Annex 8. Current status of environmental risk management

1. Suppression of generation

The basic principle of risk management for impacts of chemical substances is to prevent exposure to humans and other organisms. Chemical substances either intentionally produced or non-intentionally generated have the potential to enter the environment during a variety of stages, such as production, use and disposal. While most of the chemical substances entering the environment are non-biologically decomposed or biologically degraded in a relatively short time, the rest remain in the environment for a long time and contaminate a wide variety of media. Even those that originally have a relatively short life time in the environment may exist continuously at a constant concentration if they are continuously discharged into the environment in large amounts. Consequently, both human and other organisms are exposed to chemical substances discharged into the environment through respiration, drinking water, food and prey. To prevent exposure to chemical substances, it is necessary to block the flow of chemical substances at any of these stages. It is desirable to block this flow at a point as close as possible to its headstream, because blocking it upstream of this flow prevents all potential risks caused by chemical substances downstream in the flow.

Risk management at the point closest to the headstream of the flow of chemical substances would involve suppression of their intended production/use and unintentional generation as by-products. For unintentionally generated chemical substances, suppression (or reduction) of risk(s) may be accomplished by reassessing the human activities leading to the risk(s). For dioxins as a typical example, the first attempt to suppress their generation was to terminate production/use of agricultural chemicals containing them as impurities. The second approach was to cope with refuse incineration as a major source of dioxins emitted into the environment by reassessing conditions of the incineration itself, as well as those for the exhaust gas treatment. These countermeasures, together with concomitant suppression of emission (an action to block the flow of dioxins at a step downstream of the suppression of their generation), have greatly reduced the emission of dioxins into the environment.

2. Restriction of use

For chemical substances intentionally produced or used, the principal measure for managing the environmental risk posed by them is to conduct risk assessment for identification of those with a high environmental risk and to prohibit or restrict production/use of such high-risk chemical substances.

In Japan, three major laws are implemented to suppress production/use of chemical

substances with a view to suppressing their environmental risk: 1) The Law Concerning Examination and Regulation of Manufacture and Handling of Chemical Substances (Chemical Substances Control Law) for management of common chemical substances; 2) The Agricultural Chemicals Regulation Law for regulating agricultural chemicals; and 3) The Law Concerning the Protection of the Ozone Layer through the Control of Specified Substances and Other Measures (Ozone Layer Protection Law) for ozone-depleting substances.

The Chemical Substances Control Law requires pre-marketing examination of new chemical substances to test for persistence in the environment, bioaccumulation and toxicity. The Law prohibits or restricts production/used of chemical substances with a high environmental risk demonstrated in this examination. Although toxicity tests previously required by the Law were intended to assess the risk to human health only, the amendment in 2003 additionally calls for assessment of the environmental risk as well. For chemical substances that had already been produced and used before establishment of the Law (designated as "existing chemical substances"), the Japanese Government has examined them to test their environmental risk. However, a great many existing chemical substances had been produced and used without examination. In an attempt to correct this situation, cooperation of business operators in collecting and reporting data required for the examination of existing chemical substances has been sought to accelerate the examination process.

The Agricultural Chemicals Regulation Law prohibits marketing/use of agricultural chemicals without registration. Registration is required once every 3 years, not only for new agricultural chemicals, but also for those produced/used prior to the establishment of the Law in 1948. On registration of an agricultural chemical, risk assessment is required for a wider variety of endpoints than that required for common chemical substances according to The Chemical Substances Control Law. Registration of agricultural chemicals is withdrawn and their use is prohibited if they pose a high risk. Although the Law had previously required assessment of the adverse effects of agricultural chemicals on aquatic organisms, standards for withholding registration of agricultural chemicals were amended in 2004 to introduce a more strict procedure for environmental risk assessment.The Ozone Layer Protection Law gradually prohibits production/use of chemical substances with a high ozone-depleting activity, in accordance with a related international convention.

Even if a chemical substance has some risk, there in no alternative but to use it if they are useful. Agricultural chemicals are obviously toxic to organisms considering their intended use, but total prohibition of their production/use is impossible due to the serious consequences of this action on agricultural production. However, it is necessary to minimize the entry of chemical substances posing a risk into the environment when producing or using

them. Entry into the environment due to inappropriate handling or by emission of exhaust gas, wastewater and waste should be carefully prevented. Since it is difficult to control entry of agricultural chemicals into the environment while they are being sprayed, their usage is defined in detail to reduce the risk posed by them to human health due to persistence in crops as well as to both human health and the environment through environmental pollution.

