

CHAPTER 1

Organization and Function of the Ministry of Health, Labour and Welfare

The Ministry of Health, Labour, and Welfare (MHLW) (Koseirodosho in Japanese) was established by a merger of the Ministry of Health and Welfare (MHW) and the Ministry of Labour, on January 6, 2001 as part of the government program for reorganizing government ministries. The MHLW, which was originally established in 1938, has been in charge of the improvement and promotion of social welfare, social security and public health, and the new organization has the same tasks.

It consists of the ministry proper, affiliated institutions, councils, local branches, and external organizations. The ministry proper includes the Minister's Secretariat, 11 bureaus, and the Director-General for Policy Planning and Evaluation.

Councils include the Social Insurance Council, Pharmaceutical Affairs and Food Sanitation Council (PAFSC), and other organizations. Affiliated institutions include the National Institute of Health Sciences and the National Institute of Infectious Diseases. Local branches are regional bureaus of health and welfare and prefectural labor bureaus. The external organizations are the Social Insurance Agency and the Central Labor Relations Commission (**Fig. 1. Organization of Ministry of Health, Labour, and Welfare**).

The MHLW is in charge of pharmaceutical regulatory affairs in Japan (veterinary drugs are under the jurisdiction of the Ministry of Agriculture, Forestry and Fisheries), and the Pharmaceutical and Food Safety Bureau (PFSB) undertakes main duties and functions of the Ministry; it handles clinical studies, approval reviews and post-marketing safety measures, i.e., approvals and licensing. The Health Policy Bureau handles promotion of R&D, production, distribution policies, and drug pricing, i.e., functions related to pharmaceutical companies. The Pharmaceuticals and Medical Devices Evaluation Center (Evaluation Center) in the National Institute of Health Sciences was established to strengthen approval reviews and to introduce a specific system for reviewing tasks for drugs, etc. on July 1, 1997. To confirm the reliability of reviews and application data, the Organization for Pharmaceutical Safety and Research (OPSR) conducted compliance reviews on application data. The OPSR also began offering consultation services on protocols at the clinical trial stage.

This was followed by the integration of the aforementioned Evaluation Center, OPSR, and part of the Medical Devices Center on April 1, 2004 to form a new independent administrative organization, the Pharmaceutical and Medical Devices Agency (PMDA, KIKO). The role of the PMDA is to provide consultations concerning the clinical trials of new drugs and medical devices, and to conduct approval reviews and surveys of the reliability of application data.

Following this reorganization, the MHLW and PMDA handle a wide range of activities from clinical studies to

approval reviews, reviews throughout post-marketing stage, and pharmaceutical safety measures. (**Fig. 2. Organization of Pharmaceutical and Food Safety Bureau (PFSB) and Pharmaceuticals and Medical Devices Agency (PMDA)**).

1. PHARMACEUTICAL AND FOOD SAFETY BUREAU (PFSB)

The Pharmaceutical and Food Safety Bureau (PFSB) (except for the Department of Food Safety) is one of the 11 bureaus of the MHLW. In addition to policies to assure the efficacy and safety of drugs, quasi-drugs, cosmetics and medical devices, and policies for safety in medical institutions, the PFSB tackles problems directly related to the lives and health of the general public including policies related to blood supplies and blood products, and narcotics and stimulant drugs. This new bureau consists of a Secretary-General, Councilor in charge of drugs, five divisions, and one office* (**Fig. 2. Organization of Pharmaceutical and Food Safety Bureau (PFSB) and Pharmaceuticals and Medical Devices Agency (PMDA)**). These divisions have the functions described below.

1.1 General Affairs Division

- 1) Overall planning and coordinating activities for the Pharmaceutical and Food Safety Bureau
- 2) Matters related to pharmacists
- 3) Supervision of the PMDA (excluding areas under the control of the Evaluation and Licensing Division and Safety Division, and Compliance and Narcotics Division)
- 4) Issues related to PFSB not governed by other divisions

• Office of Drug Induced Damages

- 1) The relief systems operated by the PMDA for damage caused by adverse drug reactions including biological products-induced infection
- 2) Measures for handling health injury caused by drugs, quasi-drugs, cosmetics, and medical devices (drugs, etc.)

1.2 Evaluation and Licensing Division

- 1) Technical guidance and supervision concerning the production of drugs, quasi-drugs, cosmetics, and medical devices (drugs, etc.)
- 2) Manufacturing/marketing business licenses and approvals to manufacture and market drugs, etc.
- 3) Reexamination and reevaluation of drugs
- 4) Issues related to the Japanese Pharmacopoeia (JP)
- 5) Standards and specific precautions concerning drugs, etc.
- 6) Designation of orphan drugs
- 7) Work related to the PMDA (KIKO) (limited to approval to manufacture and market drugs, medical devices, etc.)

