports may be withdrawn at the request of reporters. Reports concerning items not classified as patient-submitted adverse drug reaction reports (including reports concerning quasi-drugs, cosmetics, and nutraceuticals) are excluded.*

1-4) PMDA's detailed investigation on reports from medical institutions

PMDA has worked to collect adverse drug reaction reports from medical institutions more comprehensively, by directing its inquiries to medical institutions on some of serious cases for the purpose of investigation.

Specifically, cases of suspected serious adverse drug reactions that reflect either of the following circumstances are subject to investigation by PMDA: no information was provided by a medical institution to a MAH; or 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.

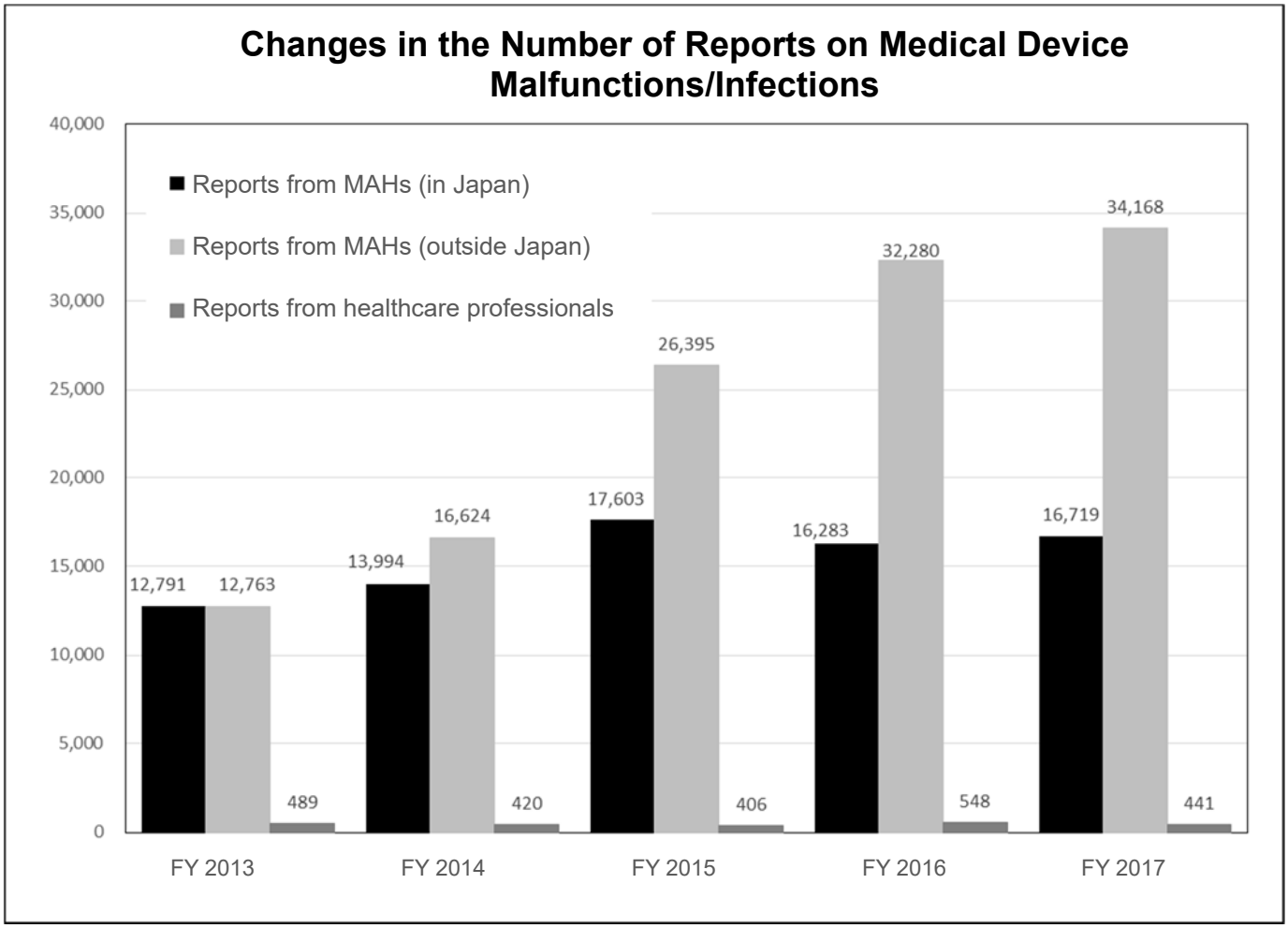
The numbers of cases investigated by PMDA in previous fiscal years are provided in the table below.

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of cases investigated by PMDA	862	1,067	1,100	1,132	1,453

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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Reports from MAHs	27,303	32,490	46,406	52,063	56,081
(Medical device malfunctions, in Japan)	(12,791)	(13,994)	(17,603)	(16,283)	(16,719)
(Medical device malfunctions, outside Japan)	(12,763)	(16,624)	(26,394)	(32,280)	(34,168)
(Infections caused by drugs, in Japan)	(0)	(0)	(0)	(0)	(0)
(Infections caused by drugs, outside Japan)	(0)	(0)	(1)	(0)	(0)
(Research reports)	(5)	(20)	(598)	(1,289)	(2,701)
(Foreign safety measure reports)	(1,669)	(1,779)	(1,742)	(2,144)	(2,437)
(Periodic infection reports)	(75)	(73)	(68)	(67)	(56)
Reports from healthcare professionals	489	420	406	548	441
Total	27,792	32,910	46,812	52,611	56,522



- In total, 78.6% of medical device malfunction/infection reports from MAHs in Japan, were submitted electronically (online reporting),[1] and 57.0% of medical device malfunction reports from healthcare professionals were submitted electronically (by email).[2]

*1 *2 Including reports exempted from reporting requirements (e.g., follow-up reports).

3) Number of reports relating to regenerative medical products

	FY 2014*	FY 2015	FY 2016	FY 2017
Reports from MAHs	17	49	122	144
(Medical device malfunctions, in Japan)	(12)	(35)	(88)	(110)
(Medical device malfunctions, outside Japan)	(0)	(0)	(0)	(0)
(Infections caused by drugs, in Japan)	(0)	(0)	(0)	(0)
(Infections caused by drugs, outside Japan)	(0)	(0)	(0)	(0)
(Research reports)	(0)	(0)	(0)	(0)
(Foreign safety measure reports)	(0)	(0)	(0)	(0)
(Periodic infection reports)	(5)	(14)	(34)	(34)
Reports from healthcare professionals	0	0	0	0
Total	17	49	122	144

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

3.3.(ii) Sophistication of safety measures

3.3.(ii).a. Introduction of the risk management system and implementation of appropriate safety measures based on the risk management plan for drugs

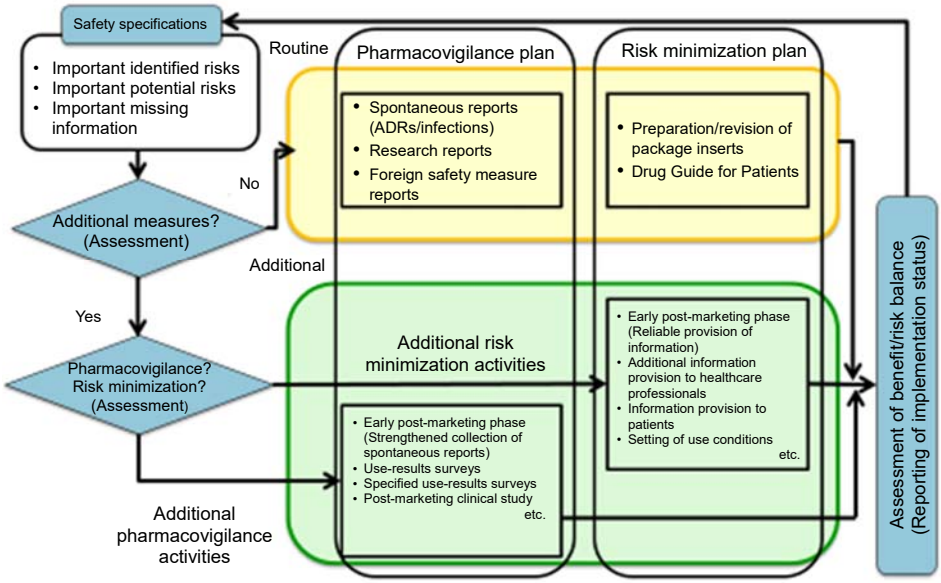
- PMDA launched a full-scale risk management system in FY 2011, and has been improving the system to consistently manage drug safety from the development phase to the post-marketing phase by having Risk Managers also work in Offices of New Drugs. As of March 2018, 14 Risk Managers were assigned to each 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, PMDA's Safety and Review offices cooperate to evaluate proposed RMPs for products under review by identifying safety specifications and assessing the appropriateness of pharmacovigilance and risk minimization activities. To ensure that these activities are appropriately conducted, PMDA directs inquiries regarding RMPs to applicants during the review process. While providing guidance and instructions through discussions with applicants, evaluation of RMPs is completed by the end of review process.

  In May 2016, PMDA published its first "Summary RMPs" (a list of the contents of different RMPs) as well as more detailed information concerning RMPs on the PMDA website, to promote the use of RMPs in medical practice. As of the end of March 2018, Summary RMPs are available on the website for all RMPs submitted.

  In FY 2017, new RMPs for 63 products and revised RMPs for 252 products (total) were posted on the PMDA website. The number of RMPs available on the PMDA website as of the end of FY 2017 is shown in the table entitled "Number of Information Documents Released on the PMDA's Website as of the End of FY 2017."

Outline of Risk Management Plan

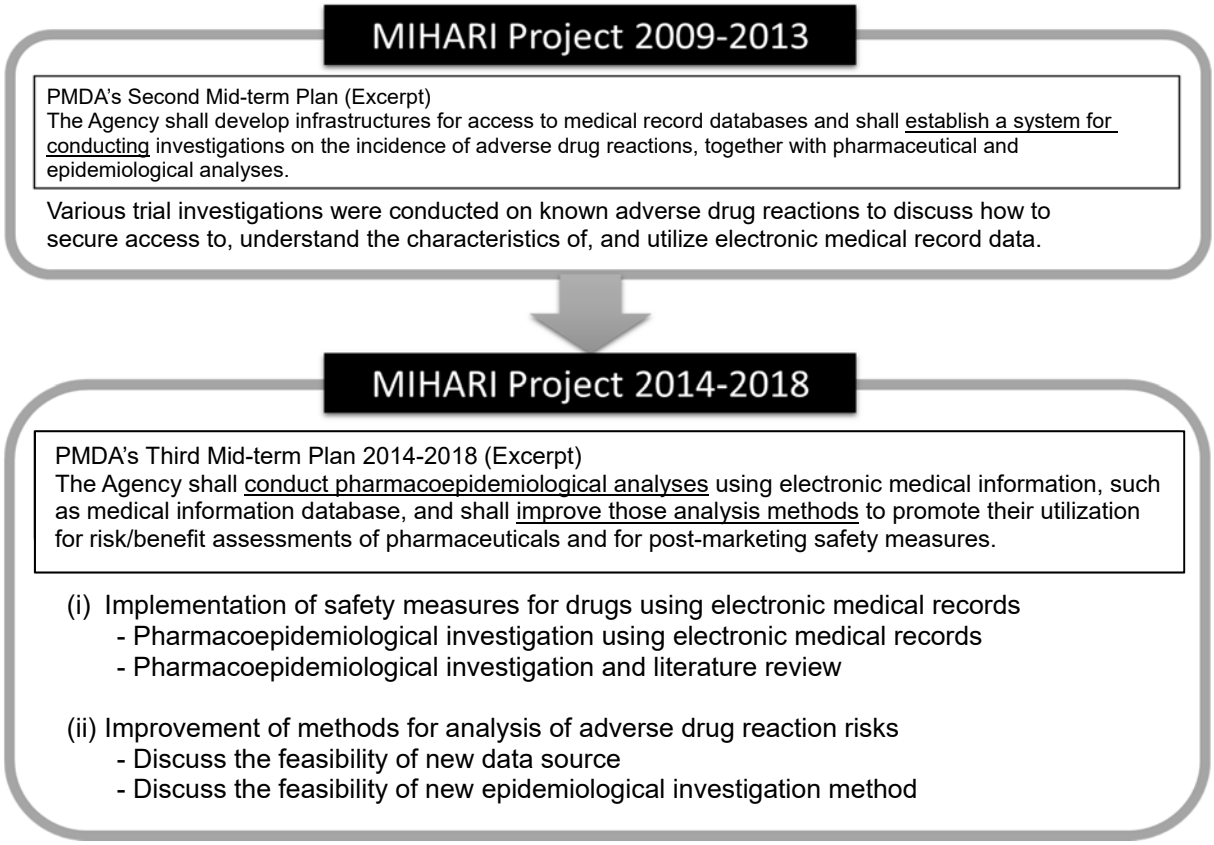


3.3.(ii).b. Use of electronic medical records etc.

- In accordance with the Third Mid-term Plan, PMDA plans 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 incorporating electronic medical records (including claims data and hospital information system data) for post-marketing drug safety evaluation (see below figure).

Course for the MIHARI Project under the Third Mid-term Plan

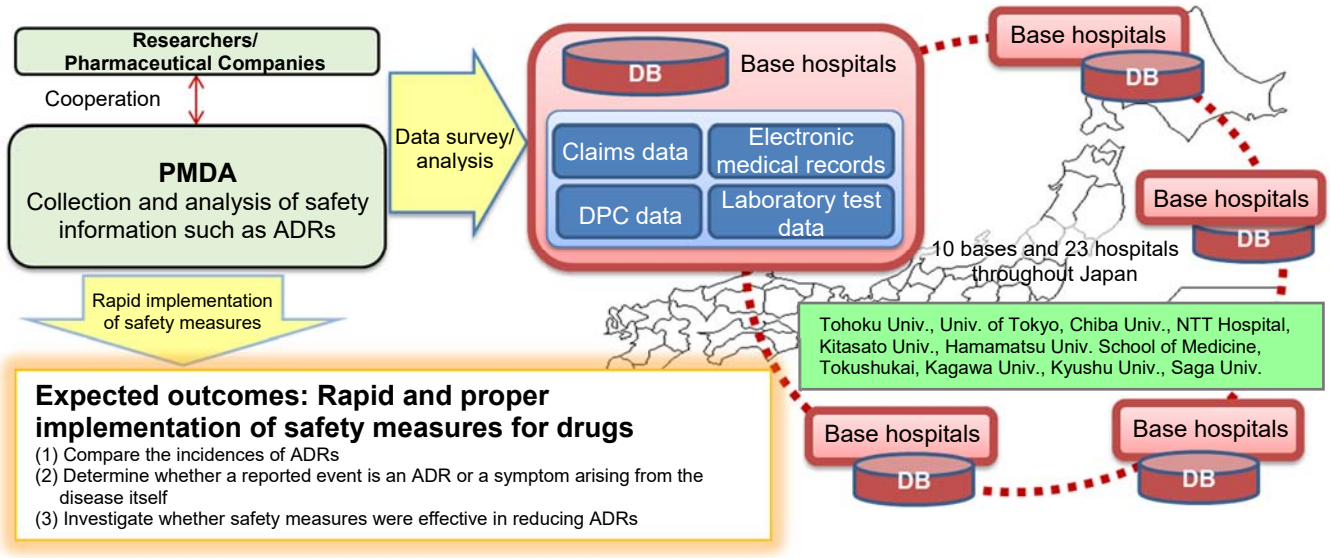


In FY 2017, PMDA's Offices of New Drugs in its Review Division and its Offices of Safety worked together to conduct (a) reviews of post-marketing surveillance plans submitted by pharmaceutical companies and the pharmacoepidemiological research literature; and (b) a survey to investigate the status of prescription drugs and analyze risks by using databases (information from the survey and risk analysis is intended to be used as data to support regulatory decision-making). PMDA completed its analysis of "Comparison of cardiovascular risk by antidiabetic drug class" using the National Claim Data managed by the MHLW Health Insurance Bureau as a new data source. PMDA then published the results of this analysis in a journal. In a working group with the pharmaceutical industry, hosted by MHLW, PMDA identified epidemiology-related issues to be addressed by the government (e.g., the launch of an "epidemiology consultation" service), to discuss the use of various medical information databases for safety measures or re-examination. As a result, the following notifications were issued in FY 2017: "Basic Principles on the Use of Medical Information Databases in Post-marketing Pharmacovigilance," "How to Proceed with Discussions to Formulate a Post-marketing Surveillance Protocol," and "Entry Guideline for Post-marketing Database Survey Protocol". PMDA officially launched a new consultation service, "Consultation on Epidemiological Surveys" in November 2017.

The Office of Healthcare Policy, Cabinet Secretariat, held discussions in preparation for enforcement of the Next Generation Medical Infrastructure Act. PMDA supported the discussions, thereby contributing to solving problems that may hinder enforcement of the Act.

- 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

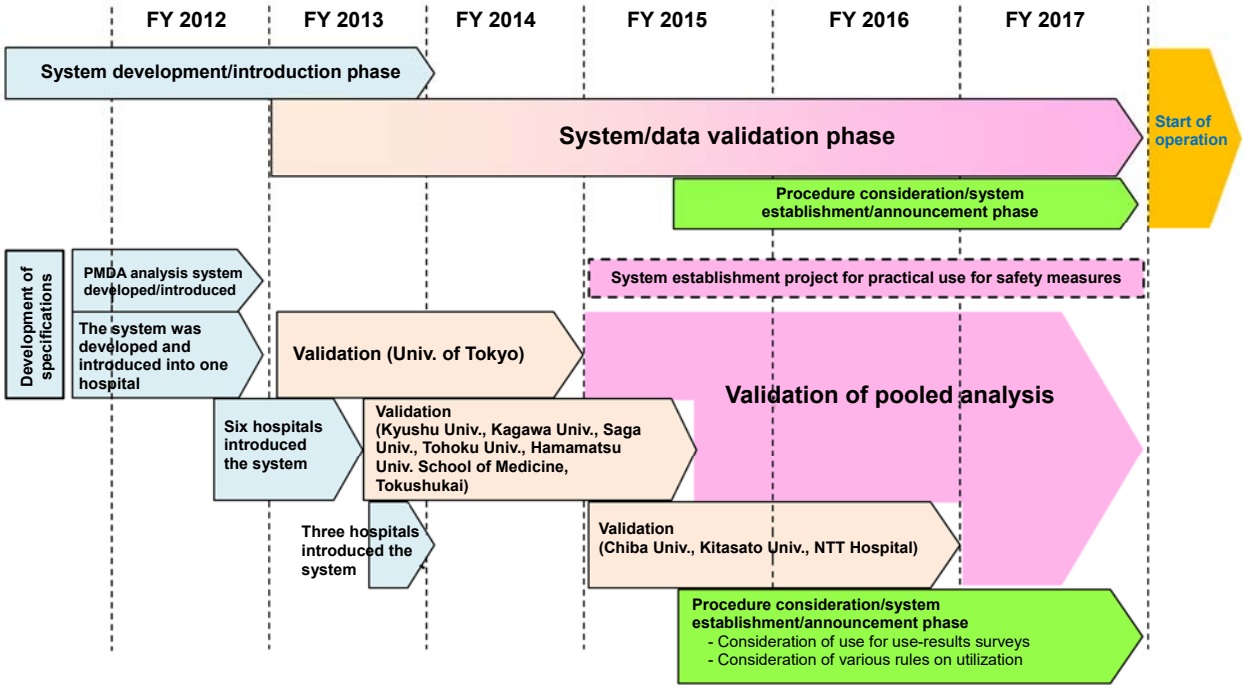
through open recruitment and is also developing its analytical system to enable the database to be used for safety measures (see the diagram below).



In FY 2017, PMDA conducted the following operations in preparation for full-scale implementation from FY 2018 onward.

- As in FY 2016, 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 4 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 10 medical institutions. As a result, PMDA clarified the characteristics of using MID-NET®.
- PMDA participated in discussions at the “Workshop on Medical Information Database Operation” established by MHLW in January 2016, and discussed utilization rules, expenses, etc. under the assumption of full-scale operation of the medical information database, including pharmaceutical companies’ access to the database, starting from FY 2018. As a result, PMDA reached a conclusion, based upon which PMDA organized specific use rules and launched an on-site center for external users.
- PMDA exchanged opinions with the US FDA, the Sentinel Project database secretariat office at Harvard University, and other related organizations, and shared issues concerning data quality control and data utilization between the US and Japan.

Progress and Plan for Development of the Medical Information Database Infrastructure



3.3.(ii).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 April 2017, management of the J-MACS Project was transferred to the J-MACS Committee of the Japanese Association for Thoracic Surgery (JATS). As of August 31, 2017, 873 patients (749 for IVADs, 124 for extracorporeal VADs) have been enrolled in J-MACS at 44 medical institutions nationwide (disclosed on the JATS website).

3.3.(ii).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 June 2017, PMDA concluded an agreement with the Japanese Society for Regenerative Medicine to lease the system developed by PMDA free of charge. Three regenerative medical products have been approved to date, and patient registration takes place using databases of academic societies or those developed by MAHs. To enhance understanding, the operation status of individual registries was presented at a workshop on the project for the patient registration system for regenerative medical products.
- 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) Roles of the working group and the sub-working group for the patient registration system for regenerative medical products; a list of working/sub-working group members; and materials for a working group meeting held in August 2017

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

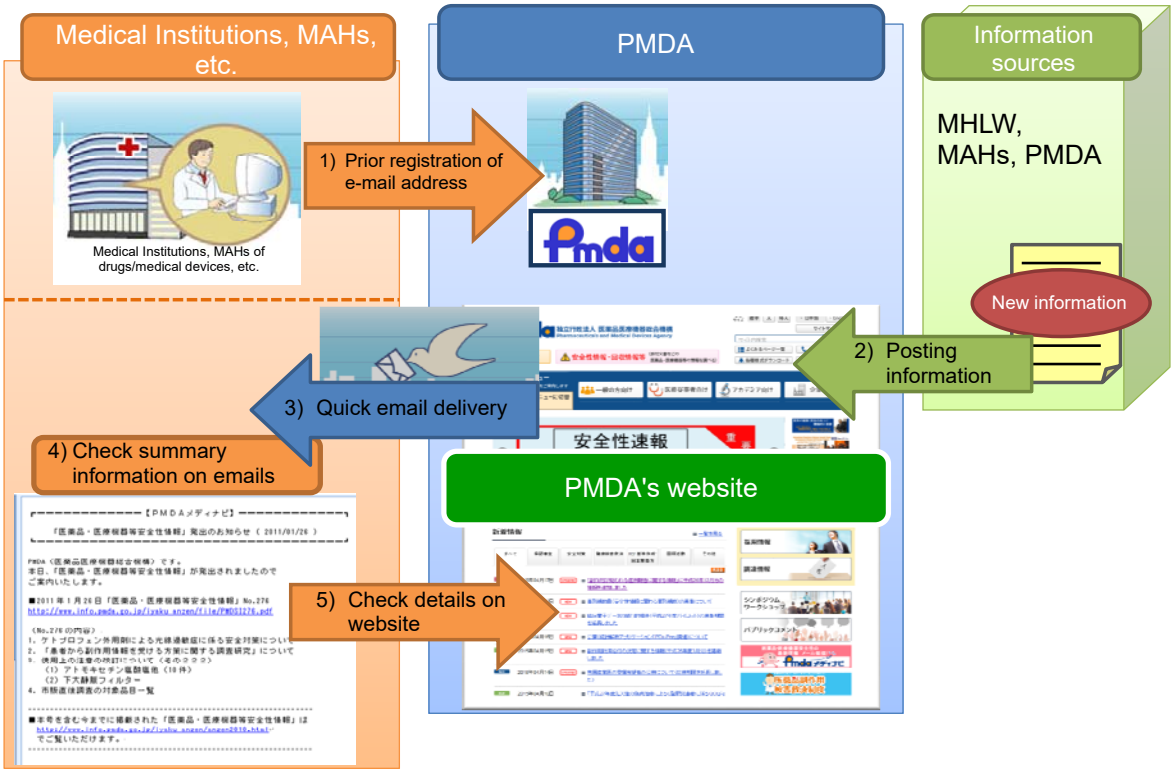
3.3.(iii).a. Provision of information via website content and e-mail distribution (use of the pharmaceuticals and medical devices information e-mail service (PMDA medi-navi))

- PMDA promptly posts important safety information including revisions to precautions in package inserts on the PMDA 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 the PMDA website.
- In February 2017, MHLW issued a notification, “Revisions to Safety Control Procedures for Use of Lenalidomide and Pomalidomide Products (request for precaution and dissemination of information to medical institutions)” (PSEHB/PED Notification No. 0215-1 and PSEHB/SD Notification No. 0215-1, dated February 15, 2017, jointly issued by the Director of the Pharmaceutical Evaluation Division and the Director of the Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW). In response to the notification, PMDA released the latest procedures for management of thalidomide, lenalidomide, and pomalidomide products, in cooperation with MHLW and the MAHs of the relevant products, to reinforce information provision services.
- The OTC version of the Drug Safety Update (DSU) (editor, Japan Federation of Self-Medication Industries; supervising editor, PSEHB, MHLW) became available on the PMDA website in July 2017. PMDA began distributing the relevant information through its e-mail service (PMDA medi-navi).
- 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. In FY 2017, PMDA hosted symposiums and lectures to ensure better understanding of the information it provides. PMDA also carried out PR activities for the medi-navi service, including banner advertisements on its website and distribution of leaflets, in cooperation with the MHLW, related organizations, related academic societies, etc.
- The February and March 2018 Issues of the JMA Journal published an interview between the Executive Director of PMDA and the President of the Japan Medical Association (JMA). This article was intended for physicians at clinics. The issues carried as an insert the PMDA Medi-Navi Registration Form.
- The “Notice that RMPs are Available on the PMDA Website” distributed via PMDA medi-navi, included a link to the RMPs of individual products, which allowed users to directly access the RMP page from the e-mail text, to enhance their usability.
- The “My Drug List for Safety Updates” is an additional service offered by the PMDA medi-navi. In order to familiarize users with the service, an article describing its functions and uses was

published in Pharmaceuticals and Medical Devices Safety Information No. 346 and Generic Drugs Quality Information No. 9.

- As a result of the efforts described above, the number of subscribers to the PMDA medi-navi service was 164,821 at the end of FY 2017, showing an increase of 11,225 compared with the end of FY 2016. (This exceeded the target increase of 10,000 or more.) The breakdown of subscribers is as follows:
  Approximately 48,700 hospitals or clinics (with an increase of approx. 2,900);
  Approximately 59,000 pharmacies (with an increase of approx. 3,900);
  Approximately 9,500 dental clinics or other medical facilities (with an increase of approx. 500);
  Approximately 21,900 MAHs or distributors (with an increase of approx. 1,700)
- As of the end of FY 2017, there were 14,258 subscribers to the “My Drug List for Safety Update,” which was an increase of 17% (2,027) from FY 2016.
- MAHs are required to post their product information (e.g., package inserts, Drug Guide for Patients) on the PMDA website via the exclusive webpages for MAHs, to ensure that product information is widely disseminated through the website. PMDA upgraded the exclusive webpages and added FAQ entries so that MAHs could properly and efficiently update their product information on the PMDA website.

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



Breakdown of Content Distributed through the PMDA medi-navi during FY 2017*

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)	7
Product Recalls (Class I)	32	Approval information (prescription drugs)	26
Product Recalls (Class II)	318	Approval information (regenerative medical products)	0
Pharmaceuticals and Medical Devices Safety Information	10	Notifications on drugs Notifications on medical devices	46
Drug Safety Update (DSU)	10	Information on proper use of drugs	5
DSU (OTC version)	3	Information on drug risk under evaluation	10
Revision of PRECAUTIONS (drugs)	12	Information on products submitted for public knowledge-based applications, covered by national health insurance	3
Revision of PRECAUTIONS (medical devices)	1	Notice of decision on payment/non-payment of adverse reaction relief benefits	12
Revision of PRECAUTIONS (quasi-drugs and cosmetics)	0	Risk Management Plan (RMP)	36
Revision of PRECAUTIONS (regenerative medical products)	0	Information on generic drugs	5
Notification on self-check (medical devices)	0	Others	25
PMDA Medical Safety Information	3		

** The number of e-mails distributed by medi-navi differs from the figures in the table because one distributed issue of medi-navi e-mail covers several items in its contents.*

Number of Information Documents Released on the PMDA's Website as of the End of FY 2017[*1]

			FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Package insert (labeling) information							
	Prescription drugs		12,921	14,912	14,843	14,639	14,812
	Medical devices [*2]		19,309	20,504	22,001	23,754	26,815
		Class I	-[*3]	-[*3]	-[*3]	-[*3]	10,290
		Class II	-[*3]	-[*3]	-[*3]	-[*3]	9,069
		Class III	-[*3]	-[*3]	-[*3]	-[*3]	4,524
		Class IV	-[*3]	-[*3]	-[*3]	-[*3]	2,931
	Regenerative medical products		-	2	3	4	4
	OTC drugs		10,234	11,127	11,360	11,385	11,425
	BTC drugs		-	20	15	16	16
	In vitro diagnostics		4,076	4,247	4,238	4,178	4,390
Drug Guide for Patients			2,155	2,701	3,213	3,366	3,873
Guidance for persons receiving vaccination			-	72	73	72	74
Safety information issued by MHLW							
	Directions for revision of package inserts (drugs)		257	272	284	297	309
	Notification of safety measures (drugs)		-[*3]	-[*3]	40	56	74
	Directions for revision of package inserts (medical devices)		48	50	53	54	55
	Notification of safety measures (medical devices)		-[*3]	-[*3]	83	88	95
	Notification concerning self-check		51	52	52	52	52
	Pharmaceuticals and Medical Devices Safety Information		168	178	188	198	208
	MHLW Press release		69	69	73[*4]	87[*4]	97[*4]
Dear Healthcare Professional Letters of Emergent Safety Communications (Yellow Letters)			27	30	24	24	24
Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)					15[*5]	15[*5]	15[*5]
Risk Management Plan (RMP)			6[*6]	117[*6]	180	270	333
Drug Safety Update (by Federation of Pharmaceutical Manufacturers' Associations of Japan [FPMAJ])			101	111	121	132	142
DSU (OTC version [JFSMI])			-	-	-	-	4

***Number of Information Documents Released on the PMDA's Website as of the End of FY 2017*[1]**

		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Information about case reports						
	Information about case reports on suspected ADR	292,720	338,224	387,162	440,485	498,809
	Information about case reports on suspected malfunction	84,766	98,407	116,182	133,159	149,696
	Information about case reports on suspected malfunction of regenerative medical products	-	-	35	91	191
	Information about case reports on suspected malfunction in the mechanical part of combination drugs	-	-	6	339	1,459
Notification related to medical safety measures		96	108	119	130	147
PMDA Medical Safety Information		43	45	48	50	53
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		700 active ingredients (1,416 products)	834 active ingredients (1,652 products)	*7	*7	*7
Information on recalls[*8]						
	Drugs (including *in vitro* diagnostics)	1,913	1,817	375	351	375
	Quasi-drugs			49	42	42
	Cosmetics			229	242	242
	Medical devices			1,223	1,224	1,258
Pharmaceuticals and Medical Devices Information E-mail Service (PMDA medi-navi)						
	E-mails issued	215	234	223	557	556
	Subscribed	102,790	112,079	135,487	153,596	164,821

**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 Including one medical device labeling showing no term name. (The term name of a medical device is determined according to the medical device classification defined by the MHLW ministerial announcement No. 298 dated July 20, 2004.)*

**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 Section 3.4.(4).*

**8 Number of information documents released over the past 2 years.*

3.3.(iii).b. Provision of information on package inserts

- The number of package inserts available on the PMDA website as of the end of FY 2017 is shown in the table entitled "Number of Information Documents Released on the PMDA's Website as of the End of FY 2017."
- When a notification requiring revisions of package inserts of drugs is issued, PMDA releases the information on its website and distributes a PMDA medi-navi e-mail within 2 days of issuance.
- Upon the issuance of MHLW notifications requiring the revision of package inserts of drugs, PMDA releases these notifications on its website and provides a link to the corresponding package inserts.
- MHLW issued a notification entitled "Instructions for Package Inserts of Prescription Drugs, etc." (PSEHB Notification No. 0608-1, dated June 8, 2017, by the Director General of the Pharmaceutical Safety and Environmental Health Bureau, MHLW). In response to the notification, PMDA developed a system associated with XML conversion of package insert information and

modified the related systems in FY 2017. Prior to the introduction of the system, PMDA also implemented a test to confirm the definitions of the XML schema (pilot test 1) in February 2018.

- PMDA added a new webpage to the exclusive website for MAHs, in order to provide the latest information on (a) consultations on the “Instructions for Package Inserts of Prescription Drugs, etc.” and (b) system upgrading associated with XML conversion to MAHs.
- 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. Also for medical devices, PMDA has been providing links between notifications mandating revisions and the corresponding package inserts, similarly to drugs.
- PMDA prepared a leaflet calling for registration etc. with the Medical Device Database associated with barcode labeling requirements for medical devices etc. PMDA then required MAHs of medical devices to place a barcode on their products, register them with the medical device database, and post labeling information on the PMDA website.

3.3.(iii).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 2017, PMDA had posted a total of 498,809 reports submitted by medical institutions and MAHs by November 2017.
- 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, 149,696 reports (submitted by November 2017) were posted by the end of FY 2017.

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, 191 reports on regenerative medical products (submitted by November 2017) and 1,459 reports on combination drugs (submitted by November 2017) were published by the end of FY 2017.

3.3.(iii).d. Provision of the Request for Proper Use of Drugs and Medical Devices

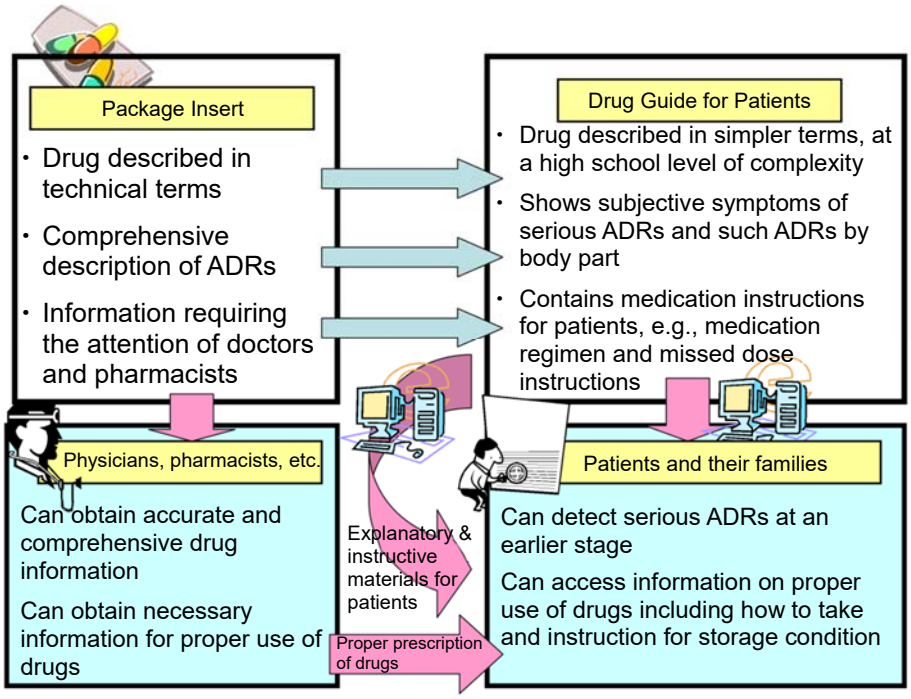
- If specific measures concerning the proper use (including dose and frequency as well as frequency of testing for adverse reactions) of a drug have already been recommended in its package insert or other materials prepared by the applicable MAH, but it is later determined that improper use persists 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 notice "PMDA Request for Proper Use of Drugs" has been available on the PMDA website since FY 2010.
- In some cases, the same malfunctions and infections due to medical devices occur repeatedly without reduction in the number of reports, despite the precautionary statements in the labeling of medical devices. To address such cases, PMDA prepares precautionary documents known as "PMDA Request for Proper Use of Medical Devices," to provide easy-to-understand information to healthcare professionals. In FY 2014, PMDA prepared a "PMDA Request for Proper Use of Medical Devices" for aortic stent-grafts (entitled "Adverse Events in Patients Using Aortic Stent-Grafts") and released it on its website.