3. Restriction of emission

The Air Pollution Prevention Law and The Water Pollution Prevention Law control emission concentation/volume for exhaust gas and wastewater, while The Waste Management Law controls disposal of wastes. All these laws are aimed at reducing the risk by defining environmental limits as target values in the control of emission on the basis of the concentration or total volume. However, to implement regulation that forces certain burden on business operators, information that serves as evidence for environmental limits to be established should be thoroughly collected and openly provided. Therefore, the number of chemical substances currently subjected to regulation is only several tens, too small compared with the number of chemical substances intentionally produced and used. Even if enough information is not yet availabe to start regulation based on scientific evidence, it is still important to minimize entry of chemical substances with potential risk into the environment. For this purpose, a legistalive system to promote voluntary improvement of the management of chemical substances by business operators has been implemented.

The Law concerning Reporting, etc. of Releases to the Environment of Specific Chemical Substances and Promoting Improvements in Their Management (Pollutant Release and Transfer Register (PRTR) Law) requires business operators to determine and report the amount of chemical substances they emit into the environment or transfer outside of their business facilities, to promote voluntary improvement of the management of chemical substances by business operators and facilitate reduction of emission into the environment. A total of 354 chemical substances are currently subject to regulation under the Law. Since this regulatory system was started in 2001, the overall volume of chemical substances emitted or transferred has decreased. The Air Pollution Prevention Law requires for 12 harmful air pollutants reduction of emission into the environment based on a voluntary management plan developed by business operators, which has greatly reduced emission of these target substances into the environment.

4. Reduction of risk

The strategy for reducing emission of chemical substances by combined restriction of production/use and voluntary management is effective for preventing new environmental

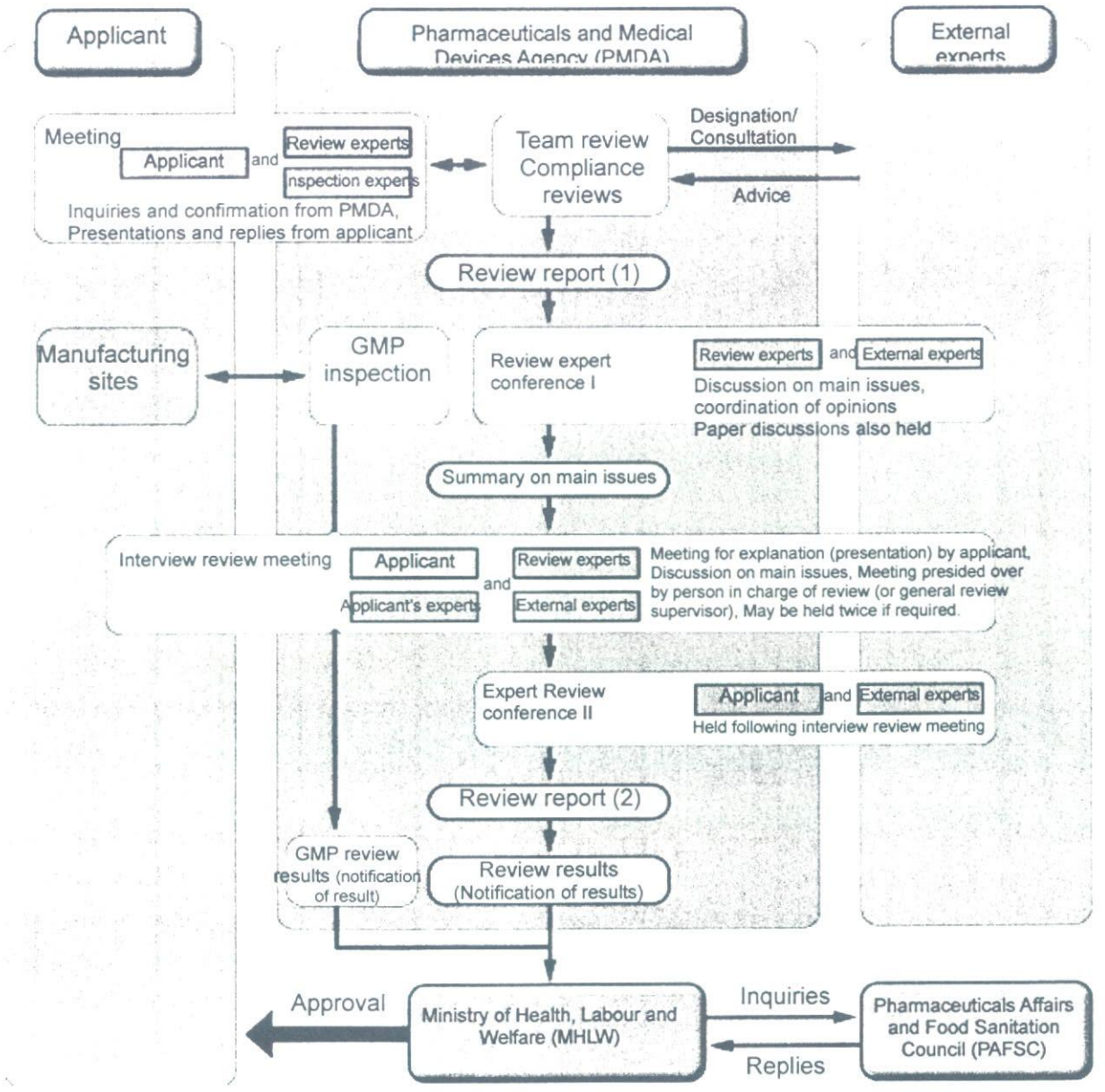
pollution. As for highly persistent pollutants previously generated, used and emitted, blocking their entry into the environment alone cannot improve the situation and environmental cleanup by human work is necessary. The Anti-Farm Soil Pollution Law was implemented in an attempt to avoid the risk of farm soil pollution that caused serious damage to human health at an early stage of the incident. According to this Law, the Japanese Government implemented measures to reduce the risk to both human health and the environment at the expense of the polluter.

