

# Profile of Services

## 2017-2018





# Our Philosophy

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

We conduct our mission in accordance with the following principles:

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

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# Greetings from the Chief Executive



The Pharmaceuticals and Medical Devices Agency (PMDA) focuses on three key service areas: relief services for persons injured by adverse health effects of medical products, product reviews, and safety measures. Through comprehensive management of the lifecycles of drug and medical device products from the earliest stages of development to the post-marketing stage, the PMDA contributes to the improvement of the public health and safety of all people in Japan.

The PMDA has always executed all of its operations with a firm rooting in the concept of “regulatory science,” and has advanced a variety of innovations. As a result, the PMDA has succeeded in shortening its review period for new products, one of the most ambitious objectives set forth in its Third Mid-term Plan\*; the new product reviews conducted by the PMDA are now among the fastest in the world. In the future, the PMDA will make every effort to improve public health in Japan by focusing not only on speed, but also on continuously improving the quality and rationality of its operations through further advancement of regulatory science and innovative measures such as strengthening international partnerships.

The PMDA has noted growing expectations regarding its activities in recent years from both Japanese and overseas stakeholders, who demand the development of and access to innovative drug and medical device products. As one of the world’s leading regulatory agencies, the PMDA will steadfastly explore new ideas and tackle the most difficult issues in order to continue to ensure the swiftest possible delivery of safe and effective drugs and medical devices to all people in Japan.

August 2017

Tatsuya Kondo, MD, PhD

Chief Executive  
Pharmaceuticals and Medical Devices Agency

\*Mid-term Plan: As the PMDA is classified as an agency managed by medium-term objectives, the Mid-term Plans to which the PMDA must adhere are created to reflect medium-term objectives decided by the Minister of Health, Labour and Welfare, and must obtain Ministerial approval to gain effect. The period of implementation of the Third Mid-term Plan extends from April 2014 until March 2019.

# Outline of the Pharmaceuticals and Medical Devices Agency (PMDA)

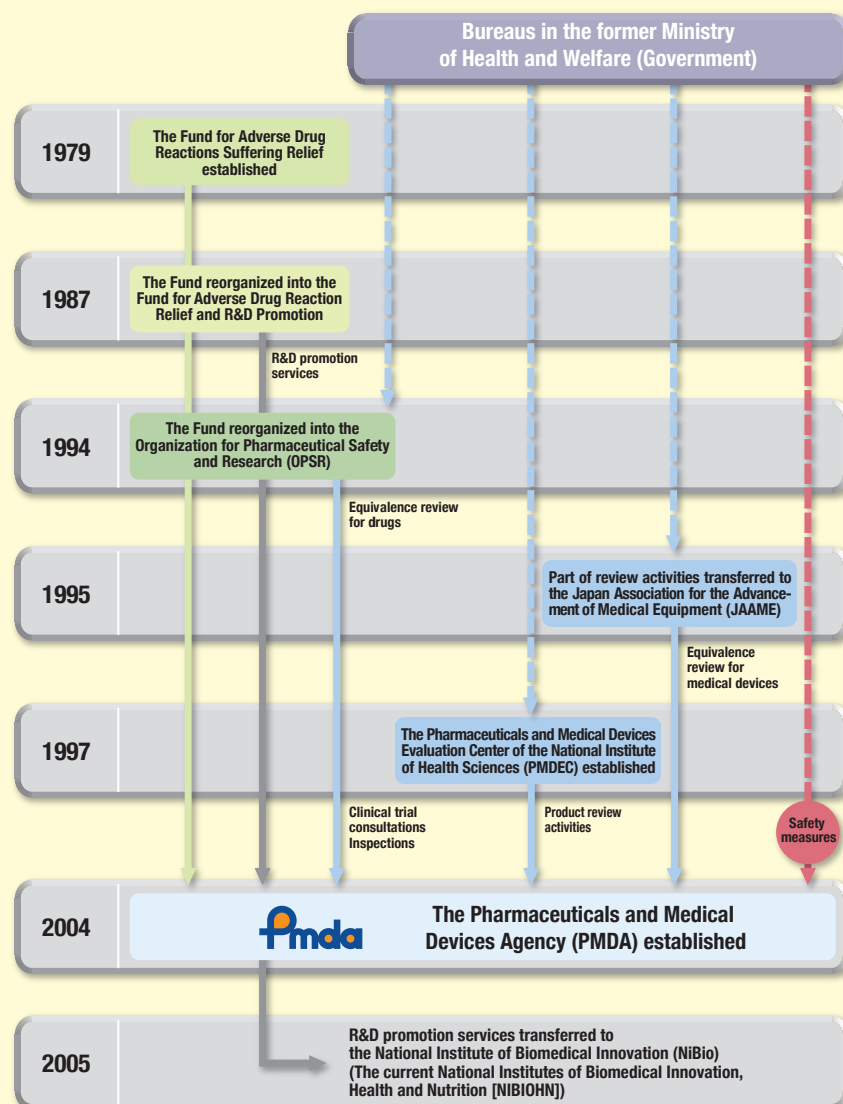
## History of PMDA

Following the Reorganization and Rationalization Plan for Special Public Corporations, which was approved at a Cabinet meeting in 2001, the Pharmaceuticals and Medical Devices Agency (PMDA) was established and came into service on April 1, 2004, under the Act on the Pharmaceuticals and Medical Devices Agency, with an aim to consolidate the services of the Pharmaceuticals and Medical Devices Evaluation Center of the National Institute of Health Sciences (PMDEC), the Organization for Pharmaceutical Safety and Research (OPSR), and part of the Japan Association for the Advancement of Medical Equipment (JAAME).

**Name:** Pharmaceuticals and Medical Devices Agency (PMDA)

**Established:** April 1, 2004

**Legal classification:** Agency managed by medium-term objectives



## Change in Number of Full-time Employees

	April 1, 2012	April 1, 2013	April 1, 2014	April 1, 2015	April 1, 2016	April 1, 2017
Total (including executives)*	678	708	753	820	873	906
Review Department**	438	460	492	532	560	578
Safety Department***	136	140	152	165	185	190
Relief Department	33	33	33	36	37	39

\* The total number includes 6 executives (including one part-time auditor). However, the total number of executives was 5 as of April 1, 2014.

\*\* The Review Department consists of Director of the Center for Product Evaluation, Director of the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, Associate Executive Directors (except the ones responsible for the Office of Regulatory Science and the Information Technology Promotion Group), Associate Center Directors (except the one responsible for the Office of Planning and Coordination), Advanced Review with Electronic Data Promotion Group, Office of International Programs, Office of International Cooperation, International Coordination/Liaison Officers, Office of Review Administration, Office of Review Management, Coordination Officer for Review of Breakthrough Products (Sakigake), Coordination Officer for Pharmaceutical Affairs Consultation on R&D, Coordination Officer for the Practical Application of Innovation Advancements, Office of Standards and Guidelines Development, Offices of New Drug I to V, Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products, Office of OTC/Quasi-drugs, Office of Generic Drugs, Offices of Medical Devices I to III, Office of In Vitro Diagnostics, Office of Non-clinical and Clinical Compliance, Chief of Kansai Branch, Consultation Division of Kansai Branch, principal senior scientists, senior scientists, International Senior Training Coordinators, and International Training Coordinators. In addition to the executives mentioned above, two executives served as Deputy Center Directors (non-permanent appointment until May 31, 2017) in the Review Department.

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

# Safety Triangle

## — Comprehensive Risk Management through the Three Functions —

### ■ Services of PMDA

PMDA's mission is to help improve public health in Japan by providing swift relief to people who have suffered health damage caused by adverse drug reactions or infections from biological products (Relief Services for Adverse Health Effects), offering guidance and conducting reviews on the quality, efficacy and safety of drugs and medical devices through a system that integrates the entire process from pre-clinical research to approval (Product Reviews), and by collecting, analyzing and providing post-market safety information (Post-marketing Safety Measures).

#### ● Relief Services for Adverse Health Effects

- Relief service for adverse drug reactions
- Relief service for infections acquired through biological products
- Health allowances etc., for SMON patients
- Health allowances for HIV-positive and AIDS patients
- Financial assistance under 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”

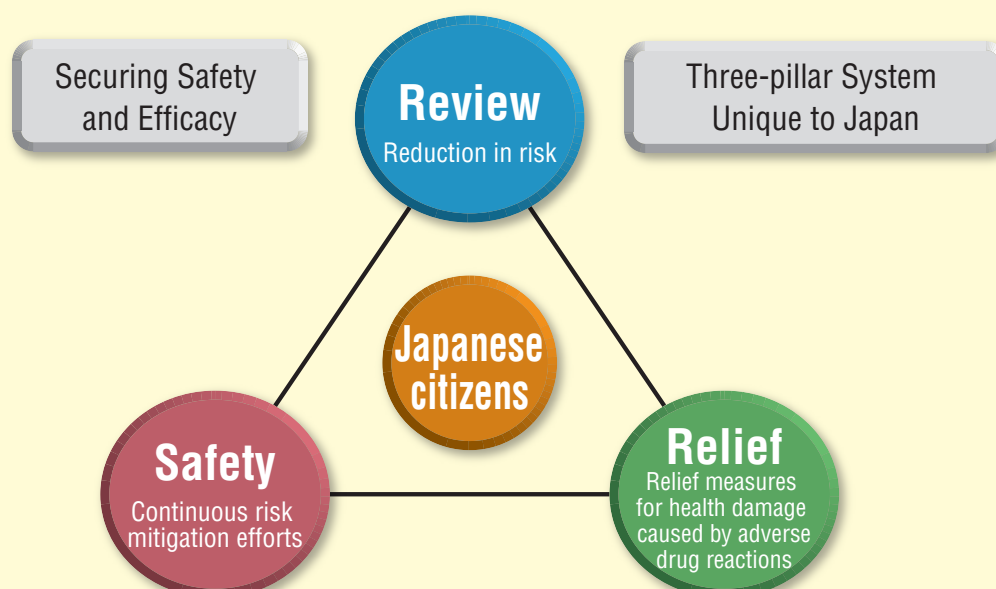
#### ● Product Reviews

- Consultations on clinical trials and other issues
- Regulatory review of drugs, medical devices and regenerative medical products
- Re-examinations/re-evaluations
- GLP/GCP/GPSP compliance assessments for regulatory submission documentation
- GMP/QMS/GCTP inspections of manufacturing processes and facilities
- Inspection of registered certification bodies
- Development of standards e.g., Japanese Pharmacopoeia

