

The Basic Concept on Regulatory Science in PMDA

Pharmaceuticals and Medical Devices Agency

The Pharmaceuticals and Medical Devices Agency (PMDA) has the philosophy to contribute actively to the public health and safety of Japanese people by correctly carrying out the three services, e.g., reviewing marketing authorisation applications of pharmaceuticals and medical devices, conducting safety measures and providing relief to people who have suffered from adverse drug reactions. Hence PMDA is required to make consistent efforts to improve the quality of these services in all aspects from development to use of pharmaceuticals and medical devices.

For further improvement of the quality of the three services, PMDA needs to make exact prediction, assessment, and judgement based on convincing evidence adopting the latest scientific knowledge, and so, promotion of regulatory science research does become important. Regulatory science is defined as “the science to adjust the achievements of science and technology with a view to make use of them for people and society in the most desirable way, by making exact prediction, assessment and judgement based on evidence” (Report to the Consultation No 11 “Concerning the basic policy for science and technology” by the Expert Panel on the Basic Policy, the Council for Science and Technology Policy. 24 Dec 2010). PMDA will actively promote regulatory science research on pharmaceuticals and medical devices from the viewpoint of protecting/promoting the health of Japanese people, and make use of the research outcomes to carry out PMDA’s three services. These may lead not only to increase public’s confidence in PMDA and Pharmaceutical Administration in Japan, but to promote international harmonisation and to play the expected role in the international community.

Such is the situation where the document lays down the basic policy for PMDA to conduct regulatory science researches smoothly and properly while ensuring transparency and fairness. In addition to the compliance with relevant legislation and the ethical guideline for epidemiological studies, PMDA conducts regulatory science researches in accordance with the basic rule outlined below..

I. Scope of application

This basic rule is applied to the researches conducted by the all PMDA staffs. However, in case the PMDA staff also belongs to an external institution and the research is independently conducted at that institution without identifying PMDA affiliation, such research is out of the scope of this rule..

II. Objective of researches

The purpose of regulatory science researches in PMDA is to carry out fairly, precisely and swiftly the three services, i.e., reviews of pharmaceuticals and medical devices, safety measures and relief services for adverse drug reactions, and to contribute actively to the improvement of the public health and safety. The

promotion of the researches allows PMDA to provide more effective and safer pharmaceuticals/medical devices to the medical front in a quicker manner and to make more exact judgements of efficacy and safety from the scientific viewpoint. This is expected to promote international harmonisation and enable the Agency to actively play the expected role in the international community.

To promote regulatory science research which comes up to the objective other than that described above, e.g., Health Technology Assessment, Measures against infectious diseases, PMDA will fulfil the expected role through cooperative researches with related external institutions.

Given the fact that regulatory science is the science of prediction, assessment and harmonisation based on data, regulatory science research in PMDA is considered to have an aspect which aims to show ideal direction and way of thinking based on certain facts, data and results, to develop various arguments and to integrate them into a certain direction.

III. Establishment of Committee

On all regulatory science researches in PMDA, just like general academic researches, the principle that reproducibility by a third person is ensured should be respected.. At the same time, appropriate protection of personal information and intellectual property is the critical component of the compliance called for the PMDA staff as well as the obligation of confidentiality laid down in Art. 13 of Pharmaceuticals and Medical Devices Agency Act. An appropriate management of conflict of interest of the PMDA staff is also required to ensure the fairness and credibility of research.

To ensure that the basic concept described above will be adhered to, PMDA shall establish the Regulatory Science Research Steering Committee (hereinafter called “Committee”), which contains external learned individuals as members, for making recommendations to the Chief Executive of PMDA to make a final decision on issues in the implementation of regulatory science research and its appropriateness.

IV. Relationship between the research and the services

Regulatory science researches undertaken at PMDA shall be categorized into two types below.

- ① Designated research: the research implemented as part of the official duties and designated by the Chief Executive,
- ② Voluntary research: the research other than the designated ones in which PMDA staff themselves identify research subjects and conduct it voluntarily during their off-duty time.

As for the designated research, proposals for new research subjects may be organised in view of opinions of PMDA staffs. Final decision for which subjects are selected as a designated research is made by the Chief Executive, after considerations of the proposed subjects by the Committee, taking into account the objective of the research, relationship with PMDA’s three services, appropriateness of the methodology and handling of data, the necessity of the research. In conducting the designated research, the effort ratio

(the proportion of the research to the total duty hours) of each researcher shall be designated in advance. In addition to a research activity as an official duty, PMDA recommends voluntary initiative on various research subjects with a free idea, but such voluntary research is not treated as official duty.

V. Data handled in research and the way of its management

It is envisaged that data comprised in a variety of PMDA-related documents including assessment reports of pharmaceuticals and medical devices, their application dossiers, materials on the implementation of various safety measures, case examples of the relief for drug adverse reactions and activity reports are used to conduct regulatory science research.

Main data used in the research are generally public or able-to-disclose ones, e.g., published papers, information posted on the PMDA website, disclosed information for the public and to be published information if information disclosure request is to be made. On the other hand, by conducting various analysis of the data comprised in PMDA-related documents, it may contribute to the public interest by improving the quality of development and assessment and streamlining them, for example. Hence unpublished data (the data that PMDA obtains in the course of the services and its disclosure for the public is legally prohibited) may also be the subject of PMDA's regulatory science research.