3.3.(iii).e. Provision of Safety Information to the Public (Patients)

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, issued by the Director General of the Pharmaceutical and Food Safety Bureau, MHLW) and have been available on the PMDA website since January 2006. In FY 2017, 118 Drug Guides for Patients (including 6 for generic drugs) were prepared for products newly marketed or products for which the Precautions had been revised. The number of Drug Guides for Patients available on the PMDA website as of the end of FY 2017 is shown in the table entitled "Number of Information Documents Released on the PMDA's Website as of the End of FY 2017."
- PMDA prepared a draft revision of the adverse drug reaction terminology used for preparation and revision of Drug Guides for Patients so that the public can understand them better.

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, issued by the Director General of the Pharmaceutical and Food Safety Bureau, MHLW). In FY 2017, no additional Guides for Patients Receiving Vaccinations were prepared concerning any products. The number of Guides for Patients Receiving Vaccinations available on the PMDA website as of the end of FY 2017 is shown in the table entitled “Number of Information Documents Released on the PMDA’s Website as of the End of FY 2017.”

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.

  MHLW has been implementing a 5-year plan (since FY 2016) to revise and update these manuals based on the latest knowledge. In FY 2017, MHLW revised 2 manuals: the manual for Stevens-Johnson syndrome and the manual for toxic epidermal necrolysis (Lyell syndrome). PMDA published the revised versions on its website and notified the revisions via PMDA medi-navi to the subscribers.

- The number of manuals available on the PMDA website as of the end of FY 2017 is shown in the table entitled “Number of Information Documents Released on the PMDA’s Website as of the End of FY 2017.”

4) Provision of other information to the public

- An open forum was co-hosted by PMDA and an AMED research group conducting “Study on How to Communicate Risk Minimization Information of Drugs etc. to Patients and Healthcare

Professionals” in November 2017, to improve risk communication among relevant parties including patients.

3.3.(iii).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 2017, 3,584 cases associated with drugs and 400 cases associated with medical devices were evaluated and the results were reported to MHLW. These 3,984 cases were posted on the PMDA website as shown in the following table.

Cases	Drugs	Medical Devices
Total applicable cases: 3,984	3,584	400
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	1
2) Cases for which measures have already been taken, or are currently under consideration, by the MAHs, etc.	24	8
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.	3,558	391

- 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 2017, the following 3 issues were posted on the PMDA web page.

PMDA Medical Safety Information

No.	Posted on	Title
No.51	September 2017	Mix-up of Drugs Due to Similarity of Nonproprietary Names
No.52	December 2017	Precautions When Using an Open Ventricular Drainage Circuit
No.53	Revised March 2018	Introduction of Connectors that Prevent Misconnection

3.3.(iii).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.”

3.3.(iii).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.

  PMDA also translated information on revised precautions, summaries of survey results, and "PMDA Request for Proper Use of Medical Devices" into English, and posted them on its website.

  PMDA also provided English-language translations of past notifications issued by MHLW and PMDA. In FY 2017, 2 translated notifications were posted on the PMDA website. PMDA also continued providing package insert information, including revision information, to regulatory agencies in Asian countries, in addition to information provision under confidentiality agreements to foreign regulatory agencies. In 2018, Azerbaijan was added to the list of countries participating in this information provision.

3.3.(iii).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 2017 is shown below:

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs	776	869	991	795	818
Medical devices	95	325	772	1,597	2,741
Medical safety	31	72	116	78	91
Regenerative medical products	-	0*	4	3	1

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

- Consultations for medical safety conducted in FY 2017 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.

3.3.(iii).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 2017, the number of persons receiving consultations was 11,327 (12,729 calls) for drugs and 401 (453 calls) for medical devices.

- PMDA has identified and compiled a list of consultations related to generic drugs 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Persons receiving consultations on drugs [persons/day]	10,244 [42.0]	11,556 [47.4]	12,551 [51.7]	13,448 [55.3]	11,327 [46.4]
(of which consultations on generic drugs)	(626)	(543)	(600)	(495)	(346)
Persons receiving consultations on medical devices [persons/day]	547 [2.2]	370 [1.5]	406 [1.7]	415 [1.7]	401 [1.6]

3.3.(iii).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.
- PMDA conducted surveys of the status of procurement, communication, and use of safety information of drugs* in hospitals and pharmacies, in FY 2014 and FY 2015, respectively. In FY 2017 (i.e., January and February 2018), PMDA conducted a follow-up survey of the status of procurement, communication, and use of safety information of drugs in hospitals (10% of hospitals nationwide) and pharmacies (5% of health insurance pharmacies nationwide). The survey results will be released on the PMDA website in FY 2018.

  * The survey of the status of procurement, communication, and use of safety information of drugs was conducted in 8,481 hospitals nationwide in FY 2014, and in 10% of health insurance pharmacies nationwide (5,664 pharmacies) in FY 2015.

- PMDA communicated the results of the surveys (hospital survey in FY 2014; pharmacy survey in FY 2015) and issues arising from the surveys at academic conferences, lecture meetings, and other occasions in collaboration with professional organizations, to promote the appropriate procurement, communication, and use of safety information in clinical practice. In collaboration with professional organizations and academic societies, PMDA developed e-learning materials and RMP-related materials to provide a better understanding of the RMP, which has recently been drawing attention. The information materials were published on the websites of the relevant professional organizations.

➢ ***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 of 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 of 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 of 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 of 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 of 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. Use 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 of 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>

FY	Title	Target	Period	Remarks
2015	Survey of the status of procurement, communication, and use of drug safety information	10% of general clinics *limited to institutions providing healthcare services as stipulated by health insurance (8,737 institutions)	October 6, 2015 to December 14, 2015	Questionnaire survey (response rate: 53.1%)
		Summary of survey results (excerpt) 1. Use of the PMDA website and the PMDA Medi-navi 2. Obtaining important information promptly and comprehensively 3. Obtaining information based on characteristics of the distribution media 4. Sharing patient information between clinics and pharmacies		
		10% of health insurance pharmacies (5,664 institutions)	October 6, 2015 to December 14, 2015	Questionnaire survey (response rate: 68.2%)
		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		
2017	Survey of the status of procurement, communication, and use of drug safety information	10% of hospitals nationwide	January 9, 2018 to February 16, 2018	Questionnaire survey
		5% of health insurance pharmacies	January 9, 2018 to February 16, 2018	Questionnaire survey

** 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:

  - Annual Meeting of the Japanese Society of Drug Informatics (A symposium was held.)
  - Japan Pharmaceutical Association Congress of Pharmacy & Pharmaceutical Science (A session was held.)
  - Japanese Society of Hospital Pharmacists: Workshops

3.3.(iii).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

3.4.(1).(i) Promotion of the PMDA "Rational Medicine" Initiative

- PMDA promoted the concept of its "Rational Medicine" Initiative across the world to promote regulatory science aimed to evaluate drugs, medical devices, and regenerative medical products with the focus on realizing a more rational basis for the provision of medical care with patient's needs and well-being firmly rooted at its core.

3.4.(1).(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.
- In FY 2017, PMDA provided a draft proposal of issues to be discussed at the fourth-term Science Board meetings from FY 2018 (April 2018 to March 2020) to the Science Board. To further accelerate the use of the Science Board in FY 2018, PMDA also reviewed the operation system of the Science Board to ensure immediate discussion of leading-edge scientific issues by the Board.
- The third-term Science Board (April 2016 to March 2018) prepared the following 3 reports that summarize discussions in the respective subcommittees in FY 2017. Among them, the report (2) was released on the PMDA website in February 2018.

  (1) Subcommittee on Rare Cancers:
  Current state of therapeutic development for rare cancers in Japan, and proposals for improvement

  (2) Subcommittee on Pharmaceuticals Development:
  Issues in and Proposals for Facilitating Drug Discovery by Collaboration between Academia and Industry 2017 - In the Trend of Rapidly Advancing Science -

  (3) Subcommittee on AI (Artificial Intelligence):
  Regulatory Science on AI-based Medical Devices and Systems

  To share the results of its research and considerations with interested parties around the world, PMDA published an English summary of reports (1) and (3) above in journals during FY 2017.

  The English summary of report (1) was accepted by the Journal of Cancer Science in March 2018, following the peer review process, and gained scholarly acclaim. The English summary of report (3) was in the process of peer review by the Journal of Advanced Biomedical Engineering as of the end of March 2018.

  In line with the progress of publication of summary reports in English in the journals, PMDA will release reports (1) and (3) on its website.

- PMDA disclosed materials and meeting minutes of the Science Board and the Subcommittees (excluding confidential information) on the PMDA website.

3.4.(1).(iii) Enhancement of regulatory science research

- With respect to electronic submission of clinical trial data for new drugs, see Section 3.2.(1).A.(ii).b.
- To conduct effective and consistent 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 2017, 8 projects (4 new projects and 4 ongoing projects) were selected as designated research, and the projects were implemented. The results of 5 of these projects were published in journals or lecture meetings (3 published in papers, 2 lectures) (reposted).
- For innovative products, see Section 3.2.(2).(i).
- PMDA conducted regulatory science research in collaboration with external organizations such as academic institutions. (33 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 2018 based on the relevant rules. As in the last year, PMDA held a meeting where the final report on designated research was presented. The outcomes of 3 projects concluded in FY 2016 and 6 projects concluded in FY 2017 were published in journals and presented at lecture meetings, and have been academically appreciated.
- PMDA re-organized tasks related to conflicts of interest (COI) management in regulatory science research to reinforce governance and secure transparency. Firstly, it has been clearly documented that employees are allowed to conduct independent research only if it is related to their operations in PMDA. This requires employees to submit a "report on financial conflicts of interest" concerning independent research.
- 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 (10 projects) and improved the environment and systems for such research activities.
- As in the previous fiscal years (i.e., since FY 2015), PMDA held an exhibition (poster sessions in FY 2017) on regulatory science research, leading to active discussions. For the first time, PMDA announced in advance the schedule for the exhibition to external parties. As a result, the exhibition was visited by prospective employees and job seekers.
- Research in humans implemented by PMDA employees was reviewed at the Ethics Committee. From this fiscal year, employees participating in such research are required to undergo research ethics education.
- Since FY 2015, PMDA has allowed employees to describe their engagement in designated research projects in the personnel evaluation sheet. In FY 2017, 5 employees requested that their performance on research be recorded on the sheet.

- In the working groups (WGs) for the 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 (Pediatric Drugs WG, Omics WG, Cardiovascular Risk Evaluation 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 [2 academic presentations/lectures and 1 paper], Pediatric Drugs WG [10 academic presentations and 3 papers], Orphan Drugs WG [2 explanatory meetings], ICH Q12 WG [7 academic conferences/lectures and 1 explanatory meeting], Clinical Innovation Network (CIN) WG [5 academic conferences/lectures and 1 paper], Innovative Manufacturing Technology WG (8 academic conferences/lectures and 2 papers], and Cardiovascular Risk Evaluation WG [1 academic conference/lecture and 3 papers]).
- The Projects Across Multi-Offices exchanged opinions about evaluation policy and other issues with drug development companies, related industry groups, academic societies, etc. (6 occasions for Companion Diagnostics WG, 1 occasion for ICH Q12 WG, 3 occasions for CIN WG, 1 occasion for Innovative Manufacturing Technology WG, and 3 occasions for Cardiovascular Risk Evaluation WG).
- Each WG for the Projects Across Multi-Offices, opinions were exchanged among the industry, academia, and government through cooperation in related AMED research projects (ICH Q12 WG, CIN WG, Innovative Manufacturing Technology WG, and Cardiovascular Risk Evaluation WG).

3.4.(1).(iv) Enhancement of staff training

3.4.(1).(iv).a. Lectures and guidance given by experts and on-site training

See Section 2.4.(2) Systematic implementation of staff training.

3.4.(1).(iv).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 U.S. Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) in April and October 2017. 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.

3.4.(1).(v) Promotion of interaction with outside researchers and collaboration on investigative research

3.4.(1).(v).a. 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, with the National Center of Neurology and Psychiatry, Tohoku University, and National Center for Global Health and Medicine in FY 2016, and with the National Cerebral and Cardiovascular Center and National Center for Child Health and Development in FY 2017. 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 2017, 5 employees of the National Cancer Center Japan (NCC) worked at PMDA, and 1 PMDA staff member at the Center as part of personnel exchange program. PMDA officers/employees provided 6 lectures at the NCC. Eight PMDA staff members participated in 3 exclusive training programs (limited to PMDA employees) offered by NCC (1 study tour program to visit the ethics committee and 2 on-site study tour programs to visit Center's pharmacists engaged in outpatient cancer chemotherapy). PMDA invited a lecturer from the NCC to speak at the PMDA Asia Training Center (ATC) Multi-Regional Clinical Trial (MRCT) Seminar. PMDA established a liaison office for the NCC research project, and conducted information sharing and opinion exchanges between NCC and PMDA staff members. Staff members from Office of New Drug V participated, as research collaborators, in an NCC-initiated 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." Also, an opinion exchange session was jointly held by NCC and PMDA staff members.
- One person from Hiroshima University worked at PMDA as part of personnel exchange program.
- One person from Keio University worked at PMDA as part of personnel exchange program. PMDA officers/employees provided 3 lectures at the university. A total of 12 PMDA staff members participated in the 5 training programs offered by the university.
- One person from University of Tsukuba worked at PMDA as part of personnel exchange program. PMDA officers/employees provided 8 lectures at the university.
- One person from the National Center of Neurology and Psychiatry (NCNP) worked at PMDA and 1 PMDA staff member at the NCNP, as part of personnel exchange program. PMDA staff provided 1 lecture at NCNP. Seven PMDA staff members participated in 2 exclusive training programs (limited to PMDA employees) offered by NCNP (a study tour program to visit the IRB and a study tour program to visit the ethics committee). Three workshops were jointly held by NCNP and PMDA staff members.
- Four people from Tohoku University worked at PMDA and 1 PMDA staff member at the university, as part of personnel exchange program. A PMDA officer/employee provided 1 lecture at the university.
- Three individuals from the National Center for Global Health and Medicine (NCGM) worked at PMDA as part of personnel exchange program. A PMDA staff member lectured at the NCGM. Six PMDA staff members participated in 4 exclusive training programs (limited to PMDA employees) offered by NCGM (a study tour program on clinical study management operations, a study tour program to visit the IRB, etc.). As part of mutual collaboration in international business services between the two institutions, NCGM provided lectures at a pharmaceuticals seminar (held in Vietnam) and an MRCT seminar, both of which were implemented by the ATC, whereas participants in training programs of ATC visited NCGM facilities. Staff members of the Tanzania Food and Drug Authority (TFDA) visited PMDA as part of the expansion program for testing

devices in Africa. As part of the NCGM's project on the promotion of globalization of medical technologies etc., PMDA staff members provided lectures at training sessions pertaining to the project to reinforce transfusion and hematopoietic stem cell transplant medicine for Myanmar government staff members (these lectures are unrelated to ATC-unrelated programs,).

- PMDA concluded a partnership agreement with the National Cerebral and Cardiovascular Center (NCVC) on July 24, 2017. One person from NCVC worked at PMDA as part of personnel exchange program. PMDA officers/employees provided 3 lectures at NCVC. Five PMDA staff members participated in an exclusive training program (limited to PMDA employees) offered by NCGM.
- PMDA concluded a partnership agreement with the National Center for Child Health and Development (NCCHD) on January 22, 2018. One person from NCCHD worked at PMDA as part of personnel exchange program.
- PMDA collaborates with the NCC, NCNP, and NCGM individually, 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 (7 delegated and 33 non-delegated PMDA officers/employees) gave 47 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:

3.4.(2).(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

- In FY 2017, PMDA planned and implemented the seminars listed in the table below at the "Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC)," which was established to provide officers in foreign regulatory agencies with training on a continuous basis not only in Japan but outside Japan (a total of 9 seminars with a total of 235 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 mock inspections) 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 government's office and the PMDA-ATC Training Institute in the Hokuriku Branch Office. PMDA utilized the resources of its ATC to arrange a study tour to visit plants as part of the seminar involving review of safety measures for drug products.

  Based on the achievements of seminars conducted at the PMDA-ATC, PMDA was certified as an "APEC Life Sciences Innovation Forum (LSIF) Regulatory Harmonization Steering Committee (RHSC) Training Center of Excellence (CoE) for Regulatory Science" in the areas of global clinical trials/GCP inspections and pharmacovigilance. In FY 2017, PMDA held seminars on global clinical trials of drugs and pharmacovigilance, as workshops of the APEC LSIF RHSC CoE. The Joint Statement of ASEAN-Japan Health Ministers Meeting announces that the Asian Training Center for Pharmaceutical and Medical Devices (PMDA-ATC) would be utilized to improve and

harmonize the national regulatory system of pharmaceutical products and medical devices in ASEAN member states. This has been highly appreciated internationally (July 2017).

	Seminar content/area	Date	Venue	No. of participants (No. of countries/ regions)
1	Risk Management Plan (RMP)	May 18 and 19, 2017	Jakarta, Indonesia	30 (1)
2	Pharmaceuticals Review	June 26-30, 2017	Tokyo (PMDA) and Toyama, Japan	28 (11)
3	Good Manufacturing Practice (GMP)	July 31 to August 4, 2017	Hikari City, Yamaguchi, Japan	13 (13)
4	Pharmaceuticals	October 3-4, 2017	Hanoi, Vietnam	30 (1)
5	Good Registration Management (GRM)*	October 31 to November 2, 2017	Taipei	30 (8)
6	Medical Devices	November 6-10, 2017	Tokyo (PMDA), Japan	30 (12)
7	Pharmaceuticals Review	December 12-15, 2017	Bangkok, Thailand	20 (2)
8	Multi-Regional Clinical Trial (MRCT)*	January 15-18, 2018	Tokyo (PMDA), Japan	25 (11)
9	Pharmacovigilance*	February 5-8, 2018	Tokyo (PMDA), Japan	29 (17)

** Workshops of APEC LSIF RHSC Training Centers of Excellence (CoE).*

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 Confidentiality 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 engaged in cluster activities to regularly exchange information with European countries and the US. PMDA was actively involved in cluster activities regarding pediatrics, biosimilars, regenerative medical products, and pharmacovigilance, and exchanged opinions in a closer manner.
- 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 US FDA and EMA in April and October 2017. 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 the United States (US FDA), Europe (EMA), the United Kingdom (MHRA), India (CDSCO), South Korea (MFDS), China (CFDA), Denmark (DKMA), Saudi Arabia (SFDA), Ireland (HPRA), Taiwan (TFDA), Iran (FDA), Malaysia (NPRA), Thailand (FDA), Singapore (MoH), Indonesia (BPOM), Vietnam (DAV), and Myanmar (FDA), to further reinforce the collaborative relationships.

  PMDA also concluded a confidentiality agreement (CA) with the regulatory authority in Sweden (Medical Products Agency [MPA]) and the regulatory authority in Poland (Office for Registration of

Medicinal Products, Medical Devices and Biocidal Products [URPL WMiPB]), to further reinforce the collaborative relationships.

- To deepen the collaborative relationship with China, PMDA's Chief Executive and officers of MHLW visited China to hold a meeting with CFDA executive officials as a public-private mission in July 2017, as in the previous year. As a result, the collaborative relationship between China and Japan has continued and progressed.

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, modeling & 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 also established a framework under which to regularly accept EMA staff members dispatched from Europe. In FY 2017, PMDA accepted EMA staff members under this system for the first time. This activity was undertaken to deepen the understanding of the Japanese regulatory system among EMA staff, explore the potential of a more collaborative partnership, and to exchange information.

GLP, GCP, GMP, and QMS

- PMDA conducted mutual acceptance of GLP investigation reports based on the OECD's mutual data acceptance system.
- As for information exchange of quality control-related inspection results, PMDA exchanged information on QMS inspections with Taiwan and reinforced the collaborative partnership. PMDA exchanged GMP inspection reports with the US FDA, Brazil ANVISA, Thailand FDA, and other agencies to improve inspection efficiency.
- PMDA was permitted to participate, on a pilot basis, in the EMA-US FDA GCP initiative, which is intended to ensure efficient GLP/GCP/GPSP inspections. As a result, PMDA took part in regular teleconferences and exchanged opinions via e-mail. Mutual attendance at inspections and other achievements, such as the prevention of overlapping inspections and reference to results, were appreciated, and discussions on PMDA's full-scale participation in the initiative are under way.

PMDA conducted the following activities to build a relationship based on trust with foreign 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 supported the negotiations between Japan (MHLW) and the EU to expand the coverage of mutual recognition agreements (MRA) related to the GMP of drugs. As a result, PMDA has confirmed that GMP requirements and implementation in Japan are equivalent to those in the EU.

  PMDA has also participated in an international GMP inspection rationalization program for drug substance manufacturers. By exchanging information on GMP inspections, including inspection plans and results etc., with foreign regulatory authorities, PMDA started international cooperation to ensure more efficient and effective GMP inspections.

Japanese Pharmacopoeia

- PMDA participated in the 8th International Meeting of World Pharmacopoeia co-hosted by WHO and other organizations, held in Brazil in July 2017. A PMDA staff member served as the chair of the meeting and took the initiative to finalize the Good Pharmacopoeial Practices (GPhP). PMDA also took this opportunity to hold bilateral meetings with the staff of the US Pharmacopeia (USP), the Brazilian Pharmacopoeia, and the Pharmacopeia of the People's Republic of China, to address mutual issues to be solved and to establish a cooperative framework. Furthermore, to promote mutual understanding among the pharmacopoeias, PMDA collaborated with WHO in conducting a questionnaire survey about the latest information regarding individual pharmacopoeias.
- PMDA participated in the European Pharmacopoeia (EP) Board meetings as an observer three times a year (June 2017, November 2017, and March 2018), and actively engaged in reinforcement of the collaborative framework and information collection. PMDA also held bilateral meetings by taking this opportunity to promote harmonization activities.
- PMDA concluded a CA in the area of pharmacopoeia with USP in June 2017. 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.

Regular bilateral meetings and symposiums

- PMDA collaborated with regulatory authorities in India, South Korea, Indonesia, and Taiwan, and held the following symposiums and meetings.

  (1) The 2nd Japan-India Medical Products Regulation Symposium and Bilateral Meeting between the regulatory authorities (April 2017)

  (2) The 2nd Japan-South Korea Medical Products Regulation Symposium and Bilateral Meeting between the regulatory authorities (May 2017)

  (3) The 3rd Indonesia-Japan Symposium and Bilateral Meeting between the regulatory authorities (May 2017)

  (4) The 5th Joint Conference of Taiwan and Japan on Medical Products Regulation and Bilateral Meeting between the regulatory authorities (November to December 2017)

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

Major actions taken concerning drug products

- The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) held conferences in Montreal (Canada) in May 2017. PMDA served as the vice chair of the ICH Assembly and the Management Committee and led discussions. The ICH held a conference in Geneva (Switzerland) in November 2017, at which time re-election of the chair and the vice chair of the Management Committee was discussed. As a result, PMDA was successfully re-elected as the chair.

  PMDA also contributed to the finalization of several guidelines on pharmaceutical regulations (e.g., the guideline for global clinical trials, and revision of the guideline for clinical trials of drugs in pediatric populations). ICH organizational rules and discussion procedures were reviewed so that discussions at ICH could be facilitated under the leadership of Japan.

Major actions taken concerning medical devices

- PMDA participated in the Management Committee meetings of the International Medical Device Regulators Forum (IMDRF) held in Ottawa (Canada) in September 2017 and in Shanghai (China) in March 2018. At the meetings, PMDA worked to finalize various IMDRF guidance documents (e.g., IMDRF/AE WG/N43 FINAL:2017 (Edition 1, 2) “IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes”; IMDRF/SaMD WG/N41 FINAL:2017 “Software as a Medical Device (SaMD): Clinical Evaluation”; IMDRF/ Registry WG/N46 FINAL:2017 “Tools for Assessing the Usability of Registries in Support of Regulatory Decision-Making”). PMDA also coordinated the revision of the IMDRF membership agreement and formulated the direction of future activities. In addition, PMDA actively participated in individual working group meetings and coordinated opinions to ensure that Japanese opinions could be adopted.
- Harmonization by Doing (HBD) Town Hall Meetings were held within cardiology-related academic conferences in Japan and the US (held in Kyoto in July 2017, Denver in October 2017, and Washington DC in March 2018). In addition, HBD East 2017 Think Tank Meeting was held in Tokyo in December 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. To expand the scope of HBD activities with potential to advance, PMDA exchanged opinions with members of US and Japanese industry, government, and academia to discuss the course of future activities.
- In addition, PMDA staff 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

- PMDA and MHLW co-hosted the 12th conference of the Summit of Heads of Medicines Regulatory Agencies (HMRA), which unites top officials of drug regulatory authorities mainly in advanced countries, in Kyoto in October 2017. This was the first time that the HMRA Summit was held in Japan, and the conference was attended by a total of 86 representatives of regulatory authorities from 29 countries and regions around the world. At this Summit, Japan was able to achieve considerable results, including an agreement on regulations of regenerative medical products and on promotion of international regulatory harmonization of the utilization of real world data.

  Following the Summit, PMDA convened an International Coalition of Medicines Regulatory Authorities (ICMRA) meeting and bilateral meetings with 9 countries and regions. PMDA also

hosted an Asian Network meeting, inviting Asian countries participating in the summit conference, for the first time.

As an event related to the Summit of Heads of Medicines Regulatory Agencies, PMDA also held a public symposium for the first time, which was attended by approximately 1,500 participants.

- At the ICMRA meeting held in Kyoto in association with the 12th conference of the Summit of Heads of Medicines Regulatory Agencies, the attendees agreed to start an innovation project (early-phase regulatory response to innovative technologies). To proceed with the project, it was agreed that Japan, as the chair of the meeting, would lead the discussions on the analysis of horizon scanning methodology implemented by individual nations. PMDA has been playing a central role in the maintenance of the ICMRA official website, which was developed by PMDA in FY 2015 and became available to the public in March 2016. In FY 2017, PMDA renovated the website to increase its functions and design, thereby contributing to increased awareness of ICMRA activities.
- PMDA participated in the Pharmacopoeial Discussion Group (PDG) meeting (a review committee meeting of Japan-US-Europe Pharmacopoeias) held in Rockville (US) in September 2017. PMDA also participated in monthly teleconferences. Through these meetings, PMDA had intense information exchanges with EP and USP. This led to the new harmonization of 1 testing method and the revision of 4 excipients.

  PMDA also contributed to the conclusion of the agreement on the revision of the operating procedure for promoting efficient PDG harmonization process, which was proposed at the Tokyo meeting in October 2016. PMDA sought public comments in Japan on the prospective new harmonization of 1 testing method and 1 excipient and the prospective revision of 1 testing method and 2 excipients.
- Seven consultations concerning applications for international nonproprietary names (INN) were conducted and PMDA participated in the WHO-hosted INN meetings held in April and October 2017.
- The Asia-Pacific Economic Cooperation Life Science Innovation Forum Regulatory Harmonization Steering Committee (APEC-LSIF-RHSC) convened in Vietnam in August 2017 and Singapore in February 2018. (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.

  As a result of appreciation of its achievements, the PMDA-ATC was certified as a “Training Center of Excellence (CoE)” that provides training programs to enhance the capacity of regulators and relevant persons, at the APEC-LSIF-RHSC meeting. Among 6 working areas established by APEC-LSIF-RHSC, PMDA held seminars at the PMDA-ATC as a CoE in the areas of global clinical trials/GCP inspections (January 2018) and pharmacovigilance (February 2018). PMDA reported this achievement at the APEC-LSIF-RHSC meeting in Singapore (February 2018), which was internationally highly appreciated.
- PMDA participated in the International Generic Drug Regulators Programme (IGDRP) meetings held in Ottawa (Canada) in June 2017, 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 study group for IPRF/IGDRP organizational integration and exchanged opinions with individual regulatory authorities about the future operation system. The new organization IPRP was established in January 2018. PMDA contributed to its establishment through the above efforts.

- PMDA participated in the 11th International Cooperation on Cosmetics Regulation (ICCR-11) meeting held in Brazil in July 2017 and exchanged information on the regulations of cosmetics with regulators from the U.S., the European Union, Canada, and Brazil.
- PMDA also hosted the 4th meeting of the Self-Medication Collaborative Asian Regulator Expert Roundtable (Self-CARER) in Taipei (Taiwan) in March 2018. PMDA, as the chair, led discussions with regulators from Asian countries to achieve regulatory harmonization in the region.
- PMDA contributed to the Project on Promotion of an International Standardization Strategy for Innovative Medical Devices, implemented by MHLW. Based on the road map prepared in the inaugural year (FY 2014) of the project (Former Project on Promotion of an International Standardization Strategy for Medical Devices), 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 worked on important themes, e.g., medical robots and additive manufacturing systems, for which international standardization should be promoted in a strategic manner. PMDA participated in 136 conferences of the ISO/IEC specification review committee on such themes (25 international conferences, 86 meetings of the Japanese committee, and 25 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 2017 PMDA dispatched 2 experts in 2 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. The experts dispatched to the academia in FY 2016 were appointed as the chair of two working groups in FY 2017.

  Furthermore, PMDA held 2 meetings of the “Standards Review Council Liaison Office,” which were organized by the Japan Federation of Medical Devices Associations (with 17 technical committees [TCs], including ISO/TC276 [Biotechnology], ISO/TC261 [Additive manufacturing], and ISO/TC299 [Robotics]) in FY 2017. PMDA provided information, issues to be solved, etc. to achieve international standardization of innovative medical devices, etc. and coordinated information sharing among regulatory agencies in Japan, . 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. As the first step, PMDA held workshops on specifications and standards focusing on the topic of “Essential Principles,” in Vietnam (22 participants), Indonesia (55 participants), and Malaysia (60 participants) at the AMDC meetings in FY 2017. 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 FY 2017, PMDA proceeded with the formulation of a draft guidance document on the role of international specifications used on the government side.
- 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.

3.4.(2).(iii) Promotion of personnel exchanges

- PMDA dispatched a total of 11 staff members to the Thailand FDA on 3 occasions in July 2017, November 2017, and March 2018, to share its policy for operations and how actual operations have been implemented by PMDA.
- In addition to the implementation of training seminars by the PMDA-ATC, PMDA accepted trainees as needed from the regulatory authorities in China, Indonesia, Thailand, etc.
- PMDA held bilateral symposiums and meetings between the regulatory authorities (India in April 2017, South Korea and Indonesia in May 2017, Taiwan in November and December 2017), and promoted understanding of Japanese pharmaceutical regulations, etc. PMDA also exchanged opinions on human capacity building.

  PMDA also held meetings with regulatory authorities, e.g., SFDA in Saudi Arabia, NPRA in Malaysia, FDA in Thailand, BPOM in Indonesia, DAV in Vietnam, FDA in Myanmar, etc., discussed information exchanges and collaborative projects, and exchanged opinions on human capacity building.

3.4.(2).(iv) Development of internationally-oriented human resources with excellent communication skills

Presentations and other events in English

- PMDA arranged a presentation in English on PMDA's latest activities at the DIA (Drug Information Association) meeting.
- PMDA made efforts to cultivate 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 offered an English language training program specifically designed for employees scheduled to be dispatched overseas for a long period to improve their practical English abilities. 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 (one-on-one lessons for all). Employees who use English when conducting their operations, (e.g., attendance at international conferences) received English training programs (one-on-one lessons, group lessons, and correspondence courses) to improve their English skills. PMDA also provided new training programs in good practice for learning English and making presentations offered by in-house staff, in order to enhance the motivation of all employees to learn English and raise their awareness of presentation skills, to improve the English ability of all employees.

3.4.(2).(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 2017 [39 drugs and 1 regenerative medical product]).

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 2017, PMDA received 437 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 also gained a slot for its session and had booth exhibitions at the DIA Annual Meetings in Europe and the US to familiarize attendees with PMDA's policies etc. PMDA also coordinated opinions with the Program Committee to gain a slot for its session at the Regulatory Affairs Professionals Society (RAPS) Annual Meeting in FY 2018.

- 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 the PMDA website. (A total of 946 certification standards, a basic requirement conformance checklist, etc. were published until FY 2017).

  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 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

3.4.(4).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.

3.4.(4).b. Releasing information related to review reports

- 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) at MHLW (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 2017, PMDA released 99 review reports, 54 summaries of product applications, and 62 re-examination reports.

  The percentage of review reports released within 1 month after approval was 100% in FY 2017 (100% in FY 2016). The percentage of summaries of product applications released within 3 months after approval was 100% in FY 2017 (100% in FY 2016); the median time from approval to release was 66 days, showing an achievement of 136% 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 7 days for review reports, 66 days for summary of product applications, and 5 days for re-examination reports.

Review reports on new medical devices

- In FY 2017, PMDA released 11 review reports, 12 summaries of product applications and 10 re-examination reports for new medical devices.

  The percentage of review reports released within 1 month after approval was 100% in FY 2017 (100% in FY 2016). The percentage of summaries of product applications released within 3 months after approval was 92% in FY 2017 (90% in FY 2016); the median time from approval to release was 87 days, showing an achievement of 103% 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 26 days for review reports, 87 days for summary of product applications, and 4 days for re-examination reports.

Review reports on new regenerative medical products

- In FY 2017, PMDA released 0 review reports and 0 summaries of product applications for new regenerative medical products.

Review reports on BTC drugs and quasi-drugs

- In FY 2017, PMDA released 3 review reports and 3 summaries of product applications for BTC drugs, and 1 review report and 1 summary of product applications for a quasi-drug.

Number of review reports released

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
New drugs	120	130	118	108	99
New medical devices	19	9	16	9	11
New regenerative medical products	-	-	2	1	-
BTC and OTC drugs	5	3	2	1	3
Quasi-drugs	0	1	3	1	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 Section 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 (current Kansai Pharmaceutical Industries Association), the Osaka Pharmaceutical Manufacturers Association, the Osaka Chamber of Commerce and Industry, and the Kansai Economic Federation, PMDA launched a video conference consultation system at its Kansai Branch in order to improve the convenience of this service for applicants based in the Kansai region. In FY 2017, PMDA conducted 59 video conference consultations, etc. PMDA also conducted 61 RS Strategy Consultations (R&D) (pre-consultations) through the web-based conference system.
- 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 further modified the system to increase the usability in response to requests from applicant companies.

- In line with the progress of discussions on ICH eCTD version 4.0, PMDA procured operations for requirement definition and basic designing to develop a system to receive and access eCTD version 4.0. In FY 2017, PMDA completed the requirement definition and proceeded with preparatory work on the basic designing phase starting in FY 2018. PMDA held a briefing session on eCTD version 4.0 specifications and related operational systems to expand the level of development vendors applying for procurement.