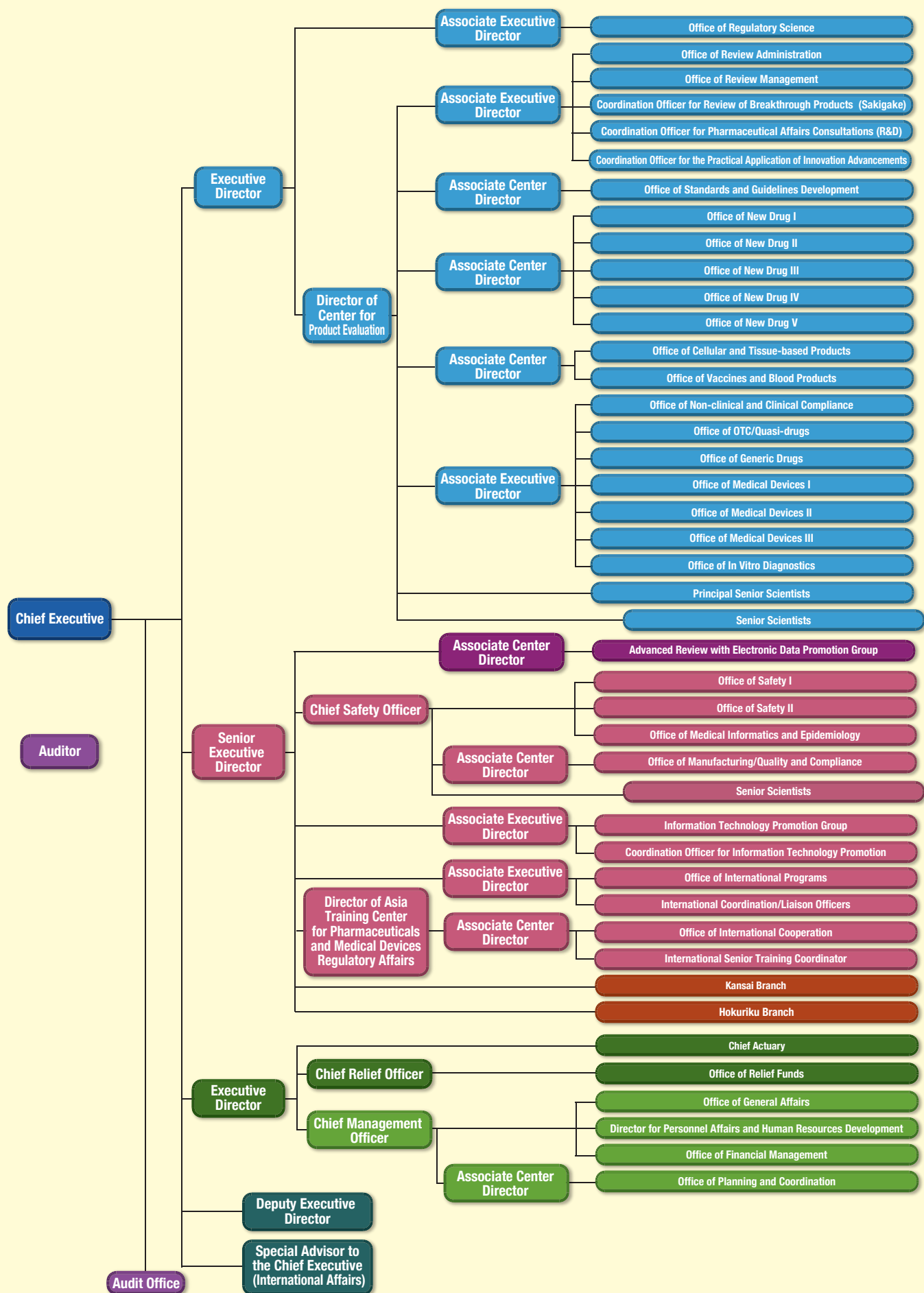
#### ● Post-marketing Safety Measures

- Acceptance of submitted labeling information (package inserts)
- Collection and organization of safety information from marketing authorization holders (MAHs) or medical institutions
- scientific research and analysis of collected information
- Consultation services on safety measures for MAHs
- Consultation services for consumers
- Provision of information on drugs, medical devices, and regenerative medical products

### ■ Safety Triangle



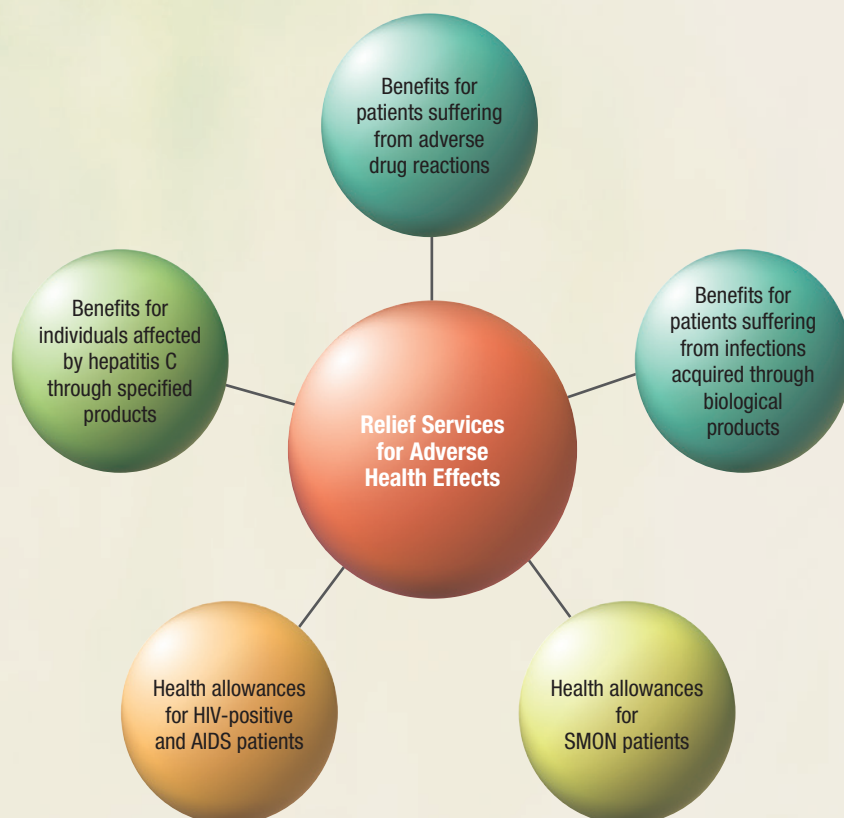
## Organization Chart (As of July 1, 2017)



# Relief Services for Adverse Health Effects

*PMDA is dedicated to providing swift relief for the people suffering from adverse health effects by conducting active public relations and dissemination of information.*

## Five Relief Services for Adverse Health Effects





Based on the lessons learned from drug-induced tragedies such as subacute myelo-optico-neuropathy (SMON) and thalidomide-induced birth defects, the Fund for Adverse Drug Reactions Suffering Relief (a predecessor of PMDA) was established in October 1979 to swiftly provide relief benefits to patients who have suffered health damage caused by adverse drug reactions.

Drug products, medical devices, and regenerative medical products are indispensable for human health and welfare, but their efficacy and safety must be ensured before they can be marketed. It is equally important that those products are used properly in order to ensure their efficacy and safety. And yet even if great care is taken in all these respects, it is almost impossible to completely prevent adverse drug reactions or infections from biological products.

Therefore, when drugs etc., used to treat illnesses cause health damage such as infectious diseases or adverse reactions, it is vital to provide relief immediately. The Relief System for Adverse Drug Reactions (since May 1980) and the Relief System for Infections Acquired through Biological Products (since April 2004) have been established for this purpose.

In addition to the above relief services, PMDA provides the following relief benefits: healthcare allowances and nursing care expenses to SMON patients for whom a settlement has been reached in court, healthcare expenses or healthcare allowances to patients who have become infected with human immunodeficiency virus (HIV) due to treatment with blood products, and financial assistance under 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.”

Following the enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (hereinafter referred to as the “PMD Act”), PMDA’s relief and safety departments share information on claims for relief benefits, which results in effective use of such information in safety measures.

## Relief Service for Adverse Drug Reactions

The Relief System for Adverse Drug Reactions is intended to provide relief benefits related to health damage such as diseases and disabilities requiring hospitalization that were caused by adverse reactions to prescription drugs prescribed at hospitals or clinics, over-the-counter (OTC) drugs purchased at pharmacies/drug stores, and regenerative medical products, even if such drugs were properly used.

These relief benefits cover health damage caused by adverse reactions to drugs and regenerative medical products that were used properly on or after May 1, 1980 and November 25, 2014, respectively (however, some of the cases may not be eligible for these benefits).

In addition to providing relief benefits, PMDA, as part of its health and welfare services, conducts investigative research on serious and rare cases of adverse health effects caused by drugs.

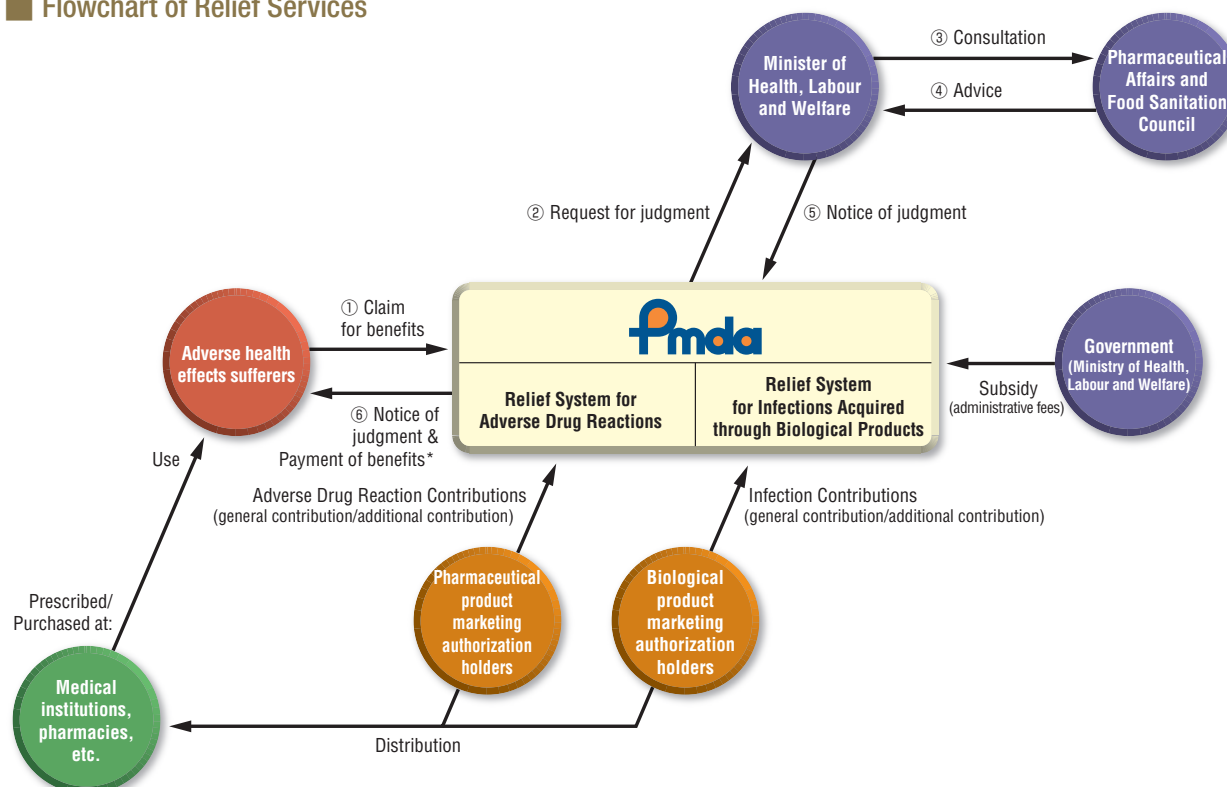
## Relief Service for Infections Acquired through Biological Products

The Relief System for Infections Acquired through Biological Products is intended to provide relief benefits to patients who have suffered health damage such as diseases and disabilities requiring hospitalization that were caused by infections acquired through biological products or regenerative medical products manufactured using ingredients and materials of biological origin, even if such products were properly used. Treatment to prevent the onset of disease following infections and cases of patients with secondary infection are also eligible for these relief benefits.

These Relief benefits cover health damage caused by infections acquired through biological products and regenerative medical products that were properly used on or after April 1, 2004 and November 25, 2014, respectively (however, some of the cases may not be eligible for these benefits).