• Office of Medical Devices and Regenerative

Medicine Products Evaluation

- 1) Technical guidance and supervision concerning the production of medical devices, extracorporeal diagnostic medicines and regenerative medicine products
- 2) Manufacturing business licenses for regenerative medicine products and manufacturing business registrations for medical devices and extracorporeal diagnostic medicines, as well as approvals to manufacture and market medical devices, extracorporeal diagnostic medicines and regenerative medicine products
- 3) Reexamination and reevaluation of regenerative medicine products
- 4) Evaluation of treatment outcomes of medical devices and extracorporeal diagnostic medicines
- 5) Business license and approvals to market, loan, or repair medical devices (excluding areas under the control of Health Policy Bureau [HPB])
- 6) Standards and specific precautions concerning medical devices, extracorporeal diagnostic medicines and regenerative medicine products
- 7) Designation of orphan medical devices and orphan regenerative medicine products
- 8) Work related to the Pharmaceutical and Medical Devices Agency, Independent Administrative Agency (limited to work listed in Article 15, Paragraph 1, Item (5) (a) to (d) of the Law on Pharmaceuticals and Medical Devices Agency, Independent Administrative Agency (Law No. 192 of 2002) (with respect to work listed in (a), (b) and (d) of said item, limited to work relating to medical devices, extracorporeal diagnostic medicines and regenerative medicine products and, with respect to work listed in (c) of said item, only manufacturing business licenses for regenerative medicine products and manufacturing business registrations for medical devices and extracorporeal diagnostic medicines, as well as approvals to manufacture and market medical devices, extracorporeal diagnostic medicines and regenerative medicine products, reexamination and reevaluation of regenerative medicine products, evaluation of treatment outcomes of medical devices and extracorporeal diagnostic medicines, standards and specific precautions concerning medical devices, extracorporeal diagnostic medicines and regenerative medicine products, and control and dissemination of Industrial standards for medical devices, other hygiene products and regenerative medical products, and other industrial standards) and work incidental thereto, as well as work listed in said Article, Paragraph 2, Item 2 (limited to work related to medical devices, extracorporeal diagnostic medicines and regenerative medicine products.))
- 9) Control and dissemination of industrial standards for medical devices, other hygiene products, and regenerative medicine products, and other industrial standards

• Office of Chemical Safety

- 1) Enforcement of laws pertaining to poisonous and deleterious substances (excluding areas under the

control of the Compliance and Narcotics Division)

- 2) Regulations related to evaluation of chemicals that might cause damage to the health of humans, animals, and plants from the standpoint of environment and public health, as well as regulations related to manufacturing, importing, using, and other handling of such chemicals
- 3) Control of household products containing harmful substances
- 4) Establishment of tolerable daily intake (TDI) of dioxins and related compounds

1.3 Safety Division

- 1) Planning and drafting of policies to assure the safety of drugs, quasi-drugs, cosmetics, and medical devices (drugs, tc.)
- 2) Manufacturing/marketing business licenses to manufacture and market drugs, etc.
- 3) Review of the safety of drugs, etc. (excluding items handed by the Evaluation and Licensing Division)
- 4) Guidance and advice concerning biological preparation and storage of records of biological products and designated medical devices
- 5) Work related to the PMDA (KIKO) (limited to matters related to improve safety of drugs, etc. and excluding items handed by the Evaluation and Licensing Division)

1.4 Compliance and Narcotics Division

- 1) Control of poor quality or falsely labeled drugs, quasi-drugs, cosmetics, and medical devices (drugs, etc.)
- 2) Guidance and supervision related to advertising of drugs, etc.
- 3) Testing and government certification of drugs, etc.
- 4) Matters related to pharmaceutical inspectors, etc.
- 5) Control of substances designated by the Law on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Law)
- 6) Matters related to inspectors of poisonous and deleterious substances
- 7) Control of narcotics, psychotropics, cannabis, opium, and stimulants
- 8) Duties of narcotics control officers and staff as judicial police officials
- 9) Cooperation with international criminal investigations concerning narcotics, psychotropics, cannabis, opium, and stimulants
- 10) Work related to the PMDA (KIKO) (limited to matters related to on-site inspection, etc. by the PMDA)

1.5 Blood and Blood Products Division

- 1) Regulation of blood collection services
- 2) Promotion of blood donation
- 3) Assurance of proper use of blood products and

assurance of stable supply of blood products

- 4) Maintenance of stable supply of blood products
- 5) Promotion, improvement, and coordination concerning production and marketing of biological products

2. HEALTH POLICY BUREAU

With the aging of society, changes in disease structure, and increasing demands from the public for better quality health care, the Health Policy Bureau is drafting policies aimed at achieving a high quality, efficient health care supply system for the 21st century.