III. SUPPLEMENTARY INFORMATION

Reviews and Safety Measure Services

1. New drug application review services

Number of approved products

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Prescription drugs	4,003	3,944	3,664	3,660	3,611
BTC and OTC drugs	916	844	752	646	537
In vitro diagnostics	166	109	172	199	187
Quasi-drugs	2,028	1,779	2,495	1,924	1,891
Cosmetics	0	0	0	0	0
Total	7,113	6,676	7,083	6,429	6,226

Number of approved new drug applications

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of approved new drug applications	138	118	116	112	104
Priority review products among these new drugs	42	44	37	38	38

Reference 1 Approved new drug applications (only those with new active ingredients)

Total review time for new drugs (priority review products)

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time (months)	9.1	9.1	9.5	9.2	8.9
Number of approved applications	15	24	17	19	13

Reference

Regulatory review time (months)	3.4	3.8	3.8	3.8	4.3
Applicant's time (months)	5.3	5.4	6.0	5.6	5.7

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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	70th	70th	80th
Total review time (months)	11.9	12.1	11.2	12.0	12.1
Number of approved applications	24	28	25	22	25

Reference

Regulatory review time (months)	6.2	6.5	5.9	7.0	6.3
Applicant's time (months)	5.4	6.5	6.7	7.3	7.6

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 2 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	60th	60th	70th	70th	80th

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	60th	70th	70th	80th	80th

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 2017	0	0	0	0	0	6	0	4	0	1	9	35	7	533	29	624
Products approved in FY 2017	0	0	0	0	0	11	0	6	0	1	2	22	2	480	13	537

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 2017, 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 2017	0	3	0	1	2	5	12	593	1,063
Products approved in FY 2017	0	1	0	5	0	0	11	620	1,112

	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 2017	26	42	77	1,824	-	-	-	1,824
Products approved in FY 2017	31	24	60	1,864	3	24	27	1,891

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.

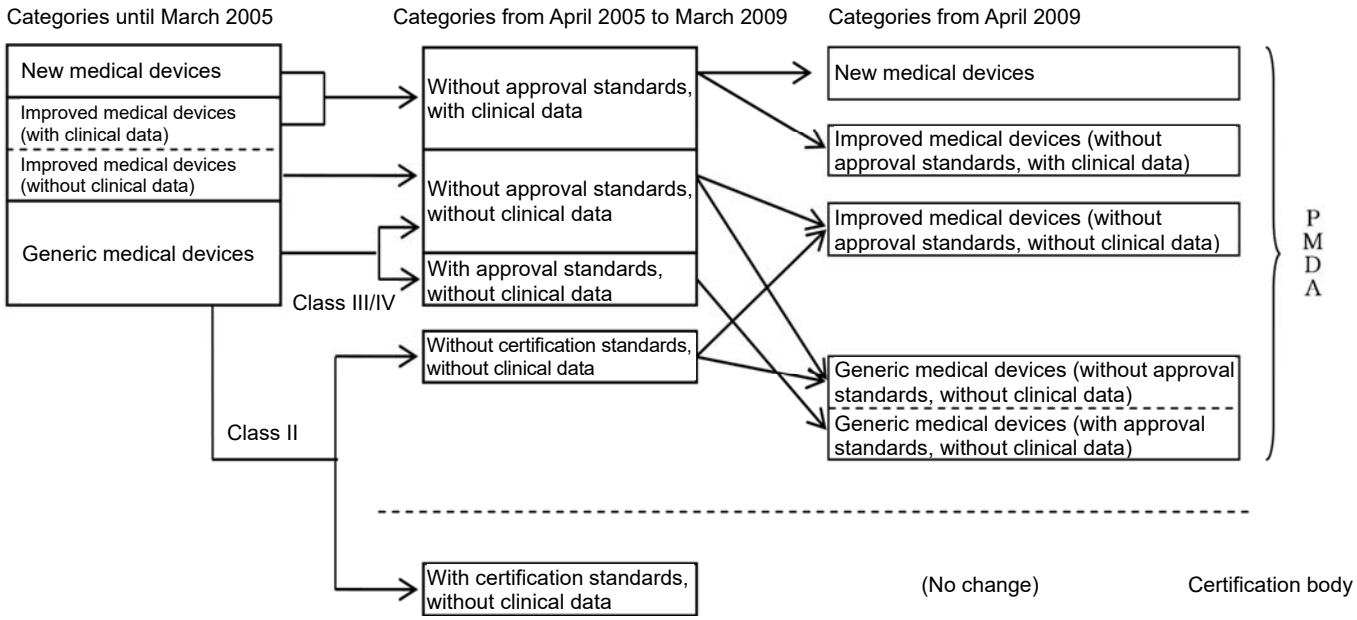
Note 4: The numbers of "Products approved in FY 2016" were calculated by category at the time of approval.

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 revised 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 2013	FY 2014	FY 2015	FY 2016	FY 2017
Medical devices		1,347	1,235	1,217	1,120	1,153
Priority review products (included in above figures)		14	5	8	1*	3
Re-listed	New medical devices	94	67	56	26	27
	Improved medical devices (with clinical data) (From FY 2009 onward)	60	35	53	44	42
	Improved medical devices (without clinical data) (From FY 2009 onward)	227	213	240	225	215
	Generic medical devices (From FY 2009 onward)	943	917	868	825	868
	Without approval standards, with clinical data	1	0	0	0	0
	Without approval standards, without clinical data	17	3	0	0	1
	With approval standards, without clinical data	1	0	0	0	0
	Controlled medical devices (without approval and certification standards, without clinical data)	1	0	0	0	0
	Improved medical devices (until FY 2004)	3	0	0	0	0
	Generic medical devices (until FY 2004)	0	0	0	0	0

** One new medical device is included.*

Reference 1 Approval status of and review time for new medical devices

Approval status of and review time for new medical devices (priority review products)

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Percentile	50th	60th	60th	70th	70th
Total review time (months) (reference, 80%)	9.0 (10.0)	8.8 (8.9)	7.9 (8.2)	8.0 (8.0)	8.3 (9.6)
Number of approved applications	14	5	8	1	3

Note: In FY 2017, a total review time of 10 months was achieved for 2 of 3 products, with an achievement rate of 66.7%; the target for the total review time was achieved from the standpoint of the percentiles of the products but was not achieved from the standpoint of the achievement rate.

Reference

Regulatory review time (months)	5.1	4.0	4.2	3.2	5.5
Applicant's time (months)	3.5	3.3	3.8	4.8	3.0

Note 1: Figures are calculated based on the products submitted in or after April 2004.

Note 2: The FY 2016 and FY 2017 results exclude standalone medical device software newly categorized as "medical devices" from November 25, 2014 according to the PMD Act, if the software 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."

Reference 2 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	60th	60th	70th	70th	80th

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	60th	60th	70th	70th	80th

Reference 3 Breakdown of approved products for which clinical trial data were submitted

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of medical devices with Japanese clinical trial data only	24	10	23	9	14
Number of medical devices with foreign clinical trial data only	32	24	23	25	26
Number of medical devices with global trial data	2	0	2	3	2
Number of medical devices with clinical evaluation reports	52	37	23	13	11
Others	8	5	10	4	2

Note 1: Others cover products with both foreign and Japanese clinical trial data etc.

2.(2) Review service for *in vitro* diagnostic products

2.(2).(i) Approved *in vitro* diagnostic products and their review times

Approximately 88% (164 of 187) of *in vitro* diagnostics applications approved in FY 2017 were processed within the standard administrative processing period (6 months).

Approved in vitro diagnostics applications and their review times

Fiscal Year (FY) of submission	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of approved applications	166	109	172	199	187
Median total review time (months)	5.4	5.3	7.2	6.4	5.2
Median regulatory review time (months)	2.7	2.6	3.9	3.5	2.9
Achievement rate	[81%]	[80%]	[71%]	[76%]	[88%]

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.)

2.(2).(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 of 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 of clinical trial notifications for new regenerative medical products started in November 2014.

The number of clinical trial notifications for drugs in FY 2017 is shown below. Among them, surveys of 131 notifications were completed, and 3 notifications were withdrawn.

Number of clinical trial notifications for drugs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Initial clinical trial notification	127 (6)	151 (20)	127 (10)	134 (10)	136 (3)
n-th clinical trial notification	474 (25)	450 (33)	530 (45)	511 (63)	557 (59)
Protocol change notification	4,356	4,321	4,566	4,998	5,200
Trial completion notification	446	498	507	469	456
Trial discontinuation notification	61	67	70	93	65
Development discontinuation notification	78	117	102	111	100
Total	5,542	5,604	5,902	6,316	6,514

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

The number of clinical trial notifications for equipment/devices in FY 2017 is shown below. Among them, surveys of 26 notifications were completed, and 0 notifications were withdrawn.

Number of clinical trial notifications for equipment/devices

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Initial clinical trial notification	31 (4)	31 (7)	31 (8)	34 (8)	25 (9)
n-th clinical trial notification	14 (0)	6 (2)	10 (0)	20 (1)	9 (2)
Protocol change notification	253	240	283	315	353
Trial completion notification	30	33	22	22	39
Trial discontinuation notification	6	6	5	2	8
Development discontinuation notification	6	2	2	7	6
Total	340	318	353	400	440

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

The number of clinical trial notifications for processed cells, etc. in FY 2017 is shown below. Among them, surveys of 16 notifications were completed, and 1 notification was withdrawn.

Number of clinical trial notifications for processed cells, etc.

	FY 2014	FY 2015	FY 2016	FY 2017
Initial clinical trial notification	3 (1)	10 (2)	16 (7)	13 (8)
n-th clinical trial notification	1 (1)	3 (2)	5 (0)	14 (10)
Protocol change notification	2	19	52	93
Trial completion notification	0	0	1	3
Trial discontinuation notification	0	0	0	3
Development discontinuation notification	0	0	0	1
Total	6	32	74	127

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

3.(2) Survey of 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.
The number of reports on adverse drug reactions etc. from clinical trials in FY 2017 is shown below.

Adverse drug reaction reports from clinical trials

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of ADR reports from clinical trials	58,275	71,689	86,039	87,876	95,008
(In Japan)	780	910	1,339	1,458	1,220
(Outside Japan)	57,495	70,779	84,700	86,418	93,788

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.

The number of device malfunction reports from clinical trials in FY 2017 is shown below.

Device malfunction reports from clinical trials

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Number of malfunction reports from clinical trials	1,518	2,119	2,966	1,971	2,252

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.

The number of processed cell-related malfunction reports from clinical trials in FY 2017 is shown below.

Number of processed cell-related malfunction reports from clinical trials

	FY 2014	FY 2015	FY 2016	FY 2017
Number of malfunction reports from clinical trials	0	50	129	196

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).

The number of DMF registrations filed or granted in FY 2017 is shown below.

Number of DMF registrations filed and registered

		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Registrations filed		1,918	2,017	2,019	3,163	2,126
Breakdown	New registrations filed	251	282	295	259	253
	Registration change filed	146	160	186	190	166
	Minor change filed	1,149	1,179	1,189	2,438	1,424
	Other applications/notifications*	372	396	349	276	283
Registrations granted		387	443	502	449	423
Breakdown	New registration granted	244	282	305	260	258
	Registration change granted	143	161	197	189	165

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

**: Other applications/notifications include applications for revision, reissuance, and transfer of the registration certificate.*

Table 1. Number of Drugs, etc. Filed and Approved (FY 2013 - 2017)

Application Category \ Fiscal Year			Number of products filed					Number of products approved				
			FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Drugs, etc.	New drugs	New	142	115	162	124	143	160	142	109	131	126
		Partial change	326	364	350	349	441	344	362	320	337	389
		Total	468	479	512	473	584	504	504	429	468	515
	Generic drugs	New	1,468	1,166	905	834	582	1,438	1,325	635	731	805
		Partial change	2,425	2,286	2,597	2,329	1,569	2,066	2,122	2,600	2,461	2,291
		Total	3,893	3,452	3,502	3,163	2,151	3,504	3,447	3,235	3,192	3,096
	BTC/OTC drugs	New	747	671	523	513	453	657	638	589	450	401
		Partial change	266	211	193	187	171	259	206	163	196	136
		Total	1,013	882	716	700	624	916	844	752	646	537
	In vitro diagnostics	New	51	89	83	63	73	69	40	80	91	70
		Partial change	85	74	113	86	123	97	69	92	108	117
		Total	136	163	196	149	196	166	109	172	199	187
	Quasi-drugs	New	2,002	1,666	2,329	1,808	1,585	1,763	1,631	2,322	1,694	1,645
		Partial change	296	162	230	254	239	265	148	173	230	246
		Total	2,298	1,828	2,559	2,062	1,824	2,028	1,779	2,495	1,924	1,891
	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	4,410	3,707	4,002	3,342	2,836	4,087	3,776	3,735	3,097	3,047
		Partial change	3,398	3,097	3,483	3,205	2,543	3,031	2,907	3,348	3,332	3,179
		Total	7,808	6,804	7,485	6,547	5,379	7,118	6,683	7,083	6,429	6,226

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 as "administrative review category." The same applies to the other categories.

Table 2. Number of Medical Devices Filed and Approved (FY 2013 - FY 2017)

Application Category \ Fiscal Year		Number of products filed					Number of products approved				
		FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
New medical devices	New	28	37	14	11	20	51	24	22	10	13
	Partial change	44	63	16	18	17	43	43	34	16	14
	Total	72	100	30	29	37	94	67	56	26	27
Improved medical devices (with clinical data) (in or after FY 2009)	New	36	36	23	43	46	54	27	43	38	36
	Partial change	10	9	4	6	14	6	8	10	6	6
	Total	46	45	27	49	60	60	35	53	44	42
Improved medical devices (without clinical data) (in or after FY 2009)	New	137	194	144	155	103	172	156	151	154	153
	Partial change	50	68	74	62	63	55	57	89	71	62
	Total	187	262	218	217	166	227	213	240	225	215
Generic medical devices (in or after FY 2009)	New	375	418	319	355	373	355	396	351	329	344
	Partial change	544	544	469	574	491	588	521	517	496	524
	Total	919	962	788	929	864	943	917	868	825	868
Medical devices (with clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	1	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	1	0	0	0	0
Medical devices (without approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	6	0	0	0	1
	Partial change	-	-	-	-	-	11	3	3	0	0
	Total	-	-	-	-	-	17	3	3	0	1
Medical devices (with approval standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	1	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	1	0	0	0	0
Controlled medical devices (without approval standards or certification standards, without clinical study data) (FY 2005 - FY 2008)	New	-	-	-	-	-	1	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	1	0	0	0	0
Improved medical devices (in or before FY 2004)	New	-	-	-	-	-	2	0	0	0	0
	Partial change	-	-	-	-	-	1	0	0	0	0
	Total	-	-	-	-	-	3	0	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	-	-	-	-	-	0	0	0	0	0
	Partial change	-	-	-	-	-	0	0	0	0	0
	Total	-	-	-	-	-	0	0	0	0	0
Total	New	576	685	500	564	542	643	603	567	531	547
	Partial change	648	684	563	660	585	704	632	653	589	606
	Total	1,224	1,369	1,063	1,224	1,127	1,347	1,235	1,220	1,120	1,153

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 - FY2017)

Fiscal year / Application Category		Number of products filed				Number of products approved			
		FY 2014	FY 2015	FY 2016	FY 2017	FY 2014	FY 2015	FY 2016	FY 2017
Regenerative Medical Products	New	2	0	0	0	0	2	0	0
	Partial change	0	3	1	1	0	2	1	2
	Total	2	3	1	1	0	4	1	2

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 as "administrative review category."

Table 4. New Drugs Approved in FY 2017

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
1	May 18, 2017	1	Asacol Tablets 400 mg (Zeria Pharmaceutical Co., Ltd.)	Change	Mesalazine	A drug with a new dosage indicated for the treatment of ulcerative colitis (excluding severe cases).
1	May 18, 2017	2	Remicade for I.V. Infusion 100 (Mitsubishi Tanabe Pharma Corporation)	Change	Infliximab (genetical recombination)	A drug with a new dosage indicated for the treatment of Crohn's disease. [Orphan drug]
1	Jun. 26, 2017	3	Oldamin for Injection 1 g (Fuji Chemical Industries Co., Ltd.)	Change	Monoethanolamine oleate	A drug with a new additional indication and a new dosage indicated for the regression of gastric varices.
1	Jul. 3, 2017	4	Jadenu Granules Sachet 90 mg Jadenu Granules Sachet 360 mg (Novartis Pharma K.K.)	Approval Approval	Deferasirox	Drugs in a new dosage form indicated for the treatment of chronic iron overload due to blood transfusions (in patients for whom injection of iron chelating agents is inappropriate).
1	Aug. 25, 2017	5	Kenketu Nonthron 500 for injection Kenketu Nonthron 1500 for injection (Nihon Pharmaceutical Co., Ltd.)	Change Change	Lyophilized human antithrombin III concentrate	Drugs with a new additional indication and a new dosage for the treatment of portal vein thrombosis associated with decreased antithrombin III.
1	Aug. 25, 2017	6	Revolade Tablets 12.5 mg Revolade Tablets 25 mg (Novartis Pharma K.K.)	Change Change	Eltrombopag olamine	Drugs with a new additional indication and a new dosage for the treatment of aplastic anemia. [Orphan drug]
1	Aug. 25, 2017	7	Neoral Oral Solution 10% Neoral 10 mg Capsules Neoral 25 mg Capsules Neoral 50 mg Capsules (Novartis Pharma K.K.)	Change Change Change Change	Ciclosporin	Drugs with a revised indication and a new dosage for the treatment of aplastic anemia which is not severe. [Expedited review]
1	Sep. 22, 2017	8	Pariet Tablets 5 mg Pariet Tablets 10 mg (Eisai Co., Ltd.)	Change Change	Rabeprazole sodium	Drugs with a new dosage indicated for the treatment of reflux esophagitis.
1	Sep. 27, 2017	9	Rectabul 2 mg Rectal Foam 14 Doses (EA Pharma Co., Ltd.)	Approval	Budesonide	A drug with a new route of administration indicated for the treatment of ulcerative colitis which is not severe.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
1	Dec. 25, 2017	10	Zyprexa Tablets 2.5 mg Zyprexa Tablets 5 mg Zyprexa Tablets 10 mg Zyprexa Fine Granules 1% Zyprexa Zydis Tablets 2.5 mg Zyprexa Zydis Tablets 5 mg Zyprexa Zydis Tablets 10 mg (Eli Lilly Japan K.K.) Olanzapine Tablets 2.5 mg "DSEP" Olanzapine Tablets 5 mg "DSEP" Olanzapine Tablets 10 mg "DSEP" Olanzapine Fine Granules 1% "DSEP" Olanzapine OD Tablets 2.5 mg "DSEP" Olanzapine OD Tablets 5 mg "DSEP" Olanzapine OD Tablets 10 mg "DSEP" (Daiichi Sankyo Espha Co., Ltd.) Olanzapine Tablets 2.5 mg "Nichi-Iko" Olanzapine Tablets 5 mg "Nichi-Iko" Olanzapine Tablets 10 mg "Nichi-Iko" Olanzapine Fine Granules 1% "Nichi-Iko" Olanzapine OD Tablets 2.5 mg "Nichi-Iko" Olanzapine OD Tablets 5 mg "Nichi-Iko" Olanzapine OD Tablets 10 mg "Nichi-Iko" (Nichi-Iko Pharmaceutical Co., Ltd.) Olanzapine Fine Granules 1% "Pfizer" (Mylan Seiyaku Ltd.) Olanzapine Tablets 2.5 mg "Nipro" Olanzapine Tablets 5 mg "Nipro" Olanzapine Tablets 10 mg "Nipro" Olanzapine Fine Granules 1% "Nipro" Olanzapine OD Tablets 5 mg "Nipro" Olanzapine OD Tablets 10 mg "Nipro" (Nipro Corporation) Olanzapine Tablets 2.5 mg "Pfizer" Olanzapine Tablets 5 mg "Pfizer" Olanzapine Tablets 10 mg "Pfizer" Olanzapine OD Tablets 2.5 mg "Pfizer" Olanzapine OD Tablets 5 mg "Pfizer" Olanzapine OD Tablets 10 mg "Pfizer" (Daito Pharmaceutical Co., Ltd.)	Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change Change	Olanzapine	Drugs with a new additional indication and a new dosage indicated for the treatment of gastrointestinal symptoms (nausea and vomiting) associated with the administration of antineoplastic drugs (cisplatin, etc.). [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
1	Jan. 19, 2018	11	Nexium Capsules 10 mg Nexium Capsules 20 mg Nexium Granules for Suspension 10 mg Nexium Granules for Suspension 20 mg (AstraZeneca K.K.)	Change Change Approval Approval	Esomeprazole magnesium hydrate	Drugs with a new additional pediatric dosage and in additional dosage forms indicated for the treatment of gastric ulcer, duodenal ulcer, anastomotic ulcer, reflux esophagitis, non-erosive reflux disease, and Zollinger-Ellison syndrome.
1	Jan. 19, 2018	12	Goofice Tablets 5 mg (EA Pharma Co., Ltd.)	Approval	Elobixibat hydrate	A drug with a new active ingredient indicated for the treatment of chronic constipation (excluding constipation due to organic diseases).
1	Feb. 23, 2018	13	Certican Tablets 0.25 mg Certican Tablets 0.5 mg Certican Tablets 0.75 mg (Novartis Pharma K.K.)	Change Change Change	Everolimus	Drugs with a new additional indication and a new dosage for the inhibition of rejection in liver transplantation.
1	Mar. 23, 2018	14	Orkedia Tablets 1 mg Orkedia Tablets 2 mg (Kyowa Hakko Kirin Co., Ltd.)	Approval Approval	Evocalcet	Drugs with a new active ingredient indicated for the treatment of secondary hyperparathyroidism in patients on maintenance dialysis.
1	Mar. 23, 2018	15	Rapalimus Gel 0.2% (Nobelpharma Co., Ltd.)	Approval	Sirolimus	A drug with a new route of administration indicated for the treatment of skin lesions associated with tuberous sclerosis complex. [Orphan drug, SAKIGAKE designation]

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2	Jun. 26, 2017	16	Rituxan Injection 10 mg/mL (Zenyaku Kogyo Co., Ltd.)	Change	Rituximab (genetical recombination)	A drug with a new additional indication and a new dosage for the treatment of chronic idiopathic thrombocytopenic purpura. [Public knowledge-based application after preliminary assessment by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)]
2	Jul. 3, 2017	17	Parmodia Tab. 0.1 mg (Kowa Company, Ltd.)	Approval	Pemafibrate	A drug with a new active ingredient indicated for the treatment of hyperlipidaemia (including familial hyperlipidaemia).
2	Sep. 27, 2017	18	Atozet Combination Tablets LD Atozet Combination Tablets HD (MSD K.K.)	Approval Approval	Ezetimibe/ Atorvastatin calcium hydrate	New combination drugs indicated for the treatment of hypercholesterolemia and familial hypercholesterolemia.
2	Sep. 27, 2017	19	Revatio Tablets 20 mg Revatio Dry Syrup for Suspension 900 mg Revatio OD Film 20 mg (Pfizer Japan Inc.)	Change Approval Approval	Sildenafil citrate	Drugs with a new additional pediatric dosage and in additional dosage forms indicated for the treatment of pulmonary arterial hypertension. [Orphan drug]
2	Jan. 19, 2018	20	Ibulief I.V. Injection 20 mg (Senju Pharmaceutical Co., Ltd.)	Approval	Ibuprofen L-lysine	A drug with a new active ingredient indicated for the treatment of patent ductus arteriosus in premature infants when conservative treatment (fluid restriction, diuretic use, etc.) is not sufficiently effective.
2	Mar. 23, 2018	21	Azilect Tablets 0.5 mg Azilect Tablets 1 mg (Takeda Pharmaceutical Company Limited)	Approval Approval	Rasagiline mesilate	Drugs with a new active ingredient indicated for the treatment of Parkinson's disease.
3-1	Jul. 3, 2017	22	Bipresso Extended Release Tablets 50 mg Bipresso Extended Release Tablets 150 mg (Astellas Pharma Inc.)	Approval Approval	Quetiapine fumarate	Drugs with a new indication in new dosage form indicated for the improvement of depressive symptoms in patients with bipolar disorder.
3-1	Jul. 3, 2017	23	Spinraza Intrathecal injection 12 mg (Biogen Japan Ltd.)	Approval	Nusinersen sodium	A drug with a new active ingredient indicated for the treatment of infantile spinal muscular atrophy. [Orphan drug]
3-1	Jul. 3, 2017	24	Depromel Tablets 25 Depromel Tablets 50 Depromel Tablets 75 (Meiji Seika Pharma Co., Ltd.) Luvox Tablets 25 Luvox Tablets 50 Luvox Tablets 75 (AbbVie GK)	Change Change Change Change Change Change	Fluvoxamine maleate	Drugs with a new additional pediatric dosage indicated for the treatment of obsessive-compulsive disorder.
3-1	Aug. 25, 2017	25	Leuplin SR for Injection Kit 11.25 mg (Takeda Pharmaceutical Company Limited)	Change	Leuprorelin acetate	A drug with a new additional indication for inhibiting progression of spinal and bulbar muscular atrophy. [Orphan drug]
3-1	Aug. 25, 2017	26	Vimpat Tablets 50 mg Vimpat Tablets 100 mg (UCB Japan Co., Ltd.)	Change Change	Lacosamide	Drugs with a revised indication for the treatment of partial seizures (including secondary generalized seizures) in patients with epilepsy.

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3-1	Sep. 22, 2017	27	Spinraza Intrathecal injection 12 mg (Biogen Japan Ltd.)	Change	Nusinersen sodium	A drug with a revised indication and a new dosage for the treatment of spinal muscular atrophy. [Orphan drug]
3-1	Dec. 25, 2017	28	Soliris for Intravenous Infusion 300 mg (Alexion Pharma G.K.)	Change	Eculizumab (genetical recombination)	A drug with a new additional indication and a new dosage indicated for the treatment of generalized myasthenia gravis (for use only in patients whose symptoms cannot be sufficiently controlled with high-dose intravenous immunoglobulin or plasmapheresis). [Orphan drug]
3-1	Jan. 19, 2018	29	Rexulti Tablets 1 mg Rexulti Tablets 2 mg (Otsuka Pharmaceutical Co., Ltd.)	Approval Approval	Brexpiprazole	Drugs with a new active ingredient indicated for the treatment of schizophrenia.
3-1	Mar. 23, 2018	30	Hernicore 1.25 Units for Intradiscal Inj. (Seikagaku Corporation)	Approval	Condoliase	A drug with a new active ingredient indicated for the treatment of lumbar disc herniation with subligamentous extrusion that has not adequately responded to conservative treatment.
3-2	Sep. 22, 2017	31	Remitch Capsules 2.5 μg Remitch OD Tablets 2.5 μg (Toray Industries, Inc.) Nopicor Capsules 2.5 μg (Toray Medical Co., Ltd.)	Change Change Change	Nalfurafine hydrochloride	Drugs with a revised indication for the improvement of pruritus in patients on peritoneal dialysis (for use only in patients who have not responded sufficiently to conventional treatments).
3-2	Jan. 19, 2018	32	Naruvein Injection 2 mg Naruvein Injection 20 mg (Daiichi Sankyo Propharma Co., Ltd.)	Approval Approval	Hydromorphone hydrochloride	Drugs with a new route of administration indicated for management of moderate to severe pain in various types of cancer.
4	May 18, 2017	33	Zosyn for Intravenous Injection 2.25 Zosyn for Intravenous Injection 4.5 Zosyn for I.V. Infusion bag 4.5 (Taiho Pharmaceutical Co., Ltd.)	Change Change Change	Tazobactam/Piperacillin hydrate	Drugs with additional indications and new dosages for the treatment of "bacterial skin infections mainly involving the dermis and/or subcutaneous tissues" and "secondary bacterial infections of pre-existing skin ulcers and/or erosion".
4	Jul. 3, 2017	34	Amenalief Tab. 200 mg (Maruho Co., Ltd.)	Approval	Amenamevir	A drug with a new active ingredient indicated for the treatment of herpes zoster.
4	Sep. 27, 2017	35	Zinplava for Intravenous Infusion 625 mg (MSD K.K.)	Approval	Bezlotoxumab (genetical recombination)	A drug with a new active ingredient indicated for the prevention of recurrent *Clostridium difficile* infection.
4	Sep. 27, 2017	36	Maviret Combination Tablets (AbbVie GK)	Approval	Glecaprevir hydrate/ Pibrentasvir	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. [Priority review]
4	Jan. 19, 2018	37	Nailin Capsules 100 mg (Sato Pharmaceutical Co., Ltd.)	Approval	Fosravuconazole L-lysine ethanolate	A drug with a new active ingredient indicated for the treatment of onychomycosis due to *Trichophyton* species.