# Relief Services for Adverse Health Effects

## Flowchart of Relief Services



\* A person having a complaint about the decision on his/her eligibility to receive a relief benefit may file a request for a review of the decision with the Minister of Health, Labour and Welfare.

## Relief Services for Adverse Drug Reactions

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims filed	1,280	1,371	1,412	1,566	1,843
Number of claims judged (Of which: Withdrawn)	1,216 (4)	1,240 (1)	1,400 (4)	1,510 (10)	1,754 (3)
Claims processed within 6 months versus total judged claims (Target: 60%)	45.5%	60.8%	61.9%	60.6%	67.4%
Number of claims in progress*	779	910	922	978	1,067
Amount paid (unit: million yen)	1,921	1,959	2,113	2,087	2,268

## Relief Services for Infections Acquired through Biological Products

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Number of claims filed	4	7	3	6	1
Number of claims judged (Of which: Withdrawn)	6 (0)	4 (0)	7 (0)	2 (0)	5 (0)
Claims processed within 6 months versus total judged claims (Target: 60%)	83.3%	100.0%	42.9%	50.0%	20.0%
Number of claims in progress*	2	5	1	5	1
Amount paid (unit: million yen)	3	3	3	3	1

\*"Number of claims in progress" indicates the value at the end of each fiscal year.

Note: The figures in the table above for "Number of claims filed" and "Number of claims judged" represent the number of those filed or judged in each fiscal year. "Amount paid" shows the amount of the benefits paid for both newly and previously judged claims.

## Healthcare Allowances, etc. for SMON Patients

Since December 1979, PMDA or its predecessor has provided healthcare allowances to SMON patients for whom the judicial settlement was reached, and nursing care expenses to patients with grade III SMON who have very severe or extremely severe symptoms, under commission from drug manufacturers liable for causing SMON in such patients.

Since FY 1982, PMDA or its predecessor has also provided nursing care expenses to patients with grade III SMON who have severe disabilities (excluding patients with very severe or extremely severe disabilities), under commission from the Japanese government.

### Classification of Severity of Disability

Severity Grade	Degree of Disability	
Grade I	A person who is considered to have significant limitations in daily activities	
Grade II	A person with disabilities falling somewhere between Grade I and III	
Grade III	Severe disability	A person with significant limitations in daily activities who needs nursing care and whose disability is not classified as being very severe or extremely severe
	Very severe disability	A person who falls under any one of the following categories: 1. A blind person or a person with equivalent visual disabilities 2. A person with a walking disability or a person with equivalent walking disabilities 3. A person with combined symptoms of impaired eyesight and gait disturbance that result in disabilities classified as being equivalent to the above 1 or 2 category.
	Extremely severe disability	A person with disabilities of the above 1 and 2 categories.

## Healthcare Allowances for HIV-positive and AIDS Patients

PMDA, under commission from the *Yu-ai* Welfare Foundation, provides the following services to patients who have become infected with HIV due to treatment with blood products. To help prevent the development of AIDS, PMDA provides healthcare expenses to HIV-positive patients who have not yet developed AIDS in exchange for reports on their health condition.

PMDA provides healthcare allowances to AIDS patients who have been infected with HIV due to treatment with blood coagulation factor products and for whom a settlement has been reached in court. The pur-

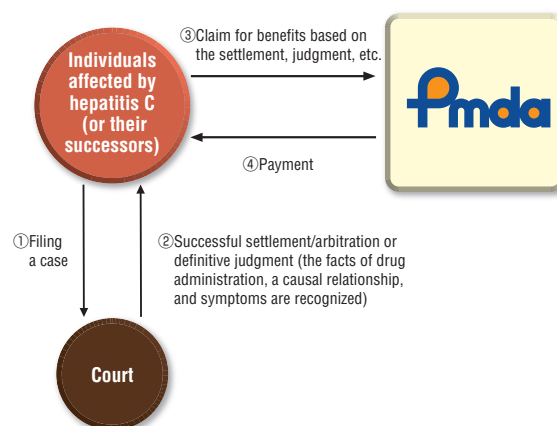
pose of these healthcare allowances is to improve the welfare of AIDS patients by reducing the cost of monitoring their health.

Patients with secondary and tertiary infections are also eligible for these benefits.

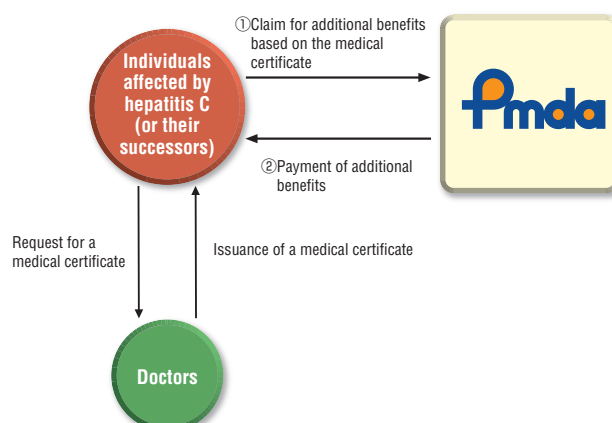
## Financial Assistance under the “Act on Special Measures concerning the Payment of Benefits to Assist Individuals Affected by Hepatitis C through Specified Fibrinogen Products and Specified Blood Coagulation Factor IX Products Contaminated by Hepatitis C Virus”

Since January 2008, PMDA has provided benefits under 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.”

### Flowchart of Claiming for Benefits



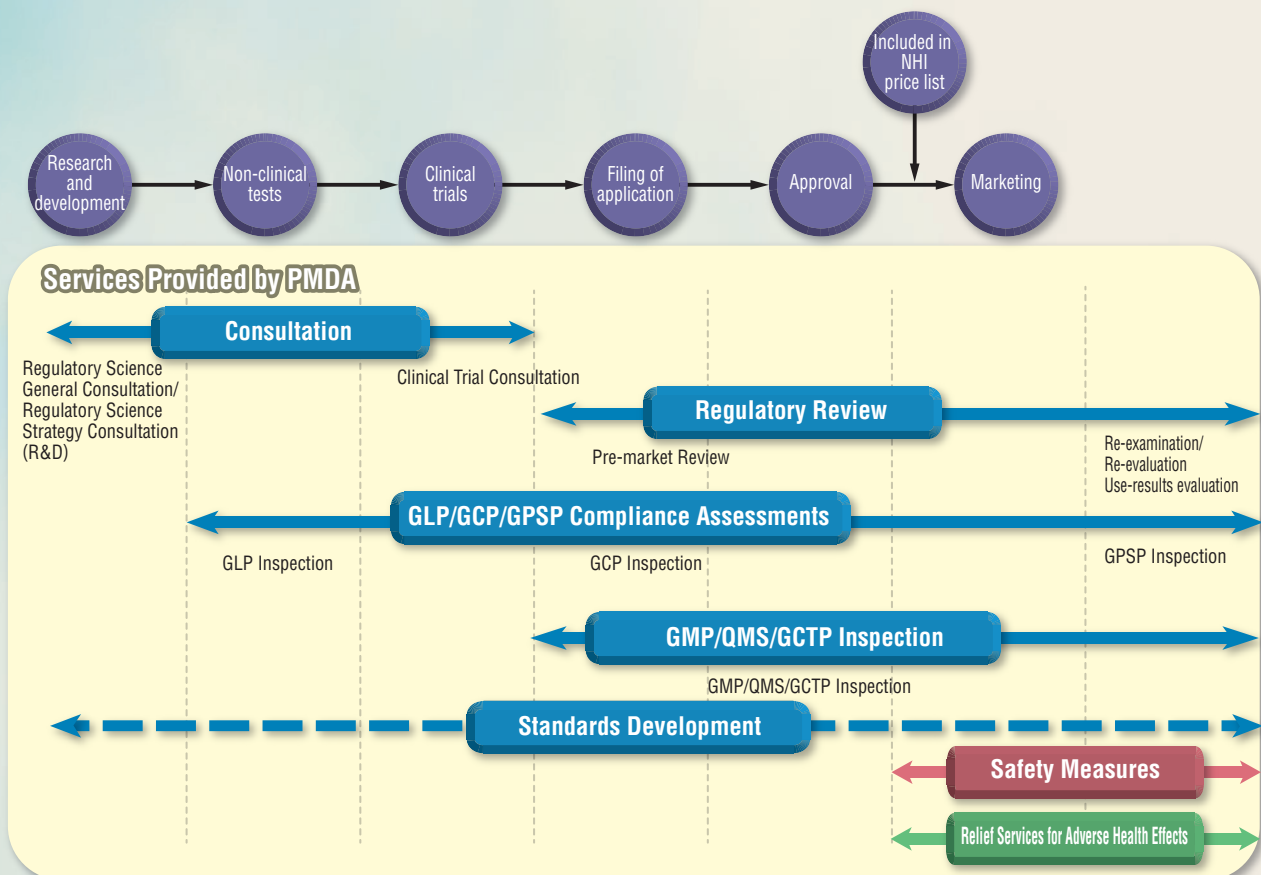
### Flowchart of Claiming for Additional Benefits (in the case of aggravation of symptoms)



# Reviews and Related Services

*In order to enable patients to have faster access to more effective drugs, medical devices, and regenerative medical products, PMDA is committed to reviewing applications for such products in a prompt and appropriate manner.*

## Life Cycle of Drug or Medical Device: From Development to Marketing





During the review process, PMDA evaluates the quality, efficacy, and safety of drugs, medical devices, and regenerative medical products in light of current scientific and technological standards. In addition, PMDA's reviews and related services consist of various activities, such as "consultations" providing advice in relation to regulatory submission, GLP/GCP/GPSP inspections to ensure that the submitted data are in compliance with the ethical and scientific standards, and GMP/QMS/GCTP inspections to ensure quality management of the manufacturing facility for the product submitted for approval.

To provide faster access to safer and more effective drugs, medical devices, and regenerative medical products, PMDA has endeavored to implement various measures to expedite and improve product reviews, such as by increasing the number of reviewers and inspectors with expertise in relevant areas, expanding and improving consultations, and establishing the system of advanced review and consultation with electronic data.

For the purpose of promotion of international regulatory harmonization, PMDA participates in international conferences on the regulation of drugs, medical devices, and regenerative medical products, including the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the International Medical Device Regulators Forum (IMDRF), and the Harmonization by Doing (HBD), while improving its review system for medical devices by actively incorporating the topics discussed at international conferences as well as standards such as those of the International Organization for Standardization (ISO).

Moreover, taking into account the Japan Revitalization Strategy (Cabinet decision on June 14, 2013), the Healthcare and Medical Strategy (Cabinet decision on July 22, 2014), the PMD Act, and the Act on the Safety of Regenerative Medicine, PMDA is making efforts to further accelerate and improve its review of medical products, such as by introducing the SAKIGAKE Designation System, in order to promote the practical application of innovative drugs, medical devices, and regenerative medical products ahead of the rest of the world.

#### ● What Is the Advanced Review and Consultation with Electronic Data?

This initiative enables PMDA to perform more advanced analysis of electronic clinical study data submitted for new drug applications, thereby improving the quality of reviews and consultations and contributing to a decrease in the workload of sponsors for regulatory submission.