The Economic Affairs Division and the Research and Development Division, the two divisions most closely related to the pharmaceutical industry, have the functions described below.

2.1 Economic Affairs Division

- 1) Promotion, improvement and coordination related to production, marketing and consumption of drugs, quasi-drugs, medical devices, sanitary materials, and other hygiene-related products (drugs, etc.) (excluding items handled by PFSB and the Research and Development Division)
- 2) Advancement, improvement, and coordination of manufacturing of drugs, etc. (excluding items handled by the Research and Development Division)
- 3) Matters related to foreign trade (import and export) of drugs, etc.
- 4) Matters related to outsourcing the work of managers of hospitals, clinics, and maternity clinics (hospitals, etc.)
- 5) Guidance on enterprises related to the improvement of the management of hospitals, etc. (excluding those governed by the national and local governments)
- 6) Issues related to hygiene inspection offices. This Division includes the Office of Direction for Health-Related Services with the following functions.

• Office of Medical Device Policy

- 1) Promotion, improvement and coordination of manufacturing, marketing and consuming medical devices and other sanitary products (other than those handled by PFSB and the Research and Development Division)
- 2) Promotion, improvement and coordination of business of manufacturing, manufacturing/marketing, selling, leasing and repairing medical devices and other sanitary products (other than those handled by the Research and Development Division)
- 3) Foreign trades (import and export) of medical devices and other sanitary products
- 4) Installation and use of medical devices (other than medical, dental, and sanitary supplies) (other than those handled by the Guidance of Medical Service Division)

2.2 Research and Development Division

- 1) Matters related to research and development of drugs, etc. (excluding items handled by PFSB)
- 2) Matters related to the cultivation and production of medicinal plants
- 3) Promotion, improvement, and coordination of manufacturing business of drugs, etc. (limited to items related to research and development)
- 4) Matters related to installation and use of medical devices (excluding medical supplies, dental supplies, and hygiene-related products) (excluding items handled by the Guidance of Medical Service Division of the HPB)
- 5) Matters related to the improvement of health care information-processing and management system
- 6) Matters related to the evaluation of medical technology (excluding those handled by other bureaus of MHLW)

• Office of Clinical Trial Promotion

Promotion of clinical trials specified in Article 2, Paragraph 16 of the Pharmaceutical Affairs Law (Law No. 145 issued in 1960) (other than those handled by PFSB)

3. NATIONAL INSTITUTE OF HEALTH SCIENCES

In July 1997, the name of the former National Institute of Hygienic Sciences was changed to the National Institute of Health Sciences. In addition to its long-standing work related to testing and research on drugs, quasi-drugs, cosmetics, medical devices, foods, poisonous and deleterious substances, the Institute supervised the Pharmaceuticals and Medical Devices Evaluation Center to undertake the reviews required for approval to manufacture or import drugs, quasi-drugs, cosmetics and medical devices, as well as the reexamination and the reevaluation of drugs, and medical devices. Thereafter, the Evaluation Center was incorporated into the Pharmaceuticals and Medical Devices Agency (PMDA, KIKO) in April 2004.

4. PHARMACEUTICALS AND MEDICAL DEVICES AGENCY (PMDA), AN INDEPENDENT ADMINISTRATIVE ORGANIZATION

In accordance with the special corporation rationalization plan passed by the Cabinet in December 2001, and enactment of the Pharmaceuticals and Medical Devices Agency Law in December 2002, the PMDA (KIKO) was established in April 2004, through the integration of the Pharmaceutical and Medical Devices Evaluation Center in the National Institute of Health Sciences, the OPSR, and part of the Medical Devices Center, and the PMDA started handling all consultation and review work from the preclinical stage to approvals and post-marketing surveillance.

The work of the PMDA can be divided into three main categories: ADR relief work, review work and safety measures.

The PMDA consists of 25 offices, 3 groups, and the Kansai branch as shown in Fig. 2, and, the duties are indicated below.