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
4	Jan. 19, 2018	38	Sirturo Tablets 100 mg (Janssen Pharmaceutical K.K.)	Approval	Bedaquiline fumarate	A drug with a new active ingredient indicated for the treatment of pulmonary multidrug-resistant tuberculosis. [Orphan drug]
4	Feb. 16, 2018	39	Harvoni Combination Tablets (Gilead Sciences, Inc.)	Change	Ledipasvir acetonate/Sofosbuvir	A drug with a new additional indication for the improvement of viremia in patients with chronic hepatitis C or compensated cirrhosis type C in serogroup 2 (genotype 2).
4	Feb. 23, 2018	40	Xofluza Tablets 10 mg Xofluza Tablets 20 mg (Shionogi & Co., Ltd.)	Approval Approval	Baloxavir marboxil	Drugs with a new active ingredient indicated for the treatment of influenza A or B virus infections. [SAKIGAKE designation]
4	Mar. 23, 2018	41	Sivextro Tablets 200 mg Sivextro Intravenous Infusion 200 mg (Bayer Yakuhin, Ltd.)	Approval Approval	Tedizolid phosphate	Drugs with a new active ingredient indicated for the treatment of bacterial skin infections mainly involving the dermis and/or subcutaneous tissues, secondary bacterial infections of pre-existing skin ulcers and/or erosion, and secondary bacterial infections of trauma, burn, and surgical wounds.
4	Mar. 23, 2018	42	Prevymis Tablets 240 mg Prevymis Intravenous Infusion 240 mg (MSD K.K.)	Approval Approval	Letermovir	Drugs with a new active ingredient indicated for the prophylaxis of cytomegalovirus disease in allogeneic hematopoietic stem cell transplant recipients. [Orphan drug]
5	Mar. 23, 2018	43	Onepal No. 1 Injection Onepal No. 2 Injection (AY Pharmaceuticals Co., Ltd.)	Approval Approval	N/A for this combination drug	Combination prescription drugs with similar formulations indicated for the supplementation of water, electrolytes, amino acids, calories, 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.
6-1	Jun. 26, 2017	44	Actemra 162 mg Syringe for SC Injection Actemra 162 mg Auto-injector for SC Injection (Chugai Pharmaceutical Co., Ltd.)	Change Change	Tocilizumab (genetical recombination)	Drugs with a new dosage indicated for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not responded sufficiently to conventional treatments.
6-1	Jul. 3, 2017	45	Olumiant Tablets 4 mg Olumiant Tablets 2 mg (Eli Lilly Japan K.K.)	Approval Approval	Baricitinib	Drugs with a new active ingredient indicated for the treatment of rheumatoid arthritis (including prevention of structural joint damage) in patients who have not responded sufficiently to conventional treatments.
6-1	Jul. 3, 2017	46	Prolia Subcutaneous Injection 60 mg Syringe (Daiichi Sankyo Company, Limited)	Change	Denosumab (genetical recombination)	A drug with a new additional indication and a new dosage indicated for inhibiting progression of bone erosion associated with rheumatoid arthritis.
6-1	Aug. 25, 2017	47	Actemra 162 mg Syringe for SC Injection Actemra 162 mg Auto-injector for SC Injection (Chugai Pharmaceutical Co., Ltd.)	Change Change	Tocilizumab (genetical recombination)	Drugs with new additional indications and a new dosage for the treatment of Takayasu arteritis and giant cell arteritis in patients who have not responded sufficiently to conventional treatments. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
6-1	Sep. 27, 2017	48	Cedarcure Japanese Cedar Pollen Sublingual Tablets 2,000 JAU Cedarcure Japanese Cedar Pollen Sublingual Tablets 5,000 JAU (Torii Pharmaceutical Co., Ltd.)	Approval Approval	N/A	Drugs with a new active ingredient indicated for the treatment of Japanese cedar pollinosis (desensitization therapy).
6-1	Sep. 27, 2017	49	Kevzara 150 mg Syringe for SC Injection Kevzara 200 mg Syringe for SC Injection Kevzara 150 mg Auto-injector for SC Injection Kevzara 200 mg Auto-injector for SC Injection (Sanofi K.K.)	Approval Approval Approval Approval	Sarilumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of rheumatoid arthritis in patients who have not responded sufficiently to conventional treatments.
6-1	Sep. 27, 2017	50	Rupafin Tablets 10 mg (Teikoku Seiyaku Co., Ltd.)	Approval	Rupatadine fumarate	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. 27, 2017	51	Benlysta for I.V. Infusion 120 mg Benlysta for I.V. Infusion 400 mg Benlysta for S.C. Injection 200 mg Autoinjector Benlysta for S.C. Injection 200 mg Syringe (GlaxoSmithKline K.K.)	Approval Approval Approval Approval	Belimumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of systemic lupus erythematosus in patients who have not responded sufficiently to conventional treatments.
6-1	Jan. 19, 2018	52	Allesaga Tape 4 mg Allesaga Tape 8 mg (Hisamitsu Pharmaceutical Co., Inc.)	Approval Approval	Emedastine fumarate	Drugs with a new route of administration indicated for the treatment of allergic rhinitis.
6-1	Jan. 19, 2018	53	Dupixent 300 mg Syringe for S.C. Injection (Sanofi K.K.)	Approval	Dupilumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of atopic dermatitis in patients who have not responded sufficiently to conventional treatments.
6-1	Jan. 19, 2018	54	Fasenra Subcutaneous Injection 30 mg Syringe (AstraZeneca K.K.)	Approval	Benralizumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of bronchial asthma (for use only in patients with intractable bronchial asthma whose asthmatic responses are uncontrollable with conventional therapies).
6-1	Feb. 16, 2018	55	Miticure House Dust Mite Sublingual Tablets 3,300 JAU Miticure House Dust Mite Sublingual Tablets 10,000 JAU (Torii Pharmaceutical Co., Ltd.)	Change Change	*Dermatophagoides farinae* extract, *Dermatophagoides pteronyssinus* extract	Drugs with a new additional pediatric dosage for children aged under 12 years. These drugs comprise allergen immunotherapy for the treatment of house dust mite antigen-induced allergic rhinitis.
6-1	Feb. 16, 2018	56	Actair 100 IR Sublingual Tablets-HDM Actair 300 IR Sublingual Tablets-HDM (Shionogi & Co., Ltd.)	Change Change	*Dermatophagoides farinae* extract bulk powder, *Dermatophagoides pteronyssinus* extract bulk powder	Drugs with a new additional pediatric dosage for children aged under 12 years. These drugs comprise allergen immunotherapy for the treatment of house dust mite antigen-induced allergic rhinitis.
6-1	Feb. 23, 2018	57	Orencia for I.V. Infusion 250 mg (Bristol-Myers Squibb K.K.)	Change	Abatacept (genetical recombination)	A drug with a new additional indication and a new dosage indicated for the treatment of polyarticular-course juvenile idiopathic arthritis 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 (underlined: new active ingredient)	Notes
6-1	Mar. 23, 2018	58	Tremfya Subcutaneous Injection 100 mg Syringe (Janssen Pharmaceutical K.K.)	Approval	Guselkumab (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	Mar. 23, 2018	59	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 Humira 40 mg for S.C. Injection in pre-filled pen 0.4 mL Humira 80 mg for S.C. Injection in pre-filled pen 0.8 mL (AbbVie GK)	Change Change Change Change Change	Adalimumab (genetical recombination)	Drugs with a new additional indication and a new dosage indicated for the treatment of pustular psoriasis in patients who have not responded sufficiently to conventional therapies.
6-2	May 18, 2017	60	Teribone Inj. 56.5 μg (Asahi Kasei Pharma Corporation)	Change	Teriparatide acetate	A drug with a new dosage indicated for the treatment of osteoporosis with high risk of fracture.
6-2	Jul. 3, 2017	61	Canalia Combination Tablets (Mitsubishi Tanabe Pharma Corporation)	Approval	Teneligliptin hydrobromide hydrate/Canagliflozin hydrate	A new combination drug indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of teneligliptin hydrobromide hydrate with canagliflozin hydrate is deemed appropriate).
6-2	Nov. 30, 2017	62	Norditropin FlexPro Injection 5 mg Norditropin FlexPro Injection 10 mg Norditropin FlexPro Injection 15 mg Norditropin S Injection 10 mg (Novo Nordisk Pharma Ltd.)	Change Change Change Change	Somatropin (genetical recombination)	Drugs with a new additional indication for the treatment of short stature associated with Noonan syndrome with no epiphyseal closure.
6-2	Mar. 23, 2018	63	Ozempic Subcutaneous Injection 2 mg (Novo Nordisk Pharma Ltd.)	Approval	Semaglutide (genetical recombination)	A drug with a new active ingredient indicated for the treatment of type 2 diabetes mellitus.
6-2	Mar. 23, 2018	64	Sujanu Combination Tablets (MSD K.K.)	Approval	Sitagliptin phosphate hydrate/Ipragliflozin L-proline	A new combination drug indicated for the treatment of type 2 diabetes mellitus (only when a concomitant use of sitagliptin phosphate hydrate with ipragliflozin L-proline is deemed appropriate).
6-2	Mar. 23, 2018	65	Galafold Capsules 123 mg (Amicus Therapeutics, Inc.)	Approval	Migalastat hydrochloride	A drug with a new active ingredient indicated for the treatment of Fabry disease in patients with *GLA* mutations categorized as amenable to treatment with migalastat. [Orphan drug]
6-2	Mar. 23, 2018	66	Signifor LAR Kit for i.m. injection 10 mg Signifor LAR Kit for i.m. injection 30 mg Signifor LAR Kit for i.m. injection 20 mg Signifor LAR Kit for i.m. injection 40 mg (Novartis Pharma K.K.)	Approval Approval Change Change	Pasireotide pamoate	Drugs with a new additional indication and a new dosage and in additional dosage forms indicated for the treatment of Cushing's disease (when surgical therapies are not sufficiently effective or are difficult to perform). [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
In vivo diagnostics	Aug. 25, 2017	67	Ovisot for Injection 0.1 g (Daiichi Sankyo Company, Limited)	Change	Acetylcholine chloride	A drug with a new route of administration indicated for the induction of coronary spasm in a drug-induced coronary spasm provocation test during coronary angiography. [Public knowledge-based application after PAFSC's preliminary assessment]
In vivo diagnostics	Sep. 27, 2017	68	Alaglio Granules sachets 1.5 g (SBI Pharmaceuticals Co., Ltd.)	Approval	Aminolevulinic acid hydrochloride	A drug with a new additional indication and a new dosage in an additional dosage form for the visualization of tumor tissues of the non-muscle invasive bladder cancer in transurethral resection of bladder tumor. [Orphan drug]
Radio-pharmaceuticals	Sep. 27, 2017	69	Vizamyl Intravenous Injectable (Nihon Medi-Physics Co., Ltd.)	Approval	Flutemetamol (18F)	A drug with a new active ingredient indicated for visualization of beta-amyloid plaques in the brains of patients with cognitive impairment suspected to be Alzheimer's disease.
Radiopharmaceuticals	Feb. 16, 2018	70	FDGscan Injectable (Nihon Medi-Physics Co., Ltd.)	Change	Fludeoxyglucose (^{18}F)	A drug with a new additional indication for visualization of inflammatory sites in the diagnosis of large-vessel vasculitis. [Public knowledge-based application after PAFSC's preliminary assessment]
Oncology drugs	May 18, 2017	71	Xalkori Capsules 200 mg Xalkori Capsules 250 mg (Pfizer Japan Inc.)	Change Change	Crizotinib	Drugs with a new additional indication for the treatment of unresectable advanced/relapsed ROS1 fusion gene-positive non-small-cell lung cancer. [Orphan drug]
Oncology drugs	May 18, 2017	72	Kyprolis for Intravenous Injection 10 mg Kyprolis for Intravenous Injection 40 mg (Ono Pharmaceutical Co., Ltd.)	Change Change	Carfilzomib	Drugs with a new dosage and other characteristics indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Jun. 26, 2017	73	Stivarga Tablets 40 mg (Bayer Yakuhin, Ltd.)	Change	Regorafenib hydrate	A drug with a new additional indication for the treatment of unresectable hepatocellular carcinoma which has progressed after cancer chemotherapy. [Priority review]
Oncology drugs	Jul. 3, 2017	74	Difolta Injection 20 mg (Mundipharma K.K.)	Approval	Pralatrexate	A drug with a new active ingredient indicated for the treatment of relapsed or refractory peripheral T-cell lymphoma. [Orphan drug]
Oncology drugs	Jul. 3, 2017	75	Istodax Injection 10 mg (Celgene K.K.)	Approval	Romidepsin	A drug with a new active ingredient indicated for the treatment of relapsed or refractory peripheral T-cell lymphoma. [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
Oncology drugs	Jul. 3, 2017	76	Somatuline 120 mg for s.c. Injection (Teijin Pharma Limited)	Change	Lanreotide acetate	A drug with a new additional indication and a new dosage indicated for the treatment of neuroendocrine tumors of the pancreas and gastrointestinal tract.
Oncology drugs	Aug. 25, 2017	77	Abraxane I.V. Infusion 100 mg (Taiho Pharmaceutical Co., Ltd.)	Change	Paclitaxel	A drug with a new dosage indicated for the treatment of gastric cancer.
Oncology drugs	Sep. 22, 2017	78	Zykadia Capsules 150 mg (Novartis Pharma K.K.)	Change	Ceritinib	A drug with a revised indication for the treatment of unresectable advanced/relapsed ALK fusion gene-positive non-small-cell lung cancer.
Oncology drugs	Sep. 22, 2017	79	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 advanced or recurrent gastric cancer which has progressed after cancer chemotherapy. [Priority review]
Oncology drugs	Sep. 27, 2017	80	Ibrance Capsules 25 mg Ibrance Capsules 125 mg (Pfizer Japan Inc.)	Approval Approval	Palbociclib	Drugs with a new active ingredient indicated for the treatment of unresectable or recurrent breast cancer.
Oncology drugs	Sep. 27, 2017	81	Darzalex Intravenous Infusion 100 mg Darzalex Intravenous Infusion 400 mg (Janssen Pharmaceutical K.K.)	Approval Approval	Daratumumab (genetical recombination)	Drugs with a new active ingredient indicated for the treatment of relapsed or refractory multiple myeloma. [Orphan drug]
Oncology drugs	Sep. 27, 2017	82	Bavencio Injection 200 mg (Merck Serono Co., Ltd.)	Approval	Avelumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of unresectable Merkel cell carcinoma. [Orphan drug]
Oncology drugs	Sep. 27, 2017	83	Faslodex Intramuscular Injection 250 mg (AstraZeneca K.K.)	Change	Fulvestrant	A drug with a revised indication and a new dosage for the treatment of breast cancer. [Expedited review]
Oncology drugs	Nov. 30, 2017	84	Keytruda Injection 20 mg Keytruda Injection 100 mg (MSD K.K.)	Change Change	Pembrolizumab (genetical recombination)	Drugs with a new additional indication for the treatment of relapsed or refractory classical Hodgkin's lymphoma.
Oncology drugs	Dec. 25, 2017	85	Tasigna Capsules 50 mg Tasigna Capsules 150 mg Tasigna Capsules 200 mg (Novartis Pharma K.K.)	Change Change Change	Nilotinib hydrochloride hydrate	Drugs with a new pediatric dosage indicated for the treatment of chronic- or accelerated-phase chronic myeloid leukemia. [Expedited review (only Tasigna Capsules 50 mg)]
Oncology drugs	Dec. 25, 2017	86	Keytruda Injection 20 mg Keytruda Injection 100 mg (MSD K.K.)	Change Change	Pembrolizumab (genetical recombination)	Drugs with a new additional indication for the treatment of unresectable urothelial cancer which progressed after cancer chemotherapy. [Priority review]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
Oncology drugs	Jan. 19, 2018	87	Tecentriq Intravenous Infusion 1200 mg (Chugai Pharmaceutical Co., Ltd.)	Approval	Atezolizumab (genetical recombination)	A drug with a new active ingredient indicated for the treatment of unresectable advanced or recurrent non-small-cell lung cancer.
Oncology drugs	Jan. 19, 2018	88	Besponsa Injection 1 mg (Pfizer Japan Inc.)	Approval	Inotuzumab ozogamicin (genetical recombination)	A drug with a new active ingredient indicated for the treatment of relapsed or refractory CD22-positive acute lymphoblastic leukemia. [Orphan drug]
Oncology drugs	Jan. 19, 2018	89	Lynparza Tablets 100 mg Lynparza Tablets 150 mg (AstraZeneca K.K.)	Approval Approval	Olaparib	Drugs with a new active ingredient indicated for the maintenance treament of recurrent ovarian cancer in patients who are in a complete or partial response to platinum-based chemotherapy.
Oncology drugs	Feb. 16, 2018	90	Zytiga Tablets 250 mg (Janssen Pharmaceutical K.K.)	Change	Abiraterone acetate	A drug with a new additional indication for the treatment of prostate cancer in patients with high-risk prognostic factors who have not received previous endocrine therapy. [Priority review]
Oncology drugs	Mar. 23, 2018	91	Tafinlar Capsules 50 mg Tafinlar Capsules 75 mg (Novartis Pharma K.K.)	Change Change	Dabrafenib mesilate	Drugs with a new additional indication and a new dosage indicated for the treatment of unresectable advanced or recurrent BRAF mutation-positive non-small-cell lung cancer. [Orphan drug]
Oncology drugs	Mar. 23, 2018	92	Mekinist Tablets 0.5 mg Mekinist Tablets 2 mg (Novartis Pharma K.K.)	Change Change	Trametinib dimethyl sulfoxide	Drugs with a new additional indication for the treatment of unresectable advanced or recurrent BRAF mutation-positive non-small-cell lung cancer. [Orphan drug]
Oncology drugs	Mar. 23, 2018	93	Lenvima Capsule 4 mg (Eisai Co., Ltd.)	Change	Lenvatinib mesilate	A drug with a new additional indication and a new dosage indicated for the treatment of unresectable hepatic cell carcinoma.
Oncology drugs	Mar. 23, 2018	94	Velcade Injection 3 mg (Janssen Pharmaceutical K.K.)	Change	Bortezomib	A drug with a new additional indication and a new dosage indicated for the treatment of Waldenström's macroglobulinemia and lymphoplasmacytic lymphoma. [Public knowledge-based application after PAFSC's preliminary assessment]
Vaccines	Mar. 23, 2018	95	Shingrix for Intramuscular Injection (Japan Vaccine Co., Ltd.)	Approval	Freeze-dried recombinant herpes zoster vaccine (prepared from Chinese hamster ovary cells)	A drug with a new active ingredient indicated for the prevention of herpes zoster.
Vaccines	Mar. 23, 2018	96	Emulsion-adjuvanted Cell-culture Derived Influenza HA Vaccine H5N1 for Intramuscular Injection "Kaketsuken" (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change	Emulsion-adjuvanted cell-culture derived influenza HA vaccine (H5N1)	A drug with a new additional pediatric dosage indicated for the prevention of pandemic influenza (H5N1). [Orphan drug]

Review Category	Approval Date	No.	Brand Name (Applicant Company)	New Approval/ Partial Change	Active Ingredient (underlined: new active ingredient)	Notes
Vaccines	Mar. 23, 2018	97	Emulsion-adjuvanted Cell-culture Derived Influenza HA Vaccine (prototype) for Intramuscular Injection "Kaketsuken" (Kaketsuken [The Chemo-Sero-Therapeutic Research Institute])	Change	Emulsion-adjuvanted cell-culture derived influenza HA vaccine (prototype)	A drug with a new additional pediatric dosage indicated for the prevention of pandemic influenza. [Orphan drug]
Blood products	Mar. 23, 2018	98	Hemlibra s.c. 30 mg Hemlibra s.c. 60 mg Hemlibra s.c. 90 mg Hemlibra s.c. 105 mg Hemlibra s.c. 150 mg (Chugai Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval Approval	Emicizumab (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with congenital blood coagulation factor VIII deficiency with blood coagulation factor VIII inhibitors. [Orphan drug]
Blood products	Sep. 27, 2017	99	Afstyla I.V. Injection 250 Afstyla I.V. Injection 500 Afstyla I.V. Injection 1000 Afstyla I.V. Injection 1500 Afstyla I.V. Injection 2000 Afstyla I.V. Injection 2500 Afstyla I.V. Injection 3000 (CSL Behring K.K.)	Approval Approval Approval Approval Approval Approval Approval	Lonoctocog alfa (genetical recombination)	Drugs with a new active ingredient indicated for the control of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Blood products	Nov. 30, 2017	100	Adynovate Intravenous 250 Adynovate Intravenous 500 Adynovate Intravenous 1000 Adynovate Intravenous 2000 (Baxalta Japan Limited)	Change Change Change Change	Rurioctocog alfa pegol (genetical recombination)	Drugs with a new additional pediatric dosage indicated for the control of bleeding tendency in patients with blood coagulation factor VIII deficiency.
Bio-CMC	Sep. 27, 2017	101	Infliximab BS for I.V. Infusion 100 mg "Nichiiko" (Nichi-Iko Pharmaceutical Co., Ltd.) Infliximab BS for I.V. Infusion 100 mg "AYUMI" (Yakuhan Pharmaceutical Co., Ltd.)	Approval Approval	Infliximab (genetical recombination) [Infliximab biosimilar 2]	Follow-on biologics indicated for the treatment of rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Bio-CMC	Sep. 27, 2017	102	Rituximab BS Intravenous Infusion 100 mg [KHK] Rituximab BS Intravenous Infusion 500 mg [KHK] (Sandoz K.K.)	Approval Approval	Rituximab (genetical recombination) [Rituximab biosimilar 1]	Follow-on biologics indicated for the treatment of CD20-positive B-cell non-Hodgkin's lymphoma, CD20-positive B-cell lymphoproliferative disorder associated with immunosuppression, Wegener's granulomatosis, and microscopic polyangiitis.
Bio-CMC	Jan. 19, 2018	103	Etanercept BS 10 mg for S.C. Inj. "MA" Etanercept BS 25 mg for S.C. Inj. "MA" Etanercept BS 25 mg Syringe 0.5 mL for S.C. Inj. "MA" Etanercept BS 50 mg Syringe 1.0 mL for S.C. Inj. "MA" Etanercept BS 50 mg PEN 1.0 mL for S.C. Inj. "MA" (Mochida Pharmaceutical Co., Ltd.)	Approval Approval Approval Approval Approval	Etanercept (genetical recombination) [etanercept biosimilar 1]	Follow-on biologics indicated for the treatment of rheumatoid arthritis (including the prevention of structural joint damage) and polyarticular-course juvenile idiopathic arthritis 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 (underlined: new active ingredient)	Notes
Bio-CMC	Mar. 23, 2018	104	Trastuzumab BS for I.V. Infusion 60 mg "NK" Trastuzumab BS for I.V. Infusion 150 mg "NK" (Nippon Kayaku Co., Ltd.) Trastuzumab BS for I.V. Infusion 60 mg "CTH" Trastuzumab BS for I.V. Infusion 150 mg "CTH" (Celltrion Inc.)	Approval Approval Approval Approval	Trastuzumab (genetical recombination) [trastuzumab biosimilar 1]	Follow-on biologics indicated for the treatment of unresectable advanced or recurrent gastric cancer with HER2 overexpression.

Table 5. New Medical Devices Approved in FY 2017

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Robotic, ICT, and other devices (not classified as other categories)	May 26, 2017 Total review time: 365 days Regulatory review time: 128 days	Apr. 1, 2015 Foreign clinical study results	SpaceOAR System (Augmenix, Inc.)	Approval	Medical products 4 Absorbable tissue spacer for radiation therapy	A synthetic absorbable material intended to be injected and provide space between the prostate and anterior rectal wall, in order to reduce radiation exposure to the rectum during radiation therapy for prostate cancer. The components include an injection syringe and injection needle, etc. The results from a foreign clinical study which compared two groups undergoing Intensity Modulated Radiation Therapy (IMRT) with and without the device were submitted to evaluate the effectiveness in reduction of radiation exposure to the rectum.
Robotic, ICT, and other devices (not classified as other categories)	Dec. 14, 2017 Total review time: 78 days Regulatory review time: 51 days	— No clinical study results	SpaceOAR System (Augmenix, Inc.)	Change	Medical products 4 Absorbable tissue spacer for radiation therapy	A synthetic absorbable material intended to be injected and provide space between the prostate and anterior rectal wall, in order to reduce radiation exposure to the rectum during radiation therapy for prostate cancer. The application was submitted to change the manufacturing site. (A "partial change" application submitted during the post-market performance review period)
Robotic, ICT, and other devices (not classified as other categories)	Mar. 29, 2018 Total review time: 163 days Regulatory review time: 95 days	Dec. 19, 2014 No clinical study results	BRACAnalysis diagnostic system (Myriad Genetic Laboratories, Inc.)	Approval	Program 1 Analysis program for germline mutations (to determine the eligibility for an antineoplastic agent)	A companion diagnostic program used to determine if olaparib is indicated based on BRCA mutation data in patients with breast cancer. As a study used to evaluate the clinical utility of the product, the result from a foreign study assessing the equivalence between this product and the test method used for the inclusion of subjects in a phase III study of olaparibt were submitted.
Orthopedic and Plastic Surgery	May 12, 2017 Total review time: 347 days Regulatory review time: 295 days	Jul. 24, 2014 Foreign clinical study results	PRESTIGE LP Cervical Disc System (Medtronic Sofamor Danek Co., Ltd.)	Approval	Medical products 4 Total Disc Replacement Prothesis	An artificial cervical disc intended to maintain intervertebral mobility by replacing the affected cervical disc with this device after removing factors causing compression, such as herniated nucleus pulposus or osteophytes. The results from a foreign, multi-center, prospective, non-inferiority, controlled study verifying the non-inferiority to the conventional therapy (Anterior Cervical Discectomy and Fusion [ACDF]) in patients who require surgery for cervical degenerative disc disease were submitted to evaluate the efficacy and safety of this device.
Orthopedic and Plastic Surgery	Dec. 15, 2017 Total review time: 434 days Regulatory review time: 149 days	Sep. 15, 2010 Foreign clinical study results	CoolSculpting Control Unit (JMEC Co., Ltd.)	Approval	Instrument & apparatus 12 Instrument and device for cooling therapy	A device intended to partially reduce the fat layer thickness by cooling of the subcutaneous fat without surgical invasion for cosmetic reasons. This device is used with dedicated applicators and consumables such as liners and gel pads. The dedicated applicators include vacuum applicators that vacuum the skin and subcutaneous fat while cooling them, and a non-vacuum applicator. The results of foreign clinical studies were submitted to evaluate the efficacy of the product for fat thickness reduction and the risks of complications.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Aug. 3, 2017 Total review time: 486 days Regulatory review time: 206 days	Oct. 9, 2014 Foreign clinical study results; Japanese clinical study results	Lutonix Drug-Coated Balloon (DCB) Catheter (for femoropopliteal arteries) (Medicon, Inc.)	Approval	Instrument & apparatus 51 Balloon-dilating catheter for angioplasty	A balloon-dilating catheter for angioplasty used for purposes including reducing restenosis of target blood vessels in the treatment of de novo or restenotic lesions within the autogenous femoropopliteal artery (excluding those within a stent). The balloon surface of this product is coated with a drug composed of paclitaxel and excipients, polysorbate and sorbitol. The results from a foreign pivotal study conducted to evaluate the performance of the product and those from a Japanese study conducted to investigate whether the pivotal data can be extrapolated to Japanese population were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Sep. 6, 2017 Total review time: 342 days Regulatory review time: 199 days	Dec. 30, 2014 Foreign clinical study results; Japanese clinical study results	IN.PACT Admiral Drug-Coated Balloon (DCB) Catheter (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 51 Balloon-dilating catheter for angioplasty	A balloon-dilating catheter for angioplasty used for purposes including reducing restenosis of target blood vessels in de novo or non-stented restenotic lesions in the superficial femoral or popliteal arteries. The balloon surface of this product is coated with paclitaxel as drug. The results from a foreign pivotal study conducted to evaluate the performance of the product and those from a Japanese study conducted to investigate whether the pivotal data can be extrapolated to Japanese population were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Sep. 29, 2017 Total review time: 1127 days Regulatory review time: 667 days	Oct. 7, 2008 Foreign clinical study results	NeuroStar TMS Therapy System (Neuronetics,Inc.)	Approval	Instrument & apparatus 12 Repetitive transcranial magnetic stimulator	A therapy system utilizing Repetitive Transcranial Magnetic Stimulation for the treatment of adult patients with Major Depressive Disorder (MDD) who have not benefitted from conventional antidepressant medication. The results from foreign clinical studies were submitted to evaluate the efficacy and safety of this product.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Oct. 10, 2017 Total review time: 1117 days Regulatory review time: 410 days	Jun. 17, 2008 Foreign clinical study results	NeuRx Diaphragm Pacing System (DPS) (USCI Japan Ltd.)	Approval	Instrument & apparatus 12 Phrenic nerve stimulator	A diaphragm pacer that supports respiratory movement of the diaphragm by electrical stimulation to the phrenic nerve through motor points on the diaphragm in patients with respiratory failure due to diaphragmatic dysfunction of central nervous or neurogenic origin. The device is used for respiratory support in patients with ventilator-dependent spinal cord (cervical) injury or central hypoventilation syndrome. The results of a foreign clinical study for evaluation of the efficacy and safety of the device were submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 8, 2017 Total review time: 91 days Regulatory review time: 85 days	Nov. 14, 2016 No clinical study results	Lutonix Drug-Coated Balloon (DCB) Catheter (for femoropopliteal arteries) (Medicon, Inc.)	Change	Instrument & apparatus 51 Balloon-dilating catheter for angioplasty	A balloon-dilating catheter for angioplasty used for purposes including reducing restenosis of target blood vessels in the treatment of de novo or restenotic lesions within the autogenous femoropopliteal artery (excluding those within a stent). The balloon surface of this product is covered with a drug coating primarily consisting of paclitaxel. The application was submitted for an extension of expiration period from the previously approved 24 months to 36 months. (A "partial change" application submitted during the post-market performance review period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Mar. 16, 2018 Total review time: 359 days Regulatory review time: 286 days	Jun. 26, 2017 No clinical study results	MR Guided Focused Ultrasound Surgery ExAblate 4000 (InSightec Ltd.)	Change	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 application was submitted for changes including an addition of an aberration correction method in patients in whom the existing aberration correction method is inadequate, addition of a treatment mode for radiation output control based on cavitation that is detected during therapy. (A "partial change" application submitted during the post-market performance review period)
Gastroenterology, Genitourinary, and Reproductive Medicine	Oct. 31, 2017 Total review time: 154 days Regulatory review time: 102 days	Aug. 5, 2015 Foreign clinical study results	Hot AXIOS System (Boston Scientific Japan K. K.)	Approval	Instrument & apparatus 51 Prosthesis for pancreatic fistulation	A system intended to form a fistula in the wall of the gastrointestinal tract and cyst through the gastrointestinal tract with endoscopic ultrasound for treatment of the cyst with accumulation of exudate and necrotic material in a pancreatic pseudocyst or walled-off necrosis associated with acute pancreatitis including acute exacerbation of chronic pancreatitis. The system consists of a prosthesis for pancreatic fistulation and a delivery system. The results of a foreign clinical study for investigation of the efficacy and safety of the device in patients in whom endoscopic drainage is indicated were submitted.
Ophthalmology and Otorhinolaryngology	Dec. 15, 2017 Total review time: 168 days Regulatory review time: 127 days	— Japanese clinical study results	TITANBRIDGE (Nobelpharma Co., Ltd.)	Approval	Medical products 4 Fixture for thyroid cartilage	A hinge-type titanium bridge made of titanium is used to fix the thyroid cartilage with the incision gap made during type II thyroplasty to improve symptoms of adductor spasmodic dysphonia. While there has been no relatively less invasive and permanent treatment for adductor spasmodic dysphonia, the product realized the treatment based on a novel principle and its development for early commercialization was anticipated in Japan ahead of the rest of the world. Therefore, the product has been designated as an item to be reviewed under the sakigake designation fast-track review system. The results of an investigator-initiated clinical study conducted in Japan were submitted to evaluate the safety and clinical efficacy of the product. [SAKIGAKE designation, Orphan device]
Cardiopulmonary Circulation	Jun. 20, 2017 Total review time: 356 days Regulatory review time: 135 days	Aug. 12, 2016 Foreign clinical study results	EDWARDS INTUITY Elite Valve System (Edwards Lifesciences Limited)	Approval	Instrument & apparatus 7 Bovine pericardial valve	This device is a system to surgically deliver a biological valve to the aortic valve position, and has a structure added with cloth-covered frame for fixation to the company's approved product "Carpentier-Edwards Bovine Pericardial Biological Valve Magna EASE ThermaFix Process" (Approval No. 22300BZX00320000) to enable the valve to be transplanted with fewer sutures than existing valves for conventional aortic valve replacement (AVR). The results of a clinical study conducted in the United States were submitted to evaluate the efficacy and safety of the device in patients with aortic stenosis or aortic stenosis with insufficiency, both requiring AVR.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Cardiopulmonary Circulation	Jul. 28, 2017 Total review time: 357 days Regulatory review time: 144 days	Apr. 1, 2016 Foreign clinical study results	HeartLight Endoscopic Ablation System (Japan Lifeline Co., Ltd.)	Approval	Instrument & apparatus 51 Cardiovascular ablation catheter	An ablation system utilizing laser for performing percutaneous transluminal myocardial ablation to treat drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. The system consists of a balloon catheter, console, endoscope fiber, solution to expand balloon catheter and accessories. The results from a US clinical study conducted to verify the efficacy and safety of this product in patients with drug-resistant recurrent symptomatic paroxysmal atrial fibrillation and compared with the safety and efficacy of a radiofrequency ablation catheter were submitted.
Cardiopulmonary Circulation	Aug. 22, 2017 Total review time: 116 days Regulatory review time: 93 days	Sep. 28, 2012 No clinical study results	S-ICD Lead (Boston Scientific Japan K. K.)	Change	Instrument & apparatus 7 Implantable defibrillator/ pacemaker lead	A subcutaneous implantable cardioverter-defibrillator (S-ICD) lead used in patients at a high risk of sudden cardiac death caused by ventricular tachyarrhythmias. This application was submitted to add in-house model in order to optimize its design and manufactureing. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Aug. 31, 2017 Total review time: 114 days Regulatory review time: 92 days	Jun. 22, 2015 No clinical study results	CoreValve Evolut R (Medtronic Japan Co., Ltd.)	Change	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 severe symptomatic native aortic stenosis caused by the calcification of native aortic valve leaflets, and who are unable to undergo surgery. The application was submitted to add raw materials for the capsule, shaft and in-line sheath of the delivery catheter system. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Sep. 7, 2017 Total review time: 106 days Regulatory review time: 100 days	- No clinical study results	SATAKE HotBalloon Catheter (Toray Industries, Inc.)	Change	Instrument & apparatus 51 Cardiovascular ablation catheter	A balloon ablation catheter utilizing a high-frequency current to treat drug-resistant recurrent symptomatic paroxysmal atrial fibrillation. The application was submitted to modify the specifications for the performance and safety, in association with the change of the upper limit of the preset temperature for “SATAKE HotBalloon Generator” (Approval No. 22700BZX00356000), add a stirring tube different in length , and confirm the conformance to the latest specifications for leakage current. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Oct. 27, 2017 Total review time: 231 days Regulatory review time: 183 days	— No clinical study results	Jarvik 2000 Implantable Ventricular Assist Device (Century Medical, Inc.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	The device is an implantable ventricular assist device system used to improve the blood circulation until heart transplant. The device is used for severe cardiac failure patients who are qualified to receive heart transplant, shown 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. The application was submitted to correct discrepancies in descriptions of the shape, structure, and principles, raw materials, and specifications for performance and safety in the approval document. (A "partial change" application submitted during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Cardiopulmonary Circulation	Oct. 31, 2017 Total review time: 368 days Regulatory review time: 222 days	May 10, 2016 Foreign and Japanese clinical study results	MitraClip NT System (Abbot Vascular Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Percutaneous repair system for mitral valve coaptation failure	The system is intended to reduce mitral regurgitation (MR) by coapting the anterior and posterior leaflets of the mitral valve using a percutaneously inserted clip. The results of a foreign clinical study comparing the percuntaneous reduction by this system with surgery in operable patients, and Japanese and foreign clinical studies in patients with severe MR who have been determined to be at high risk for mitral valve surgery were submitted.
Cardiopulmonary Circulation	Nov. 8, 2017 Total review time: 167 days Regulatory review time: 104 days	Jul. 8, 2016 No clinical study results	Micra Transcatheter Pacing System (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 7 Implantable leadless cardiac pacemaker	An implantable electrode-integrated cardiac pacemaker intended to be percutaneously placed in the right ventricle using a catheter. Patients in whom the device is implanted may undergo limited MRI examinations only if the patients meet the set requirements. The application was submitted to add activation of the remote monitoring function and adjust the descriptions on details of approved items. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Nov. 28, 2017 Total review time: 298 days Regulatory review time: 118 days	— No clinical study results	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist device system used to improve circulation until heart transplant in patients who are considered difficult to survive without heart transplant. The application was submitted to add another type of the device with a blood pump that has been downsized and made lighter in weight and a driveline with reduced diameter, and to adjust the descriptions in the approval document. (A "partial change" application submitted during the reexamination period)
Cardiopulmonary Circulation	Dec. 7, 2017 Total review time: 252 days Regulatory review time: 100 days	— No clinical study results	Implantable Ventricular Assist System EVAHEART (Sun Medical Technology Research Corp.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	An implantable ventricular assist system is a device which is intended to support the blood circulation in end-stage heart failure patients who cannot survive without receiving heart transplantation. This application was submitted to add a self management kit of cool seal fluid which enables patients to refill the reservoir with cool seal fluid at home by themselves. (A "partial change" application submitted during the reexamination period)
Cardiopulmonary Circulation	Dec. 15, 2017 Total review time: 228 days Regulatory review time: 179 days	— No clinical study results	Jarvik 2000 Implantable Ventricular Assist Device (Century Medical, Inc.)	Change	Instrument & apparatus 7 Implantable ventricular assist device	The device is an implantable ventricular assist device system used to improve the blood circulation until heart transplant. The device is used for severe cardiac failure patients who are qualified to receive heart transplant, shown 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. The application was submitted to add double portable batteries to the methods of battery usage at night. (A "partial change" application submitted during the reexamination period)

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Cardiopulmonary Circulation	Feb. 5, 2018 Total review time: 129 days Regulatory review time: 36 days	Jun. 22, 2015 No clinical study results	CoreValve Evolut R (Medtronic Japan Co., Ltd.)	Change	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 severe symptomatic native aortic stenosis caused by the calcification of native aortic valve leaflets, and who are unable to undergo surgery. The application was submitted to add raw materials for the flush tube of the delivery catheter system. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Mar. 9, 2018 Total review time: 343 days Regulatory review time: 151 days	Jun. 22, 2015 Foreign clinical study results	CoreValve Evolut R (Medtronic Japan Co., Ltd.)	Change	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 severe symptomatic native aortic stenosis caused by the calcification of native aortic valve leaflets, and who are unable to undergo surgery. The application was submitted to add a new indication, valve implantation in an implanted surgical bioprosthetic aortic valve with failure (stenosis, insufficiency, or combined). The results of a foreign clinical study in patients with failure of an implanted surgical valve and who are unable to undergo surgery, were submitted. (A "partial change" application submitted during the post-market performance review period)
Cardiopulmonary Circulation	Mar. 22, 2018 Total review time: 146 days Regulatory review time: 76 days	May 30, 2008 No clinical study results	Impella Circulatory Assist Pump Catheter (Abiomed, Inc.)	Change	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 application was submitted to add raw materials for the motor housing part, and to change the specification of the maximum discharge performance. (A "partial change" application submitted during the post-market performance review period)