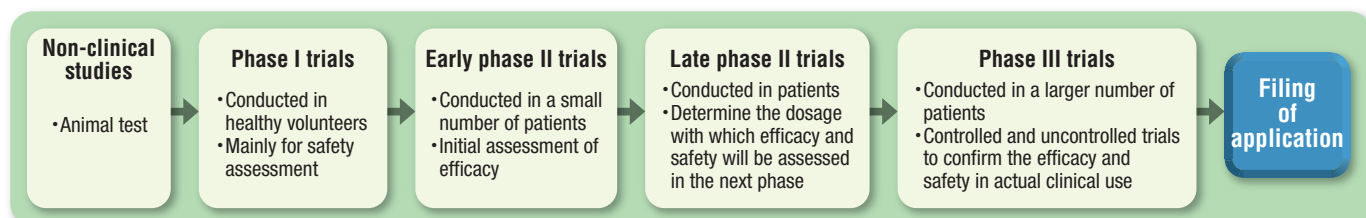
The electronic submission of study data for new drug applications started in October 2016. In the future, the use of accumulated data is expected to allow reviewers to conduct integrated review of data from multiple studies and products by using advanced modeling and simulation techniques. This will facilitate the development of new guidelines, thus contributing to an increased success rate of drug development.

#### ● What Is the SAKIGAKE Designation System?

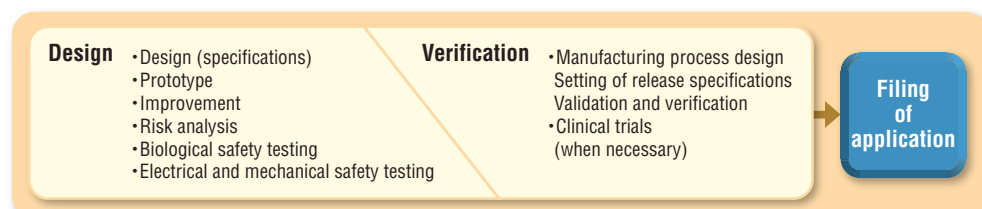
The SAKIGAKE Designation System is an expedited program intended to facilitate the development of innovative drugs, medical devices, and regenerative medical products, leading to their early practical application as the first in the world. The pilot scheme of the SAKIGAKE designation has been implemented, starting in FY 2015.

In this expedited program, innovative products including new drugs that meet certain requirements will be granted priority status for consultations on regulatory submission and for review by PMDA at a relatively early stage of development. In addition, the program ensures that the sponsor's manufacturing system is properly established in line with the schedule of product review and that the product is smoothly supplied to clinical settings once it has been approved, thereby resulting in further acceleration of practical application of the SAKIGAKE-designated product. To facilitate the clinical development of SAKIGAKE-designated products, a PMDA manager is assigned to be a review partner (also called a "concierge") who serves as a liaison between the Ministry of Health, Labour and Welfare (MHLW) and responsible offices at PMDA while managing the process of product development and review.

### ■ Standard Drug Development Process



### ■ Standard Medical Device Development Process



## Consultations

### Consultations

PMDA offers consultations to give guidance and advice on clinical trials of drugs, medical devices, and regenerative medical products as well as on data for regulatory submissions. In clinical trial consultations for new drugs, PMDA checks whether a proposed clinical trial complies with the requirements for regulatory submission, taking into consideration the ethical and scientific aspects and reliability of the clinical trial as well as the safety of trial subjects, and also gives advice that leads to an improvement in the quality of the clinical trial. Starting in FY 2009, PMDA provides prior assessment consultations, in which its reviewers evaluate data on the quality, efficacy, and safety of a product in the pre-submission stage. This consultation process constitutes part of the review of the product once the application is submitted.

In addition, PMDA coordinates and operates a variety of consultations for users' convenience, so as to meet the various requirements for advice on product development and regulatory submission, in such categories as new medical devices and regenerative medical products.

### New Consultation Categories and Operational Change

PMDA has managed the categories and contents of clinical trial consultation through several exchanges of opinions with the Ministry of Health, Labour and Welfare (MHLW) and related industries.

In FY 2016, new categories of consultation have been added, such as the consultation on compliance assessment for re-examination of drugs, in which the integrity of data for submission is assessed prior to filing of the application for re-examination of marketed drugs and the consultation on qualification of biological ingredients used for manufacturing regenerative medical products, in which guidance and advice is given on qualification of biological ingredients containing materials of human or animal origin from the view point of the virus and prion safety. In addition, some operational changes were made to the consultation for electronic study data submission for new drug applications, based on the experience so far.

#### ● What Is a Clinical Trial?

A clinical trial refers to a research study conducted to assess the efficacy of a drug, medical device, or processed cell product in humans and to identify the risk of potential adverse reactions. The data collected from such studies are submitted and subjected to regulatory reviews.

### Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D)

In order to promote the practical application of innovative drugs, medical devices, and regenerative medical products originating in Japan, PMDA conducted the Pharmaceutical Affairs Consultation on R&D Strategy starting in July 2011, mainly for universities, research institutions, and venture companies that discovered promising “seed-stage” technologies. Such consultations are intended to provide advice on the design of studies needed during the period from the final stage of drug candidate selection to the proof-of-concept (POC) trials (designed as early phase II trials) and clinical trial protocol development.

In April 1, 2017, the Pharmaceutical Affairs Consultation on R&D Strategy was reorganized for enrichment of the consultation service. Pre-consultation and full-scale consultation meetings conducted as part of the Pharmaceutical Affairs Consultation on R&D Strategy are continued under the name of the Regulatory Science Strategy Consultation (R&D). The introductory consultation was converted into the Regulatory Science General Consultation, so as to address the expanded scope of consultation.

In addition, the consultation service also provides guidance and advice on the quality and safety of regenerative medical products and on those of gene therapy products which are intended for transgene expression in a human body and used to prevent diseases (excluding ones classified as regenerative medical products, e.g., live recombinant vaccines), at an early development stage.

#### ● Examples of issues addressed

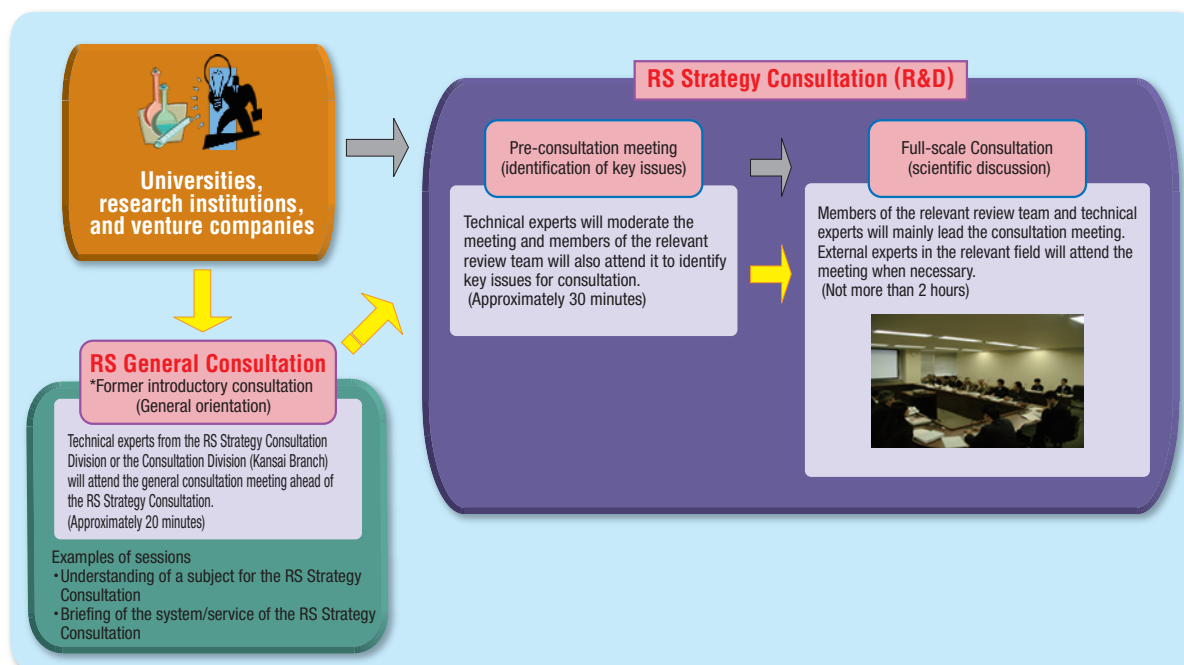
##### For drugs

- Quality and specification setting
- Nonclinical studies required before the commencement of first-in-human trials
- Protocols of early exploratory clinical trials (phase I and II trials)
- Preparation of the data package required for regulatory submission

##### For medical devices

- Nonclinical studies required before the commencement of clinical studies (trials) in humans
- Conformity to the essential principles
- Specifications on performance and safety
- Data on the safety and performance of the medical device which are required for regulatory submission (e.g., design verification and validation requirements and their summaries)
- Preparation of the data package required for regulatory submission

## ■ Outline of Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D)



## ■ Number of Consultations

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
New drugs	387	354	411	371	422
Medical devices	165	162	196	203	276
<i>In vitro</i> diagnostics	8	7	25	45	43
Regenerative medical products	—	—	6	18	28

Note: The consultation category for regenerative medical products was newly established on November 25, 2014. The figures for the regenerative medical products indicates the number of consultations provided on or after the date. (Relevant issues had been addressed by consultations for drugs or medical devices until then.)

## ■ Number of Regulatory Science Strategy Consultations (R&D) (Full-scale Consultations)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
R&D strategy for drugs	28	66	48	58	40
R&D strategy for medical devices	5	38	16	16	20
R&D strategy for regenerative medical products*	—	—	2	11	14
Quality and safety of regenerative medical products**	7 (13)	19 (32)	18 (44)	29 (55)	26 (64)
Product development planning***	—	—	1	0	0
Total	40 (46)	123 (136)	85 (111)	114 (140)	100 (138)

\* This consultation category was started on November 25, 2014. (Relevant issues had been addressed by consultations on R&D strategy for drugs or medical devices until then.)

\*\* Figures in this consultation category include the number of consultations accepted as those on R&D strategy for drugs until November 24, 2014. Figures in parentheses represent the total number of consultation sessions because some of the consultations took place over multiple days. Such multiple-day consultations were conducted to the extent necessary for adequate confirmation of the quality and safety of regenerative medical products before submission of clinical trial notifications for the products.

\*\*\* This consultation category was started on November 25, 2014.

## Drug Reviews

In the review of drug applications, PMDA reviewers, who have degrees in pharmaceutical science, medicine, veterinary medicine, physical science, biostatistics, or other specialties, form a team to evaluate the quality, pharmacology, pharmacokinetics, toxicology, clinical implications, and biostatistics regarding the particular drug product under review. During the review process, the reviewers exchange opinions with external experts (Expert Discussions) to ensure that more effective reviews are conducted by making use of their advanced expertise. In addition, PMDA participates in the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and has actively incorporated the guidelines agreed upon at ICH into its drug reviews.

PMDA strives to speed up the review process by setting target review times, while clarifying the standards for review by publishing the basic considerations for reviewers on its website.

PMDA's drug reviews encompass not only new drugs but also generic drugs, OTC drugs / "behind-the-counter (BTC)" drugs (requiring pharmacists' advice) that can be purchased at pharmacies without a doctor's prescription, and quasi-drugs. PMDA also conducts re-examinations and re-evaluations of approved drug products.

In FY 2016, a total of 6429 drugs were approved, of which 3660 were prescription drugs (including 468 new drugs), 646 were OTC drugs / BTC drugs, 199 were *in vitro* diagnostics, and 1924 were quasi-drugs.

### ● What Are Generic Drugs?

Generic drugs (or generics) refer to drug products whose active ingredients are identical to those of off-patent brand-name drugs which have already been approved for new active ingredients or additional indications, etc., based on data from clinical trials. In principle, a generic drug must contain the same amount of the same active ingredient and have the same indications, the same dosage and administration, and the same route of administration as those of the original brand-name drug. The therapeutic equivalence of the generic drug to the original brand-name drug needs to be proven by bioequivalence studies, etc.

