I. THE PHARMACEUTICALS AND MEDICAL DEVICES AGENCY

PART 1. HISTORY AND OBJECTIVE OF THE AGENCY

As lessons learned from drug-induced diseases caused by pharmaceuticals such as thalidomide and SMON (sub-acute myelo-optical-neuropathy), the Fund for Adverse Drug Reactions Suffering Relief was established in October 1979 based on stipulations in the Adverse Drug Reaction Suffering Relief Fund Law (1979, Law No. 55), for the purpose of providing prompt relief to patients suffering from adverse drug reactions. In 1987, the Fund started R&D promoting operations under the name of "The Fund for Adverse Drug Reaction Relief and R&D Promotion" and then reorganized into "The Organization for Pharmaceutical Safety and Research (OPSR/Kiko)" in 1994 to play a role in equivalency reviews of generic drugs. Later, in 1997, the organization started to provide advice on clinical trials and conduct conformity audits on applications for approval of pharmaceuticals.

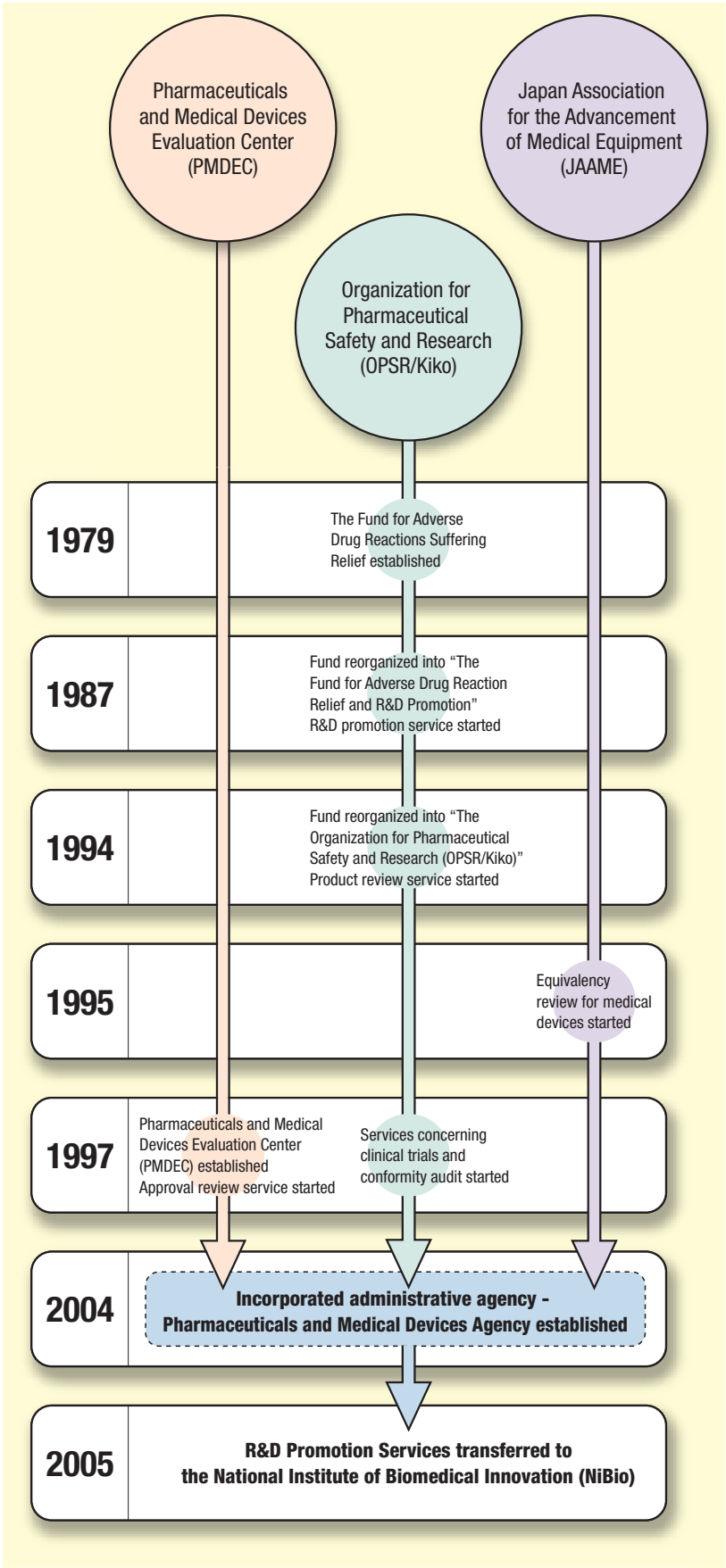
In 1997, the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) was established at the National Institute of Health Sciences in order to develop a full-scale approval review system and to make the contents of the review more advanced. At the Center, reviews were conducted by teams consisting of experts specializing in pharmaceutical science, medical science, biostatistics etc. In addition, the Japan Association for the Advancement of Medical Equipment (JAAME) began operations starting in 1995 to conduct equivalency reviews of medical devices as a designated investigative body under the Pharmaceutical Affairs Law.

From 1997 to 1999, there was a systematic and drastic increase in the number of the staff engaging in reviews 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 and developing the structure as governmental organizations.