Table 6. Improved Medical Devices (with Clinical Data) Approved in FY 2017

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Robotic, ICT, and other devices (not classified as other categories)	Nov. 16, 2017 Total review time: 324 days Regulatory review time: 179 days	— Japanese clinical study results	Hemodynamic Monitor HDM-3000 (Nihon Kohden Corporation)	Approval	Instrument & apparatus 21 Multi-item patient monitor	A multi-item monitor intended to display patient's vital signs (e.g. electrocardiogram, blood pressure, and oxygen saturation) on a screen, generate alarms, and provide continuous cardiac output estimated by a non-invasive parameter, pulse wave transit time under conditions of relatively stable hemodynamics. It is a device that is based on "Bedside Monitor: BSM-3000 Series, Life Scope VS," the previous generation device (Certification No. 22300BZX00245000), and has the added feature that it can calculate and display estimated continuous cardiac output (esCCO). esCCO is calculated by continuous pulse waves obtained by electrocardiography and pulse oximetry measurement, and calibrated by blood pressure and cardiac output known or calculated based on patient data such as body weight. The results of a clinical comparative study of the approved product, "Vigileo Monitor" (Approval No. 21700BZY00328000), as the control were submitted as materials to evaluate the clinical safety and efficacy of the function of calculating esCCO.
Robotic, ICT, and other devices (not classified as other categories)	Dec. 4, 2017 Total review time: 187 days Regulatory review time: 18 days	Apr. 13, 2017 Clinical evaluation report	Philips IntelliSite Pathology Solution (Philips Japan, Ltd.)	Approval	Instrument & apparatus 21 Diagnostic auxiliary equipment for whole-slide imaging in pathology	A system for preparation and storage of whole-slide images in pathology and assisting pathological diagnosis, consisting of a scanner for image reading and an image management system. In addition, remote pathological diagnosis is feasible by connecting to an external network. A clinical assessment report summarizing the results of foreign clinical studies was submitted to confirm the equivalenece between the diagnositic result using this product and existing light microscope.
Robotic, ICT, and other devices (not classified as other categories)	Feb. 19, 2018 Total review time: 265 days Regulatory review time: 148 days	Sep. 28, 2016 Foreign clinical study results	Medtronic MiniMed 600 Series (Medtronic Japan Co., Ltd.)	Change	Instrument & apparatus 74 Portable insulin infusion pump	An insulin infusion pump for display and storage of data on glucose levels in interstitial fluids and continuous subcutaneous insulin infusion. The application was submitted to add the feature of being able to temporarily stop insulin infusion ("Suspend on low" and "Suspend before low") if the glucose level in the interstitial fluid has decreased or is anticipated to decrease below a pre-specified value. The results of a foreign clinical study showing the efficacy and safety of the features by comparing the area under the blood glucose level curve at the onset of nocturnal hypoglycemia in the presence and the absence of the features, were submitted. The results of a clinical single-arm study performed outside Japan to confirm the safety of the "Suspend before low" feature, were also submitted.
Orthopedic and Plastic Surgery	May 30, 2017 Total review time: 967 days Regulatory review time: 203 days	— Japanese clinical study results	4-U CLS Hip Prosthesis (Teijin Nakashima Medical Co., Ltd.)	Approval	Medical products 4 Total hip prosthesis	An acetabular cup and a sleeve to be used exclusively with femoral stem of hip prosthesis to replace or reconstruct the hip joint. Both components can be fixed without bone cement and are manufactured by Electron-beam additive manufacturing using Ti-15Zr-4Nb-4Ta alloy powder. The results of a Japanese clinical study were submitted to evaluate the efficacy of the new surface treatment using GRAPE Technology, which gives bone conductivity to this device.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Orthopedic and Plastic Surgery	Jun. 27, 2017 Total review time: 256 days Regulatory review time: 176 days	Sep. 17, 2010 Japanese clinical study results	V.A.C. Ulta Wound Therapy System (KCI KK)	Approval	Medical products 4 Negative pressure wound therapy system	V.A.C. Ulta Therapy System is a negative pressure wound therapy (NPWT) system with wound cleaning function to be used for patients with refractory wounds which have not responded to and/or are considered unlikely to respond to the conventional NPWT. This device can also be used for wounds with local infection using its function to instill wound-cleansing solutions automatically and periodically to optimize the wound surface environment and clean wounds. Furthermore, it can also be used as a local NPWT without using the function of periodic and automatic instillation. The results of a Japanese clinical study were submitted to evaluate the efficacy and safety in patients with refractory wounds associated with contamination or local infection.
Orthopedic and Plastic Surgery	Aug. 21, 2017 Total review time: 263 days Regulatory review time: 110 days	Jan. 23, 2009 Japanese clinical study results	BC Corkscrew FT Anchor (Arthrex Japan G.K.)	Approval	Medical products 4 Absorbable ligament fixation	An absorbable ligament fixation made of poly-L-lactic acid/β-tricalcium phosphate composite used to attach the stump of soft tissues, such as ligaments and tendons, or artificial ligaments to bones. There have been no Japanese approvals of medical devices using the raw material. Therefore the results from a Japanese open study conducted to evaluate the safety and efficacy for rotator cuff repair using this device and “BC SwiveLock Screw” for which an application was made simultaneously, were submitted as clinical study data.
Orthopedic and Plastic Surgery	Aug. 22, 2017 Total review time: 264 days Regulatory review time: 125 days	Jan. 7, 2011 Japanese clinical study results	BC SwiveLock Screw (Arthrex Japan G.K.)	Approval	Medical products 4 Absorbable ligament fixation	An absorbable ligament fixation used to attach the stump of soft tissues, such as ligaments and tendons, or artificial ligaments to bones. As a raw material for the absorbable screw, poly-L-lactic acid/β-tricalcium phosphate composite is adopted. Until now, there have been no approvals of products for which β-tricalcium phosphate is added to poly-L-lactic acid. Therefore the results from a Japanese open study conducted to evaluate the safety and efficacy for rotator cuff repair using this device and “BC Corkscrew FT Anchor” for which an application was made simultaneously, were submitted as clinical study data.
Orthopedic and Plastic Surgery	Aug. 31, 2017 Total review time: 125 days Regulatory review time: 91 days	Sep. 15, 2011 Japanese clinical study results	BC SwiveLock Tenodesis Screw (Arthrex Japan G.K.)	Approval	Medical products 4 Absorbable ligament fixation	An absorbable ligament anchor made of poly-L-lactic acid/β-tricalcium phosphate composite used to attach the stump of soft tissues, such as ligaments and tendons, or artificial ligaments to bones. There have been no Japanese approvals of medical devices using the raw material. Therefore the results from a Japanese open study conducted to evaluate the safety and efficacy for rotator cuff repair using the company’s similar devices “BC SwiveLock Screw” and “BC Corkscrew FT Anchor” which use the raw material, were submitted as clinical study data.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Orthopedic and Plastic Surgery	Oct. 16, 2017 Total review time: 108 days Regulatory review time: 79 days	Aug. 5, 2005 Clinical evaluation report	Compress System (Zimmer Biomet G.K.)	Approval	Medical products 4 Artificial material for lower limb reconstruction	An artificial material for lower limb reconstruction intended to reconstruct lower limb function with prosthesis of the defective part of the bone, in patients who had undergone extensive bone resection, due to conditions such as malignant tumor. The structure of the system provides compressive stress on the bone-implant interface, and reduces stress shielding which is caused by the placement of implant. The device does not include a stem, and is therefore available for use in patients where necessary length of the stem for bone implant cannot be ascertained. A clinical assessment report including the results of a clinical study with follow-up in the U.S., and reports from foreign clinical literature, were submitted to demonstrate similar efficacy and safety of the product to existing artificial joints for cancer patients.
Orthopedic and Plastic Surgery	Dec. 7, 2017 Total review time: 90 days Regulatory review time: 55 days	Mar. 2, 2015 Clinical evaluation report	Mpact DM Acetabular Component (Medacta Japan Co., Ltd.)	Approval	Medical products 4 Artificial hip joint, acetabular component	The acetabular component for an artificial hip intended to replace or restore the acetabulum during hip replacement (including reimplantation), consisting of a stainless steel cup and liner made of ultra-high molecular weight polyethylene. The contact surface of the cup and acetabular roof is treated with pure titanium flame spray, and the liner is treated with crosslinking. Since the device is the first double mobility system of this company with sliding surfaces both on the in- and outside of the liner, a clinical assessment report based on a foreign clinical study of the device and foreign clinical literature on the previous generation of the product, demonstrating equivalence to this device, were submitted to confirm that the product has similar efficacy and safety to a conventional artificial hip.
Orthopedic and Plastic Surgery	Dec. 26, 2017 Total review time: 364 days Regulatory review time: 75 days	Nov. 9, 2010 Clinical evaluation report	CO2RE Carbon Dioxide Laser with Fractional Mode (Syneron Candela K.K.)	Approval	Instrument & apparatus 31 Carbon dioxide laser	A carbon dioxide laser intended for ablation of soft tissue for skin resurfacing. The device has a computer-controlled scanner by which uniform ablation is feasible based on the pattern that is selected by the physician in advance. It also has a mode of fine fractional laser irradiation. Improved points include improved safety compared to the conventional laser scalpel by smaller spots ablation instead of larger area ablation on the skin, to expand its applications to various purposes including cosmetic improvement. The product is equipped with a mode that allows its use for other purposes as a laser scalpel, similarly to conventional carbon dioxide lasers. A clinical assessment report, consisting of the results of a foreign clinical study of the device and clinical papers of similar products was submitted to evaluate that the performance of the product on skin resurfacing as well as complications due to the product are acceptable for a medical device for cosmetic use.
Orthopedic and Plastic Surgery	Feb. 2, 2018 Total review time: 310 days Regulatory review time: 114 days	May 17, 2009 Foreign clinical study results	Prontosan (B. Braun Medical AG)	Approval	Medical products 4 Antibacterial wound dressing	Antibacterial gel dressing for wounds reaching the subcutaneous adipose tissue (excluding third-degree burns) to "protect wounds," "moisten wound bed," "accelerate healing," and "alleviate pain." Ingredients of the product include polyhexanide, which has been used as a disinfectant in clinical practice, in expectation of the effect of preventing bacterial infection and diffusion in the wounds. The results of a foreign clinical study were submitted to confirm the efficacy and safety of the product as a wound dressing consisting of new raw materials, and the absence of delayed healing due to the polyhexanide content.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Orthopedic and Plastic Surgery	Feb. 28, 2018 Total review time: 258 days Regulatory review time: 178 days	Aug. 24, 2012 Clinical evaluation report	Trabecular Metal Ankle System (Zimmer Biomet G.K.)	Approval	Medical products 4 Total ankle prosthesis	A hinge-type titanium bridge made of titanium is used to fix the thyroid cartilage with the incision gap made during type II thyroplasty to improve symptoms of adductor spasmodic dysphonia. While there has been no relatively less invasive and permanent treatment for adductor spasmodic dysphonia, the product realized the treatment based on a novel principle and its development for early commercialization was anticipated in Japan ahead of the rest of the world. Therefore, the product has been designated as an item to be reviewed under the sakigake designation fast-track review system. The results of an investigator-initiated clinical study conducted in Japan were submitted to evaluate the safety and clinical efficacy of the product. [SAKIGAKE designation, Orphan device]
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	May 26, 2017 Total review time: 270 days Regulatory review time: 181 days	Jul. 9, 2015 Foreign clinical study results	SCS External Stimulation Device (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Stimulation device for pain relief	A stimulation device used in Spinal Cord Stimulation which allows physicians to locate stimulus and patients to subjectively evaluate the therapeutic effect. The application was submitted to establish a new stimulation mode (A "partial change" application). The results of a foreign clinical study using a similar product, “Prodigy MRI Dual 8 Neurostimulator” designed to demonstrate the non-inferiority to the existing stimulation mode were submitted to evaluate the efficacy and safety of the new stimulation mode which is not included in the existing system.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	May 30, 2017 Total review time: 209 days Regulatory review time: 108 days	Oct. 18, 2016 Foreign clinical study results	Proclaim Elite MRI Dual 8 Neurostimulator (St. Jude Medical Japan Co., Ltd.)	Change	Instrument & apparatus 12 Implantable stimulator for pain relief	An implantable stimulator for pain relief used in patients with chronic refractory pain in the trunk and extremities who are not sufficiently responsive to pain relief therapy with drugs or nerve block. The patients implanted with the device can conditionally undergo an MRI scan. The application was submitted to add a stimulation mode, namely “Surgical mode,” which is provided as one of safety measures when the patient has to have whole-body MRI with electrosurgical units (A "partial change" application). The results of a foreign clinical study using a similar product, “Prodigy MRI Dual 8 Neurostimulator” designed to demonstrate the non-inferiority to the existing stimulation mode were submitted to evaluate the efficacy and safety of the new stimulation mode which is not included in the existing system.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Jul. 27, 2017 Total review time: 231 days Regulatory review time: 161 days	None Foreign clinical study results	Vascular Stent-1 (Covidien Japan, Inc.)	Approval	Instrument & apparatus 7 Stent for iliac artery	An iliac arterial stent system available in nominal stent sizes of 6, 7 and 8 mm diameters for maintaining vascular patency of atherosclerotic lesions in the iliac arteries. The results from foreign clinical studies were submitted to evaluate the efficacy and safety of this device.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Jul. 27, 2017 Total review time: 231 days Regulatory review time: 188 days	Jan. 21, 2015 Foreign clinical study results	Vascular Stent-2 (Covidien Japan, Inc.)	Approval	Instrument & apparatus 7 Stent for iliac artery	An iliac arterial stent system available in nominal stent sizes of 9, 10 and 12 mm diameters for maintaining vascular patency of atherosclerotic lesions in the iliac arteries. The results from foreign clinical studies were submitted to evaluate the efficacy and safety of this device.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Sep. 15, 2017 Total review time: 267 days Regulatory review time: 203 days	Jan. 27, 2017 Foreign clinical study results	GORE VIABAHN VBX Balloon Expandable Endoprosthesis (W. L. GORE & Associates, Co., Ltd.)	Approval	Instrument & apparatus 7 Stent graft with heparin for central circulatory system	A stent graft system which consists of a balloon expandable stent graft made of stainless steel and delivery catheter used to treat de novo or restenotic lesions found in iliac arteries. The inside and outside of the stent are fused with a PTFE film which has a heparin bonding layer. The results from a foreign clinical study using this product were submitted as clinical evaluation data.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Nov. 10, 2017 Total review time: 477 days Regulatory review time: 233 days	Sep. 15, 2015 Global clinical trial	COOK Zenith Alpha Thoracic Endovascular Graft (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft used for endovascular treatment of thoracic aortic aneurysm, consisting of the stent graft and the delivery system. Based on the structure of the company's approved product, "COOK Zenith TX2 TAA Endovascular Graft" (Approval No. 22300BZX00147000), the raw material of the stent was changed from stainless steel to nitinol, the flexibility of the stent graft was increased by thinning the graft material, and the external diameter of the delivery catheter was reduced. The results of a global clinical trial were submitted to evaluate the efficacy and safety of the product for thoracic aortic aneurysm.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Dec. 8, 2017 Total review time: 161 days Regulatory review time: 71 days	— Clinical evaluation report	TMP Occlusion (Tokai Medical Products, Inc.)	Approval	Instrument & apparatus 51 Emboli-capturing catheter in the central circulatory system	An emboli-capturing catheter for carotid artery stenting and acute cerebral revascularization and so forth prevent distal embolization of cerebrovascular vessels, and the catheter has a balloon at its tip. A clinical assessment report prepared based on clinical literature reports of the device and similar products, was submitted to indicate the equivalence of the device to approved products.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 6, 2018 Total review time: 224 days Regulatory review time: 52 days	May 6, 2011 Clinical evaluation report	AFX Endovascular AAA System (Japan Lifeline Co., Ltd.)	Change	Instrument & apparatus 7 Aortic stent graft	An aortic stent graft used for endovascular treatment of infrarenal abdominal aortic aneurysms. The application was submitted mainly to add a cuff extension with a large diameter and another type of delivery catheter. To complement the performance evaluation of the cuff extension of the additional size, a clinical assessment report summarizing the clinical results of the cuff extension of the applicable size was submitted.
Brain and Circulatory Medicine, Respiratory Medicine, Neurology, and Psychiatry	Feb. 9, 2018 Total review time: 266 days Regulatory review time: 60 days	Oct. 1, 2001 Clinical evaluation report	Bactiseal Shunt Catheter (Johnson & Johnson K.K.)	Approval	Instrument & apparatus 51 Cerebrospinal catheter	A cerebrospinal catheter intended to be placed in the body as a component of a shunt system for treatment of hydrocephalus by leading excessive cerebrospinal fluid from the central nervous system to other absorptive sites in the body using a cerebrospinal fluid shunt. The device is impregnated with rifampicin and clindamycin hydrochloride to inhibit colonization of bacteria that stick to the catheter surface. It was selected as an item for early introduction at the "Japanese Ministry of Health, Labour and Welfare's Panel of experts meeting on early introduction of highly needed medical devices" on August 9, 2013. A clinical evaluation report summarizing such materials as foreign literature was submitted for safety evaluation.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Gastroenterology, Genitourinary, and Reproductive Medicine	Nov. 24, 2017 Total review time: 269 days Regulatory review time: 117 days	— Japanese clinical study results	Toray Filtryzer BK (Toray Industries, Inc.)	Approval	Instrument & apparatus 7 Hollow-fiber dialyzer	A hollow-fiber dialyzer 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 improved points are the addition of some materials to the raw materials of hollow fiber used for the approved product, "Filtryzer BK," (Approval No. 15900BZZ01740000) and myoglobin clearance as a specification for performance. Since equivalence of the raw materials of dialysis membranes for the device and those for the approved product was not confirmed, the results of a Japanese clinical study for safety evaluation were submitted in accordance with PFSB Notification No. 0301-5 dated on March 1, 2013.
Gastroenterology, Genitourinary, and Reproductive Medicine	Nov. 24, 2017 Total review time: 269 days Regulatory review time: 117 days	— Japanese clinical study results	Toray Filtryzer BG (Toray Industries, Inc.)	Approval	Instrument & apparatus 7 Hollow-fiber dialyzer	A hollow-fiber dialyzer 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 improved points are the addition of some materials to the raw materials of hollow fiber used for the approved product, "Filtryzer BG," (Approval No. 20700BZZ00293000) and myoglobin clearance as a specification for performance. Since equivalence of the raw materials of dialysis membranes for the device and those for the approved product was not confirmed, the results of a Japanese clinical study for safety evaluation were submitted in accordance with PFSB Notification No. 0301-5 dated on March 1, 2013.
Gastroenterology, Genitourinary, and Reproductive Medicine	Nov. 29, 2017 Total review time: 184 days Regulatory review time: 138 days	Mar. 20, 2015 Clinical evaluation report	AirSeal Intelligent Flow System (Conmed Japan KK)	Approval	Instrument & apparatus 25 Air and water supply device for endoscopy	An air and water supply device for endoscopy intended to secure adequate space and visualization of the surgical field required for examination and surgery by insufflating CO_2 gas into the peritoneal cavity, or retroperitoneal space and rectum to extend the space in the applicable area while eliminating smoke during endoscopy and surgery or transanal rectal surgery. The insufflation of CO_2 gas into the retroperitoneal space or rectum to aid surgery by securing the visual field has been added to the intended use or effects, and thereby makes the product available for transanal total mesorectal excision (taTME) of all layers of rectal cancer or transanal minimally invasive surgery (TAMIS) for some procedures such as mucosal stripping from the gut lumen using a rigid endoscope. A clinical assessment report summarizing the foreign literature was submitted to evaluate the efficacy and safety of insufflation into the retroperitoneal space and rectum at the implementation of taTME or TAMIS.
Dentistry and Oral Medicine	Jul. 6, 2017 Total review time: 267 days Regulatory review time: 154 days	Sep. 13, 2011 Foreign clinical study results	Episil Oral Liquid (Solasia Pharma K.K.)	Approval	Medical products 4 Wound dressing and protecting hydrogel material for topical management	The product is used for management and relief of oral pain by covering and protecting lesions/stomatitis associated with chemotherapy and/or radiotherapy. The bioadhesive oral liquid consists of lipid components such as glycerol dioleate and soy phosphatidylcholine wituout "active medicinal (pharmacuetical) components. The liquid forms a protective bioadhesive layer by the uptake of aqueous fluid i.e saliva. The results from a foreign clinical study were submitted to evaluate the efficacy and safety of the product.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Dentistry and Oral Medicine	Dec. 14, 2017 Total review time: 212 days Regulatory review time: 125 days	— Japanese clinical study results	GC Cytrans Granules (GC Corporation)	Approval	Medical products 4 Resorbable dental bone reconstruction implant material	The device is a resorbable dental implant material for bone reconstruction consisting of granular carbonate apatite used for compensation of a bone defect of the maxilla, mandible, and alveolar bone. The results of a Japanese clinical study of the efficacy and safety of the product when concurrently used with a dental implant fixture were submitted.
Ophthalmology and Otorhinolaryngology	Jun. 28, 2017 Total review time: 184 days Regulatory review time: 102 days	- Japanese clinical study results	2week Menicon PremiO (Menicon Co., Ltd.)	Change	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	Reusable colored soft contact lenses for correcting visual acuity. This silicone lens is to be replaced periodically in 2-week intervals. The application was submitted to add a progressive toric lens, which is a combination of the existing progressive design and toric design (A "partial change" application). Since the progressive toric lens has a new design, a Japanese clinical study was conducted to evaluate its efficacy and safety.
Ophthalmology and Otorhinolaryngology	Jul. 24, 2017 Total review time: 270 days Regulatory review time: 165 days	Aug. 14, 2015 Foreign clinical study results	Naída CI (Nihon Kohden Corporation)	Approval	Medical products 4 Cochlear implant system	A sound processor that constitutes the cochlear implant system used in patients with bilateral severe hearing loss who have not responded sufficiently to wearing hearing aids. The basic performance of the product is equivalent to that of the approved Auria harmony sound processor for “HiRes Auria Sound Processor” (Approval No. 22000BZY00009000). A power saving method based on the approved method of audio signal processing was added to this device. The results from a clinical study conducted in the United States were submitted to evaluate the efficacy and safety of this device.
Ophthalmology and Otorhinolaryngology	Nov. 2, 2017 Total review time: 133 days Regulatory review time: 100 days	— Foreign clinical study results	Tecnis Symfony Toric VB (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 of an aphakic eye with corneal astigmatism. The shape and structure of the device are similarly designed as "Tecnis Symfony Toric", which has a diffractive multifocal mechanism and toric structure (Approval No. 22900BZX00359000), and ultraviolet and violet light-absorbing agents were added to the raw materials.
Ophthalmology and Otorhinolaryngology	Nov. 2, 2017 Total review time: 258 days Regulatory review time: 209 days	Jul. 15, 2016 Foreign clinical study results	Tecnis Symfony Toric (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 of an aphakic eye with corneal astigmatism. The posterior optical zone has the same diffractive multifocal mechanism as the company's approved product, "Tecnis Symfony" (Approval No. 22900BZX00006000). The anterior optical zone has an aspherical surface similar to the company's approved product, "Tecnis Toric One-piece" (Approval No. 22500BZX00363000). The improved point is that it has combined optical functions of the company's approved products.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Ophthalmology and Otorhinolaryngology	Nov. 24, 2017 Total review time: 269 days Regulatory review time: 107 days	— Japanese clinical study results	Noninvasive Transtympanic Pressure Device EFET01 (Daiichi Medical Co., Ltd.)	Approval	Instrument & apparatus 12 Transtympanic pressure device	A device intended to inhibit vertiginous attacks due to Meniere's disease and delayed endolymphatic hydrops by non-invasively adding pressure to the middle ear cavity through the external auditory canal to facilitate excretion of endolymphatic fluid that has accumulated in the inner ear, consisting of an air pressure generating device, a tube with ear plugs to add pressure and a power supply. The improved point is increased reproducibility of the waveform by detailed specification of the parameters of the air pressure wave to efficiently add pressure to the middle ear space, compared to certified tympanum massagers.
Ophthalmology and Otorhinolaryngology	Nov. 27, 2017 Total review time: 262 days Regulatory review time: 199 days	— Japanese clinical study results	Clareon Aspherical Hydrophobic Acryl Intraocular Lens (Alcon Japan Ltd.)	Approval	Instrument & apparatus 72 Posterior chamber lens	A monofocal posterior chamber lens to be inserted as a substitute for a crystalline lens in the posterior chamber to correct visual acuity of an aphakic eye. The shape of the product is a one-piece type, consisting of the same raw materials in the optic and haptic. The product is a cross-linked acrylic copolymer containing the same ultraviolet and blue light-absorbing agents as the company's approved product, "Alcon AcrySof Natural Single Piece" (21800BZY10066000). The improved point is that flexibility and maneuverability are increased by changing the composition of the major component monomers.
Ophthalmology and Otorhinolaryngology	Dec. 7, 2017 Total review time: 261 days Regulatory review time: 141 days	— Clinical evaluation report	Menicon Rose K-T (Menicon Co., Ltd.)	Approval	Instrument & apparatus 72 Reusable colored contact lenses for correcting visual acuity	An oxygen-transmissible daily wear hard contact lens intended to correct visual acuity in patients with keratoconus and associated myopia and hyperopia. The improved points are that the lens blanks of products made of the same raw materials as the company's approved product, "Menicon Tinu," (21800BZZ10125000) are formed to enable patients with keratoconus to wear the lenses, and that indications are made clear in the intended use.
Ophthalmology and Otorhinolaryngology	Feb. 27, 2018 Total review time: 263 days Regulatory review time: 212 days	— Japanese clinical study results	Aktis Toric (Nidek Co., Ltd.)	Approval	Instrument & apparatus 72 Posterior chamber lens	The product is a single-piece-type monofocal posterior chamber lens intended to be inserted into the aphakic eye of patients with corneal astigmatism after cataract surgery. The shape other than the optic is similar to the company's approved product, "Nex-Acri AA 1P" (Approval No. 22100BZX00945000). The improved points are the change of raw material compositions and the addition of cylindrical power for the correction of corneal astigmatism. The results of a Japanese clinical study were submitted to evaluate the clinical efficacy, including an astigmatism correction function, and safety of the device.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Cardiopulmonary Circulation	Jun. 9, 2017 Total review time: 221 days Regulatory review time: 107 days	Apr. 28, 2017 Foreign clinical study results	Resolute Onyx Coronary Stent System (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system consisting of a zotarolimus-eluting stent used for treating patients with symptomatic ischemic cardiac disease who have a new coronary artery lesion (a lesion length of 35 mm or less) with a reference vessel diameter of 2.25-4.2 mm and a delivery catheter to place the stent at the site of stenosis. The deliverability was improved by reducing the thickness of the stent strut to lower crossing profile as compared to that of the previous product "Resolute Integrity Coronary Stent System (Approval No. 22400BZX00176000)". To maintain radiopacity, platinum-iridium alloy was used for inner core of the strut. The results of clinical studies conducted in the United States were submitted to evaluate the efficacy and safety in patients with symptomatic ischemic cardiac disease.
Cardiopulmonary Circulation	Aug. 1, 2017 Total review time: 412 days Regulatory review time: 277 days	- Foreign clinical study results	BioFreedom Drug-Coated Stent (Biosensors Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system consisting of a biolimus-coated stent and a delivery catheter for the treatment of patients with symptomatic ischemic heart disease, with de novo coronary lesions of a lesion length of 33 mm or less, and with a reference vessel diameter of 2.25-4.0 mm in size. Without the use of polymer, biolimus A9 is directly coated to the stainless steel which has a selectively micro-structured surface. The drug is absorbed in about 1 month, after which becomes a bare metal stent. This stent was developed to allow discontinuation of dual antiplatelet therapy in one month, similarly to bare metal stents. The results from Japanese and foreign clinical studies were submitted to evaluate the efficacy and safety of this device.
Cardiopulmonary Circulation	Aug. 14, 2017 Total review time: 255 days Regulatory review time: 98 days	Jul. 1, 2014 Nov. 12, 2014 Clinical evaluation report	COOK Evolution RL Controlled-Rotation Dilator Sheath Set (Cook Japan Inc.)	Approval	Instrument & apparatus 7 Pacemaker/ defibrillator lead removal kit	A pacemaker/defibrillator lead removal kit used for transvenous lead removal of implantable pacemaker leads, implantable defibrillator leads, etc. It was developed based on the approved product "COOK Lead Extraction System" (Approval No. 22700BZX00054000). Changes were made to unidirectional or bidirectional rotation of the inner sheath by handle operation and to a stainless-steel tip on the end of the inner sheath. A clinical evaluation report summarizing foreign literatures reporting this device or the previous generation device was submitted to evaluate the efficacy and safety of this device.
Cardiopulmonary Circulation	Aug. 31, 2017 Total review time: 262 days Regulatory review time: 72 days	Jul. 31, 2017 Foreign clinical study results	Avalus Bioprosthesis (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Bovine pericardial valve	A bovine pericardial valve to be used to substitute for the function of a malfunctioning native or prosthetic aortic valve. The biological valve has a frame made of polyetheretherketone and a valve leaflet treated with alpha-amino oleic acid for anticalcification. It was developed aiming at the safety of MRI and reductions of permanent deformations and corrosion risk when assuming future valve in valve procedures are performed, by using non-metallic components. The results of clinical studies conducted in EU, US, and Canada were submitted to evaluate the efficacy and safety of this product in patients with aortic valve stenosis requiring aortic valve replacement.

Review Category	Approval Date	Approval Date in US Clinical Study Results: Japanese/Foreign	Brand Name (Applicant Company)	New Approval/ Partial Change	Classification Term Name	Notes
Cardiopulmonary Circulation	Nov. 2, 2017 Total review time: 247 days Regulatory review time: 135 days	Oct. 25, 2016 Foreign clinical study results	Claria MRI CRT-D Series (Medtronic Japan Co., Ltd.)	Approval	Instrument & apparatus 7 Implantable biventricular pacing pulse generator with defibrillator function	The device is an implantable biventricular pacing pulse generator with a defibrillator function. Patients implanted with the device can conditionally undergo an MRI scan only when the patient's condition is suitable for the requirements for imaging. It is a higher-end model of the company's approved product, "Amplia MRI CRT-D Series" (Approval No. 22800BZX00219000). The major differing point is an additional feature whereby the device evaluates the efficacy of pacing with CRT during atrial fibrillation (AF), and adjusts the pacing rate based on the evaluation results (EffectivCRT during AF feature). The results of a foreign clinical study were submitted to evaluate the efficacy and safety of the EffectivCRT during AF feature.
Cardiopulmonary Circulation	Jan. 19, 2018 Total review time: 374 days Regulatory review time: 157 days	— Global clinical trial	Orsiro Sirolimus Eluting Coronary Stent System (Biotronik Japan, Inc.)	Approval	Instrument & apparatus 7 Coronary stent	A stent system consisting of a sirolimus-eluting stent used for treating patients with symptomatic ischemic cardiac disease who have a new coronary artery lesion (a lesion length of 26 mm or less) with a reference vessel diameter of 2.25 mm to 4.0 mm and a delivery catheter to place the stent at the site of stenosis. The stent platform made of cobalt chromium is coated with hydrogenated amorphous silicon carbide that inhibits metal ion release. The drug coating layer is composed of sirolimus and bioabsorbable PLLA. The results of Japanese and foreign clinical studies were submitted to evaluate the efficacy and safety of this device.
Cardiopulmonary Circulation	Jan. 24, 2018 Total review time: 239 days Regulatory review time: 140 days	Dec. 21, 2017 Foreign clinical study results	BSC OI Ablation Catheter (Boston Scientific Japan K. K.)	Change	Instrument & apparatus 51 Cardiovascular ablation catheter	A catheter designed to be inserted percutaneously into the heart through a blood vessel to deliver radiofrequency energy to the electrophysiologically identified target site of arrhythmia to treat drug-refractory recurrent symptomatic paroxysmal atrial fibrillation as well as sustained or recurrent type I atrial flutter. The device is intended for the treatment of arrhythmia by an increase in tissue temperature due to the delivery of radiofrequency energy, leading to ablation in the myocardial tissue. The application was submitted to expand the indication to drug-refractory recurrent symptomatic paroxysmal atrial fibrillation. The results of a foreign clinical study that evaluated the efficacy and safety of the device on drug-refractory recurrent symptomatic paroxysmal atrial fibrillation were submitted.

Table 7. 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 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
FY 2017	62,092	428,248	6,618	1,018	497,976	1,206

** 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 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
FY 2017	16,719	34,168	441	51,328	2,701

(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
FY 2017	110	0	0	110	0

** The number of reports after the Pharmaceutical and Medical Devices Act came into effect on November 25, 2014.*

Table 8. Revisions to PRECAUTIONS for Drugs, etc. and Other Information as Directed by MHLW during FY 2017

○ Revisions to PRECAUTIONS for drugs, etc. and other information implemented by MHLW based on PMDA reports in FY 2017

	Drugs	Medical devices
Directions concerning revisions to PRECAUTIONS in product package insert[*1]	219[*1]	0
Information published as Pharmaceuticals and Medical Devices Safety Information	17	0

*[*1] Including a report for 1 quasi drug.*

○ Revisions to PRECAUTIONS for Drugs, as Directed by MHLW during FY 2017

Date	Drug name
Apr. 20, 2017	01. Denosumab (genetical recombination) (drug product with the indication for osteoporosis) 02. Pembrolizumab (genetical recombination) 03. Caspofungin acetate
May 30, 2017	01. Treprostinil 02. Dulaglutide (genetical recombination) 03. Bosutinib hydrate 04. Pneumococcal vaccine
Jul. 4, 2017	01. Tramadol hydrochloride Tramadol hydrochloride 02. Tramadol hydrochloride 03. Tramadol hydrochloride/Acetaminophen 04. Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Chlorpheniramine maleate Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Chlorpheniramine maleate Dihydrocodeine phosphate/dl-methylephedrine hydrochloride/Chlorpheniramine maleate 05. Dihydrocodeine phosphate/Diprophylline/dl-methylephedrine hydrochloride/Diphenhydramine salicylate/Acetaminophen/Bromovalerylurea 06. Codeine phosphate hydrate/Cherry bark extract 07. Dihydrocodeine phosphate/Platycodon fluidextract/Glycyrrhiza extract/Plantago herb extract/Peony root extract 08. Codeine phosphate hydrate Codeine phosphate hydrate Codeine phosphate hydrate Codeine phosphate hydrate Codeine phosphate hydrate 09. Dihydrocodeine phosphate Dihydrocodeine phosphate Dihydrocodeine phosphate 10. Dihydrocodeine phosphate/Ephedrine hydrochloride/Ammonium chloride 11. Products containing codeine phosphate hydrate and products containing dihydrocodeine phosphate (OTC drugs) (preparations with the administration for patients younger than 2 years old) 12. Products containing codeine phosphate hydrate and products containing dihydrocodeine phosphate (OTC drugs) (preparations with the administration for patients younger than 12 years old and without the administration for patients younger than 2 years old) 13. Products containing codeine phosphate hydrate and products containing dihydrocodeine phosphate (OTC drugs) (preparations without the administration for patients younger than 12 years old)

Date	Drug name
	14. Loxoprofen sodium hydrate (cataplasms/gel patches) Loxoprofen sodium hydrate (tape) Loxoprofen sodium hydrate (gel) Loxoprofen sodium hydrate (spray) 15. Hydroxocobalamin 16. Nivolumab (genetical recombination) 17. Fluconazole Fluconazole Fluconazole Fluconazole Fluconazole 18. Fosfluconazole 19. Patch test products containing gold (I) sodium thiosulfate 20. Loxoprofen sodium hydrate (dermatologic preparation) (BTC drugs)
Aug. 3, 2017	01. Riociguat 02. Warfarin potassium Warfarin potassium Warfarin potassium 03. Azithromycin hydrate Azithromycin hydrate Azithromycin hydrate Azithromycin hydrate Azithromycin hydrate 04. Azithromycin hydrate 05. Laninamivir octanoate hydrate
Sep. 12, 2017	01. Dabigatran etexilate methanesulfonate 02. Palivizumab (genetical recombination) 03. Interferon beta
Oct. 17, 2017	01. Levetiracetam Levetiracetam Levetiracetam 02. Chlorhexidine hydrochloride/Diphenhydramine salicylate/Hydrocortisone acetate/Benzalkonium chloride concentrated solution 50 03. Chlorhexidine gluconate

Date	Drug name
	Chlorhexidine gluconate Chlorhexidine gluconate Chlorhexidine gluconate 04. Products containing chlorhexidine gluconate or products containing chlorhexidine hydrochloride (OTC drugs) 05. Linagliptin 06. Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate 07. Lansoprazole/Amoxicillin hydrate/Clarithromycin 08. Lansoprazole/Amoxicillin hydrate/Metronidazole 09. Rabeprazole sodium/Amoxicillin hydrate/Clarithromycin 10. Rabeprazole sodium/Amoxicillin hydrate/Metronidazole 11. Vonoprazan fumarate/Amoxicillin hydrate/Clarithromycin 12. Vonoprazan fumarate/Amoxicillin hydrate/Metronidazole 13. Potassium clavulanate/Amoxicillin hydrate Potassium clavulanate/Amoxicillin hydrate 14. Moxifloxacin hydrochloride (oral)
Nov. 28, 2017	01. Clozapine 02. Gadoxetate sodium 03. Gadoteridol 04. Meglumine gadoterate 05. Gadobutrol 06. Gadodiamide hydrate Gadodiamide hydrate 07. Meglumine gadopentetate Meglumine gadopentetate
Jan. 11, 2018	01. Aripiprazole Aripiprazole Aripiprazole Aripiprazole Aripiprazole Aripiprazole 02. Aripiprazole hydrate Aripiprazole hydrate 03. Teriparatide (genetical recombination) 04. Teriparatide acetate Teriparatide acetate 05. Edoxaban tosilate hydrate Edoxaban tosilate hydrate 06. Ipilimumab (genetical recombination) 07. Lenvatinib mesilate
Feb. 13, 2018	01. Gardenia fruit Gardenia fruit Gardenia fruit Gardenia fruit 02. Inchinkoto extract Inchinkoto extract Inchinkoto extract 03. Orengedokuto extract Orengedokuto extract Orengedokuto extract Orengedokuto extract

Date	Drug name
	04. Kamishoyosan extract Kamishoyosan extract Kamishoyosan extract 05. Shiniseihaito extract Shiniseihaito extract 06. Unseiin extract Unseiin extract 07. Kamikihito extract Kamikihito extract Kamikihito extract 08. Keigairengyoto extract 09. Gorinsan extract Gorinsan extract 10. Saikoseikanto extract Saikoseikanto extract 11. Shishihakuhito extract 12. Seijobofuto extract 13. Seihaito extract 14. Bofutsushosan extract Bofutsushosan extract Bofutsushosan extract 15. Ryutanshakanto extract Ryutanshakanto extract Ryutanshakanto extract 16. Efavirenz 17. Iohexol (for urinary tract, blood vessel) Iohexol (for urinary tract, blood vessel) Iohexol (for urinary tract, blood vessel, CT) Iohexol (for urinary tract, blood vessel, CT) 18. Iomeprol Iomeprol 19. Products containing gardenia fruit (OTC drugs)
Mar. 20, 2018	01. Tolvaptan 02. Selexipag 03. Clopidogrel sulfate 04. Clopidogrel sulfate/Aspirin 05. Anagliptin 06. Anagliptin 07. Linagliptin 08. Teneligliptin hydrobromide hydrate 09. Teneligliptin hydrobromide hydrate/Canagliflozin hydrate combination tablets 10. Sterile talc
Mar. 27, 2018	01. Azithromycin hydrate (tablets 250 mg/500 mg) Azithromycin hydrate (dry syrup) Azithromycin hydrate (for pediatric use) Azithromycin hydrate (for pediatric use) 02. Aztreonam 03. Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate Amoxicillin hydrate 04. Amoxicillin hydrate/Potassium clavulanate Amoxicillin hydrate/Potassium clavulanate 05. Ampicillin hydrate Ampicillin hydrate