The PMDA is currently working to achieve goals under the Third Medium Range Plan (2014-2018), including strengthening and enhancing post-marketing safety measures to ensure the quality of products and prevent the occurrence or escalation of health hazards and striving to speed up and improve the quality of reviews, in order to be the first in the world to facilitate practical use of innovative drugs, pharmaceutical medical devices and regenerative medicine products, as well conducting publicity activities so that relief systems are definitely used when necessary.

1) Drug ADR Relief Work

- **Provision of medical benefits to cover healthcare expenses, disability pensions, and survivors pensions for individuals suffering disease or disability due to adverse drug reactions or bioderived infections**
- **Provision of medical allowances for treatment of myelo-optico-neuropathy (SMON) patients and for HIV carriers and AIDS patients**
- **Surveys on damage caused by drugs and research on treatment, etc. of adverse drug reactions as health and welfare work**
- **Provision of medical allowances based on the Special Measures Law for Provision of Medical Allowances for Treatment of Hepatitis C Patients Infected by Specified Fibrinogen Concentrates or Specified Coagulation Factor XI Concentrates.**

2) Review Related Work

- **Approval reviews of new drugs and medical devices based on the Drugs and Medical Devices Law**
- **Guidance and advice related to clinical trials**
- **Reviews of GLP and GCP compliance of attached data of approval applications and reexamination and reevaluation applications**
- **Reviews of manufacturing facilities, processes, and quality control based on GMP, QMS, etc.**
- **Confirmation of reexaminations and reevaluations based on the Drugs and Medical Devices Law**

3) Safety Measures

- **Collection, analysis, and dissemination of information related to the quality, efficacy, and safety of drugs and medical devices**
- **Consultations with consumers and other parties concerning drugs and medical devices**
- **Guidance and advice for manufacturers, etc. to improve the safety of drugs and medical devices**

The work of the review and safety offices is detailed below.

4.1 Office of Review Administration

This office handles tasks related to the receipt and processing of license and other applications, drug master file (MF) registrations and modifications, clinical trial notifications, simple consultation applications on generic drugs and the issuance of manufacturing/marketing authorization letters, etc.

4.2 Office of Review Management

This office handles tasks related to the publication (disclosure) of approval review results, receipt and processing of clinical trial consultations on new drugs, and receipt and processing of reports including basic protocols for post-marketing surveillance, and periodic safety update reports (PMS, reevaluation, GVP). The office also handles pharmaceutical affairs consultation on R&D strategy on drugs and medical devices mainly for universities, research institutes, and venture companies.

4.3 Office of Standards and Guidelines Development

This office handles tasks related to the preparation of draft Japanese Pharmacopoeia, standards on medical devices, standards on drugs, master file systems, and generic names (JAN).

4.4 Office of International Programs

This office represents PMDA at bilateral talks with foreign regulatory agencies and plays a central role in international communication such as the sharing of public and non-public information with foreign regulatory agencies and organizations. The main services rendered are the promotion of international harmonization of regulatory standards/practices, planning of international activities, foreign public relations campaign, and expansion of human exchange. The office serves as the administrative office of PMDA at international conferences sponsored by PMDA.

4.5 Office of New Drug I

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluation of gastrointestinal drugs, dermatologic drugs, hormone preparations, and metabolic disease drugs (e.g., anti-diabetic, osteoporosis, gout, and congenital metabolic disorder drugs)

4.6 Office of New Drug II

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations and reevaluation of new cardiovascular drugs, drugs to treat Parkinson's disease, drugs to treat Alzheimer's disease, urogenital and anal drugs, combination drugs, radiopharmaceuticals, and contrast media.

4.7 Office of New Drug III

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluation of new central nervous system drugs, peripheral nervous system drugs, anesthetic agents, sensory organ drugs (other than drugs for inflammatory diseases), and narcotics.

4.8 Office of New Drug IV

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluation of antibacterial drugs, antiviral agents (except for anti-HIV/AIDS agents), new respiratory tract drugs, anti-allergy drugs, sensory organ drugs (limited to drugs for inflammatory diseases), and

anti-HIV/AIDS agents.

4.9 Office of New Drug V

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluations of antineoplastic drugs.

4.10 Office of Cellular and Tissue-based Products

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluations of regenerative medical products (cellular and tissue-based products and gene therapy products), preliminary reviews for approval or verification based on the Cartagena Protocol, and quality review of antibody preparations.

4.11 Office of Vaccines and Blood Products

This office confirms clinical trial notifications and adverse drug reactions of globulins, blood coagulation-factor products, vaccines, and antidotes and performs the reviews required for approval, reexamination, or reevaluation.