In contrast, measures to control urban soil pollution were not as adequate as those for farm soil pollution, because the situation of the former was more difficult to grasp as compared with that of the latter. To overcome such circumstances, The Soil Contamination Countermeasures Law was established in 2002, which requires the polluter or land owner (in case that the polluter is unknown) to conduct a survey on the situation and implement measures to reduce any risk identified. This has substantially enhanced the understanding of the actual situation of soil pollution.

Besides soil, bottom sediment is also susceptible to persistence of chemical substances. While bottom sediment pollution by mercury and PCB were recognized early and countermeasures have been implemented on the basis of anationwide field survey, environmental limits for dioxins in bottom sediment has been established only recently and actions have been initiated in various regions in Japan. Soil Contamination Countermeasures Law requires the polluter or the land owner to implement measures to reduce the risk related to the polluted land that failed to meet the criteria for soil safety. According to the Law, prevention of exposure is the action to take in principle, while cleanup of polluted soil should not be required uniformly.

When the risk is related to intake of drinking water or food, exposure to pollutants can be prevented by controlling the supply of polluted drinking water or food. Safety criteria for tap water and food are provided by The Water Supply Law and The Food Sanitation Law, respectively, to control supply of tap water and food that do not meet these criteria. Exposure to pollutants in the atmospheric environment through respiration is difficult to prevent, as supply of air to humans or other organisms cannot be blocked. Rather, prevention of generation of such pollutants would be the key countermeasure.

Annex 9. Process for examination of pharmaceuticals and medical devices



From the website of Pharmaceuticals and Medical Devices Agency of Japan 2005.10.8

Annex 10. Emission control for pharmaceuticals

Pharmaceuticals play an important role in protecting human health. Accordingly, the use of pharmaceuticals with a high therapeutic effect may reasonably be justified despite some environmental risk posed by the substance, based on the. risk-benefit balance. Nevertheless, care should be taken to minimize their emission into the environment.

In emission control for chemical substances, environmental standards as target values for control are established first, and then the emission concentration/volume as well as detailed procedure for disposal are defined to fulfill the environmental standards. As for environmental risk management of chemical substances, the environmental standard for water quality has been established with respect to zinc to date, and the emission control procedure and standard have just been defined for effluents containing zinc. Considering the route of entry of pharmaceuticals into the environment, those excreted from the human body may enter the aquatic environment via a sewage line, while unused and discarded pharmaceuticals may also enter the aquatic environment via a garbage landfill. Accordingly, the major and immediate task in emission control for pharmaceuticals is to control their emission into the aquatic environment. It would be most appropriate to apply the basic framework of emission control for chemical substances into the aquatic environment (establishment of environmental standards with subsequent development of a control procedure to satisfy the standards) to pharmaceuticals or their metabolites as necessary.

For environmental standards for water quality related to human health, a systematic procedure for reassessment has been established, involving a combination of "survey subjects" and "monitoring subjects": first, presence or absence of the target substance in the aquatic environment is examined (survey subject); second, the status of the target substance in the aquatic environment is continuously monitored (monitoring subject); third, environmental standards for the target substance are defined for emission control as required. It may be desirable for establishment of environmental standards for water quality related to environmental risk to follow a similar process.

The above-mentioned process may be applicable also to emission control for chemical substances related to pharmaceuticals in view of environmental risk management. The potential source of effluents containing pharmaceuticals include business facilities manufacturing or using pharmaceuticals, as well as wastewater treatment plants into which effluents from such business facilities enter. Also, pharmaceuticals and their metabolites excreted from people taking over-the-counter drugs for self-medication may appear in household effluents and then flow into wastewater treatment plants.

Another potential source of pharmaceuticals discharged into the environment is unused and discarded pharmaceutical products. When they are discharged as solid wastes, garbage

landfills may function as sites of emission of pharmaceuticals into the environment. As a consequence, effluents from the final disposal area for wastes should undergo emission control in a similar manner to effuents from wastewater treatment plants. It is true that no control measure for waste disposal considering environmental risk has been developed as yet. However, if such a control measure should become available in the future, discarded pharmaceuticals would be managed accordingly. Then a system for recovery and proper disposal of unused pharmaceuticals should be considered.