Date	Drug name
	06. Ampicillin sodium 07. Ampicillin sodium, Cloxacillin sodium hydrate (100 mg preparation) 08. Imipenem hydrate, Cilastatin sodium Imipenem hydrate, Cilastatin sodium 09. Erythromycin 10. Erythromycin ethylsuccinate Erythromycin ethylsuccinate 11. Erythromycin stearate 12. Ofloxacin (tablets) 13. Kanamycin monosulfate Kanamycin monosulfate 14. Kanamycin sulfate 15. Clarithromycin Clarithromycin Clarithromycin 16. Clindamycin hydrochloride 17. Clindamycin phosphate (injection) Clindamycin phosphate (injection) 18. Chloramphenicol (topical) Chloramphenicol (oral) 19. Chloramphenicol sodium succinate 20. Colistin sodium methanesulfonate (oral) Colistin sodium methanesulfonate (oral) 21. Sitafloxacin hydrate Sitafloxacin hydrate 22. Ciprofloxacin hydrochloride hydrate 23. Dibekacin sulfate (injection) Dibekacin sulfate (injection) 24. Josamycin 25. Josamycin propionate Josamycin propionate 26. Spiramycin acetate 27. Sultamicillin tosilate hydrate Sultamicillin tosilate hydrate 28. Sulfamethoxazole, Trimethoprim (oral) 29. Cefaclor Cefaclor Cefaclor 30. Cefazolin sodium hydrate Cefazolin sodium hydrate Cefazolin sodium hydrate Cefazolin sodium hydrate 31. Cefalexin Cefalexin Cefalexin Cefalexin Cefalexin Cefalexin Cefalexin 32. Cefalotin sodium 33. Cefixime hydrate 34. Cefepime dihydrochloride hydrate Cefepime dihydrochloride hydrate 35. Cefozopran hydrochloride 36. Cefotaxime sodium 37. Cefotiam hydrochloride Cefotiam hydrochloride Cefotiam hydrochloride

Date	Drug name
	38. Cefotiam hexetil hydrochloride 39. Cefoperazone sodium 40. Cefoperazone sodium, Sulbactam sodium Cefoperazone sodium, Sulbactam sodium 41. Cefcapene pivoxil hydrochloride hydrate Cefcapene pivoxil hydrochloride hydrate Cefcapene pivoxil hydrochloride hydrate 42. Cefditoren pivoxil Cefditoren pivoxil 43. Cefdinir Cefdinir Cefdinir 44. Ceftazidime hydrate Ceftazidime hydrate Ceftazidime hydrate 45. Ceftizoxime sodium 46. Ceftibuten hydrate 47. Cefteram pivoxil Cefteram pivoxil Cefteram pivoxil Cefteram pivoxil 48. Ceftriaxone sodium hydrate Ceftriaxone sodium hydrate Ceftriaxone sodium hydrate Ceftriaxone sodium hydrate 49. Cefpirome sulfate 50. Cefpodoxime proxetil Cefpodoxime proxetil 51. Cefminox sodium hydrate 52. Cefmetazole sodium Cefmetazole sodium 53. Cefmenoxime hydrochloride (injection) Cefmenoxime hydrochloride (injection) Cefmenoxime hydrochloride (for ear and nose) 54. Cefroxadine hydrate 55. Cefuroxime axetil 56. Tetracycline hydrochloride (oral) Tetracycline hydrochloride (oral) 57. Tebipenem pivoxil 58. Demethylchlortetracycline hydrochloride 59. Doxycycline hydrochloride hydrate 60. Tosufloxacin tosilate hydrate (tablets) Tosufloxacin tosilate hydrate (tablets) 61. Tobramycin (injection) 62. Doripenem hydrate 63. Nalidixic acid Nalidixic acid 64. Norfloxacin (tablets) Norfloxacin (tablets) 65. Bacampicillin hydrochloride 66. Panipenem/Betamipron 67. Vancomycin hydrochloride (powder) 68. Pipemidic acid hydrate 69. Piperacillin sodium Piperacillin sodium Piperacillin sodium 70. Faropenem sodium hydrate Faropenem sodium hydrate

Date	Drug name
	71. Prulifloxacin 72. Flomoxef sodium 73. Benzylpenicillin potassium 74. Benzylpenicillin benzathine hydrate 75. Fosfomycin calcium hydrate Fosfomycin calcium hydrate Fosfomycin calcium hydrate 76. Fosfomycin sodium (injection) Fosfomycin sodium (injection) 77. Polymyxin B sulfate (powder) 78. Minocycline hydrochloride (oral) Minocycline hydrochloride (oral) Minocycline hydrochloride (oral) Minocycline hydrochloride (oral) Minocycline hydrochloride (injection) 79. Garenoxacin mesilate hydrate 80. Metronidazole (oral) Metronidazole (injection) 81. Meropenem hydrate 82. Moxifloxacin hydrochloride (tablets) 83. Latamoxef sodium 84. Lincomycin hydrochloride hydrate Lincomycin hydrochloride hydrate Lincomycin hydrochloride hydrate Lincomycin hydrochloride hydrate 85. Levofloxacin hydrate (oral) Levofloxacin hydrate (oral) Levofloxacin hydrate (oral) Levofloxacin hydrate (oral) Levofloxacin hydrate (oral) 86. Roxithromycin 87. Lomefloxacin hydrochloride (oral)
Mar. 27, 2018	01. Propofol Propofol Propofol Propofol 02. Adrenaline (preparations indicated for emergency supplemental treatment of anaphylactic reactions caused by allergens in vespid venom, food, drugs and other allergens) 03. Adrenaline (preparations indicated for emergency supplemental treatment of acute hypotension or shock associated with various diseases or conditions) Adrenaline (preparations indicated for emergency supplemental treatment of acute hypotension or shock associated with various diseases or conditions) 04. Asenapine maleate 05. Aripiprazole Aripiprazole Aripiprazole Aripiprazole Aripiprazole Aripiprazole 06. Olanzapine Olanzapine Olanzapine Olanzapine 07. Quetiapine fumarate Quetiapine fumarate Quetiapine fumarate

Date	Drug name
	08. Clocapramine hydrochloride hydrate Clocapramine hydrochloride hydrate 09. Chlorpromazine hydrochloride Chlorpromazine hydrochloride Chlorpromazine hydrochloride 10. Chlorpromazine hydrochloride/Promethazine hydrochloride/Phenobarbital 11. Chlorpromazine phenolphthalinate 12. Spiperone 13. Zotepine 14. Timiperone Timiperone 15. Haloperidol Haloperidol Haloperidol Haloperidol 16. Paliperidone 17. Pipamperone hydrochloride 18. Fluphenazine decanoate 19. Fluphenazine maleate 20. Brexpiprazole 21. Prochlorperazine maleate 22. Prochlorperazine mesilate 23. Propericiazine 24. Bromperidol 25. Perphenazine 26. Perphenazine hydrochloride 27. Perphenazine fendizoate 28. Perphenazine maleate 29. Perospirone hydrochloride hydrate 30. Mosapramine hydrochloride 31. Risperidone (oral) Risperidone (oral) Risperidone (oral) Risperidone (oral) Risperidone (oral) 32. Levomepromazine hydrochloride 33. Levomepromazine maleate Levomepromazine maleate Levomepromazine maleate Levomepromazine maleate 34. Aripiprazole hydrate Aripiprazole hydrate 35. Paliperidone palmitate 36. Haloperidol decanoate 37. Risperidone (injection) 38. Clozapine 39. Blonanserin

**Note: More detailed information is available on the PMDA website.*

Table 9. Revisions to PRECAUTIONS for Medical Devices and Other Information, as Directed by MHLW Based on Reports from PMDA during FY 2017

Date	Title
Not applicable	Not applicable

**Note: More detailed information is available on the PMDA website.*

Table 10. FY 2017 Pharmaceuticals and Medical Devices Safety Information (No.342-351)

Date	No.	Table of Contents
April 18, 2017	342	1. Precautions for Dependence Associated with Hypnotics-Sedatives, Anxiolytics, and Antiepileptics 2. Optimal Clinical Use Guidelines 3. Important Safety Information (1) Aluminum potassium sulfate hydrate/Tannic acid 4. Revision of Precautions (No. 283) Lamotrigine (and 37 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
May 23, 2017	343	1. Project of the Japan Drug Information Institute in Pregnancy 2. Revision of Precautions (No. 284) Denosumab (and 2 others) 3. List of Products Subject to Early Post-marketing Phase Vigilance
June 27, 2017	344	1. Revision of Instructions for Package Inserts of Prescription Drugs 2. Precautions Concerning Recurrent and Similar Medical Accidents 3. Important Safety Information (1) Treprostinil (2) Bosutinib 4. Revision of Precautions (No. 285) Treprostinil (and 3 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
August 1, 2017	345	1. Summary of Guidance for Adverse Drug Reaction Reporting by Medical and Pharmaceutical Providers 2. Important Safety Information (1) Loxoprofen sodium hydrate (dermatologic preparation) (2) Fluconazole, Fosfluconazole (3) Nivolumab (genetical recombination) 3. Revision of Precautions (No. 286) Loxoprofen sodium hydrate (dermatologic preparation) (and 16 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
September 5, 2017	346	1. The Expert Committee on Quality of Generic Drug Products 2. Introduction of the “My Drug List for Safety Updates” service 3. Revision of Precautions (No. 287) Riociguat (and 4 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
October 10, 2017	347	1. Summary of the Relief System for Adverse Drug Reaction and Request of Cooperation for the System 2. Important Safety Information (1) Dabigatran etexilate methanesulfonate 3. Revision of Precautions (No. 288) Dabigatran etexilate methanesulfonate (and 2 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

Date	No.	Table of Contents
November 14, 2017	348	1. Initiative of Revision of the Manuals for Management of Individual Serious Adverse Drug Reactions 2. Prevention of Accidents with Electric Massagers for Household Use 3. Important Safety Information (1) Levetiracetam (2) Linagliptin 4. Revision of Precautions (No. 289) Levetiracetam (and 8 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
December 26, 2017	349	1. Safety of Influenza Antiviral Drugs 2. Suspected Adverse Reactions to Influenza Vaccines in the 2016 Season 3. Important Safety Information (1) Clozapine 4. Revision of Precautions (No. 290) Clozapine (and 2 others) 5. List of Products Subject to Early Post-marketing Phase Vigilance
February 6, 2018	350	1. An Incident of Distribution of Counterfeit HARVONI Combination Tablets and Government Measures Against Counterfeit Drugs 2. Important Safety Information (1) [1] Teriparatide (genetical recombination), [2] Teriparatide acetate (subcutaneous injection) (2) Edoxaban tosilate hydrate (3) Lenvatinib mesilate 3. Revision of Precautions (No. 291) (1) Aripiprazole (2) Aripiprazole hydrate (and 5 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance
March 13, 2018	351	1. Medical Information Database MID-NET (Medical Information Database NETwork) 2. Important Safety Information (1) Gardenia fruit 3. Revision of Precautions (No. 292) Gardenia fruit (and 6 others) 4. List of Products Subject to Early Post-marketing Phase Vigilance

**Note: More detailed information is available on the PMDA website.*

Table 11. FY 2017 PMDA Medical Safety Information

No.	Month and year published	Title
51	September 2017	Mix-up of Drugs Due to Similarity of Nonproprietary Names
52	December 2017	Precautions When Using an Open Ventricular Drainage Circuit
53	March 2018	Introduction of Connectors that Prevent Misconnection

**Note: More detailed information is available on the PMDA website.*

Table 12. List of User Fees for Drugs

List of user fees (revised on April 1, 2017) 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		159,900	159,900
				Article 31, Paragraph 1, Item 1 (a)	
		Document		120,400	120,400
				Article 31, Paragraph 1, Item 1 (b)	
	Renewal of existing license	On-site		105,200	105,200
				Article 31, Paragraph 1, Item 2 (a)	
		Document		59,700	59,700
				Article 31, Paragraph 1, Item 2 (b)	
	Change/addition of classification	On-site		105,200	105,200
				Article 31, Paragraph 1, Item 3 (a)	
		Document		59,700	59,700
				Article 31, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers' accreditation of drugs					
	New accreditation	On-site		143,900 + overseas travel expenses	143,900 + overseas travel expenses
				Article 31, Paragraph 2, Item 1 (a)	
		Document		62,600	62,600
				Article 31, Paragraph 2, Item 1 (b)	
	Renewal of existing license	On-site		69,700 + overseas travel expenses	69,700 + overseas travel expenses
				Article 31, Paragraph 2, Item 2 (a)	
		Document		42,900	42,900
				Article 31, Paragraph 2, Item 2 (b)	
	Change/addition of classification	On-site		69,700 + overseas travel expenses	69,700 + overseas travel expenses
				Article 31, Paragraph 2, Item 3 (a)	
		Document		42,900	42,900
				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		28,545,700 Article 32, Paragraph 1, Item 1 (a)-(1)	8,096,400 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (a)	36,642,100 (+ overseas travel expenses *1)
		Line extension products		2,956,800 Article 32, Paragraph 1, Item 1 (a)-(3)	2,023,900 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (c)	4,980,700 (+ overseas travel expenses *1)
New drugs (No. 1) (orphan drugs)		First application products		23,921,000 Article 32, Paragraph 1, Item 1 (a)-(2)	4,056,000 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (b)	27,977,000 (+ overseas travel expenses *1)
		Line extension products		2,473,800 Article 32, Paragraph 1, Item 1 (a)-(4)	1,009,800 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (d)	3,483,600 (+ overseas travel expenses *1)
New drugs (No. 2) (non-orphan drugs)		First application products		13,623,700 Article 32, Paragraph 1, Item 1 (a)-(5)	3,040,300 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (e)	16,664,000 (+ overseas travel expenses *1)
		Line extension products		1,409,100 Article 32, Paragraph 1, Item 1 (a)-(7)	760,300 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (g)	2,169,400 (+ overseas travel expenses *1)
New drugs (No. 2) (orphan drugs)		First application products		11,214,800 Article 32, Paragraph 1, Item 1 (a)-(6)	1,521,200 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (f)	12,736,000 (+ overseas travel expenses *1)
		Line extension products		1,204,900 Article 32, Paragraph 1, Item 1 (a)-(8)	382,800 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (h)	1,587,700 (+ overseas travel expenses *1)
Generic drugs		with inspections		649,100 Article 32, Paragraph 1, Item 1 (a)-(9)	346,700 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (i)	995,800 (+ overseas travel expenses *1)
		without inspection		649,100 Article 32, Paragraph 1, Item 1 (a)-(9)		649,100
BTC/OTC drugs	Switch to OTC status, etc.	First application products	with inspections	1,356,100 Article 32, Paragraph 1, Item 1 (a)-(10)	346,700 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (i)	1,702,800 (+ overseas travel expenses *1)
			without inspection	1,356,100 Article 32, Paragraph 1, Item 1 (a)-(10)		1,356,100
		Line extension products	with inspections	1,356,100 Article 32, Paragraph 1, Item 1 (a)-(10)	346,700 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (i)	1,702,800 (+ overseas travel expenses *1)
			without inspection	1,356,100 Article 32, Paragraph 1, Item 1 (a)-(10)		1,356,100
	Others		with inspections	115,800 Article 32, Paragraph 1, Item 1 (a)-(11)	346,700 (+ overseas travel expenses *1) Article 32, Paragraph 2, Item 1 (i)	462,500 (+ overseas travel expenses *1)
			without inspection	115,800 Article 32, Paragraph 1, Item 1 (a)-(11)		115,800
Quasi-drugs		New active ingredients		3,130,100 Article 32, Paragraph 1, Item 1 (b)-(1)		3,130,100
		New dosage, etc.		258,900 Article 32, Paragraph 1, Item 1 (b)-(2)		258,900
		Others		66,600 Article 32, Paragraph 1, Item 1 (b)-(6)		66,600

(*1) Overseas travel expenses (Article 32, Paragraph 3) are added to the user fees of overseas surveys.

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	5,237,200		5,237,200
				Article 32, Paragraph 1, Item 1 (a)-(12) and (b)-(3)		
			New dosage, etc.	411,800		411,800
				Article 32, Paragraph 1, Item 1 (a)-(13) and (b)-(4)		
			Others	100,200		100,200
				Article 32, Paragraph 1, Item 1 (a)-(14) and (b)-(5)		
	Cosmetics			66,600		66,600
				Article 32, Paragraph 1, Item 1 (c)		
	New application for change or replacement of brand name			37,300		37,300
				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	12,228,600	3,040,300 (+ overseas travel expenses *1)	15,268,900 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (a)	
			Line extension products	1,268,800	760,300 (+ overseas travel expenses *1)	2,029,100 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (b)	
		Others		246,100	149,000 (+ overseas travel expenses *1)	395,100 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(3)	Article 32, Paragraph 2, Item 2 (c)	
	New drugs (No. 1) (orphan drugs)	Changes in indications, etc.	First application products	10,121,100	1,521,200 (+ overseas travel expenses *1)	11,642,300 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(4)	Article 32, Paragraph 2, Item 2 (d)	
			Line extension products	1,050,700	382,800 (+ overseas travel expenses *1)	1,433,500 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(5)	Article 32, Paragraph 2, Item 2 (e)	
		Others		159,200	135,400 (+ overseas travel expenses *1)	294,600 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(6)	Article 32, Paragraph 2, Item 2 (f)	
	New drugs (No. 2) (non-orphan drugs)	Changes in indications, etc.	First application products	12,228,600	3,040,300 (+ overseas travel expenses *1)	15,268,900 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(1)	Article 32, Paragraph 2, Item 2 (a)	
			Line extension products	1,268,800	760,300 (+ overseas travel expenses *1)	2,029,100 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(2)	Article 32, Paragraph 2, Item 2 (b)	
		Others		246,100	149,000 (+ overseas travel expenses *1)	395,100 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(3)	Article 32, Paragraph 2, Item 2 (c)	
	New drugs (No. 2) (orphan drugs)	Changes in indications, etc.	First application products	10,121,100	1,521,200 (+ overseas travel expenses *1)	11,642,300 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(4)	Article 32, Paragraph 2, Item 2 (d)	
			Line extension products	1,050,700	382,800 (+ overseas travel expenses *1)	1,433,500 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(5)	Article 32, Paragraph 2, Item 2 (e)	
		Others		159,200	135,400 (+ overseas travel expenses *1)	294,600 (+ overseas travel expenses *1)
				Article 32, Paragraph 1, Item 2 (a)-(6)	Article 32, Paragraph 2, Item 2 (f)	

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			10,700,000	2,660,200 (+ overseas travel expenses *1)	13,360,200 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(7)	Article 32, Paragraph 2, Item 2 (g)	
			Line extension products			1,110,200	665,200 (+ overseas travel expenses *1)	1,775,400 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(8)	Article 32, Paragraph 2, Item 2 (h)	
		Changes based on guidelines, etc.				56,000		56,000
						Article 32, Paragraph 1, Item 2 (a)-(9)		
		Others				323,000	195,500 (+ overseas travel expenses *1)	518,500 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(10)	Article 32, Paragraph 2, Item 2 (i)	
	BTC/OTC drugs	Switch to OTC status, etc.	Changes in indications, etc.	First application products	with inspections	10,700,000	195,500 (+ overseas travel expenses *1)	10,895,500 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(7)	Article 32, Paragraph 2, Item 2 (i)	
					without inspection	10,700,000		10,700,000
						Article 32, Paragraph 1, Item 2 (a)-(7)		
				Line extension products	with inspections	1,110,200	195,500 (+ overseas travel expenses *1)	1,305,700 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(8)	Article 32, Paragraph 2, Item 2 (i)	
					without inspection	1,110,200		1,110,200
						Article 32, Paragraph 1, Item 2 (a)-(8)		
			Others		with inspections	59,200	195,500 (+ overseas travel expenses *1)	254,700 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(11)	Article 32, Paragraph 2, Item 2 (i)	
					without inspection	59,200		59,200
						Article 32, Paragraph 1, Item 2 (a)-(11)		
		Changes based on guidelines, etc.			with inspections	37,300	195,500 (+ overseas travel expenses *1)	232,800 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(12)	Article 32, Paragraph 2, Item 2 (i)	
					without inspection	37,300		37,300
						Article 32, Paragraph 1, Item 2 (a)-(12)		
		Others			with inspections	59,200	195,500 (+ overseas travel expenses *1)	254,700 (+ overseas travel expenses *1)
						Article 32, Paragraph 1, Item 2 (a)-(11)	Article 32, Paragraph 2, Item 2 (i)	
					without inspection	59,200		59,200
						Article 32, Paragraph 1, Item 2 (a)-(11)		
	Quasi-drugs					37,300		37,300
						Article 32, Paragraph 1, Item 2 (b)-(1)		
	Cosmetics					37,300		37,300
						Article 32, Paragraph 1, Item 2 (c)		
	Pest control agents					50,800		50,800
						Article 32, Paragraph 1, Item 2 (a)-(13) and (b)-(2)		

(*1) Overseas travel expenses (Article 32, Paragraph 3) are added to the user fees of overseas surveys.

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		875,000 Article 32, Paragraph 5, Item 1 (b)-(1)	875,000
				Overseas		1,104,200 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 1 (b)-(2)	1,104,200 (+ overseas travel expenses *2)
		Biological drugs/Radiopharmaceuticals, etc.		In Japan		787,800 Article 32, Paragraph 5, Item 1 (a)-(1)	787,800
				Overseas		998,800 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 1 (a)-(2)	998,800 (+ overseas travel expenses *2)
		Sterile drugs/Sterile quasi-drugs		In Japan		548,700 Article 32, Paragraph 5, Item 1 (c)-(1)	548,700
				Overseas		691,200 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 1 (c)-(2)	691,200 (+ overseas travel expenses *2)
		Other Drugs/Quasi-drugs		In Japan		398,400 Article 32, Paragraph 5, Item 1 (d)-(1)	398,400
				Overseas		501,900 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 1 (d)-(2)	501,900 (+ overseas travel expenses *2)
		Packaging, labeling, storage, external testing, etc.		In Japan		75,400 Article 32, Paragraph 5, Item 2 (a) and Paragraph 6, Item 1 (a)	75,400
				Overseas		100,200 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 2 (b) and Paragraph 6, Item 1 (b)	100,200 (+ overseas travel expenses *2)
Renewal of approval/Renewal of manufacture for export		Biological drugs/Radiopharmaceuticals, etc.	Basic	In Japan		787,800 Article 32, Paragraph 5, Item 3 (a)-(1)	787,800
				Overseas		998,800 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 3 (a)-(2)	998,800 (+ overseas travel expenses *2)
			Addition of products	In Japan		36,100 Article 32, Paragraph 5, Item 3 (a)-(1)	36,100
				Overseas		36,100 Article 32, Paragraph 5, Item 3 (a)-(2)	36,100
		Sterile drugs/Sterile quasi-drugs	Basic	In Japan		548,500 Article 32, Paragraph 5, Item 3 (b)-(1)	548,500
				Overseas		691,200 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 3 (b)-(2)	691,200 (+ overseas travel expenses *2)
			Addition of products	In Japan		14,700 Article 32, Paragraph 5, Item 3 (b)-(1)	14,700
				Overseas		14,700 Article 32, Paragraph 5, Item 3 (b)-(2)	14,700
		Other Drugs/Quasi-drugs	Basic	In Japan		398,400 Article 32, Paragraph 5, Item 3 (c)-(1)	398,400
				Overseas		501,900 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 3 (c)-(2)	501,900 (+ overseas travel expenses *2)
			Addition of products	In Japan		11,300 Article 32, Paragraph 5, Item 3 (c)-(1)	11,300
				Overseas		11,300 Article 32, Paragraph 5, Item 3 (c)-(2)	11,300
		Packaging, labeling, storage, external testing, etc.	Basic	In Japan		305,700 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	305,700
				Overseas		399,900 (+ overseas travel expenses *2) Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b)	399,900 (+ overseas travel expenses *2)
			Addition of products	In Japan		8,000 Article 32, Paragraph 5, Item 3 (d)-(1) and Paragraph 6, Item 2 (a)	8,000
				Overseas		8,000 Article 32, Paragraph 5, Item 3 (d)-(2) and Paragraph 6, Item 2 (b)	8,000

(*2) Overseas travel expenses (Article 32, Paragraph 7) are added to the user fees of overseas surveys.

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				2,545,600 Article 32, Paragraph 4, Item 1 (a)	2,545,600
		Overseas				2,817,400 + overseas travel expenses Article 32, Paragraph 4, Item 1 (b)	2,817,400 + overseas travel expenses
GCP inspection of drugs							
New GCP		First application products	In Japan	New		3,361,200 Article 32, Paragraph 4, Item 2 (a)-(1)	3,361,200
				Partial change		3,361,200 Article 32, Paragraph 4, Item 2 (b)-(1)	3,361,200
			Overseas	New		3,717,600 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(2)	3,717,600 + overseas travel expenses
				Partial change		3,717,600 + overseas travel expenses Article 32, Paragraph 4, Item 2 (b)-(2)	3,717,600 + overseas travel expenses
		Line extension products	In Japan	New		889,600 Article 32, Paragraph 4, Item 2 (a)-(3)	889,600
				Partial change		889,600 Article 32, Paragraph 4, Item 2 (b)-(3)	889,600
			Overseas	New		927,900 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(4)	927,900 + overseas travel expenses
				Partial change		927,900 + overseas travel expenses Article 32, Paragraph 4, Item 2 (b)-(4)	927,900 + overseas travel expenses
	GCP inspection of generic drugs		In Japan	New		696,700 Article 32, Paragraph 4, Item 2 (a)-(5)	696,700
				Partial change		696,700 Article 32, Paragraph 4, Item 2 (b)-(5)	696,700
			Overseas	New		1,026,200 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6)	1,026,200
				Partial change		1,026,200 + overseas travel expenses Article 32, Paragraph 4, Item 2 (b)-(6)	1,026,200
	GCP inspection of BTC /OTC drugs		In Japan	New		696,700 Article 32, Paragraph 4, Item 2 (a)-(5)	696,700
				Partial change		696,700 Article 32, Paragraph 4, Item 2 (b)-(5)	696,700
			Overseas	New		1,026,200 + overseas travel expenses Article 32, Paragraph 4, Item 2 (a)-(6)	1,026,200
				Partial change		1,026,200 + overseas travel expenses Article 32, Paragraph 4, Item 2 (b)-(6)	1,026,200
Re-examination of drugs							
Re-examination		First application products			967,800 Article 32, Paragraph 9, Item 1	3,300,100 (+ overseas travel expenses *3) Article 32, Paragraph 10, Item 1 (a)	4,267,900 (+ overseas travel expenses *3)
		Line extension products			325,800 Article 32, Paragraph 9, Item 2	1,101,100 (+ overseas travel expenses *3) Article 32, Paragraph 10, Item 1 (b)	1,426,900 (+ overseas travel expenses *3)
GLP for re-examination		In Japan				2,545,600 Article 32, Paragraph 10, Item 2 (a)-(1)	2,545,600
		Overseas				2,817,400 (+ overseas travel expenses *3) Article 32, Paragraph 10, Item 2 (a)-(2)	2,817,400 (+ overseas travel expenses *3)
GPSP		First application products	In Japan			2,707,200 Article 32, Paragraph 10, Item 2 (b)-(1)	2,707,200
			Overseas			2,974,200 (+ overseas travel expenses *3) Article 32, Paragraph 10, Item 2 (b)-(2)	2,974,200 (+ overseas travel expenses *3)
		Line extension products	In Japan			928,900 Article 32, Paragraph 10, Item 2 (b)-(3)	928,900
			Overseas			953,200 (+ overseas travel expenses *3) Article 32, Paragraph 10, Item 2 (b)-(4)	953,200 (+ overseas travel expenses *3)

(*3) Overseas travel expenses (Article 32, Paragraph 11) are added to the user fees of overseas surveys.

Table 13. List of User Fees for Medical Devices and In Vitro Diagnostics

List of user fees (revised on July 31, 2017) 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)					12,731,500 Article 33, Paragraph 1, Item 1 (a)-(1)	999,500 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (a)	13,731,000 (+ overseas travel expenses *1)
New medical devices (Class II/III)					9,086,400 Article 33, Paragraph 1, Item 1 (a)-(3)	999,500 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (a)	10,085,900 (+ overseas travel expenses *1)
Improved medical devices with clinical data (Class IV)					7,269,200 Article 33, Paragraph 1, Item 1 (a)-(2)	799,600 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (b)	8,068,800 (+ overseas travel expenses *1)
Improved medical devices with clinical data (Class II/III)					4,353,800 Article 33, Paragraph 1, Item 1 (a)-(4)	799,600 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (b)	5,153,400 (+ overseas travel expenses *1)
Improved medical devices without clinical data, without approval standards (Class IV)					2,567,400 Article 33, Paragraph 1, Item 1 (a)-(7)	76,800 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (c)	2,644,200 (+ overseas travel expenses *1)
Generic medical devices without clinical data, without approval standards (Class IV)					1,926,700 Article 33, Paragraph 1, Item 1 (a)-(8)	76,800 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (c)	2,003,500 (+ overseas travel expenses *1)
Improved/generic medical devices without clinical data, without approval standards (Class II/III)					1,536,700 Article 33, Paragraph 1, Item 1 (a)-(9)	76,800 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (c)	1,613,500 (+ overseas travel expenses *1)
Generic medical devices with approval standards (Class IV)					467,800 Article 33, Paragraph 1, Item 1 (a)-(5)	76,800 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (c)	544,600 (+ overseas travel expenses *1)
Generic medical devices with approval standards (Class II/III)					375,000 Article 33, Paragraph 1, Item 1 (a)-(6)	76,800 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (c)	451,800 (+ overseas travel expenses *1)
Re-processed single-use medical devices		(Class IV)			7,269,200 Article 33, Paragraph 1, Item 1 (a)-(2)	799,600 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (b)	8,068,800 (+ overseas travel expenses *1)
		(Class II/III)			4,353,800 Article 33, Paragraph 1, Item 1 (a)-(4)	799,600 (+ overseas travel expenses *1) Article 33, Paragraph 2, Item 1 (b)	5,153,400 (+ overseas travel expenses *1)
In vitro diagnostics	New products	Excluding companion diagnostics			2,534,000 Article 33, Paragraph 1, Item 1 (b)-(2)		2,534,000
		Companion diagnostics			4,295,000 Article 33, Paragraph 1, Item 1 (b)-(3)		4,295,000
	Out of scope of approval standards	With clinical data	Excluding companion diagnostics		2,534,000 Article 33, Paragraph 1, Item 1 (b)-(2)		2,534,000
			Companion diagnostics		4,295,000 Article 33, Paragraph 1, Item 1 (b)-(3)		4,295,000
		Without clinical data			2,362,200 Article 33, Paragraph 1, Item 1 (b)-(4)		2,362,200
	Nonconformity with approval standards	With clinical data	Excluding companion diagnostics		2,534,000 Article 33, Paragraph 1, Item 1 (b)-(2)		2,534,000
			Companion diagnostics		4,295,000 Article 33, Paragraph 1, Item 1 (b)-(3)		4,295,000
		Without clinical data			1,096,500 Article 33, Paragraph 1, Item 1 (b)-(6)		1,096,500
	Conformity with approval standards	Without clinical data			380,100 Article 33, Paragraph 1, Item 1 (b)-(5)		380,100
	Addition of series				63,300 Article 33, Paragraph 1, Item 1 (b)-(1)		63,300
Change of brand name					37,300 Article 33, Paragraph 1, Item 1 (c)		37,300

(*1) Overseas travel expenses (Article 33, Paragraph 3) are added to the user fees of overseas surveys.

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)				6,372,500	999,500 (+ overseas travel expenses *1)	7,372,000 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(1)	Article 33, Paragraph 2, Item 2 (a)	
New medical devices (Class II/III)				4,548,100	999,500 (+ overseas travel expenses *1)	5,547,600 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(3)	Article 33, Paragraph 2, Item 2 (a)	
Improved medical devices with clinical data (Class IV)				3,638,500	799,600 (+ overseas travel expenses *1)	4,438,100 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(2)	Article 33, Paragraph 2, Item 2 (b)	
Improved medical devices with clinical data (Class II/III)				2,190,700	799,600 (+ overseas travel expenses *1)	2,990,300 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(4)	Article 33, Paragraph 2, Item 2 (b)	
Improved medical devices without clinical data, without approval standards (Class IV)				1,287,500	41,600 (+ overseas travel expenses *1)	1,329,100 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(7)	Article 33, Paragraph 2, Item 2 (c)	
Generic medical devices without clinical data, without approval standards (Class IV)				963,700	41,600 (+ overseas travel expenses *1)	1,005,300 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(8)	Article 33, Paragraph 2, Item 2 (c)	
Improved/generic medical devices without clinical data, without approval standards (Class II/III)				773,300	41,600 (+ overseas travel expenses *1)	814,900 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(9)	Article 33, Paragraph 2, Item 2 (c)	
Generic medical devices with approval standards (Class IV)				236,900	41,600 (+ overseas travel expenses *1)	278,500 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(5)	Article 33, Paragraph 2, Item 2 (c)	
Generic medical devices with approval standards (Class II/III)				189,200	41,600 (+ overseas travel expenses *1)	230,800 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(6)	Article 33, Paragraph 2, Item 2 (c)	
Others (medical devices)				156,400	41,600 (+ overseas travel expenses *1)	198,000 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(10)	Article 33, Paragraph 2, Item 2 (c)	
Reprocessed single-use medical devices		With design/ manufacturing data for reprocessing	(Class IV)	3,638,500	799,600 (+ overseas travel expenses *1)	4,438,100 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(2)	Article 33, Paragraph 2, Item 2 (b)	
			(Class II/III)	2,190,700	799,600 (+ overseas travel expenses *1)	2,990,300 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(4)	Article 33, Paragraph 2, Item 2 (b)	
		Without design/ manufacturing data for reprocessing	(Class IV)	963,700	41,600 (+ overseas travel expenses *1)	1,005,300 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(8)	Article 33, Paragraph 2, Item 2 (c)	
			(Class II/III)	773,300	41,600 (+ overseas travel expenses *1)	814,900 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(9)	Article 33, Paragraph 2, Item 2 (c)	
		Others		156,400	41,600 (+ overseas travel expenses *1)	198,000 (+ overseas travel expenses *1)
				Article 33, Paragraph 1, Item 2 (a)-(10)	Article 33, Paragraph 2, Item 2 (c)	
In vitro diagnostics	Out of scope of approval standards	With clinical data	Excluding companion diagnostics	1,048,200		1,048,200
				Article 33, Paragraph 1, Item 2 (b)-(2)		
			Companion diagnostics	1,996,600		1,996,600
				Article 33, Paragraph 1, Item 2 (b)-(3)		
		Without clinical data	Excluding companion diagnostics	528,700		528,700
				Article 33, Paragraph 1, Item 2 (b)-(4)		
			Companion diagnostics	1,007,200		1,007,200
				Article 33, Paragraph 1, Item 2 (b)-(5)		
	Nonconformity with approval standards	With clinical data	Excluding companion diagnostics	1,048,200		1,048,200
				Article 33, Paragraph 1, Item 2 (b)-(2)		
			Companion diagnostics	1,996,600		1,996,600
				Article 33, Paragraph 1, Item 2 (b)-(3)		
		Without clinical data	Excluding companion diagnostics	528,700		528,700
				Article 33, Paragraph 1, Item 2 (b)-(4)		
			Companion diagnostics	1,007,200		1,007,200
				Article 33, Paragraph 1, Item 2 (b)-(5)		
	Conformity with approval standards	Without clinical data		216,500		216,500
				Article 33, Paragraph 1, Item 2 (b)-(6)		
	Addition of series			33,400		33,400
				Article 33, Paragraph 1, Item 2 (b)-(1)		
Others (*in vitro* diagnostics)				150,600		150,600
				Article 33, Paragraph 1, Item 2 (b)-(7)		

(*1) Overseas travel expenses (Article 33, Paragraph 3) are added to the user fees of overseas surveys.