4.12 Office of OTC and Generics

This office conducts reviews required for the approval, export certification, and quality reevaluations of guidance-mandatory drugs non-prescription drugs, quasi-drugs, and cosmetics.

4.13 Office of Generics

This office conducts reviews required for the approval, export certification, and quality reevaluations of generic drugs, etc. (ethical drugs excluding new drugs and extracorporeal diagnostic medicines).

4.14 Office of Medical Devices I

This office confirms clinical trial notifications and adverse drug reactions and conducts reviews required for approval, reexaminations, and reevaluation of medical devices and high-level medical electronic devices intended for use in the fields of cerebro-/cardiovascular systems, respiratory system, neurology/psychiatry, etc.

4.15 Office of Medical Devices II

This office confirms clinical trial notifications and conducts reviews required for approval, reexamination, and reevaluation of medical devices intended for use in the fields of ophthalmology, otorhinolaryngology, dentistry, gastroenterology, urology, obstetrics/gynecology, orthopedic surgery, plastic and reconstructive surgery, dermatology, and laboratory testing (in vitro diagnostics).

4.16 Office of Medical Devices III

This office performs reviews for approval applications, investigations, etc. of generic medical devices in all fields other than laboratory testing (in vitro diagnostics).

4.17 Office of Compliance and Standards

This office reviews the documentation included with applications for approval, reexamination, or reevaluation of

drugs, medical devices, and regenerative medicine products to assure that the studies on which the data is based comply with GLP, GCP, GPSP, study protocol, etc. both ethically and scientifically to determine if the documents have been prepared appropriately and accurately based on the study results in accordance with the Criteria for Reliability of Application Data (Article 43 of the Enforcement Regulations, Pharmaceutical Affairs Law) (hereinafter "Reliability Criteria") and examined on site and on paper. Compliance of facilities performing GLP-based studies is also examined and certified.

4.18 Office of Safety I

This office undertakes centralized collection and compilation of information related to the quality, efficacy, and safety of drugs and medical devices, conducts surveys and guidance on the application of such information in medical institutions, and conducts scientific analysis and evaluation of such safety information using pharmaceutical and epidemiological procedures. It also undertakes consultations and information dissemination work.

4.19 Office of Safety II

This office undertakes analysis and evaluation of adverse reactions of drugs and medical devices.

4.20 Kansai Branch

This branch undertakes pharmaceutical strategy consultations and GMP and QMS inspections in the Kansai area.

4.21 Electronic Data Promotion Group

This group makes plans and proposals concerning the use of electronic application data and undertakes surveys and adjustments associated with this. It also proposes education and training relating to the viewing and analysis of electronic application data, and gathers and organizes information concerning the use of electronic application data.

5. THE NATIONAL INSTITUTE OF BIOMEDICAL INNOVATION (INDEPENDENT ADMINISTRATIVE AGENCY)

The National Institute of Biomedical Innovation was established in April 2005 based on the Law for the National Institute of Biomedical Innovation which was approved by the 159th National Diet Session and promulgated in 2004 to make a major contribution to drug research and development by integrating basic research, research on bioresources, and promotion of research and development.

Research promotion and orphan drug development promotion, which had been conducted by the PMDA, were transferred to the institute.

6. PHARMACEUTICAL AFFAIRS AND FOOD SANITATION COUNCIL (PAFSC)

The Pharmaceutical Affairs and Food Sanitation Council (PAFSC) serves as an advisory body to the MHLW, and reviews and discusses important pharmaceutical and food sanitation-related matters (**Fig. 3. Organization of the Pharmaceutical Affairs and Food Sanitation Council. PAFSC**)

This council was created by merging of the Central Pharmaceutical Affairs Council (CPAC) and the Food Sanitation Investigation Council. It is divided into a Pharmaceutical Affairs Committee and a Food Sanitation Committee. The latter comes under the Food Sanitation Law and the former under other laws.

The Council has as members experts in various fields¹⁾ including the medical and pharmaceutical sciences.

The frequency of committee meetings differs. For example, the First Committee on New Drugs²⁾ and the Second Committee on New Drugs²⁾, which review new drug applications, each meet approximately eight times a year and the Committee on Non-prescription Drugs³⁾ meets four times a year.⁴⁾ New drugs are then reviewed or reported and approved by the Pharmaceutical Affairs Committee that meets four times a year.^{5) 6)}

Note 1) Expert areas: Nursing, life sciences, applied biochemistry, mathematics and statistics, law, and economics

Note 2) Categories of drugs for the Second Committee on New Drugs to review: Antiviral drugs, chemotherapeutic agents, anti-malignant tumor agents, blood products, and biological products. Those for the First Committee: Remaining therapeutic categories

Note 3) Categories of drugs for the Committee on Non-prescription Drugs to review: New non-prescription drugs which are apparently different from existing non-prescription drugs in active ingredient, strength, dosage/administration, indications, etc.