### ● What Are Priority Review Products?

Priority review products refer to orphan drugs (including those expected to be used by less than 50,000 patients or those indicated for the treatment of intractable diseases) and products designated for priority review by the Ministry of Health, Labour and Welfare in consideration of their clinical usefulness and the seriousness of the diseases for which they are indicated.

### ■ Total Review Time for New Drugs (Priority Review Products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentiles	50	50	60	60	70
Total review time	6.1 months	7.2 months	8.8 months	8.7 months	8.8 months
Number of approved applications	53	42	44	37	38

Note 1: Values indicate the data for approved applications that were filed in or after April 2004. The number of applications represents the number of active ingredients.

Note 2: The products submitted for public knowledge-based applications in accordance with the recommendation by the Study Group on Unapproved and Off-label Drugs of High Medical Need are included in the category of priority review products.

### ■ Total Review Time for New Drugs (Standard Review Products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentiles	50	50	60	70	70
Total review time	10.3 months	11.3 months	11.9 months	11.3 months	11.6 months
Number of approved applications	81	96	73	79	74

Note: Values indicate the data for approved applications that were filed in or after April 2004. The number of applications represents the number of active ingredients.



## Medical Device Reviews

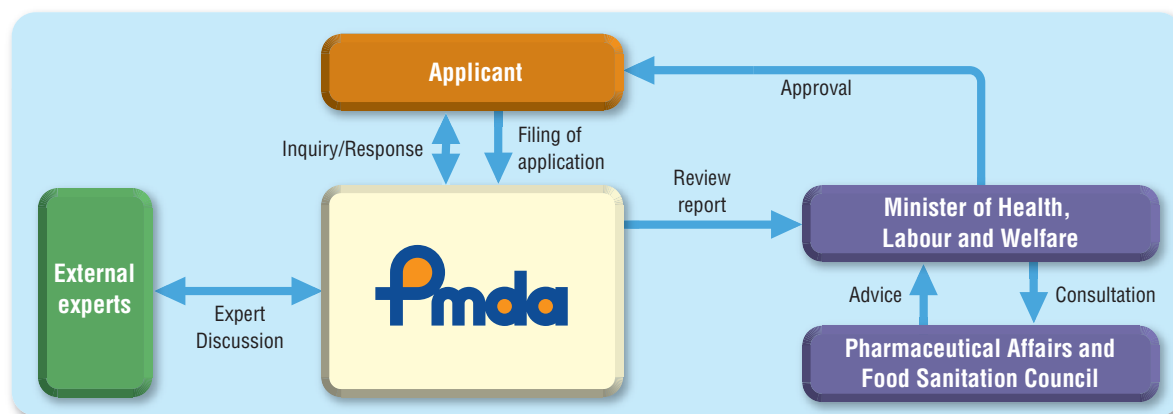
Medical devices cover a wide range of products, from adhesive bandages and forceps to magnetic resonance imaging (MRI) and pacemakers, which are characterized by a variety of usage patterns and different levels of risk. Among these products, high-risk medical devices are mainly evaluated by PMDA. As with drug reviews, PMDA has set target review times for medical devices and is working hard to achieve these targets through various efforts, such as increasing the number of reviewers.

In the medical device review process, not only reviewers who possess expertise in medical engineering, biological engineering, and biomaterials but also specialists with degrees in medicine, dentistry, pharmaceutical science, and other fields are involved in non-clinical and clinical evaluation and biostatistical analysis. During the review process, the reviewers exchange opinions with external experts (Expert Discussions) to enable more highly specialized reviews.

### ● What Are High-Risk Medical Devices?

Medical devices are classified into four categories (Classes I to IV) according to the risk-based classification system which incorporates a set of international classification rules for medical devices. Class III and Class IV medical devices represent high-risk medical devices that are classified as specially controlled medical devices under the PMD Act (e.g., artificial heart and cardiac pacemaker). Class I medical devices, such as adhesive bandages and dental forceps, are classified as general medical devices, for which marketing notification should be submitted to PMDA. Class II medical devices are classified as controlled medical devices. In the case of Class II medical devices for which certification standards have been established by the Minister of Health, Labour and Welfare (e.g., MRI and home use massage devices), third-party certification by registered certification bodies is necessary for demonstration of conformance of products to relevant standards, but otherwise regulatory approval is required in this class as with high-risk medical devices.

### ■ Review Process for Drug or Medical Device Application



### ■ Total Review Time for New Medical Devices (Priority Review Products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentiles	50	50	60	60	70
Total review time	9.3 months	9.0 months	8.8 months	7.9 months	8.0 months
Number of approved applications	5	14	5	8	1

Note: Values indicate the data for approved applications that were filed in or after April 2004.

### ■ Total Review Time for New Medical Devices (Standard Review Products)

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Percentiles	50	50	60	60	70
Total review time	12.7 months	6.3 months	5.6 months	10.1 months	12.0 months
Number of approved applications	41	80	62	48	24

Note 1: Values indicate the data for approved applications that were filed in or after April 2004.

Note 2: Since the review results in FY 2013 and FY 2014 involved a great number of applications for MRI-compatible pacemakers, the number of approved applications was temporarily increased.

## Regenerative Medical Product Reviews

Regenerative medical products have been newly defined by the PMD Act that was enforced on November 25, 2014. The regenerative medical products include products derived from processed living cells/tissues of human or animal origin and products used for gene therapy, and such products have properties different from those of conventional drugs and medical devices.

For example, the use of living cells/tissues may result in heterogeneity in product quality; therefore, collecting data to support the efficacy of a regenerative medical product is a time-consuming task. In response to these circumstances, “the conditional and time-limited authorization system” has been established under the new legislation so that regenerative medical products can be swiftly granted conditional approval for a limited time period once their efficacy is predicted and their safety is ensured.

PMDA has established a review system capable of appropriately and promptly responding to the new regulatory framework and strived to disseminate information on the new system.

In FY 2016, one regenerative medical product (with a new indication) was approved under the new regulatory system.

### What Are Regenerative Medical Products?

Regenerative medical products refer to:

1. Products derived from human or animal cells/tissues processed by methods such as cell culture, and are those used for the purposes of:
  - (a) reconstruction, restoration or formation of structures and functions of the human body; and
  - (b) prevention or treatment of diseases
2. Products transfected into human cells/tissues for the purpose of gene therapy.

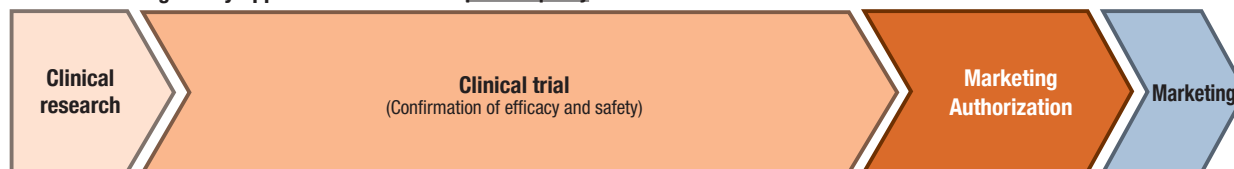
\* Since these products are all derived from processed living cells/tissues, the products are characterized by their varied quality and in that their efficacy is difficult to be confirmed in some cases.

### Regulatory System That Facilitates Practical Application of Regenerative Medical Products (Conditional and Time-limited Authorization System)

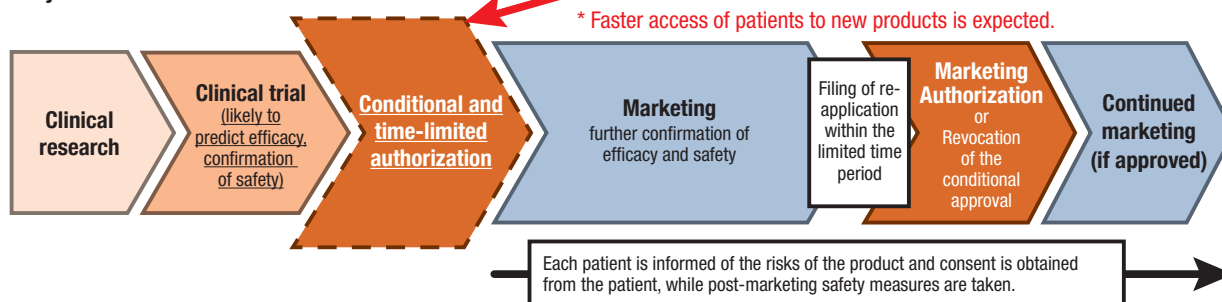
“Drawbacks of the conventional approval system for regenerative medical products”

Long-term collection and evaluation of data that support the efficacy of a product derived from processed human cells and tissues are necessary because there is heterogeneity in product quality due to individual variation.

#### Conventional Regulatory Approval Process



#### Regulatory System That Facilitates Early Patient Access



- Based on the clinical data from a limited number of patients, efficacy is predicted in a shorter time compared with the conventional process.
- Acute-phase adverse reactions etc., can be evaluated for safety in a short period of time.

(Source: the related document published by MHLW)

## GLP/GCP/GPSP Compliance Assessments

PMDA conducts compliance assessments (i.e., document-based or on-site inspections and data integrity assessments) with respect to the data submitted in support of applications for marketing approval of new products as well as those for re-examination, re-evaluation, or use-results evaluation of approved products. During the compliance assessment process, PMDA inspectors assess whether necessary tests and clinical trials were conducted in an ethically and scientifically appropriate way in compliance with Good Laboratory Practice (GLP), Good Clinical Practice (GCP) and Good Post-marketing Study Practice (GPSP), and whether the submitted data comply with the data integrity standards for regulatory submission. PMDA is also responsible for recognition of GLP compliance of testing facilities.

### ● Improvement of the Clinical Trial Environment

PMDA is responsible for GCP inspections as part of its services. GCP is a standard for the conduct of clinical trials to protect the human rights, safety, and welfare of trial subjects, as well as to ensure the scientific quality of clinical trials and the integrity of clinical trial data. The GCP inspection at medical institutions conducting the clinical trials of a proposed product is intended to verify how the safety and ethics of trial subjects are ensured and how the trials are managed.

During the GCP inspection, PMDA inspectors also offer first-hand advice to the physicians, pharmacists, clinical research coordinators and nurses at the medical institutions, thus improving the clinical trial environment in Japan.

## ■ Number of GLP/GCP/GPSP Compliance Assessments

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

Note : The figures in the table above represent the numbers of products for which inspection/assessment was completed. (The numbers of document-based assessments, on-site GCP inspections, document-based assessments for re-examination, and on-site GPSP inspections for re-examination on medical devices were tabulated until December 2013 on the basis of product applications for which both inspection and review were completed.)

## GMP/QMS/GCTP Inspections

When drug products, medical devices or regenerative medical products are manufactured, all product batches should be of the same quality as that of the product which is approved. To ensure this, the manufacturing site should have appropriate manufacturing facilities, and the manufacturing process and quality management system should be maintained and controlled properly.

PMDA conducts the following inspections.

### GMP inspection

PMDA conducts on-site and document-based inspections of manufacturing sites for products classified as “high-risk,” such as new drugs, biological products or biotechnological products (including foreign manufacturing sites), in order to ascertain whether their manufacturing facilities and manufacturing and quality controls comply with standards of the Good Manufacturing Practice (GMP), and whether the manufacturing sites have a system for manufacturing products of adequate quality. PMDA also conducts inspections in relation to accreditation of foreign manufacturers.