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 Article 33, Paragraph 5, Item 1 (a), Item 2 (a), and Item 3 (a); and Paragraph 6, Item 1 (a), Item 2 (a), and Item 3 (a)	50,400
Fee paid by MAH	New	New	New medical devices		386,600 Article 33, Paragraph 5, Item 1 (a)-(2)	386,600
			MAHs of class II medical devices		386,600 Article 33, Paragraph 6, Item 1 (a)-(2)	386,600
			Class IV		374,500 Article 33, Paragraph 5, Item 1 (a)-(3)	374,500
			Biological products		398,500 Article 33, Paragraph 5, Item 1 (a)-(1)	398,500
			MAHs of class II medical devices		398,500 Article 33, Paragraph 6, Item 1 (a)-(1)	398,500
			Other medical devices		374,500 Article 33, Paragraph 5, Item 1 (a)-(4)	374,500
			MAHs of class II medical devices		262,100 Article 33, Paragraph 6, Item 1 (a)-(3)	262,100
			In vitro diagnostics		272,900 Article 33, Paragraph 5, Item 1 (a)-(5)	272,900
		Partial change	Class IV		134,000 Article 33, Paragraph 5, Item 2 (a)-(2)	134,000
			Biological products		145,600 Article 33, Paragraph 5, Item 2 (a)-(1)	145,600
			MAHs of class II medical devices		145,600 Article 33, Paragraph 6, Item 2 (a)-(1)	145,600
			Other medical devices		127,800 Article 33, Paragraph 5, Item 2 (a)-(3)	127,800
			MAHs of class II medical devices		89,400 Article 33, Paragraph 6, Item 2 (a)-(2)	89,400
			In vitro diagnostics		93,200 Article 33, Paragraph 5, Item 2 (a)-(4)	93,200
		Renewal	Class IV		167,600 Article 33, Paragraph 5, Item 3 (a)-(2)	167,600
			Biological products		176,900 Article 33, Paragraph 5, Item 3 (a)-(1)	176,900
			MAHs of class II medical devices		176,900 Article 33, Paragraph 6, Item 3 (a)-(1)	176,900
			Other medical devices		149,200 Article 33, Paragraph 5, Item 3 (a)-(3)	149,200
			MAHs of class II medical devices		104,400 Article 33, Paragraph 6, Item 3 (a)-(2)	104,400
			In vitro diagnostics		129,700 Article 33, Paragraph 5, Item 3 (a)-(4)	129,700
	New	Design			86,100 Article 33, Paragraph 5, Item 1 (b)-(1) and Paragraph 11, Item 1 (a)	86,100
			MAHs of class II medical devices		60,200 Article 33, Paragraph 6, Item 1 (b)-(1)	60,200
		Sterilization			91,200 Article 33, Paragraph 5, Item 1 (b)-(3) and Paragraph 11, Item 1 (c)	91,200
			MAHs of class II medical devices		63,800 Article 33, Paragraph 6, Item 1 (b)-(3)	63,800
		Assembly/Cleaning			104,100 Article 33, Paragraph 5, Item 1 (b)-(2) and Paragraph 11, Item 1 (b)	104,100
			MAHs of class II medical devices		72,800 Article 33, Paragraph 6, Item 1 (b)-(2)	72,800
		Others			90,500 Article 33, Paragraph 5, Item 1 (b)-(4) and Paragraph 11, Item 1 (d)	90,500
			MAHs of class II medical devices		63,200 Article 33, Paragraph 6, Item 1 (b)-(4)	63,200
		Unregistered			87,500 Article 33, Paragraph 5, Item 1 (b)-(5) and Paragraph 11, Item 1 (e) and Paragraph 12, Item 1	87,500
			MAHs of class II medical devices		61,200 Article 33, Paragraph 6, Item 1 (b)-(5)	61,200

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					
Partial change	Design			64,400	64,400
				Article 33, Paragraph 5, Item 2 (b)-(1)	
		MAHs of class II medical devices		45,000	45,000
				Article 33, Paragraph 6, Item 2 (b)-(1)	
	Sterilization			75,900	75,900
				Article 33, Paragraph 5, Item 2 (b)-(3)	
		MAHs of class II medical devices		53,100	53,100
				Article 33, Paragraph 6, Item 2 (b)-(3)	
	Assembly/Cleaning			87,700	87,700
				Article 33, Paragraph 5, Item 2 (b)-(2)	
		MAHs of class II medical devices		61,300	61,300
				Article 33, Paragraph 6, Item 2 (b)-(2)	
	Others			75,800	75,800
				Article 33, Paragraph 5, Item 2 (b)-(4)	
		MAHs of class II medical devices		53,000	53,000
				Article 33, Paragraph 6, Item 2 (b)-(4)	
	Unregistered			75,900	75,900
				Article 33, Paragraph 5, Item 2 (b)-(3)	
		MAHs of class II medical devices		53,100	53,100
				Article 33, Paragraph 6, Item 2 (b)-(3)	
Renewal	Design			68,800	68,800
				Article 33, Paragraph 5, Item 3 (b)-(1) and Paragraph 11, Item 2 (a)	
		MAHs of class II medical devices		48,100	48,100
				Article 33, Paragraph 6, Item 3 (b)-(1)	
	Sterilization			80,100	80,100
				Article 33, Paragraph 5, Item 3 (b)-(3) and Paragraph 11, Item 2 (c)	
		MAHs of class II medical devices		56,000	56,000
				Article 33, Paragraph 6, Item 3 (b)-(3)	
	Assembly/Cleaning			97,400	97,400
				Article 33, Paragraph 5, Item 3 (b)-(2) and Paragraph 11, Item 2 (b)	
		MAHs of class II medical devices		68,100	68,100
				Article 33, Paragraph 6, Item 3 (b)-(2)	
	Others			79,600	79,600
				Article 33, Paragraph 5, Item 3 (b)-(4) and Paragraph 11, Item 2 (d)	
		MAHs of class II medical devices		55,700	55,700
				Article 33, Paragraph 6, Item 3 (b)-(4)	
	Unregistered			76,100	76,100
				Article 33, Paragraph 5, Item 3 (b)-(5) and Paragraph 11, Item 2 (e) and Paragraph 12, Item 2	
		MAHs of class II medical devices		53,200	53,200
				Article 33, Paragraph 6, Item 3 (b)-(5)	
Options	Micro machine			47,500	47,500
				Article 33, Paragraph 7, Item 1	
		MAHs of class II medical devices		33,200	33,200
				Article 33, Paragraph 8	
	Nano materials			47,500	47,500
				Article 33, Paragraph 7, Item 2	
		MAHs of class II medical devices		33,200	33,200
				Article 33, Paragraph 8	
	Others (including reprocessed single-use medical devices)			47,500	47,500
				Article 33, Paragraph 7, Item 3	
		MAHs of class II medical devices		33,200	33,200
				Article 33, Paragraph 8	
Travel expenses for on-site inspection (per day)		In Japan		212,400	212,400
				Article 33, Paragraph 9, Item 1 and Paragraph 13	
		Overseas		179,500 + overseas travel expenses	179,500 + overseas travel expenses
				Article 33, Paragraph 9, Item 2 (a) and (b)	
Re-issue/renewal of compliance certification				11,000	11,000
				Article 33, Paragraph 17	

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			2,482,000 Article 33, Paragraph 4, Item 1 (a)	2,482,000
		Overseas			2,747,000 + overseas travel expenses Article 33, Paragraph 4, Item 1 (b)	2,747,000 + overseas travel expenses
GCP inspection of medical devices						
	GCP	In Japan			764,400 Article 33, Paragraph 4, Item 2 (a)	764,400
		Overseas			1,105,200 + overseas travel expenses Article 33, Paragraph 4, Item 2 (b)	1,105,200 + overseas travel expenses
Use-results evaluation of medical devices and *in vitro* diagnostics						
	Target medical devices			588,000 Article 33, Paragraph 14, Item 1 (a)	751,600 (+ overseas travel expenses *2) Article 33, Paragraph 15, Item 1	1,339,600 (+ overseas travel expenses *2)
	Child items with multiple brand names of the target medical device			41,700 Article 33, Paragraph 14, Item 1 (b)		41,700
	Target *in vitro* diagnostics			588,000 Article 33, Paragraph 14, Item 2	751,600 (+ overseas travel expenses *2) Article 33, Paragraph 15, Item 1	1,339,600 (+ overseas travel expenses *2)
	GLP for use-results evaluation of medical devices	In Japan			2,482,000 Article 33, Paragraph 15, Item 2 (a)-(1)	2,482,000
		Overseas			2,747,000 (+ overseas travel expenses *2) Article 33, Paragraph 15, Item 2 (a)-(2)	2,747,000 (+ overseas travel expenses *2)
	GPSP	Medical devices	In Japan		734,900 Article 33, Paragraph 15, Item 2 (b)-(1)	734,900
			Overseas		1,142,000 (+ overseas travel expenses *2) Article 33, Paragraph 15, Item 2 (b)-(2)	1,142,000 (+ overseas travel expenses *2)
	GPSP	*In vitro* diagnostics	In Japan		734,900 Article 33, Paragraph 15, Item 2 (b)-(1)	734,900
			Overseas		1,142,000 (+ overseas travel expenses *2) Article 33, Paragraph 15, Item 2 (b)-(2)	1,142,000 (+ overseas travel expenses *2)

(*2) Overseas travel expenses (Article 33, Paragraph 16) are added to the user fees of overseas surveys.

Table 14. List of User Fees for Regenerative Medical Products

List of user fees (revised on April 1, 2017) 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		159,900	159,900
				Article 34, Paragraph 1, Item 1 (a)	
		Document		120,400	120,400
				Article 34, Paragraph 1, Item 1 (b)	
	Renewal of existing license	On-site		105,200	105,200
				Article 34, Paragraph 1, Item 2 (a)	
		Document		59,700	59,700
				Article 34, Paragraph 1, Item 2 (b)	
	Change/addition of classification	On-site		105,200	105,200
				Article 34, Paragraph 1, Item 3 (a)	
		Document		59,700	59,700
				Article 34, Paragraph 1, Item 3 (b)	
Assessment for foreign manufacturers accreditation of regenerative medical products					
	New accreditation	On-site		143,900 + overseas travel expenses	143,900 + overseas travel expenses
				Article 34, Paragraph 2, Item 1 (a)	
		Document		62,600	62,600
				Article 34, Paragraph 2, Item 1 (b)	
	Renewal of accreditation	On-site		69,700 + overseas travel expenses	69,700 + overseas travel expenses
				Article 34, Paragraph 2, Item 2 (a)	
		Document		42,900	42,900
				Article 34, Paragraph 2, Item 2 (b)	
	Change/addition of classification	On-site		69,700 + overseas travel expenses	69,700 + overseas travel expenses
				Article 34, Paragraph 2, Item 3 (a)	
		Document		42,900	42,900
				Article 34, Paragraph 2, Item 3 (b)	
Review for approval of regenerative medical products (new approval)					
	New regenerative medical products		12,786,000	1,003,800 (+ overseas travel expenses *1)	13,789,800 (+ overseas travel expenses *1)
			Article 35, Paragraph 1, Item 1 (a)	Article 35, Paragraph 2, Item 1	
	Regenerative medical products in case of new application for approval after the conditional time-limited authorization		6,399,700	1,003,800 (+ overseas travel expenses *1)	7,403,500 (+ overseas travel expenses *1)
			Article 35, Paragraph 1, Item 1 (b)	Article 35, Paragraph 2, Item 1	
	Application for change of brand name		37,300		37,300
			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.)		6,399,700	1,003,800 (+ overseas travel expenses *1)	7,403,500 (+ overseas travel expenses *1)
			Article 35, Paragraph 1, Item 2 (a)	Article 35, Paragraph 2, Item 2 (a)	
	Regenerative medical products (other changes)		1,388,000	44,800 (+ overseas travel expenses *1)	1,432,800 (+ overseas travel expenses *1)
			Article 35, Paragraph 1, Item 2 (b)	Article 35, Paragraph 2, Item 2 (b)	

(*1) Overseas travel expenses (Article 35, Paragraph 3) are added to the user fees of overseas surveys.

Revised on April 1, 2017

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		875,000	875,000
						Article 35, Paragraph 5, Item 1 (a)	
				Overseas		1,104,200 (+ overseas travel expenses)	1,104,200 (+ overseas travel expenses)
						Article 35, Paragraph 5, Item 1 (b) and (Article 35, Paragraph 7)	
		Packaging, labelling, or storage		In Japan		75,400	75,400
						Article 35, Paragraph 5, Item 2 (a)	
				Overseas		100,200 (+ overseas travel expenses)	100,200 (+ overseas travel expenses)
						Article 35, Paragraph 5, Item 2 (b) and (Article 35, Paragraph 7)	
		Testing institutions		In Japan		75,400	75,400
						Article 35, Paragraph 6, Item 1 (a)	
				Overseas		100,200 (+ overseas travel expenses)	100,200 (+ overseas travel expenses)
						Article 35, Paragraph 6, Item 1 (b) and (Article 35, Paragraph 7)	
	Renewal	Manufacturing sites other than those conducting only packaging, labelling, or storage	Basic	In Japan		875,000	875,000
						Article 35, Paragraph 5, Item 3 (a)-(1)	
				Overseas		1,104,200 (+ overseas travel expenses)	1,104,200 (+ overseas travel expenses)
						Article 35, Paragraph 5, Item 3 (a)-(2) and (Article 35, Paragraph 7)	
			Addition of products	In Japan		36,100	36,100
						Article 35, Paragraph 5, Item 3 (a)-(1)	
				Overseas		36,100	36,100
						Article 35, Paragraph 5, Item 3 (a)-(2)	
		Packaging, labelling, or storage	Basic	In Japan		305,700	305,700
						Article 35, Paragraph 5, Item 3 (b)-(1)	
				Overseas		399,900 (+ overseas travel expenses)	399,900 (+ overseas travel expenses)
						Article 35, Paragraph 5, Item 3 (b)-(2) and (Article 35, Paragraph 7)	
			Addition of products	In Japan		7,900	7,900
						Article 35, Paragraph 5, Item 3 (b)-(1)	
				Overseas		7,900	7,900
						Article 35, Paragraph 5, Item 3 (b)-(2)	
		Testing institutions	Basic	In Japan		305,700	305,700
						Article 35, Paragraph 6, Item 2 (a)	
				Overseas		399,900 (+ overseas travel expenses)	399,900 (+ overseas travel expenses)
						Article 35, Paragraph 6, Item 2 (b) and (Article 35, Paragraph 7)	
			Addition of products	In Japan		7,900	7,900
						Article 35, Paragraph 6, Item 2 (a)	
				Overseas		7,900	7,900
						Article 35, Paragraph 6, Item 2 (b)	

Revised on April 1, 2017

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 regenerative medical products					
	GLP	In Japan		2,492,600	2,492,600
				Article 35, Paragraph 4, Item 1 (a)	
		Overseas		2,758,700 + overseas travel expenses	2,758,700 + overseas travel expenses
				Article 35, Paragraph 4, Item 1 (b)	
GCP inspection of regenerative medical products					
	GCP	In Japan		767,700	767,700
				Article 35, Paragraph 4, Item 2 (a)	
		Overseas		1,110,100 + overseas travel expenses	1,110,100 + overseas travel expenses
				Article 35, Paragraph 4, Item 2 (b)	
GPSP inspection of regenerative medical products					
	GPSP	In Japan		738,400	738,400
				Article 35, Paragraph 4, Item 3 (a)	
		Overseas		1,146,900 + overseas travel expenses	1,146,900 + overseas travel expenses
				Article 35, Paragraph 4, Item 3 (b)	
Re-examination of regenerative medical products					
	Regenerative medical products		592,600	754,800 (+ overseas travel expenses)	1,347,400 (+ overseas travel expenses)
			Article 35, Paragraph 9	Article 35, Paragraph 10, Item 1 and (Article 35, Paragraph 11)	
	GLP for re-examination	In Japan		2,492,600	2,492,600
				Article 35, Paragraph 10, Item 2 (a)-(1)	
		Overseas		2,758,700 (+ overseas travel expenses)	2,758,700 (+ overseas travel expenses)
				Article 35, Paragraph 10, Item 2 (a)-(2) and (Article 35, Paragraph 11)	
	GPSP	In Japan		738,400	738,400
				Article 35, Paragraph 10, Item 2 (b)-(1)	
		Overseas		1,146,900 (+ overseas travel expenses)	1,146,900 (+ overseas travel expenses)
				Article 35, Paragraph 10, Item 2 (b)-(2) and (Article 35, Paragraph 11)	

Table 15. List of User Fees for Investigation

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	

Table 16. Classification of user fees, etc.

Revised January 4, 2018

(Yen)

		User fees				Timing of payment
Consultations						
Drugs/Quasi drugs	Procedural consultation for drugs	per consultation	150,900			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	261,500			
	Consultation for electronic study data submission (with recording)	per consultation	99,300			
	Consultation on bioequivalence testing, etc. for drugs	per consultation	600,400			
	Safety consultation for drugs	per consultation	1,925,300			
	Quality consultation for drugs	per consultation	1,596,500			
	Consultation before start of phase I study for drugs (non-orphan drugs)	per consultation	4,578,500			
	Consultation before start of phase I study for drugs (orphan drugs)	per consultation	3,441,000			
	Consultation before start of early phase II study for drugs (non-orphan drugs)	per consultation	1,752,800			
	Consultation before start of early phase II study for drugs (orphan drugs)	per consultation	1,320,200			
	Consultation before start of late phase II study for drugs (non-orphan drugs)	per consultation	3,737,800			
	Consultation before start of late phase II study for drugs (orphan drugs)	per consultation	2,807,000			
	Consultation after completion of phase II study for drugs (non-orphan drugs)	per consultation	7,419,900			
	Consultation after completion of phase II study for drugs (orphan drugs)	per consultation	5,573,700			
	Pre-application consultation for drugs (non-orphan drugs)	per consultation	7,419,900			
	Pre-application consultation for drugs (orphan drugs)	per consultation	5,570,400			
	Consultation on protocols of post-marketing clinical trials of drugs	per consultation	1,997,700			
	Consultation at completion of post-marketing clinical trials of drugs (preparation of application data, etc.)	per consultation	1,997,700			
	Consultation at completion of post-marketing clinical trials of drugs (review of conditions for approval, etc.)	per consultation	992,100			
	Additional consultation for drugs (non-orphan drugs)	per consultation	2,889,700			
	Additional consultation for drugs (orphan drugs)	per consultation	2,171,200			
	Consultation on epidemiological survey procedures for drugs	per consultation	150,900			
	Consultation on epidemiological survey plan for drugs	per consultation	3,007,900			
	Additional consultations on epidemiological surveys of drugs	per consultation	1,505,900			
	Consultation on prior confirmation of revision of package inserts for drugs	per consultation	99,200			
	Consultation on revision of package inserts for drugs	per consultation	4,987,400			
	Consultation on GLP/GCP/GPSP compliance for drugs	per consultation	3,549,200	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation on re-examination compliance for drugs	per consultation	1,797,200		+ overseas travel expenses	
	Consultation on compliance inspections of supporting data for revision of package inserts for drugs	per consultation	1,797,200		+ overseas travel expenses	
	Prior assessment consultation for drugs (quality)	per consultation	3,763,800			
	Prior assessment consultation for drugs (non-clinical: toxicity)	per consultation	2,544,000			
	Prior assessment consultation for drugs (non-clinical: pharmacology)	per consultation	2,544,000			
	Prior assessment consultation for drugs (non-clinical: pharmacokinetics)	per consultation	2,544,000			
	Prior assessment consultation for drugs (phase I study)	per consultation	4,301,100			
	Prior assessment consultation for drugs (phase II study)	per consultation	5,551,000			
	Prior assessment consultation for drugs (phase II / III study)	per consultation	8,622,300			
	Consultation on drug product eligibility for priority review	per consultation	1,016,100			
	Consultation on drug product eligibility for priority review (with pre-application consultation for drugs)	per consultation	208,200			
	Consultation on drug product eligibility for conditional expeditious approval	per consultation	1,016,100			
	Consultation on drug product eligibility for conditional expeditious approval (with pre-application consultation for drugs)	per consultation	208,200			
	Consultation on pharmacogenomics/biomarkers (qualification)	per consultation	3,270,600			
	Consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	1,199,900			
	Additional consultation on pharmacogenomics/biomarkers (qualification)	per consultation	995,700			
	Additional consultation on pharmacogenomics/biomarkers (key points of clinical trial protocols)	per consultation	435,300			
	Consultation on bioequivalence of generic drugs	per consultation	1,077,300			
	Quality consultations for generic drugs	per consultation	531,100			
	Consultation before minor change notification	per consultation	319,900			
	Pre-application consultation for switch OTC drugs	per consultation	1,621,200			
	Consultation on key points of clinical trial protocols for OTC drugs	per consultation	542,600			
	Consultation on appropriateness of development of new OTC drugs	per consultation	215,000			
	Consultation for human study plan confirmation for quasi drugs	per consultation	499,800			
	Consultation on new excipient development for quasi drugs	per consultation	249,800			
	Post-consultation for drugs (with recording)	per consultation	99,200			
	Consultation on GCP/GLP/GPSP for drugs	per consultation	347,000	(Conducted at the Kansai branch)** +280,000 yen		

(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 finalization of application dossiers for medical devices		per consultation	390,100			
	Consultation on finalization of application dossiers for medical devices (additional consultation)		per consultation	196,000			
	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	(Conducted at the Kansai branch)** +280,000 yen		
		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			

Revised January 4, 2018

(Yen)

			User fees				Timing of payment
Consultations							
Medical devices	Evaluation consultation for medical devices	Safety (2 tests)	per consultation	196,000			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	(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			
	Consultation on the evaluation of reprocessed single-use medical devices (QMS compliance confirmation)		per consultation	1,498,600		+ overseas travel expenses	

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(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 the development program of companion diagnostics		per consultation	1,541,600		
	Consultation on the development program of companion diagnostics (preliminary consultation completed)		per consultation	1,512,200		
	Consultation on protocol for *in vitro* diagnostics	Quality	per consultation	127,400		
		Quality (after the preparatory interview)	per consultation	89,100		
		Quality (additional consultation)	per consultation	60,800		
		Performance (other than quality) (1 test)	per consultation	127,400		
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	89,100		
		Performance (other than quality) (1 test) (additional consultation)	per consultation	60,800		
		Performance (other than quality) (2 tests)	per consultation	254,800		
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	216,500		
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	127,400		
		Performance (other than quality) (3 or more tests)	per consultation	381,900		
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	343,700		
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	191,100		
		Correlation	per consultation	254,800		
		Correlation (after the preparatory interview)	per consultation	216,500		
		Correlation (additional consultation)	per consultation	127,400		
		Clinical performance studies	per consultation	735,300		
		Clinical performance study (after the preparatory interview)	per consultation	688,000	(Conducted at the Kansai branch)** +280,000 yen	
		Clinical performance study (additional consultation)	per consultation	367,600		
		Clinical performance study for companion diagnostics	per consultation	2,353,100		
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	2,323,700		
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	1,176,500		
	Application procedure consultation for *in vitro* diagnostics		per consultation	78,300		
	Consultation on evaluation for *in vitro* diagnostics	Quality	per consultation	127,400		
		Quality (after the preparatory interview)	per consultation	89,100		
		Quality (unevaluated protocol)	per consultation	191,100		
		Quality (unevaluated protocol) (after the preparatory interview)	per consultation	150,100		
		Quality (additional consultation)	per consultation	60,800		
		Performance (other than quality) (1 test)	per consultation	127,400		
		Performance (other than quality) (1 test) (after the preparatory interview)	per consultation	89,100		
		Performance (other than quality) (1 test) (unevaluated protocol)	per consultation	191,100		
		Performance (other than quality) (1 test) (unevaluated protocol) (after the preparatory interview)	per consultation	150,100		
		Performance (other than quality) (1 test) (additional consultation)	per consultation	60,800		
		Performance (other than quality) (2 tests)	per consultation	254,800		
		Performance (other than quality) (2 tests) (after the preparatory interview)	per consultation	216,500		
		Performance (other than quality) (2 tests) (unevaluated protocol)	per consultation	381,900		
		Performance (other than quality) (2 tests) (unevaluated protocol) (after the preparatory interview)	per consultation	343,700		
		Performance (other than quality) (2 tests) (additional consultation)	per consultation	127,400		
		Performance (other than quality) (3 or more tests)	per consultation	381,900		
		Performance (other than quality) (3 or more tests) (after the preparatory interview)	per consultation	343,700		
		Performance (other than quality) (3 or more tests) (unevaluated protocol)	per consultation	573,500		
		Performance (other than quality) (3 or more tests) (unevaluated protocol) (after the preparatory interview)	per consultation	535,300		
		Performance (other than quality) (3 or more tests) (additional consultation)	per consultation	191,100		

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			User fees				Timing of payment
Consultations							
In vitro diagnostics	Consultation on evaluation for*in vitro* diagnostics	Correlation	per consultation	254,800	(Conducted at the Kansai branch)** +280,000 yen		Payment by the date of consultation application after arrangement of the consultation date
		Correlation (after the preparatory interview)	per consultation	216,500			
		Correlation (unevaluated protocol)	per consultation	381,900			
		Correlation (unevaluated protocol) (after the preparatory interview)	per consultation	343,700			
		Correlation (additional consultation)	per consultation	127,400			
		Clinical performance studies	per consultation	440,700			
		Clinical performance study (after the preparatory interview)	per consultation	396,600			
		Clinical performance study (unevaluated protocol)	per consultation	808,600			
		Clinical performance study (unevaluated protocol) (after the preparatory interview)	per consultation	764,500			
		Clinical performance study (additional consultation)	per consultation	220,500			
		Clinical performance study for companion diagnostics	per consultation	1,470,700			
		Clinical performance study for companion diagnostics (after the preparatory interview)	per consultation	1,441,300			
		Clinical performance study for companion diagnostics (unevaluated protocol)	per consultation	2,647,200			
		Clinical performance study for companion diagnostics (unevaluated protocol) (after the preparatory interview)	per consultation	2,617,700			
		Clinical performance study for companion diagnostics (additional consultation)	per consultation	733,000			
Regenerative medical products	Procedural consultation for regenerative medical products		per consultation	141,600	(Conducted at the Kansai branch)** +280,000 yen		
	Consultation before the start of expanded clinical trials for regenerative medical products		per consultation	261,400			
	Pre-development consultation for regenerative medical products		per consultation	314,700			
	Pre-development consultation for regenerative medical products (additional consultation)		per consultation	157,300			
	Non-clinical consultation for regenerative medical products (effectiveness)		per consultation	944,400			
	Non-clinical consultation for regenerative medical products (effectiveness) (additional consultation)		per consultation	472,100			
	Non-clinical consultation for regenerative medical products (safety)		per consultation	993,500			
	Non-clinical consultation for regenerative medical products (safety) (additional consultation)		per consultation	496,800			
	Quality consultation for regenerative medical products		per consultation	993,500			
	Quality consultation for regenerative medical products (additional consultation)		per consultation	496,800			
	Consultation on qualification of materials for regenerative medical products		per consultation	496,800			
	Consultation before therapeutic exploratory study for regenerative medical products		per consultation	1,153,400			
	Consultation before therapeutic exploratory study for regenerative medical products (additional consultation)		per consultation	577,100			
	Consultation after therapeutic exploratory study for regenerative medical products		per consultation	1,318,200			
	Consultation after therapeutic exploratory study for regenerative medical products (additional consultation)		per consultation	659,600			
	Prior assessment consultation for regenerative medical products (safety, quality, effectiveness)		per consultation	2,878,300			
	Prior assessment consultation for regenerative medical products (therapeutic exploratory study)		per consultation	1,318,200			
	Prior assessment consultation for regenerative medical products (confirmatory clinical study)		per consultation	2,878,300			
	Pre-application consultation for regenerative medical products		per consultation	2,878,300			
	Pre-application consultation for regenerative medical products (additional consultation)		per consultation	1,439,100			
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)		per consultation	1,318,200			
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)		per consultation	659,600			
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)		per consultation	989,400			
	Consultation on protocols of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)		per consultation	494,600			
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol)		per consultation	1,318,200			
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (with protocol) (additional consultation)		per consultation	659,600			
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation)		per consultation	989,400			
	Consultation at completion of clinical trials for regenerative medical products after the conditional time-limited authorization (only for investigation) (additional consultation)		per consultation	494,600			

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		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	1,318,200	(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	659,600			
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	989,400			
	Consultation on protocols of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	494,600			
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol)	per consultation	1,318,200			
	Consultation at completion of post-marketing clinical trials for regenerative medical products (with protocol) (additional consultation)	per consultation	659,600			
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation)	per consultation	989,400			
	Consultation at completion of post-marketing clinical trials for regenerative medical products (only for investigation) (additional consultation)	per consultation	494,600			
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products	per consultation	479,600			
	Consultation on GLP/GCP (including GCTP) compliance for regenerative medical products (additional consultation)	per consultation	237,500			
	Pre-consultation for regenerative medical products (with recording)	per consultation	99,200			
	Post-consultation for regenerative medical products (with recording)	per consultation	99,200			
SAKIGAKE comprehensive evaluation consultation	SAKIGAKE comprehensive evaluation consultation for drugs (quality)	per consultation	3,597,200	(Conducted at the Kansai branch)** +280,000 yen		
	SAKIGAKE comprehensive evaluation consultation for drugs (non-clinical)	per consultation	5,999,500			
	SAKIGAKE comprehensive evaluation consultation for drugs (clinical)	per consultation	7,193,800			
	SAKIGAKE comprehensive evaluation consultation for drugs (reliability)	per consultation	3,589,000			
	SAKIGAKE comprehensive evaluation consultation for drugs (GMP)	per consultation	3,586,800		+ 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	1,799,600			
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (non-clinical)	per consultation	2,997,300			
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (clinical)	per consultation	3,598,500			
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (reliability)	per consultation	1,798,300			
	SAKIGAKE comprehensive evaluation consultation for regenerative medical products (GCTP)	per consultation	1,798,300		+ overseas travel	
Regulatory Science (RS) Strategy Consultation (R&D)	RS Strategy Consultation (R&D) for drugs	per consultation	1,541,600	(Conducted at the Kansai branch)** +280,000 yen		
	RS Strategy Consultation (R&D) 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			
	RS Strategy Consultation (R&D) for medical devices	per consultation	874,000			
	RS Strategy Consultation (R&D) for medical devices (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	87,400			
	RS Strategy Consultation (R&D) for regenerative medical products	per consultation	874,000			
	RS Strategy Consultation (R&D) for regenerative medical products (universities/research institutions and venture companies meeting requirements specified separately*)	per consultation	87,400			
	RS Strategy Consultation (R&D) for development plans, etc.	per consultation	73,600			

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(Yen)

					Timing of payment
Consultations					
Simple consultations	Generic drugs		per consultation	22,600	Payment by the date of consultation application after arrangement of the consultation date
	OTC drugs		per consultation	22,600	
	Quasi-drugs (including pest control agents)		per consultation	22,600	
	Medical devices or *in vitro* diagnostics		per consultation	39,400	
	Simple consultations on the prior confirmation of protocol change notifications for medical devices		per consultation	39,400	Payment by the date of written consultation application
	New drugs		per consultation	22,600	Payment by the date of consultation application after arrangement of the consultation date
	Regenerative medical products		per consultation	22,600	
	GCP/GLP/GPSP for drugs		per consultation	20,300	
	GCP/GLP/GPSP for medical devices		per consultation	19,400	
	GCP/GLP/GPSP for regenerative medical products		per consultation	20,400	
	GMP/QMS inspection		per consultation	25,400	
	GCTP inspection		per consultation	26,700	
GLP inspection of test facilities					
All test items	Basic fee	With animal-rearing facility	per facility	1,364,500	Request to PMDA after advanced payment
		Without animal-rearing facility	per facility	839,400	
	Additional fee for target tests	General toxicity studies	per study	419,600	
		Reproduction toxicity studies	per study	209,800	
		Safety pharmacology core battery (only for drugs)	per study	209,800	
		Hemocompatibility studies (only for medical devices)	per study	209,800	
		In vitro studies	per study	209,800	
		Other studies (dependence, TK, pathology, and other studies)	per study	209,800	
	Additional fee for target classification	Drugs	per facility	209,800	
		Medical devices	per facility	209,800	
		Regenerative medical products	per facility	209,800	
Additional compliance accreditation			per facility	1,007,200	
Additional inspection			per inspection from the second inspection onwards	416,300	
Confirmation of certification on drugs, etc.					
GMP certification on investigational products (with on-site inspection)			per product of one facility	798,900	Request to PMDA after advanced payment
GMP certification on investigational products (without on-site inspection)			per product of one facility	16,200	
Certification of drug products			per product	16,200	
Other certifications (including GMP/QMS certification)			per matter of one product	9,100	
Fee for the video conference system at the Kansai Branch (consultations on safety measures)					
			per consultation	70,000	Payment by the date of consultation application after scheduling
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 video conference 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], simple consultations, and consultations on safety measures)

Appendix 1

Mid-term Targets of the Pharmaceuticals and Medical Devices Agency (PMDA)
(Provisional Translation)

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

Instruction No. 0307-73 (dated March 7, 2014) of
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare (MHLW)

Targets to be achieved by the Pharmaceuticals and Medical Devices Agency in its operation management shall be established as below, based on the provision of Article 29, Paragraph 1 of the Act on General Rules for Incorporated Administrative Agency for Incorporated Administrative Agency (Act No. 103, 1999),.

March 7, 2014

Minister of Health, Labour and Welfare
Norihisa Tamura

Part 1
Effective Period for Mid-term Targets
The effective period for Mid-term Targets according to Article 29, Paragraph 2, Item 1 of the Act on General Rules for Incorporated Administrative Agency (Act No. 103, 1999) shall be 5 years, from April 2014 through March 2019.

Part 2
Matters Regarding Improvement in Operation Management of the Overall Corporation and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public
The targets related to the overall corporation regarding improvement in efficiency of operations, as stipulated in Article 29, Paragraph 2, Item 2 of the Act on General Rules for Incorporated Administrative Agency, and the targets regarding improvement in the quality of services and other operations rendered to the public, as stipulated in Article 29, Paragraph 2, Item 3 of the Act on General Rules for Incorporated Administrative Agency, shall be as follows.

1) Efficient and Flexible Management of Operations

a) The Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the “PMDA”) shall establish an efficient and flexible system for managing operations, confirm the way of operational control and methods for implementing operations through external evaluation, and improve the management of operations based on the following points.
- Improve internal controls including the way of implementing duties in accordance with instructions from accounting auditors, and proactively disclose measures taken.
- Examine the way of internal control by utilizing professional knowledge from experts of third-parties.
- PMDA shall refer to the matters that were notified to each evaluation committee of the incorporated administrative agencies of the government ministries, which are opinions on the report (*Internal Control and Evaluation in Incorporated Administrative Agencies*) released by the Study Group on Internal Control and Evaluation in Incorporated Administrative Agencies held by the Ministry of Internal Affairs and Communications, and opinions on evaluation results of the operating performance in incorporated administrative agencies from the Ministry of Internal Affairs and Communications and the Evaluation Committee of Incorporated Administrative Agencies.

b) Promote computerization of the operations to increase efficiency of the operation management system.

c) Based on a re-examination of systems control operation of the common information and the review operation, PMDA shall control costs by re-examining the system configuration of the overall PMDA and its procurement method, in order to reduce system costs, to ensure transparency of system procurement, and to streamline operation management.
For this reason, PMDA shall promote approaches to optimize operations and systems by integrating the individual review systems and by establishing a system to promote information sharing among review services, post-marketing safety measures, and relief services for adverse health effects, based on the Optimization Plan for Operations and Systems established at the end of FY 2007.