Note 4) The First and Second Committees on New Drugs meet in January, February, April, May, July, August, October, and November in principle. The Committees on Non-prescription Drugs meets in February, May, August, and November in principle.

Note 5) The Pharmaceutical Affairs Committee meets in March, June, September, and December in principle.

Note 6) For recent new drugs, refer to the homepage on drug information.

(<http://www.info.pmda.go.jp>)

7. NATIONAL INSTITUTE OF INFECTIOUS DISEASES

In April 1997, the name of the National Institute of Health was changed to the National Institute of Infectious Diseases. The institute undertakes basic and applied research, reference and surveillance activities, and collection, analysis, and supply of information pertaining to infectious diseases, performs research on the quality control of antibiotics and other biological products, and undertakes national certification/testing and activities related to international cooperation.

- **Infectious Diseases Information Center**

This Center was established in April 1997 to undertake surveys and research, and collect and supply information on infectious diseases, etc.

- **AIDS Research Center**

This Center was established in April 1988 to undertake HIV basic research and to develop methods of prevention and treatment of AIDS.

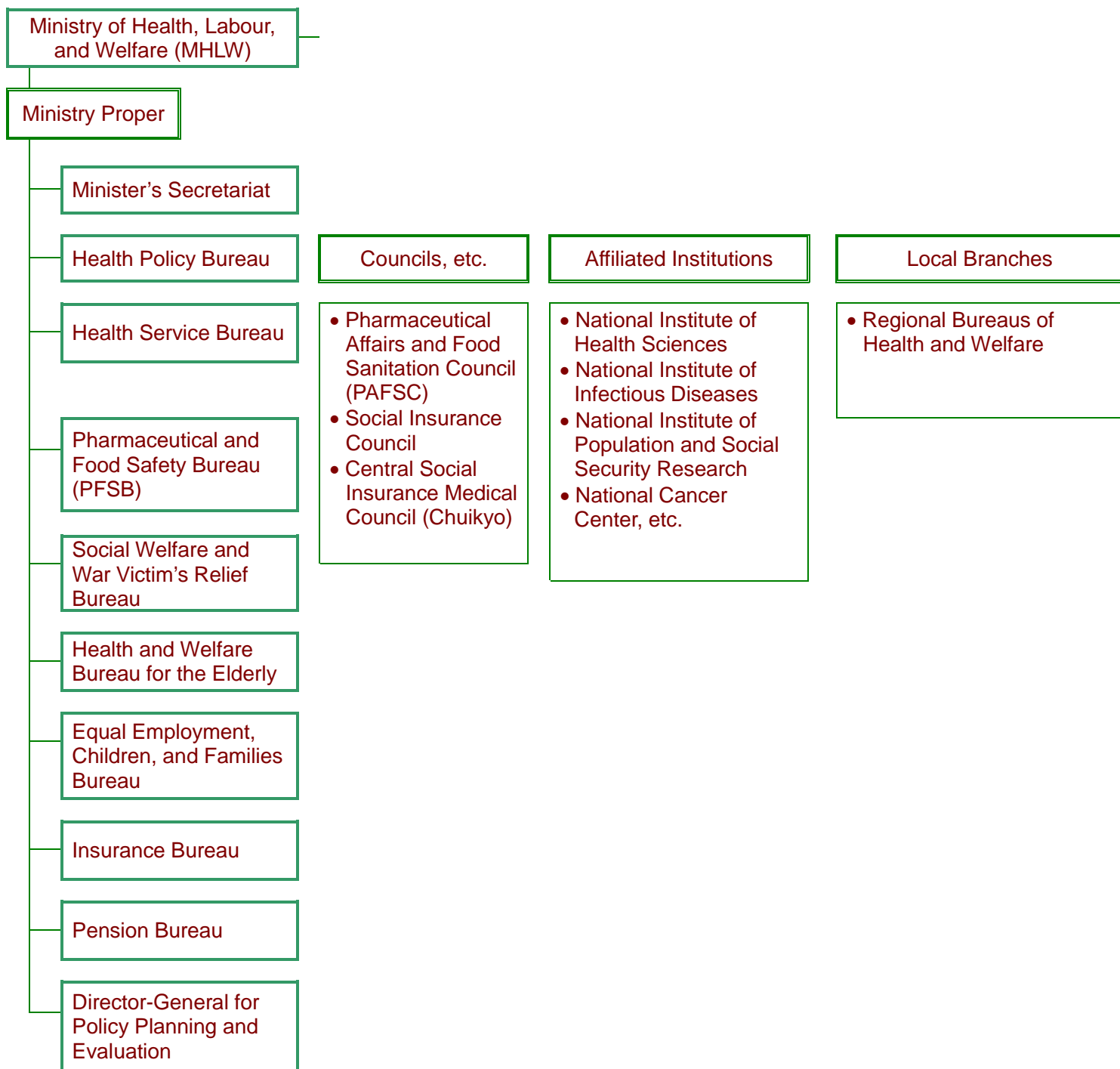


Fig. 1 Organization of Ministry of Health, Labour, and Welfare (Health-related organizations only)