### QMS inspection

PMDA conducts on-site and document-based inspections for marketing authorization holders of medical devices or *in vitro* diagnostics and the relevant registered manufacturing sites (of products under review or approved) located in Japan or overseas, in order to ascertain whether their manufacturing facilities and manufacturing and quality controls comply with standards of the Quality Management System (QMS), and whether the marketing authorization holders ensure that products of adequate quality are manufactured and marketed in accordance with the standards.

### GCTP inspection

PMDA inspects manufacturing sites of regenerative medical products in Japan or overseas, in order 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 (GCTP). PMDA also conducts inspections on compliance with the standards for buildings and facilities, for-cause inspections, and inquiries on cell processing facilities, in response to the enforcement of the Act on Safety of Regenerative Medicine.

## Assessment of Registered Certification Bodies

Any person who intends to market medical devices and *in vitro* diagnostics that are designated in accordance with standards established by the Minister of Health, Labour and Welfare must obtain the certification by a registered certification body. PMDA conducts compliance assessments to confirm that registered certification bodies (including organizations which intend to become a registered certification body) meet the requirements for registration. In addition, PMDA receives reports from registered certification bodies when certification is granted or cancelled for a marketing authorization holder.

Furthermore, the Ministry of Health, Labour and Welfare (MHLW) and PMDA have participated in the Medical Device Single Audit Program (MDSAP), which serves as part of international cooperation activities for ensuring the quality of medical devices.

In the conventional regulatory framework, medical device manufacturers need to cope with each of on-site QMS inspections performed by regulatory authorities of different countries. Under the MDSAP program,\* a single audit of a medical device manufacturer’s quality management system is performed by a recognized third-party auditing organization in accordance with the MDSAP QMS that incorporates the regulatory requirements in the participating countries. This program is thus expected to reduce the burden of QMS inspections/audits on medical device manufacturers.

### Number of GMP/QMS Inspections

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs (excluding <i>in vitro</i> diagnostics)	1,593 (198)	1,415 (168)	1,672 (163)	1,647 (165)	1,783 (171)
<i>In vitro</i> diagnostics	48 (0)	67 (1)	38 (1)	147 (33)	83 (44)
Quasi-drugs	2 (0)	3 (1)	6 (0)	2 (0)	3 (0)
Medical devices	954 (81)	883 (61)	512 (42)	2,032 (351)	952 (251)
Regenerative medical products	—	—	0 (0)	8 (3)	0 (0)
Total	2,597 (279)	2,368 (231)	2,228 (206)	3,836 (552)	2,818 (466)

Note: Figures in parentheses indicate the number of on-site inspections.



The participating regulatory authorities assess relevant third-party auditing organizations for compliance with the MDSAP QMS. PMDA plays a role in the assessment of auditing organizations, thereby contributing to the full implementation of the MDSAP.

\* A program in which medical device manufacturers are audited by MDSAP-recognized third-party auditing organizations and QMS audit reports are prepared by the auditing organizations. The audit reports will be used by the participating regulatory authorities of Japan, the United States, Canada, Australia, and Brazil.

## Standards Development

PMDA is involved in developing the Japanese Pharmacopoeia (JP) as an official compendium containing specifications and standards related to the quality of drugs in Japan. PMDA organizes JP Expert Committees, which consist of external experts and are responsible for developing and revising General Tests and monographs included in JP. These committees prepare draft monographs for JP and seek public comments on the PMDA website before reporting the draft monographs to the MHLW.

In addition to JP, certification standards and guidelines which provide guidance for review of medical devices are developed at PMDA. These standards and guidelines have been released on the agency's website.

To facilitate harmonization with international standards, PMDA participates in international conferences on drugs, such as the meetings of the Pharmacopoeial Discussion Group (PDG) consisting of the European Pharmacopoeia, Japanese Pharmacopoeia, and United States Pharmacopoeia and the WHO International Nonproprietary Names (INN) meetings, and those on medical devices, such as the International Organization for Standardization (ISO)/ International Electrotechnical Commission (IEC) meetings.

The projects across multi-offices for standards development are ongoing in PMDA. These projects are intended to address issues related to the assessment and development of drugs and medical devices, contributing to formulation of new standards and guidelines. In each project, specific topics are discussed across the related offices of PMDA, in consideration with international regulatory convergence.

## Operations in Kansai Branch

On October 1, 2013, PMDA established its Kansai Branch which offers the Regulatory Science General Consultation and Regulatory Science Strategy Consultation (R&D) (for pre-consultation meeting) and undertakes GMP/QMS/GCTP inspection.

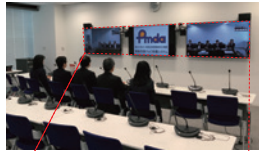
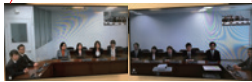
The high-performance video conferencing system introduced in June 2016 allows a live video connection between the PMDA headquarters in Tokyo and the Kansai branch office. The system enables approximately 20 reviewers from the Tokyo headquarters to attend a full-scale consultation meeting taking place between the two offices.

### Consultations available in Kansai Branch through Video Conferencing

Regulatory Science Strategy Consultation (R&D)	<ul style="list-style-type: none"> <li>• Consultation on R&amp;D strategy for drugs</li> <li>• Consultation on R&amp;D strategy for medical devices</li> <li>• Consultation on R&amp;D strategy for regenerative medical products</li> </ul>
Consultation	<ul style="list-style-type: none"> <li>• Clinical trial consultation for new drugs</li> <li>• Clinical trial consultation for new medical devices</li> <li>• Clinical trial consultation for regenerative medical products</li> <li>• Clinical trial consultation for generic drugs</li> </ul>



### Video Conferencing in Kansai Branch

A video conference room of the Kansai branch office

The monitors show live images of the room of the Tokyo headquarters.  
\*The center monitor is used as a presentation monitor.

A video conference room of the Tokyo headquarters

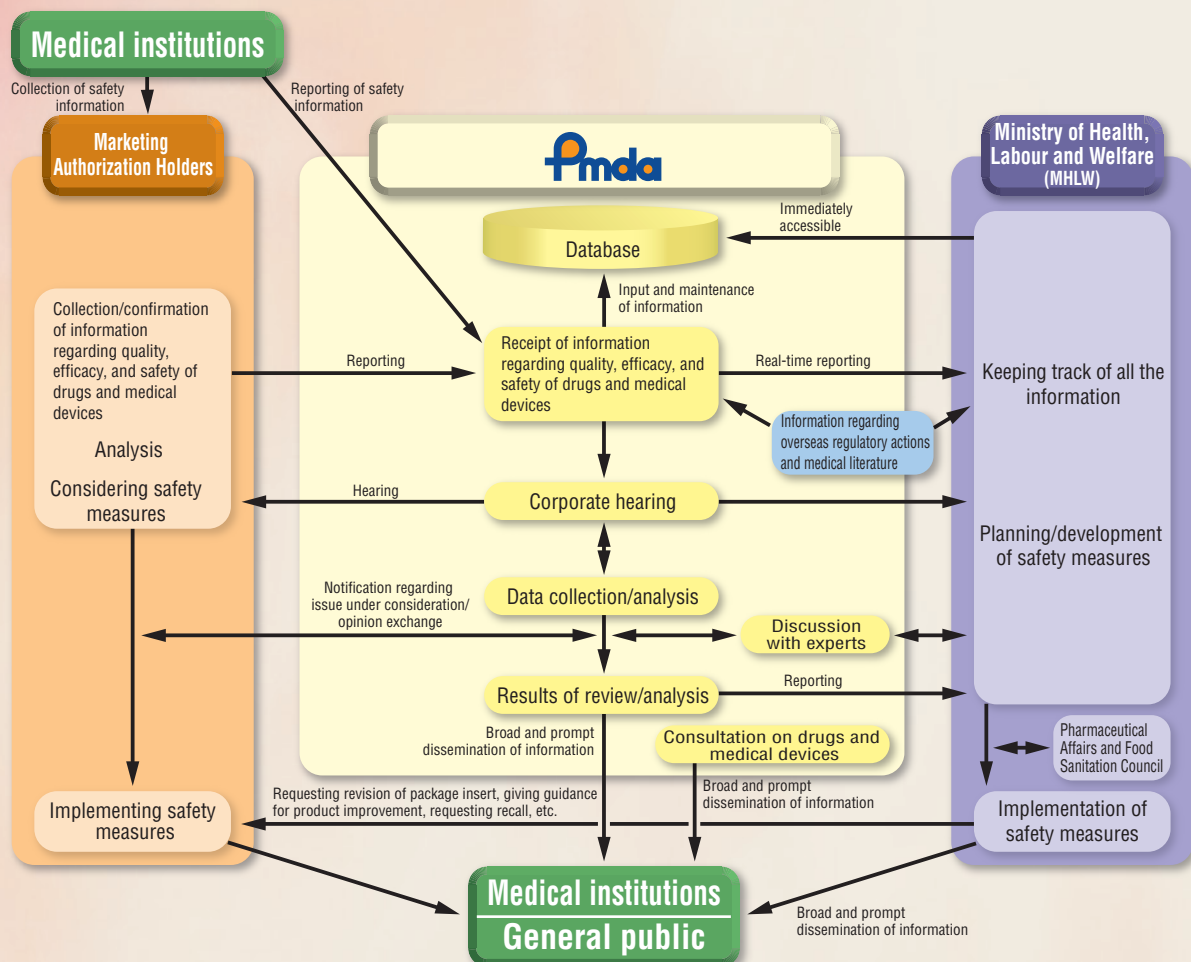
The monitors show live images of the room of the Kansai branch office.

The video conferencing system provides high-definition images and clear sounds.  
The simultaneous translation system is available.  
The zoom function enables users to zoom in to view materials on hand.

# Post-marketing Safety Measures

*In cooperation with the Ministry of Health, Labour and Welfare, PMDA is dedicated to improving the safety and reliability of drugs, medical devices, and regenerative medical products.*

Flowchart of Safety Measures



Drugs, medical devices, and regenerative medical products are essential for protecting our health and lives. Thanks to advancements in science and technology, humans have conquered many difficulties over the years; the drugs, medical devices, and regenerative medical products created by human ingenuity have allowed us to overcome many diseases.

However, the drugs, medical devices, and regenerative medical products used for diagnosing or treating diseases may also cause unexpected adverse reactions, so they should be used considering the balance between risk and benefit. It is extremely important that healthcare professionals use drugs, medical devices, and regenerative medical products properly at all times; safety is achieved through the ceaseless efforts of people who are involved in all stages of the life cycle of these products. And it is this safety that gives users peace of mind.

In cooperation with the Ministry of Health, Labour and Welfare (MHLW), PMDA is dedicated to improving the safety and reliability of drugs, medical devices, regenerative medical products.

## Acceptance of Labeling Information (Package Inserts) Submitted

Under the PMD Act, marketing authorization holders (MAHs) of drugs (prescription drugs and BTC drugs), medical devices (Class IV medical devices), or regenerative medical products are required to develop a package insert for each of their products based on the latest findings and to submit it to the Minister of Health, Labour and Welfare. At the same time, the submitted package insert needs to be published on the PMDA website.

PMDA accepts the package inserts for drugs etc., from MAHs, and publishes them on its website.

## Collection and Organization of Safety Information

MAHs and medical institutions need to report adverse drug reactions (ADRs), infections caused by regenerative medical products, and malfunctions of medical devices if those cases are detected during the clinical development and post-marketing periods. PMDA accepts or collects such safety information promptly and efficiently.

PMDA also consolidates a variety of safety information collected from overseas regulatory agencies and other sources such as conference papers and research reports. The collected information is then promptly compiled into a database and shared with the MHLW.