2) Improvement of Operation Management

a) By continuously improving the operation and increasing efficiency in management, the following reduction in the budget for the Mid-term Plan is expected to have been achieved by the end of the effective period for Mid-term Targets, regarding general administrative expenses (excluding personnel expenses) in which the administrative subsides are to be applied.
- No less than 15% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase in personnel, etc.).

b) By increasing efficiency in operations, the following reduction, regarding operating expenses (excluding personnel expenses, and single fiscal-year expenses, etc., that were paid for the establishment of operations) in which the administrative subsidies are to be applied, is expected to be made by the end of the effective period for Mid-term Targets.
- No less than 5% as compared to FY 2014.
- Appropriately utilize outsourcing (outsource when possible to prevent increase of personnel, etc.).

c) Yearly administrative subsidies are to be rigorously calculated with consideration of its debt balance.

d) Promote efficiency and improvements of operations by consolidating the management of the marketing authorization holder’s product data, etc. of contributions for adverse drug reaction (ADR), contributions for relief for infections, and contributions for post-marketing safety measures.

e) As a general rule, contracts shall be concluded through open competitive bidding, etc., and the following approaches shall be made.
- Fully secure competitiveness and transparency even when contracts are not concluded by open competitive bidding such as planning competition and invitation to bids.
- Conduct bids and conclude contracts appropriately, by having them thoroughly checked by auditors and accounting auditors as well as by utilizing opinions of experts.

f) Provide and disseminate genuinely useful information from the public perspective
Let the public be aware of the services and role of PMDA by disseminating and providing information from the public’s perspective, which enables the public and patients to readily access to the information they need. Enhance the consultation system and ensure transparency of operations and its details in order to improve the services rendered to the public.

g) Analyze issues of the operation system
Analyze the issues of the operation system appropriately and revise them if necessary.
h) Considerations related to financial base
Consider a financial base that is appropriate for the role of PMDA and take necessary measures.

Part 3
Matters Regarding Improvement in Operation Management of Each Division and Matters Regarding Improvement in the Quality of Services and Other Operations Rendered to the Public

1. Relief Fund Services for Adverse Health Effects

With regard to the relief fund services for Adverse Health Effects (hereinafter referred to as "relief services"), it is important not only to fully disseminate more people the Adverse Drug Reaction Relief System and the Relief System for Infections Acquired through Biological Products (hereinafter referred to as "relief systems") and appropriately operate them, but also adequately and promptly provide relief for those suffering from ADR and infections acquired through biological products or regenerative medical products (hereinafter, including cellular and tissue-based products and gene therapy products).

Based on this concept, the following targets shall be achieved.

1) Enhance Public Relations and Dissemination of Information Regarding the Relief Systems

a) Conduct proactive public relations so that the relief systems are definitely utilized when necessary.
b) Make more efficient operations by reducing the number of cases where inadequate operations of claim documents, etc., result in need of extra processing time.

2) Promptly Process Relief Benefit Claims by Investigating and Organizing the Facts of the Claims

a) Promptly process relief benefit claims
b) Set up standard administrative processing times* and steadily achieve those standards.
* Standard administrative processing time includes a certain period for medical and pharmaceutical judgments of the Ministry of Health, Labour and Welfare. However, administrative processing time shall exclude the period when processing could not be continued because additional or supplementary documents and investigations of the claimant or medical institutions were required to make medical and pharmaceutical judgments.

3) Promote Appropriate Information Transmission in cooperation with Divisions

Cooperation shall be promoted among the divisions of PMDA, and information especially regarding cases of relief payment shall be appropriately disseminated to the Review Divisions and the Safety Measures Divisions, with attention to ensuring protection of personal information.

4) Implement Appropriate Health and Welfare Services

Steadily implement health and welfare services.

5) Appropriately Provide Healthcare Allowances to SMON Patients and Patients infected with HIV through Blood Products

Appropriately conduct services regarding healthcare allowances to SMON patients and HIV-positive patients infected with blood products.

6) Appropriately Pay Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus

Appropriately conduct services regarding payment of benefits to assist individuals affected by hepatitis C through specified fibrinogen products and specified blood coagulation factor IX products contaminated by hepatitis C virus.

2. Reviews and Related Services

In the review services and post-marketing safety measures, PMDA shall enable better pharmaceuticals and medical devices, etc., to be provided to medical settings more promptly and safely, so that the public can use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

Along with this conception, and based on the Japan Revitalization Strategy (adopted by the Cabinet on June 14,2013) and the Healthcare and Medical Strategy (an agreement among the Chief Cabinet Secretary, Minister of Health, Labour and Welfare, and Minister of Internal Affairs and Communications on June 14, 2013) , Act to Ensure Quality, Efficacy, and Safety of Pharmaceuticals and Medical Devices (Act No. 145, 1960) that were revised as a result of the Act for Partial Revision of the Pharmaceutical Affairs Act, (Act No. 84, 2013) , as well as the Act to Ensure Safety of Regenerative Medicine (Act No. 85, 2013), etc. , PMDA shall accelerate reviews speed for s and medical devices, aim to achieve elimination of review lag*, and aim to improve the quality of the reviews, etc. Pharmaceutical Affairs Consultation on R&D Strategy, etc., shall also be enhanced as a support to eliminate the developmental lag*.
In order to achieve these targets, PMDA's financial resources shall be utilized in enhancing the system.
*Drug lag and device lag are defined as delay of approvals of pharmaceuticals and medical devices, respectively, from United States in Japan. Drug lag or device lag can be divided into review lag, which are differences in review time (time from application to approval) between the United States and Japan, and development lag, which are differences in time at which the companies submit applications to the regulatory agencies of the United States and Japan (from the Japan Revitalization Strategy [approved by the Cabinet on June 14, 2013]).
The overall lag shall be eliminated by eliminating the review lag and development lag.

Following measures shall be promoted in order for the above mentioned measures to be implemented appropriately and smoothly, while maintaining cooperation with MHLW.

1) Make pharmaceuticals, medical devices, etc. accessible by the public more quickly

Efforts shall be made to enable the public and healthcare professionals to promptly gain advantage of advanced and safe pharmaceuticals and medical devices, etc., based on their needs so that they can receive the maximum benefit from them.
PMDA shall proactively support and cooperate with MHLW and its approaches, including acceleration of clinical trials, to promote development of pharmaceuticals and medical devices that are still unapproved in Japan but are of high medical need, in order to reduce development lag.

a) Conduct various measures, while evaluating and verifying their state of progress, and take additional measures when necessary.
b) In order to achieve reduce review lag while improving the quality of reviews, PMDA shall improve the services by setting time reduction targets (targets at ordinary times without any exceptional cases such as substantial changes in the systems or social conditions) for the processing time of applications (regulatory review time for products approved in the respective years) that were submitted after April 1, 2004. PMDA shall develop a review system to achieve these targets.
c) Promote multiregional clinical trials by cooperating with the United States, Europe, and Asian countries.
d) Prioritize clinical trial consultations for pharmaceuticals and medical devices that are expected to be highly useful by enhancing pre-application consultations, so as to reduce review period.

Correctly understand the accurate needs of companies at the stage of development and reevaluate system of the consultation service whenever necessary.

e) Improve PMDA's own scientific levels for skills of consultations and reviews, with consideration of the rapid development of the latest technologies such as biotechnology, genomics, and regenerative medicine, and shall take necessary measures for the consultations and reviews along with the development of new pharmaceuticals, new medical devices, and regenerative medical products that utilize the latest technologies.

f) Take necessary measures to accelerate reviews for generic drugs, etc., as in the case of new pharmaceuticals.

g) Take measures to accelerate reviews for behind-the-counter (BTC) drugs*, over-the-counter (OTC) drugs, and quasi-drugs as with new pharmaceuticals.
*Behind-the counter (BTC) drugs are defined as switch OTC drugs and powerful OTC drugs which require pharmacist's intervention.

h) Set targets to aim for eliminating review lag for medical devices, as with new pharmaceuticals, and take measures to accelerate reviews. Develop a review system to achieve these targets.
Regarding reviews of improved medical devices and generic medical devices, PMDA shall take measures to systematically and intensively review items which had taken long time for the reviews after submission, and shall make efforts to reduce the applicant's time (the time within the review time that is necessary for the applicants to reply to inquiries from the regulatory side).

i) Take measures to accelerate reviews for regenerative medical products by enhancing the relevant review divisions necessary to conduct accurate and prompt reviews, while introducing conditional and time-limited approval system as well as setting target review times.

j) Appropriately and efficiently conduct conformity inspections.

k) Conduct appropriate and efficient GMP/QMS/GCTP (Good gene, Cellular and Tissue Practice) etc. inspections.

2) Provide Support to be the First in the World to Facilitate Practical Use of Innovative Pharmaceuticals, Medical Devices, and Regenerative Medical Products

Make the following approaches in order to be first in the world to facilitate practical use of innovative pharmaceuticals, medical devices, and regenerative medical products.

a) Establish and update review standards for innovative products.

b) Proactively conduct Pharmaceutical Affairs Consultation on R&D Strategy, etc.

c) Operate the approval system based on the characteristics of regenerative medical products.

3. Safety Measures

In the review services and post-marketing safety measures, PMDA shall promptly and safely provide superior pharmaceuticals and medical devices, etc., to medical settings in order to enable the public to use global standard pharmaceuticals and medical devices, etc., at ease. It is important to ensure that pharmaceuticals and medical devices, etc., are appropriately used, prevent health hazards from occurring while accurately and promptly taking measures in cases where health hazards occur, and make pharmaceuticals and medical devices, etc., fulfill their mission in the long term.

In accordance with this concept, utilize finances including PMDA's own financial resource and enhance the system when necessary to improve post-marketing safety measures of pharmaceuticals and medical devices, etc., based on the Act for Partial Revision of the Pharmaceutical Affairs Act that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.

a) Systematically and continuously conduct comprehensive evaluations of information on ADR, Malfunction, and Adverse Reaction (here in after ADR, etc.), by substantially enhancing assemble of information on ADR, etc., and its evaluation analysis system in order to accurately respond to the advanced and specialized evaluation of information on ADR, etc. Furthermore, find out new relationships among multiple ADR information, and establish an efficient and effective evaluation system for safety information such as researching and utilizing methods to identify and analyze new safety information, and improved it when necessary, by using IT technology.

b) Have healthcare professionals and companies increase utilization of feedback information on the analysis results of collected safety information, etc., and enhance methods of disseminating information on appropriate use to the patients, in order to enhance the rigorous system for disseminating safety information to improve safety measures at medical institutions. At the same time, PMDA shall also establish standards that enable the accomplishments of safety measures to be more accurately understood in a manner in which the public are able to understand easily.

c) Conduct appropriate post-marketing safety measures based on the Risk Management Plan of pharmaceuticals.

d) Cooperation shall be promoted among the relief services and the review services to enable appropriate assessment of safety.

e) Establish a system that enables confirmation of the current status and effectiveness of post-marketing safety measures taken by PMDA in companies and medical institutions, etc.

f) Appropriately collect information on Adverse Reaction reports regulated in the Preventive Vaccination Act and appropriately conduct investigations and analyses.

4. Promotion of Regulatory Science, Globalization, etc.

Note: Regulatory science = Science for coordinating results of science and technology into the most desirable form for harmonizing people and society, by conducting accurate and evidence-based estimations, evaluations, and decisions in order for the results of science and technology to be used for people and society. (from the Science and Technology Basic Plan, adopted by the Cabinet on August 19, 2011)

a) Enhance regulatory science research
Develop an environment and system for conducting regulatory science research (hereinafter referred to as the "RS research") aimed at improving the quality of the services provided by PMDA. Make efforts to train human resources to be experts in RS research through conducting it, and make efforts to contribute to increase the efficiency of development of pharmaceuticals, etc., through establishment of guidelines, etc.

b) Response to globalization
Reinforce partnerships with foreign regulatory agencies, promote global harmonization activity to proactively collect foreign information, and make efforts to promote dissemination of information in English.
Furthermore, enhance the English website of PMDA, and enhance measures in order for Asian countries to increase their understanding of Japanese regulations and standards regarding pharmaceutical applications, etc.

c) Enhance staff training
By enhancing staff training, PMDA shall establish a group of engineering supervisors that have a global level in review services and post-marketing safety measures so as to increase the quality of the services, and shall make efforts to train human resources to be experts in RS research.

d) Promote interaction with external researchers and investigative research
Promote investigative research by proactively interacting with external researchers in order to contribute to activate development and to establish guidelines regarding innovative seed-stage resources.

e) Promptly facilitate practical use of pharmaceuticals for intractable diseases and orphan diseases.
f) Promote further transparency of review services and post-marketing safety measures such as revealing in public review reports.
g) Develop an information system basis that ensures reliability and increases efficiency of review services and post-marketing safety measures.

Part 4
Matters Regarding Improvement in Financial Affairs

The following is the target for improving financial affairs specified in Article 29, Paragraph 2, Item 4 of the Act on General Rules for Incorporated Administrative Agency.

For matters specified in Part 2, items 1) and 2) of this Mid-term Targets, a Mid-term budget shall be developed with an estimation of cost reductions, and PMDA shall operate based on this budget.

Part 5
Important Matters Regarding Other Operation Management

The following are important targets regarding other operation management specified in the Article 29, Paragraph 2, Item 5 of the Act on General Rules for Incorporated Administrative Agency.

1) Matters Regarding Personnel Affairs
a) Secure enough personnel necessary to reviews and post-marketing safety measures, based on the Act for Partial Revision of the Pharmaceutical Affairs Act, etc., that reflects the details of Japan Revitalization Strategy, the Healthcare and Medical Strategy, and the final recommendation of the Committee for Investigation of Pharmaceutical-induced Hepatitis Cases and Appropriate Regulatory Administration to Prevent Similar Sufferings, etc.
In order to avoid any suspicion of inappropriate relationships with pharmaceutical companies, etc., PMDA shall take appropriate measures in employment, allocation, post-retirement reemployment, etc., of executives and employees, while thoroughly ensuring its neutrality, etc.
PMDA shall make efforts to adjust the salary levels of the employees to achieve an appropriate and efficient level, taking into consideration competitiveness for stable securement of excellent human resources.
b) Appropriately develop personnel capacities by having them interact with external institutions to increase their expertise, and appropriately conduct personnel evaluations based on their work performance. PMDA shall also increase motivation of the personnel through these measures, etc.

2) Ensure Security
Ensure security of the offices, etc. and take all measures to thoroughly manage information, in order to thoroughly protect information of personal, corporate, etc.

3) Matters Regarding Disposition of the Reserve Funds Specified in Article 31, Paragraph 1 of the Act on the Pharmaceuticals and Medical Devices Agency
Appropriately dispose the reserve funds that are still left even after adjusting profit and loss according to Article 44 of the Act on General Rules for Incorporated Administrative Agency at the end of the last fiscal-year of the effective period for the Second Mid-term Targets.

4) Other Matters
Steadily conduct approaches based on the government policy indicated in past Cabinet decisions, etc.

Appendix 2

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.

Appendix 3

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.

Appendix 4

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.

Appendix 5

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.

Appendix 6

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.

Appendix 7

Budget for FY 2017 (after the passage of the first supplementary budget for FY 2017)

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			979	985	1,963				1,963
Governmental subsidies	179	121	392	940	1,332				1,632
Contributions	4,249	100		3,416	3,416	3,650			11,415
User fees			10,373		10,373				10,373
Commissioned operations			248		248		955	647	1,850
Management income	299	68	1	0	2				368
Miscellaneous income	1	0	30	6	36	0	1	1	40
Total	4,728	288	12,023	5,347	17,370	3,650	956	648	27,641
Expenditure									
Operating expenses	3,143	204	11,241	4,663	15,904	5,731	948	643	26,573
Personnel expenses	244	26	5,762	1,386	7,149	20	45	22	7,505
Administrative expenses	2,899	178	5,478	3,277	8,755	5,711	903	621	19,067
General administrative expenses	216	16	2,501	672	3,174	2	8	5	3,421
Personnel expenses	67		708	192	900				966
Non-personnel expenses	150	16	1,793	481	2,274	2	8	5	2,455
Total	3,359	220	13,742	5,336	19,077	5,733	956	648	29,993

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

Appendix 8

Income and Expenditure Plan for FY 2017 (after the passage of the first supplementary budget for FY 2017)

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	5,763	367	14,749	5,599	-42	20,306	5,734	958	642	33,769
Relief benefits	2,445	32								2,477
Operating expenses for health and w elfare	31	104								135
Operating expenses for review s			3,820			3,820				3,820
Operating expenses for safety measures				2,371		2,371				2,371
Specified relief benefits							5,688			5,688
Benefits (healthcare allow ances, etc.)								885		885
Benefits (special allow ances, etc.)									245	245
Operating expenses for research and study									351	351
Provision for liability reserve	2,341	132								2,473
Other administrative expenses	722	82	8,321	2,534		10,855	43	62	40	11,804
Personnel expenses	225	24	5,162	1,278		6,439	18	41	21	6,767
Depreciation expenses	67	15	1,267	926		2,193	0	1	2	2,278
Retirement benefit expenses	10	2	249	60		309	1	1	0	324
Provision for accrued bonuses	8	1	304	46		350	1	2	1	363
Other expenses	412	41	1,340	224		1,564	23	16	16	2,072
General administrative expenses	222	16	2,606	693	-42	3,258	3	9	5	3,514
Personnel expenses	65		627	177		804				869
Depreciation expenses	0		197	0		197				197
Retirement benefit expenses	0		29	6		36				36
Provision for accrued bonuses	2		47	11		58				60
Other expenses	156	16	1,706	499	-42	2,164	3	9	5	2,353
Financial expenses	0		1	0		1				1
Miscellaneous losses	1	1		1		1		1	1	5
Ordinary income	4,689	285	12,081	5,074	-42	17,113	5,734	956	648	29,425
Governmental subsidies	179	121	392	534		926				1,226
Administrative subsidies			979	970		1,948				1,948
Other governmental grants							46			46
Contributions	4,249	100		3,416		3,416				7,765
User fees			10,373			10,373				10,373
Gain on reversal of specified relief fund deposit received							5,688			5,688
Commissioned operations			248			248		955	647	1,850
Reversal of asset offset subsidies			32	130		162	0			162
Reversal of asset offset administrative subsidies			0	24		24				24
Reversal of asset offset gifts received			4			4				4
Financial income (no operating income)	261	64	1	0		2				327
Miscellaneous income			52	0	-42	10		1	1	12
Ordinary net income or loss	-1,073	-82	-2,667	-525		-3,193	0	-2	6	-4,344
Current net income or loss before tax	-1,073	-82	-2,667	-525		-3,193	0	-2	6	-4,344
Current net income or loss	-1,073	-82	-2,667	-525		-3,193	0	-2	6	-4,344
Reversal of appropriated surplus	-	-	1,616	942		2,558	-	-	-	2,558
Current gross income or loss	-1,073	-82	-1,051	417		-634	0	-2	6	-1,786

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

Appendix 9

Cash Flow Plan for FY 2017 (after the passage of the first supplementary budget for FY 2017)

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	3,404	246	13,920	5,114	-45	18,988	5,733	971	649	29,991
Relief benefits	2,456	31								2,487
Operating expenses for health and welfare	32	104								136
Operating expenses for reviews			5,747			5,747				5,747
Operating expenses for safety measures				3,069		3,069				3,069
Administrative expenses	455	53					23	16	10	558
Specified relief benefits							5,688			5,688
Benefits (healthcare allowances, etc.)								885		885
Benefits (special allowances, etc.)									245	245
Operating expenses for research and study									351	351
General administrative expenses	151	31	1,751	270		2,021	2	8	4	2,218
Personnel expenses	298	24	6,172	1,506		7,679	19	44	22	8,085
Repayment money	1	1		1		1		1	1	5
Other cash outflow from operating activities	11	1	249	267	-45	472	1	16	15	515
Cash outflow from investing activities	4,009	500	369	350		719			8	5,237
Amount carried forward to next fiscal year	2,909	511	8,156	2,502		10,658	727	27	132	14,963
Total	10,322	1,257	22,444	7,966	-45	30,366	6,459	998	789	50,191
Cash Inflows										
Cash inflows from operating activities	4,731	289	13,508	5,360	-45	18,823	3,641	956	648	29,089
Contributions	4,249	100		3,416		3,416	3,641			11,406
Administrative subsidies			979	985		1,963				1,963
Governmental subsidies	179	121	392	940		1,332				1,632
User fees			11,746			11,746				11,746
Commissioned operations			248			248		955	647	1,850
Amount of interests received	299	68	1	0		2				368
Other incomes	4	1	141	19	-45	116	0	1	1	124
Cash inflows from investing activities	2,701	500								3,201
Amount carried forward from previous fiscal year	2,890	467	8,936	2,606		11,543	2,818	42	141	17,901
Total	10,322	1,257	22,444	7,966	-45	30,366	6,459	998	789	50,191

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

Appendix 10

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.

Appendix 11

Balance Sheet (corporate basis)

(As of March 31, 2018)

Unit: yen

Account item	Amount		Account item	Amount	
Assets			Liabilities		
I Current assets			I Current liabilities		
Cash and deposits		21,232,673,760	Accrued benefits		332,077,221
Securities		3,602,350,538	Accounts payable		2,007,037,271
Expenses for work-in-process reviews, etc.		1,416,017,114	Advances received		8,308,782,281
Prepaid expenses		2,500,260	Deposits received		137,544,960
Accounts due		375,593,887	Allowance		
Accrued income		44,541,510	Accrued bonuses	573,575,946	573,575,946
Other current assets		354,081	Total of current liabilities		11,359,017,679
Total of current assets		26,674,031,150	II Fixed liabilities		
			Per contra liabilities for property acquisition		
			Administrative subsidies for assets as per contra	58,284,337	
II Fixed assets			Governmental subsidies, etc. for assets as per contra	515,949,176	
Tangible fixed assets			Contributions for assets as per contra	28,050,784	
Tools, equipment and fixtures	3,857,166,826		Amount of received goods for assets as per contra	457,240	602,741,537
Cumulative total of depreciation	-2,535,473,050	1,321,693,776	Deposits of specific relief funds		
Building and accompanying facilities	58,867,674		Long-term deposit subsidy, etc.	98,282,351	
Cumulative total of depreciation	-6,340,683	52,526,991	Deposit contribution	3,003,436,642	3,101,718,993
			Allowances		
			Allowances for retirement benefits	2,948,099,936	2,948,099,936
Total of tangible fixed assets		1,374,220,767	Liability reserve		25,347,394,341
			Total of fixed liabilities		31,999,954,807
Intangible fixed assets			Total of liabilities		43,358,972,486
Software		3,533,231,510	Net assets		
Software in progress		115,236,000	I Capital funds		
Telephone subscription right		286,000	Government investment		1,179,844,924
Total of intangible fixed assets		3,648,753,510	Total of capital funds		1,179,844,924
Investments and other assets			II Capital surplus		
Investment securities		37,133,534,045	Capital reserves		4,670,640
Rental deposit		13,272,360	Cumulative total of depreciation that are not recorded as expenses (-)		-677,118,623
Total of investments and other assets		37,146,806,405	Loss on retirement or sale of fixed assets that are not recorded as expenses (-)		-113,407,005
			Total of capital surplus		-785,854,988
Total of fixed assets		42,169,780,682	III Retained earnings		25,090,849,410
			Total of net assets		25,484,839,346
Total of assets		68,843,811,832	Total of liabilities and net assets		68,843,811,832

Appendix 12

Profit and Loss Statement (Corporate basis)

(From April 1, 2017 to March 31, 2018)

Unit: yen

Account item	Amount		
Ordinary expenses			
Adverse reaction relief benefits		2,351,544,702	
Infection relief benefits		586,866	
Operating expenses for health and welfare		123,924,597	
Operating expenses for reviews		2,980,865,722	
Operating expenses for safety measures etc.		1,628,735,093	
Specific relief benefits		1,020,000,000	
Benefits for healthcare allowances, etc.		855,350,672	
Benefits for special allowances, etc.		219,265,200	
Investigative research		283,700,200	
Provision of liability reserves		2,682,250,772	
Other operating expenses			
Personnel expenses	6,559,491,713		
Depreciation expenses	2,263,522,381		
Retirement benefit expenses	647,509,233		
Provision for accrued bonuses	382,899,078		
Estate rental fees	1,575,679,505		
Other expenses	454,357,036	11,883,458,946	
General administrative expenses			
Personnel expenses	867,971,332		
Depreciation expenses	211,433,390		
Retirement benefit expenses	78,526,628		
Provision for accrued bonuses	68,827,485		
Estate rental fees	229,155,456		
Other expenses	1,280,795,785	2,736,710,076	
Financial expenses			
Interest paid		436,316	
Miscellaneous losses		25,050,888	
Total of ordinary expenses			26,791,880,050
Ordinary revenues			
Administrative subsidies		1,966,614,643	
User fees		11,225,163,292	
Contributions		7,931,248,300	
Commissioned operations for government		50,606,309	
Commissioned operations for others		1,459,468,936	
Revenue from governmental subsidies		825,212,312	
Reversal of provision for deposits of specific relief funds			
Revenues from contributions		1,020,000,000	
Revenue from contributions		20,423,146	
Return of administrative subsidies for assets as per contra		23,785,445	
Return of subsidies, etc. for assets as per contra		172,865,259	
Return of contributions for assets as per contra		3,543,258	
Return of amount of received goods for assets as per contra		265,102	
Return of liability reserves		996,261	
Financial revenue			
Interest received	193,963		
Interest on securities	327,847,180	328,041,143	
Miscellaneous gains		10,685,184	
Total of ordinary revenues			25,038,918,590
Ordinary losses			-1,752,961,460
Extraordinary losses			
Loss on disposal of fixed assets		299,101	299,101
Current net losses			-1,753,260,561
Reversal of reserve carried forward from the previous Mid-term target period			2,665,137,488
Current gross profit			911,876,927

Appendix 13

Cash Flow Statement (corporate basis)

(From April 1, 2017 to March 31, 2018)

Unit: yen

Account item	Amount
I. Cash flow from operating activities	
Expenditure for adverse reaction relief benefits	-2,340,073,657
Expenditure for infection relief benefits	-586,866
Expenditure for operating expenses for health and welfare	-123,919,618
Expenditure for operating expenses for reviews	-3,650,435,553
Expenditure for operating expenses for safety measures	-1,424,201,714
Expenditure for specific relief benefits	-1,020,000,000
Expenditure for benefits for healthcare allowances, etc.	-865,387,392
Expenditure for benefits for special allowances, etc.	-215,850,100
Expenditure for expenses for investigative research	-285,157,200
Expenditure for personnel expenses	-7,969,774,642
Expenditure for money refunded for settlement of subsidies, etc.	-10,557,007
Other operating expenditures	-3,970,431,303
Income from administrative subsidies	1,963,292,000
Income from commissioned operations for government	51,169,703
Income from commissioned operations for others	1,573,997,914
Income from user fees	11,856,256,477
Income from contributions	8,214,034,300
Income from governmental subsidies	1,164,802,000
Income from contributions	20,423,146
Income from subsidies	6,020,000
Other incomes	144,242,372
Subtotal	3,117,862,860
Interest paid	367,390,083
Interest received	-436,316
Cash flow from operating activities	3,484,816,627
II. Cash flow from investing activities	
Expenditure for acquisition of investment securities	-4,820,549,000
Income from redemption of investment securities at maturity	3,200,000,000
Expenditure for acquisition of tangible fixed assets	-42,542,548
Expenditure for acquisition of intangible fixed assets	-702,122,556
Cash flow from investing activities	-2,365,214,104
III. Cash flow from financing activities	
Expenditure for repayment of finance lease obligations	-31,441,685
Cash flow from financing activities	-31,441,685
IV. Increase in funds	1,088,160,838
V. Beginning-of-term balance of funds	20,144,512,922
VI. End-of-term balance of funds	21,232,673,760

Appendix 14

Government Service Implementation Cost Statement (corporate basis)

(From April 1, 2017 to March 31, 2018)

Unit: yen

Account item	Amount		
I. Operating expenses			
(1) Expenses in the profit and loss statement			
Adverse reaction relief benefits	2,351,544,702		
Infection relief benefits	586,866		
Operating expenses for health and welfare services	123,924,597		
Operating expenses for reviews	2,980,865,722		
Operating expenses for safety measures	1,628,735,093		
Specific relief benefits	1,020,000,000		
Benefits for healthcare allowances, etc.	855,350,672		
Benefits for special allowances, etc.	219,265,200		
Expenses for investigative research	283,700,200		
Provision of liability reserves	2,682,250,772		
Other operating expenses	11,883,458,946		
General administrative expenses	2,736,710,076		
Financial expenses	436,316		
Miscellaneous losses	25,050,888		
Extraordinary losses	299,101	26,792,179,151	
(2) (Exemption) Self-generated income, etc.			
Income from user fees	-11,225,163,292		
Income from contributions	-8,951,248,300		
Income from commissioned operations for government	-50,606,309		
Income from commissioned operations for others	-1,459,468,936		
Revenue from contributions	-20,423,146		
Return of contributions for assets as per contra	-3,543,258		
Return of liability reserves	-996,261		
Financial revenue	-328,041,143		
Miscellaneous gains	-10,685,184	-22,050,175,829	4,742,003,322
Total of operating expenses			
II. Amount equivalent to depreciation that are not recorded as expenses			10,601,894
III. Amount equivalent to loss on retirement and sale that are not recorded as expenses			1
IV. Estimated amount of non-allowance bonuses			20,943,535
V. Estimated increased amount of non-allowance retirement benefits			198,440,862
VI. Opportunity costs			
Opportunity costs of investments by the government or local governments, etc.			227,406
VII. Government service implementation costs			4,972,217,020

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. The percentage-of-period method is employed to deal with all administrative activities, except those where progress is clearly correlated with administrative subsidies.

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 0.045%, by reference to the 10-year Japanese government bond yield at the end of March 2018.

9. Methods of accounting for lease transactions

Finance release transactions for which the total of lease fees is 3 million yen or more are handled by accounting method according to the method for usual sales transactions.

Finance release transactions for which the total of lease fees is less than 3 million yen are handled by accounting method according to the method for usual lease transactions.

10. Methods of accounting for consumption tax, etc.

These are handled by the tax-included method.

II. Items to note

1. Notes for balance sheets

(1) Notes regarding matters including current prices of financial products

[1] Items related to the status of financial products

Deposits are to be deposits for settlement.

Also, investments in financial products for purposes of funds management are limited to long-lived deposits, public and corporate bonds, and similar categories of securities. As investment securities, the PMDA holds only public bonds, FILP agency bonds, and class A or higher corporate bonds and does not hold stocks, etc. based on rules such as the provisions of Article 47 of the Act on General Rules for Incorporated Administrative Agencies.

[2] Items related to matters including current prices of financial products

Balance sheet amounts, current prices, and amounts of difference between them on closing date are as follows.

(Unit: yen)

Classification	Balance sheet amount	Current price on closing date	Amount of difference
A. Cash and deposits	21,232,673,760	21,232,673,760	0
B. Securities and investment securities	40,735,884,583	41,652,280,000	916,395,417
C. Accounts payable	(2,007,037,271)	(2,007,037,271)	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	36,868,126,741	37,794,330,000	926,203,259
Bonds with current prices not exceeding balance sheet amount	3,867,757,842	3,857,950,000	-9,807,842
Total	40,735,884,583	41,652,280,000	916,395,417

2) Scheduled amounts of redemption after closing date for held-to-maturity bonds

(Unit: yen)

Classification	≤1 year	>1 and ≤5 years	>5 and ≤10 years	>10 years
Government bonds	1,100,000,000	8,400,000,000	900,000,000	0
Government-guaranteed bonds	1,700,000,000	6,600,000,000	7,200,000,000	0
Local government bonds	0	0	700,000,000	0
Corporate bonds	800,000,000	0	7,300,000,000	0
FILP agency bonds	0	0	5,600,000,000	0
Total	3,600,000,000	15,000,000,000	21,700,000,000	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: 116,936,015 yen

(3) Estimated amount of non-allowance retirement benefits

Estimated amount of retirement benefits to be covered by the administrative subsidies: 325,978,387 yen

2. Notes for profit and loss statements

(1) Expenses for health and welfare services are expenses required for investigative research conducted to improve the QOL (Quality of Life) of people such as those covered by the system who suffered a serious and rare adverse drug reaction for which supports are not necessary sufficient when taking general measures intended for disabled people. These expenses consist of rewards for cooperation for investigation, etc.

(2) Expenses for reviews and related services are expenses required for the operation of reviews and related services for drugs, medical devices, etc. These expenses consist of rewards, travel expenses, expenses at government offices in charge of clerical tasks, etc. Also, expenses for safety measures, etc. are expenses required for the operation of post-marketing safety measures for drugs, medical devices, etc. These expenses also consist of rewards, travel expenses, expenses at government offices in charge of clerical tasks, etc.

(3) Expenses for investigative research are expenses required for investigative research of persons infected with HIV through blood products for the purpose of contributing to the prevention of the onset and spread of AIDS. All of these expenses are classified as healthcare expenses for HIV-infected persons.

(4) Income from user fees is income paid by applicants for drug or medical device product approval, and is utilized as a financial resource for conducting review services for drugs and other regulated products.

(5) Income from contributions is income paid by drug and medical device marketing and manufacturing authorization holders as a financial resource for conducting relief services for victims of regulated product-related adverse health effects and post-marketing safety operations.

3. Notes for cash flow statements

Relationship between the end-of-term balance of funds and money amounts of accounting items shown in the balance sheet

Cash and deposits: 21,232,673,760 yen

End-of-term balance of funds: 21,232,673,760 yen

4. Notes for government service implementation cost statements

The estimated increased amount of non-allowance retirement benefits includes 58,360,400 yen for executives and regular employees temporally transferred from the government.

5. Notes for asset retirement obligations

The PMDA has obligations for restoration to original state at the time of leaving business office based on the real estate leasehold contract, but the actual period of use of lease assets related to these obligations are not clear.

As such, it is difficult to predict when these obligations will be implemented, and it is not possible to reasonably estimate asset retirement obligations. For this reason, asset retirement obligations that match these obligations have not been allocated.

6. Notes for allowances for retirement benefits

(1) Outline of the retirement benefits system employed

The PMDA has established a retirement lump sum grants system as a defined-benefit system.

(2) Reconciliation between beginning-of-term and end-of-term retirement benefit obligations of FY 2017.

(Unit: yen)

Classification	April 1, 2017 - March 31, 2018
[1] Beginning-of-term retirement benefit obligations	2,745,938,159
[2] Service expenses	329,815,882
[3] Interest expenses	9,495,658
[4] Actuarial difference of the current term	-166,447,718
[5] Retirement benefits paid	-137,149,763
[6] End-of-term retirement benefit obligations ([1] + [2] + [3] + [4] + [5])	2,781,652,218

(3) Reconciliation of retirement obligation and allowances for retirement benefits reported on the balance sheet

(Unit: yen)

Classification	As of March 31, 2018
[1] Retirement benefit obligations	2,781,652,218
[2] Unrecognized actuarial difference	166,447,718
[3] Allowance for retirement benefits ([1] + [2])	2,948,099,936

(4) Profit and Loss of retirement benefit

Classification	April 1, 2017 - March 31, 2018
[1] Service expenses	332,478,922
[2] Interest expenses	9,620,175
[3] Amortization expenses for actuarial difference	380,312,827
[4] Retirement benefit funded from the administrative subsidies	3,623,937
[5] Retirement benefits expenses ([1] + [2] + [3] + [4])	726,035,861

Note: Retirement benefit expenses for workers temporally transferred from other institutions are included: [1] 2,663,040 yen for service expenses; and [2] 124,517 yen for interest expenses.

(5) Items related to basic calculation of actuarial

Classification	As of March 31, 2018
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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