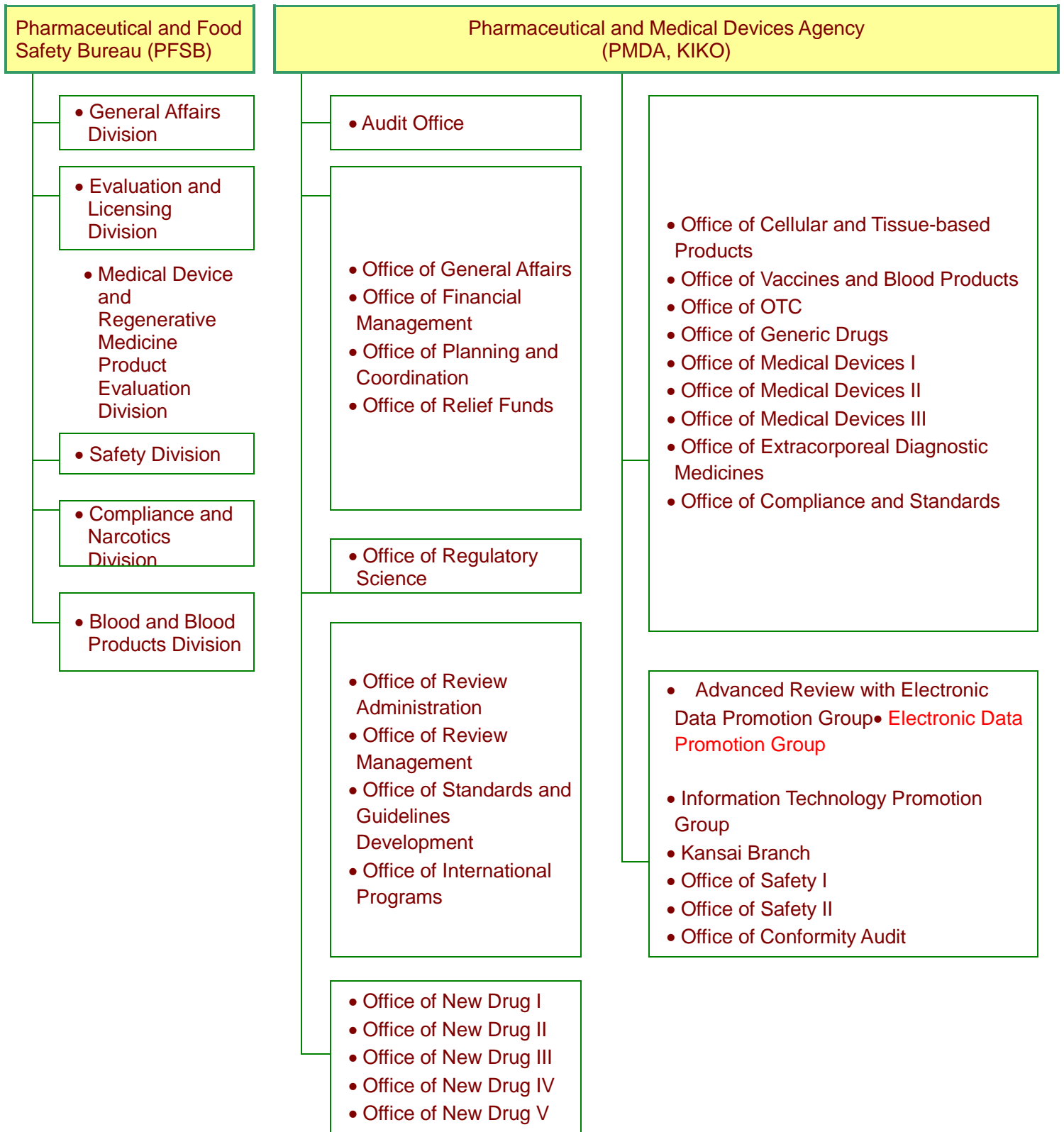
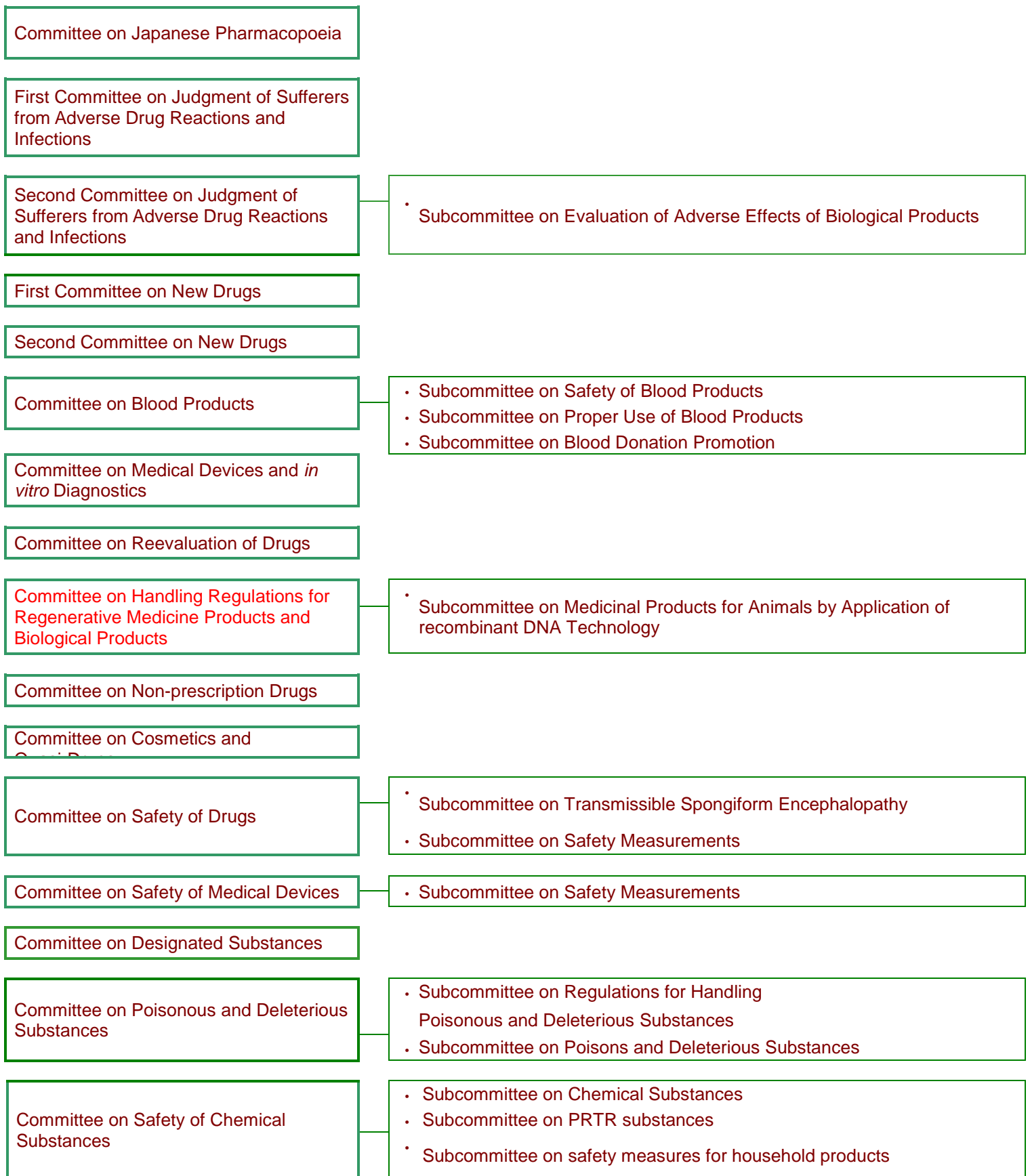


Fig. 2 Organization of Pharmaceutical and Food Safety Bureau (PFSB) and Pharmaceuticals and Medical Devices Agency (PMDA [KIKO])





**Fig. 3 Organization of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC)
(17 Committees and 19 Subcommittees)**