PMDA started the service to collect reports on adverse drug reactions directly from patients at the end of 2011, on a trial basis.

### Number of Adverse Drug Reaction Reports

From	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
MAHs (cases in Japan)	41,413	38,427	49,276	51,065	55,817
MAHs (cases out of Japan)	261,862	266,539	300,216	345,193	393,825
Healthcare professionals	4,147	5,420	6,180	6,129	6,047

### Number of Medical Device Malfunction Reports

From	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
MAHs (cases in Japan)	11,242	12,791	13,994	17,603	16,283
MAHs (cases out of Japan)	10,992	12,763	16,624	26,395	32,280
Healthcare professionals	522	489	420	406	548

### Number of Regenerative Medical Product Malfunction Reports

From	FY 2014	FY 2015	FY 2016
MAHs (cases in Japan)	12	35	88
MAHs (cases out of Japan)	0	0	0
Healthcare professionals	0	0	0

Note: The figures in the table above represent the numbers of regenerative medical product malfunctions reported from each source on or after November 25, 2014.

## Scientific Research and Analyses

PMDA conducts research and reviews of the collected information through scientific analyses, interviews with companies, and discussions with experts, to determine whether there is any case requiring urgent measures, whether the risk/benefit profile is favorable, and what the optimal safety measures are. All these efforts lead to safety measures of drugs, medical devices, and regenerative medical products.

To take effective safety measures, the safety staff work together with the review and relief departments as well as the MHLW, as required. In FY 2016, PMDA submitted 152 reports for drugs (the number of active ingredients) and 6 reports for medical devices (the number of term names) to the MHLW, because these reports suggested the need of measures such as the revision of the package insert.

Meanwhile, when application for a new drug or a follow-on biologic (biosimilar) is filed in or after April 2013, the applicant is required to include a Risk Management Plan (RMP) in the application. To facilitate this regulatory framework, risk managers have been appointed in the Office of Safety II, who concurrently serve as members of the Office of New Drug. PMDA thus strives to enhance safety measures by utilizing RMPs based on the cooperation between the safety and drug review offices.

To enhance and advance safety measures, PMDA takes various approaches such as the introduction of data mining methods (which involve statistical analysis of ADRs as reported by companies or medical institutions, thereby detecting signals of ADRs that may warrant further investigation) and safety evaluation of drugs based on pharmacoepidemiological methods utilizing electronic medical records (known as the MIHARI Project), and construction of medical information database (MID-NET).

### ● What Is Risk Management Plan (RMP)?

To ensure the safety of drugs, appropriate measures for management of the risks associated with the drugs should be assessed consistently from the development phase through to the post-marketing phase.

The RMP is a document comprising summaries of the following elements: Safety Specification (which includes important identified risks of a drug product, important potential risks, and important missing information), Pharmacovigilance Plan (which includes the planned collection and review of information on Safety Specification), and Risk Minimization Action Plans.

The submitted RMPs have been posted on the PMDA website.

■ Numbers of Reports Submitted to MHLW for Cases Requiring Revision of Package Insert and for Analysis of Medical Safety Information

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
Drugs*	198	160	100	87****	152
Medical devices**	15	14	4	28	6
Regenerative medical products	—	—	0***	0	0
Medical Safety	6	6	6	6	6

\* The figures for drugs indicate the number of active ingredients.

\*\* The figures for medical devices indicate the number of term names.

\*\*\* The figure indicates the number of reports after the enforcement of the PMD Act on November 25, 2014.

\*\*\*\* The figures indicate the sum of 84 reports for drugs and 3 reports for *in vitro* diagnostics.



## Consultation Services

### **Consultations for companies**

PMDA offers consultations for companies on a broad range of product safety issues, such as how to revise package inserts, how to promote proper use of products to prevent serious ADRs, and how to develop and update Risk Management Plans (RMPs) for drugs in the post-marketing stage. In such consultations, PMDA gives specific advice and guidance to companies in order to help promote the safety of drug products, medical devices, or regenerative medical products, while also raising corporate awareness of safety measures.

### **Consultations for general public**

PMDA's telephone consultation service is also available for the general public so that they can obtain safety information on products such as drugs prescribed by doctors (prescription drugs), drugs purchased at pharmacies (OTC drugs or BTC drugs), home-use medical devices purchased in stores while seeking advice on those products.

In order for generic drugs to be used without feeling uneasy, PMDA also offers consultation services on the quality, efficacy, and safety of generic drugs and provides the related information.

## Information Services

A wide range of information on the quality, efficacy, and safety of drug products, medical devices and regenerative medical products is provided on the PMDA website in a timely manner, including the package inserts for drug products, medical devices, and regenerative medical products, Risk Management Plans (RMPs) for drugs, recalls, and emergent safety communications ("Dear Healthcare Professional" Letters). All cases of adverse drug reactions and medical device malfunctions reported by companies or healthcare professionals on or after April 1, 2004 (the date PMDA was established) are posted on the same web page every month.

PMDA provides information not only to healthcare professionals but also to the general public, such as the "Drug Guide for Patients," which is an easy-to-understand explanation for patients to teach them about prescription drugs with warnings labels, and the "Manuals for Management of Individual Serious Adverse Drug Reactions (for the general public)," which outline individual ADRs, initial symptoms, and key points for early detection and treatment in an easy-to-understand manner.

In addition, the Agency offers an email information service called "PMDA medi-navi" (available in Japanese only), through which important safety information posted on its website is distributed to healthcare professionals who subscribe to the service.

### ● What Is "PMDA medi-navi"?

The "PMDA medi-navi" (i.e., the pharmaceuticals and medical devices information e-mail service) is an e-mail service that delivers important information on the quality, efficacy, and safety etc., of drug products, medical devices, and regenerative medical products, to previously registered e-mail addresses of subscribers, immediately at the time such information is issued.

Anyone can subscribe to this service free of charge to obtain important safety information.

The PMDA medi-navi mainly includes:

- Dear Healthcare Professional Letters regarding Emergent/Rapid Safety Communications
- MHLW notifications for instructions on revision of precautions
- Information on Recall (for classes I and II)
- Information on product approvals
- Drug risk information under review

Please scan the QR code to register.



# International Activities

While formulating the PMDA International Vision and other policy statements during the period covered by the First and Second Mid-term Plans (FY 2004 to 2013), PMDA has actively promoted international activities such as strengthening partnerships with the US, the EU, and Asian and other countries; participation in and contribution to international harmonization activities; and dissemination of information to the international community in a timely manner. PMDA's efforts have been highly regarded internationally and the agency has been the focus of calls for greater international contribution largely as a result of the substantial reduction in review times for drug and medical device approvals (known as "review lag") that was achieved during the term of the same Mid-term Plans. Accordingly, PMDA must further contribute to international society.

Under these circumstances, in response to recent changes in the environment surrounding the regulatory agencies and in light of the International Pharmaceutical Regulatory Harmonization Strategy set forth by the Ministry of Health, Labour and Welfare (MHLW) in June 2015, the Agency developed the PMDA International Strategic Plan 2015 that specifies international activities the Agency should implement within the period covered by its Third and Fourth Mid-term Plans (FY 2014 to 2023).

As the development, manufacture, and distribution of drugs, medical devices, and regenerative medical products are becoming increasingly globalized, PMDA must increase its efforts to cooperate closely with foreign regulatory authorities, as well as industry and academia. In line with the PMDA International Strategic Plan 2015, PMDA aims to maximize the common health benefits to Japan and the world by building on its experience with international activities, and by making the most of its scientific knowledge, human resources, and electronic information. The three visions and five strategies set out in the strategic plan will serve as the main pillars of PMDA's international activities.

## ● PMDA International Strategic Plan 2015

### Three Visions

#### **Vision I: To contribute to the world through regulatory innovation**

PMDA will, based on regulatory science, promote public health globally by communicating the outcomes of its first-in-the-world product reviews, safety measures, and relief services

#### **Vision II: To maximize the common health benefits to other countries/regions**

PMDA will, in order to realize quicker access to more effective and safer medical products for patients around the globe, communicate more closely with countries around the world to promote regulatory harmonization and collaboration

#### **Vision III: To share the wisdom with other countries/regions**

PMDA will, by fully utilizing the accumulated knowledge and experience, contribute to the public health of partner countries/regions through provision of information and training that are essential for building regulatory capacity in those countries

### Five Strategies

#### **Strategy 1: Taking the lead, and disseminating the information around the globe**

- Establish the "Regulatory Science Center" and other schemes

#### **Strategy 2: Promotion of international regulatory harmonization and global cooperation**

- Expediting the global utilization of the Japanese Pharmacopoeia (JP)
- Strengthening the communication with overseas regulatory authorities through mutual personnel exchange

#### **Strategy 3: Increase efficiency of inspections that may lead to future international work-sharing**

- Streamline international collaboration in GXP/QMS inspections

#### **Strategy 4: Contribution to international regulatory harmonization activities**

- Proactively propose to create guidelines, etc. leading to common health benefit

#### **Strategy 5: Provision of information and training programs that are essential for building regulatory capacity in partner countries**

- Launch of "Asian Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs" and other programs



■ A view of a session at the DIA Annual Meeting (in Philadelphia, USA, June 2016)



■ A group photograph of participants at the 11th International Summit of Heads of Medicines Regulatory Agencies and the meeting of the International Coalition of Medicines Regulatory Authorities (ICMRA) (in Interlaken, Switzerland, October 2016)

## ■ Bilateral Cooperation between PMDA and Foreign Regulatory Authorities (as of the end of July 2017)



- ★ Confidentiality Arrangement signed    ■ PMDA staff stationed at the agency    ● Joint symposium held    ▲ Memorandum of Cooperation  
 ▲ Memorandum of Cooperation (related to the pharmacopoeia)

\* The Memorandum of Understanding has been signed between the Interchange Association of Japan and the East Asia Relations of Taiwan for the Establishment of the Framework of the Cooperation on Medical Products Regulation.

## Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

In line with the objectives of the PMDA International Strategic Plan 2015, in April 2016, PMDA established the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC), a training center for members of the staff of Asian regulatory authorities. The mission of the PMDA-ATC is to promote greater understanding of Japanese regulations pertaining to pharmaceuticals and medical devices among Asian regulatory authorities. PMDA plans to take a proactive approach to information sharing and idea exchange with other Asian regulators regarding its understanding of regulatory science in Japan and accumulated regulatory experience and knowledge.

In addition, PMDA established a Hokuriku branch office located in Japan's Toyama prefecture in June 2016. The PMDA-ATC plans to offer training courses focusing on GMP inspections in cooperation with the new Hokuriku branch office.

Details of seminars and training programs offered by the PMDA-ATC will be posted and updated as necessary on the PMDA website.

In FY 2016, PMDA-ATC organized seven training seminars both in and outside Japan and a total of 161 regulators from 27 countries/regions participated in the seminars.

PMDA-ATC's achievements have been highly evaluated, and the training center was officially endorsed as the APEC LSIF RHSC Training Centers of Excellence for Regulatory Science (CoE) in the fields of multi-regional clinical trials, GCP inspections, and pharmacovigilance in February 2017. As a result, PMDA-ATC has come to be recognized globally.

## ■ Activities of PMDA-ATC





# Promotion of Regulatory Science

PMDA's scientific activities must consist of accurate prediction, evaluation, and judgment based on clear evidence, while incorporating the latest scientific findings. To improve such activities, it is important to advance regulatory science, which forms the basis of regulatory activities.