In the midst of this kind of situation, the Cabinet adopted "Special Service Agency Restructuring Plan" in December 2001, in which it was decided that the OPSR/Kiko should be dissolved, and the Pharmaceutical and Medical Devices Agency (PMDA) should be newly founded by consolidating the operations allocated to the PMDEC, OPSR/Kiko and JAAME in order to further enhance reviews and safety measures. In 2002, a legislative bill for the Law for the Pharmaceuticals and Medical Devices Agency was discussed and passed at the 155th extraordinary session of the Diet, resulting in the establishment of the PMDA on April 1, 2004 in accordance with the Law for the Pharmaceuticals and Medical Devices Agency (2002, Law No.192).

The objective of the Agency is to contribute to the improvement of national health by providing prompt relief services for sufferers of adverse health effects resulting from infections derived from biological products in addition to adverse health reactions caused by pharmaceuticals (Relief for Adverse Health Effects); providing guidance and reviews regarding the quality, efficacy and safety of pharmaceuticals and medical devices through a system that is consistent from pre-clinical research to approval (Reviews); and collecting, analyzing and providing information on post-marketing safety (Safety Measures).

Previously, one of the objectives of the Agency was to promote basic research and development of pharmaceuticals and medical devices that contribute to maintaining and advancing 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 (NiBio) in April 2005, in order to allow the Agency to focus specifically on reviews, safety measures and relief services for adverse health effects.


Pharmaceuticals and Medical Devices Evaluation Center (PMDEC)
Japan Association for the Advancement of Medical Equipment (JAAME)
Organization for Pharmaceutical Safety and Research (OPSR/Kiko)
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/Kiko)" Product review service started
1995
Equivalency review for medical devices started
1997
Pharmaceuticals and Medical Devices Evaluation Center (PMDEC) established Approval review service started
Services concerning clinical trials and conformity audit started
2004
Incorporated administrative agency - Pharmaceuticals and Medical Devices Agency established
2005
R&D Promotion Services transferred to the National Institute of Biomedical Innovation (NiBio)

PART 2. OVERVIEW OF OPERATIONS

1. Relief Services for Adverse Health Effects

As a service inherited from the OPSR/Kiko, the Agency provides benefits for medical expenses, disability pensions and bereaved family pensions to the sufferers of illnesses or disabilities caused by adverse drug reactions (Adverse Drug Reaction Relief Service).

In April 2004, the Agency also started providing benefits to sufferers of adverse health effects caused by infections from pharmaceuticals and medical devices created by using ingredients and materials derived from biological entities (Relief Service for Infections Derived from Biological Products).

The Agency is also commissioned by the government and pharmaceutical companies to provide healthcare allowances and nursing care expenses to SMON patients (Service for Healthcare Allowances). In addition, the Agency works under the commission of the Yu-ai Welfare Foundation to make payments for healthcare expenses for HIV positive and AIDS patients (Service for Healthcare Allowances).

2. Review Services

In accordance with the Pharmaceutical Affairs Law, the Agency reviews the efficacy, safety and quality of pharmaceuticals and medical devices for which applications for approval review have been submitted, based on the current scientific and technological standards. In addition, the Agency conducts re-examinations/re-evaluations of pharmaceuticals and medical devices and reviews of applications for pre-clinical assurance of products processed with cell tissue, as well as reviews of applications for genetically modified biological entities in accordance with the Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms" (Law No. 97, 2003) (Approval Review Services).

In response to requests from clinical trial sponsors, the Agency provides face-to-face guidance and consultations on clinical trials for new drugs and new medical devices, as well as on clinical trials for re-examinations/re-evaluations of approved products (Face-to-face Consultation Service).

For items for which applications were made for approval reviews and re-examinations/re-evaluations, on-site and document inspections are implemented to determine whether materials attached to approval application documents conform to GLP (Good Laboratory Practice), GCP (Good Clinical Practice) and reliability standards for application materials (Conformity Audit Services).

In addition, on-site and document inspections are conducted to determine whether manufacturing facilities and manufacturing control methods for new drugs and new medical devices, etc., conform with ministry ordinances relating to standards for manufacturing control and quality

control, and whether there is a system for manufacturing products of an appropriate quality (GMP/QMS Conformity Audits Services).

3. Safety Measures

The Agency is cooperating with the Ministry of Health, Labour and Welfare on the following services to improve the safety of marketed pharmaceuticals and medical devices as well as to enable for patients and people involved in the medical field to use pharmaceuticals and medical devices appropriately and with a peace of mind.

(1) Services for collecting information in an unified manner and organizing such information relating to the safety of pharmaceuticals and medical devices from a broad range of sources, such as reports from the private sector, information from medical institutions, information from foreign regulatory agencies and conference papers, relating to adverse drug reactions, malfunctions and infections (Collection and Organization of Information).

(2) Services for conducting research and reviews relating to safety measures based on the information collected in (1) above (Research and Review Services).

(3) Services for giving guidance and advice to marketing authorization holders, as well as providing advice in response to consultations from consumers (Consultation Services).

(4) Services to provide information on the safety of pharmaceuticals and medical devices widely to healthcare professionals, patients, and private companies, etc., in a timely manner (Information Provision Services).

(5) Surveys related to developing various standards, such as the Japanese Pharmacopoeia that is stipulated in the Pharmaceutical Affairs Law (Standards Development).

[Structure of the Agency (FY2006)]