

Chemical Substance Management

The pharmaceutical industry uses many types of chemical substances for the research, development, and production of drugs that protect human health. Some of these chemical substances may harm people's health or our ecosystem if released into the environment.

Therefore, in the pharmaceutical industry, release of such chemical substances should be as little as possible. We vigorously promote the voluntary control of chemical substances.

Recently, reports that components of pharmaceuticals have been detected in river water or from sewerage processing plant discharge,

mainly in the U.S. and Europe, are drawing attention. Similar reports have been made in Japan, but as the concentration was extremely low, it is thought to have entered the aquatic environment from human excrement via the sewerage processing plants. Very little is known about health effects from the extremely small quantity of pharmaceuticals in the environment entering the human body via aquatic organisms or drinking water. There may be a number of ways to investigate by setting up a method that can assess environmental effects. We recognize the need within JPMA to act in cross-sectoral cooperation.

At JPMA

JPMA began voluntary PRTR research activities in FY 1997 that include quantitative monitoring of the environmental release and movement of chemical substances that are handled or manufactured in the pharmaceutical industry and publishing of the results. We also devised a voluntary control plan of harmful atmospheric pollutants as part of our efforts in

reducing the atmospheric emission of organic chlorine chemical substances.

As for assessing the pharmaceuticals' environmental effects, a Drug Evaluation Committee and Environment & Safety Committee will work collaboratively to share information on the assessment methods in Europe and the U.S., the outcome of research in Japan, etc., and to investigate which methods are most proper and efficient.

Voluntary Control Plan of Harmful Atmospheric Pollutants



Target

Third Term Plan To reduce, by FY 2007, the quantity of aerial emissions of dichloromethane, 1,2-dichloroethane, and chloroform by 20% of the emissions in FY 2003

We developed a voluntary control plan of aerial emission reduction for the organic chlorides such as dichloromethane and 1,2-dichloroethane in FY 1998 and have since made efforts towards our reduction target. The second term concluded at the end of March 2004, with the targets exceedingly achieved.

As for other substances, member companies have also endeavored at each business establishment to control the emissions of formaldehyde,

benzene, etc., into the environment and have achieved over 50% reductions, as a result of enhancement of activities, for examples, installation of activated carbon adsorption equipment.

For the third term (four years) plan, member companies and affiliate companies have been making efforts towards achieving the target of further reducing aerial emissions of dichloromethane, 1,2-dichloroethane, and chloroform.

Examples of emission reduction measures implemented by member companies in FY 2005

- Change and termination of medium / solvent use
- Installation of filtering facilities using filters such as activated carbon adsorption equipment
- Sealing of the system
- Improvement in existing filtering facilities (change operational protocols, renew active charcoal filter, etc.)

According to a survey conducted in June 2006, as of the end of FY 2005, dichloromethane was reduced by 47.5%, 1,2-dichloroethane was reduced by 82.9%, and chloroform was reduced by 34.8%; therefore, the target 20% reduction was exceedingly achieved.

Aerial emissions (tons)

	dichloromethane	1,2-dichloroethane	chloroform
FY 2003	736	143	50.2
FY 2004	490	104	52.4
FY 2005	383	25	32.7
FY 2007(Target)	589	114	40.2



● PRTR Research

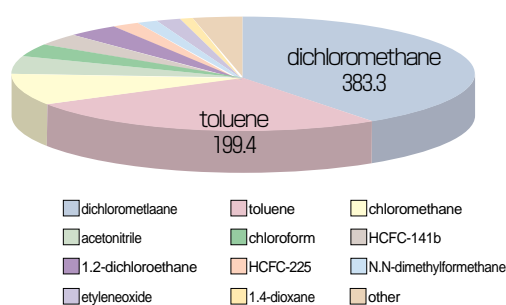
We have continued our research from FY 2006 in which we are investigating 354 of the chemical substances designated as class I (excluding the dioxins). The 75 companies that responded (responses received from every JPMA member company) altogether handled 23,114 tons (a 6% reduction compared to last year) of class I substances, from which 851 tons (31% reduction compared to last year) were released into the atmosphere, 32 tons (26% reduction compared to prior year) into the water, and nil into the soil.

In terms of quantity handled, dichloromethane was recorded as being handled the most, 5,000 tons more, same as last year, followed by toluene, acetonitrile, N,N-dimethylformamide, Bis(2-ethylhexyl)phthalate and Acrylonitrile, all quantity of 1,000 tons or more.

In terms of atmospheric emission, the two substances dichloromethane 383 tons (490 tons) and toluene 199 tons (347 tons) exceeded 100 tons, followed by nine substances with over 10 tons of emission: chloromethane, acetonitrile, chloroform, 1,1-dichloro-1-fluoroethane (HCFC-141b), 1,2-dichloroethane,

dichloropentafluoropropane (HCFC-225), N,N-dimethylformamide, ethylene oxide and 1,4-dioxane. Total emission of these 11 substances was 822 tons, comprising 97% of total atmospheric emissions.

Substances with 10 tons or more of atmospheric emission



(Unit: tons, subjects of research: JPMA member companies (257 business establishments, including subsidiary and affiliated companies))

TOPICS

Efforts for Assessment of Environmental Risks from Pharmaceuticals



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We occasionally hear news that drugs such as antibiotics and analgesics and their metabolic derivatives or degradation byproducts have been detected in the natural environment, such as in the rivers. While some say that this is caused by the increasing use of drugs, mainstream thinking is that this is due to improved analysis technology leading to increased detection sensitivity (lowering of detection limits). Compared to general chemical substances, pharmaceuticals are manufactured and used in smaller quantities; therefore, the levels detected in the environment are lower. However, the Environmental Assessment (EA) of pharmaceuticals, chemicals that are designed to have physiological activity, is still important.

The effects of chemical substances discharged into nature not only impact human health through environmental pollution, but also secondary effects to the natural ecosystem are of concern. The effects on the ecosystem of synthetic chemicals, agricultural chemicals, and drugs for animals discharged into environment are assessed through the EA. Conducting an EA for chemical substances became compulsory after the Amendment to Chemical Control Law in April 2003. As for pharmaceuticals, the FDA guidelines in the US in 1998 and the EMEA guidelines in EU in 2006 were established to assess medicine's environmental effect, and the submission of environmental effect assessment data, alongside efficacy and safety data, has become compulsory when lodging an application for

approval of a new drug.

In Japan, the "Law concerning the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Control Law)" and "Agricultural Chemicals Regulation Law" regulate general chemical substances, except pharmaceuticals, and agricultural chemicals, and assess effects on the environment and its flora/fauna, and restrict importation, manufacturing and use. However, the Pharmaceutical Affairs Law does not have articles pertaining to environmental effect of the pharmaceutical. Although drugs are essential to maintain human health and treat diseases, they should still be subject to scientific assessment, as are general chemical substances and agricultural chemicals, since there is still the issue of the impact administered drugs have on the environment.

The MHLW has set up the "Environmental effect assessment method for pharmaceuticals study group" in Japan and investigation has moved towards legislation. In 2003, when the Chemical Control Law introduced EA, Japan Pharmaceutical Manufacturers Association created a task force with its main members from the Drug Evaluation Committee Basic Research Subcommittee to prepare and streamline for the legislation of EA of pharmaceuticals. This task force has provided information to member companies and hosted training courses, as well as taken part in the