Regulatory science plays an important role in adapting the achievements of technology to social and human needs in the most optimal way, by making precise prediction, evaluation and judgment based on evidence. The practical application of outcomes of medical research and development activities requires regulatory assessment. In such an assessment process, regulatory science serves to appropriately and promptly predict, evaluate, and determine the quality, efficacy, and safety of a newly developed product in light of current scientific findings.

PMDA is committed to promoting regulatory science and fostering regulatory scientists through expansion of training programs for employees, implementation of research on PMDA's three services (product reviews, safety measures, and relief services for adverse health effects), utilization of the Science Board, and education by way of the Collaborative Graduate School Program.

## Science Board

In May 2012, PMDA established the Science Board in order to respond to the rapid progress of medical innovations in recent years and to properly address scientific challenges in the field of advanced science and technology. The Science Board consists of external experts in areas such as medicine, dentistry, pharmaceutical science, and engineering.

PMDA actively utilizes the Science Board, thereby reinforcing collaboration and communication with scientists in universities and research institutions and healthcare professionals to discuss the evaluation methods of innovative drugs, medical devices, and regenerative medical products. Furthermore, PMDA endeavors to appropriately deal with state-of-the-art technology products through its review and related services and safety measures in addition to the Regulatory Science Strategy Consultation (R&D).

The third term Subcommittees (April 2016 to March 2018) of the Science Board are currently working on the following topics: measures for rare cancers, drug development, and artificial intelligence (AI).

### ● The outcome documents of the Science Board meetings

#### The First Term: May 2012 to March 2014

- 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
- Summary of Discussion on the Assessment of the Current Status of Personalized Medicine related to Development and Regulatory Review
- Summary of Discussion on Non-clinical Pharmacology Studies on Anticancer Drugs

#### The Second Term: April 2014 to March 2016

- Current Status and Perspectives of Placebo-controlled Studies
- Report on the Use of Non-clinical Studies in the Regulatory Evaluation of Oncology Drugs
- Report on the Use of Numerical Analysis for Strength Evaluation of Orthopedic Implants
- Discussions on Evaluation of Medical Devices in Pediatric Use
- Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products



## Comprehensive Partnership Agreement

PMDA has made efforts to promote regulatory science and foster younger researchers through post-graduate education by concluding agreements with several graduate schools on Collaborative Graduate School Program launched in 2009.

Since April 2015, the program has been expanded to include medical and research institutions that conduct high-quality clinical research, in addition to universities, and thereby to establish an extensive collaborative framework that exceeds conventional research or education. PMDA intends to develop enhanced partnership programs under a comprehensive partnership agreement, which allows distinctive and diversified features of collaboration based on the strengths of individual specialized organizations.

- As of the end of July 2017, PMDA has concluded the comprehensive partnership agreements with eight institutions:

National Cancer Center Japan  
Hiroshima University  
Keio University  
University of Tsukuba  
National Center of Neurology and Psychiatry  
Tohoku University  
National Center for Global Health and Medicine  
National Cerebral and Cardiovascular Center  
(Listed in order of signing)

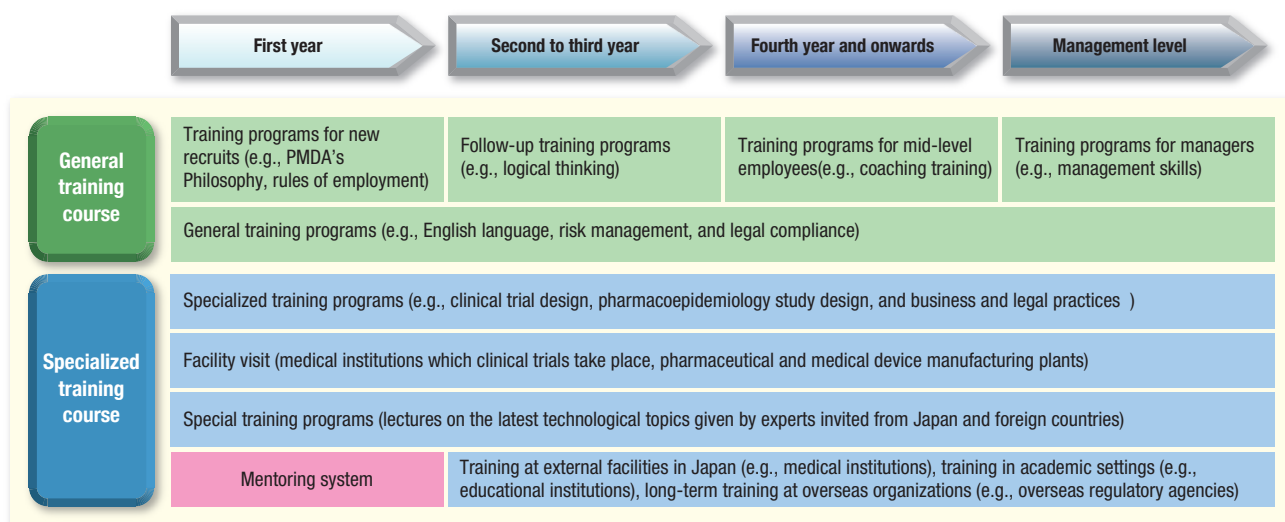
- Graduate schools with which PMDA has concluded the agreement on the collaborative graduate school program

- University of Tsukuba Graduate School of Comprehensive Human Sciences;
- Yokohama City University Graduate School of Medicine;
- Yamagata University Graduate School of Medical Science;
- Gifu Pharmaceutical University Graduate School of Pharmaceutical Science;
- Kobe University Graduate School of Medicine;
- Chiba University Graduate School of Medical and Pharmaceutical Sciences/Graduate School of Medicine;
- Musashino University Graduate School of Pharmaceutical Sciences;
- United Graduate School of Drug Discovery and Medical Information Sciences, Gifu University;
- Teikyo University Graduate School of Medicine/Graduate School of Pharmaceutical Sciences;
- Shujitsu University Graduate School of Clinical Pharmacy;
- Graduate School of Integrated Pharmaceutical and Nutritional Sciences, University of Shizuoka;
- Osaka University Graduate School of Medicine;
- Kyoto Pharmaceutical University Graduate School of Pharmaceutical Sciences;
- Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences;
- Nagoya University Graduate School of Medicine;
- Nagoya City University Graduate School of Pharmaceutical Sciences;
- Hokkaido University Graduate School of Medicine;
- Kanazawa University Graduate School of Medical Sciences; and
- Kumamoto University Graduate School of Medical Sciences.  
(Listed in order of signing)

## Training and Human Resource Development

PMDA's services such as reviews, relief services for adverse health effects, and post-marketing safety measures all require a high level of expertise. In addition, science and technology for development of drugs and medical devices are rapidly advancing these days. PMDA strives to enhance the quality of its services by providing its employees with organized training opportunities.

### ■ Training Programs at PMDA



# Contact & Map

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## Contact Information

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*\*Please contact us via our online contact form.*

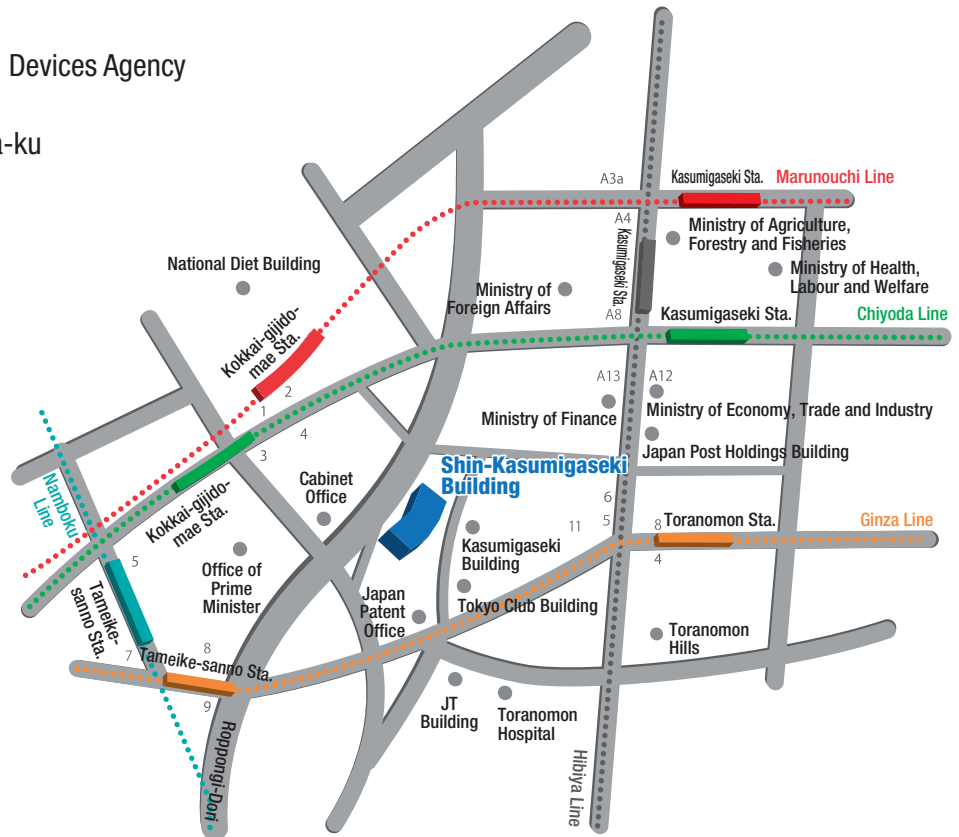
Website: <http://www.pmda.go.jp>

English site: <http://www.pmda.go.jp/english/index.html>

# How to Find Us - Location Maps

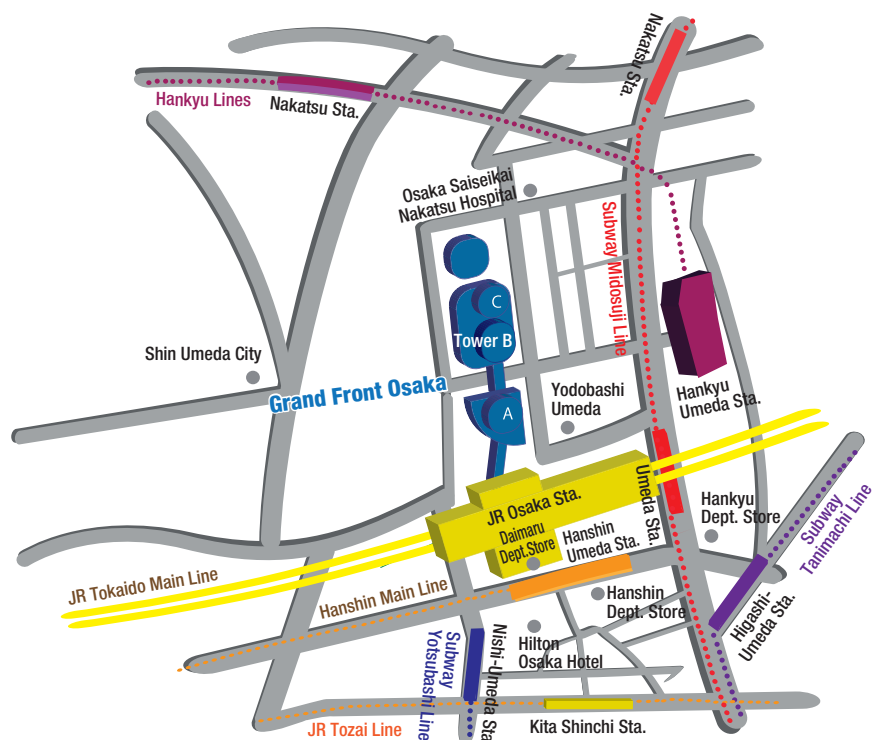
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