In light of the above noted, the published/able-to-disclose data can be used in both designated and voluntary research on the condition that its source be clearly stated, while the use of undisclosed data is permitted only in the designated research. In publication of the research outcome using undisclosed data, all researchers should pay due attention to confidentiality of data and proprietary information and make sure that an individual item, such as name of product and company, may not be identified. In order to maintain high scientific quality of research, an outline of the data used should be published as much as possible so that reproduction of research by a third party may be allowed.

If the individual product may be identified by the publication, PMDA will inform the organization which has the source data for the PMDA's research in advance of the intent to conduct a research. The research can be conducted only when the permission is gained from the organization. The referral to the organization concerned is conducted in writing and it shall be clearly stated in the letter that, if they decline the use of undisclosed data, they shall not be penalized.

VI. Procedures in research

(1) Initiation of research

The designated research starts after the designation by the Chief Executive. In the voluntary research, researchers may start it with submitting the research plan to the director of the office he/she belongs to.

(2) Implementation process of research

- ① In the designated research, a group to the research subject is set up in view of the expertise of the PMDA staff involved, followed by designation of a principal researcher. The principal researcher will ensure appropriate implementation of the research and compliance with the rules, and be in charge of managing and supervising research activities by the researchers within the group. In the voluntary research, a principal researcher shall also be appointed and the compliance with rules should be ensured.
- ② In the designated research, PMDA shall check appropriateness of the data handling and the progress of the research periodically.
- ③ In the voluntary research, PMDA shall check whether the research contains only published/able-to-disclose data and not include undisclosed data prior to the publication.
- ④ When a critical issue in the implementation of the research arises, it should be reported to the Chief Executive without delay and it will be considered accordingly in the Committee.

(3) Joint research with an external institution

- ① As for the joint designated research with an external institution, the necessity of joint research to achieve the objective and the appropriateness of the external institute in question shall be evaluated. In a joint research with an external institute in which undisclosed data are used, the principal researcher shall manage/supervise the research so that the external researchers may not to access the source material which enables them to identify the individual products.
- ② In the voluntary research, joint research with external institution(s) may be conducted if needed on the condition that the necessity is clearly identified in its research plan.

(4) Publication of the research outcome

From the viewpoint of ensuring transparency, the result of the designated research, in principle, should be published, and that of the voluntary research is also encouraged to be published. To publish the result of their research, an appropriate way to each research subject, such as publishing articles in the PMDA's business report or scientific journals or other publications and giving a presentation in related academic conferences, should be selected. Publications in a peer-reviewed scientific journal in English should be considered in view of the international contribution and ensuring high scientific quality. In the process for publication of the research outcome, the following should be taken into consideration.

- ① For the designated research, the Chief Executive shall make a decision as to whether it should be published or not, after checking on the appropriateness of data handling, publication means and contents for publication.
- ② For the voluntary research, prior to the publication, the director of the office the principal researcher belongs to shall check appropriateness of the data handling by reference to the opinion of the PMDA senior staff members with relevant competence (but the director shall not interfere with the research contents in principle).

- ③ All the research results are tracked and maintained in an integrated manner and are reported periodically to the Committee.
- ④ All publications by PMDA staff should generally include a disclaimer stating that they do not represent the official views of PMDA in a unified format.

(5) Research Fund

To implement regulatory science research in PMDA in a smooth and appropriate manner, and to have its stable development, it is of importance that PMDA secures a sufficient budget required for research and also leverages it with external competitive research funds such as the Health and Labour Sciences Research Fund. For the purpose, the system should be improved for proper implementation of the research budget, management of potential conflicts of interests, and other funding issues.

For the designated research, PMDA shall bear the expenses necessary for the business trip for making a presentation at an academic conference and the publication in peer-reviewed scientific journal (fees for corrections and proofreading by English native speaker, paper submission, publication and offprints) as well as the cost of research implementation.

For the voluntary research, after the internal assessment of the research objective, its relevance with PMDA's three services, the necessity of the research, PMDA shall subsidize the expense for the publication by request, setting an upper limit for payment in each research subject within the limits of the budget. However, if the researcher receives an external monetary assistance for a voluntary research, the research is outside the scope of the subsidization.

Regulatory Science Research Steering Committee

(Objective)

1. The objective of the Regulatory Science Research Steering Committee is to provide opinions in response to the consultation by the Chief Executive as well as based on the Committee's voluntary initiative, so that regulatory science research activities in PMDA shall be conducted in a smooth and an appropriate manner ensuring its transparency and fairness.

(Organisation)

2. The Committee consists of the following members.
 - (1) Four members who possess expertise on one of the following areas: medicine, dentistry, pharmaceutical science and other specialised knowledge related to drugs and medical devices (at least one in the four is an expert in regulatory science research in the pharmaceutical affair)
 - (2) A legal expert in view of intellectual property right
 - (3) Two members from the pharmaceutical and medical device industry organisation (one from the pharmaceutical sector, one from the medical device sector)
 - (4) A learned person other than those listed above
 - (5) Three Executive directors of PMDA

(Tasks)

3. The Committee considers and reports to the Chief Executive on the followings:
 - (1) Matters to do with the implementation of designated researches conducted in PMDA
 - (2) Matters to do with the proper use of data handled in researches based on Art. 13 of the Pharmaceuticals and Medical Devices Agency Act
 - (3) Matters to do with the assessment and management of the conflict of interest laid down in the guideline on the management of conflict of interest in the Health and Labour Sciences Research (Decision by Director of Health Science Division, Notification No. 0331001, 31 March 2008)
 - (4) Any other matters to do with necessary measures for implementing regulatory science researches