Section 2. Promotion of Measures to Provide Better Drugs Safely and Promptly

1. Measures for Safety of Drugs

Because drugs basically provide medication for patients by affecting human bodies, it is inevitable not only to cure diseases as expected but also to occur unexpected adverse drug reactions. As it is important to balance effectiveness and safety, drugs are evaluated on both their effectiveness and safety using data from clinical trials for obtaining approval from the Minister of Health, Labour and Welfare before being allowed on the market. However, drug safety information obtained through clinical trials before approval is limited, it is necessary to collect information on adverse drug reactions after launch, then to analyze and evaluate that information, and to promptly implement measures to secure safety of drugs.

(1) Report System for Adverse Drug Reactions

In accordance with the “Drug Safety Information Report System”, information on post-marketing adverse drug reactions is reported from authorized license holders of drugs and medical professionals to the Minister of Health, Labour and Welfare. When the authorized license holders of drug find out the occurrence of diseases that are suspected of being induced by adverse drug reactions, they must report that information to the Minister of Health, Labour and Welfare and also to medical institutions. Medical professionals such as doctors, dentists, and pharmacists are also required to report any such information to the Minister of Health, Labour and Welfare in accordance with the “Drug Safety Information Report System”. The annual number of adverse drug reaction cases in accordance with the Pharmaceutical Affairs Law is approximately 32,000 domestic cases and 95,000 abroad cases. For medical devices the number is approximately 14,000 domestic cases and 3,000 abroad cases. In addition, authorized license holders of drug are obliged to conduct post-marketing surveillance on those drugs that require careful verification of safety such as newly approved drugs. They must also provide information of rational drug use and promptly detect occurrence of serious drug adverse reactions by, for example, visiting medical facilities.

(2) Evaluation and Provision of Information on Adverse Drug Reactions

The Ministry of Health, Labour and Welfare conducts immediate and

appropriate evaluations of information on adverse drug reactions reported by manufacturers/distributers and related medical institutions in cooperation with the Pharmaceuticals and Medical Devices Agency, and implements safety measures based on the results of the evaluations. In particular for urgent and important information, the Ministry orders manufacturers/distributors to distribute emergency safety alert information (so-called a doctor letter) in order that medical institutions are promptly informed. In addition, information such as revision of instruction for use is provided through the monthly publication of “Safety Information on Drugs and Medical Devices”.

(3) Prediction- and Prevention-Oriented Safety Measures

In addition to these current safety measures, in medical institutions that plan to enhance and strengthen prediction- and prevention-oriented safety measures in cooperation with related academic societies, other medical facilities, and manufacturers/distributors, to detect and deal with patients serious adverse reactions in early phase, the Ministry have created and provided "Manual for Detection and Treatment of Serious Adverse Reactions by Type" that summarize early symptom, detection and medication in collaboration with related academia since FY2005.

In addition, “Pregnancy and Drug Information Center” within the National Center for Child Medical Health and Development collect information of perinatal effect of drugs through consultations with pregnant women who are worried about their effect.

Furthermore, the Pharmaceuticals and Medical Devices Agency has published reports on adverse drug reactions from drug manufacturers and “Patient Medication Guide” about drugs which require patients’ special attention prepared by drug manufacturers, and provided them for medical professions and patients and their families since January 2006 through its website (http://www.info.pmda.go.jp).

2. Speeding up Approval Review of pharmaceuticals and Others

(1) Measures to Provide Pharmaceuticals and Others Promptly

While the development of pharmaceuticals and medical devices is making rapid progress it has been pointed out that pharmaceuticals and medical devices used abroad are not being made promptly available in Japan. It is expected to provide safe and effective drugs and others to people in a timely manner.

Under this circumstance, measures for faster and better review will be implemented aiming for reducing the period before marketing of new drugs by 2.5 years based on the “5-Year Strategy for Creation of Innovative Pharmaceuticals and Medical Devices” formulated jointly by the Ministry of Health, Labour and Welfare, the Ministry of Economy, Trade and Industry, and the Ministry of Education, Culture, Sports, Science and Technology in April 2007.

More concretely, the following measures will be implemented: ① doubling the number of pharmaceutical reviewers and quality improvement (increase of 236 staff members over 3 years), ② clarifying the review processes and standards and improved implementation of GCP (Good Clinical Practice), ③ establishing a guidance on global clinical trials, ④ discussions on the possible introduction of parallel scientific advice program for global clinical trials between regulators of Japan, the United States, and Europe, ⑤ promoting rationalization and simplification of clinical trials practice and approval review while securing the safety of medical devices, ⑥ expansion and improvement of medical device review staff, and ⑦ improvement in the operation of medical device GCP .

(2) Discussion on the Issues of Using Unapproved Drugs

With regard to domestically unapproved drugs that have been approved in the United States and Europe, the status of approval in the United States and Europe as well as requests from academic societies and patients have been regularly identified by a “Study Group on Unapproved Drugs” made up of experts since January 2005. The study group has been securing safety and opportunity for use of unapproved drugs by scientifically evaluating the clinical necessity and appropriateness of use and by leading them to domestic execution of clinical trials. The study group had a total of 16 meetings by March 2008. So far the study group has reached conclusions on 46 cases where clinical trials should start early and requested related enterprises to promptly conduct clinical trials on them.

(3) Discussion on Early Introduction of Medical Devices of High Medical Need

The “Study Group on Early Introduction of Medical Devices etc. of High Medical Need” (hereinafter referred to as the “Study Group on Need”) is held to discuss the early introduction of domestically unapproved or off-label use of medical devices and

in-vitro diagnostics (IVDs) . The study group has met 6 times to date and selected 13 types of prioritized medical devices. Discussions are being made on concrete measures for early introduction of these products. Early introduction of medical devices and IVDs of high medical need will be promoted in the future and will include making additional selection of products to be discussed by the Study Group.

3. Revision of Sales System for Over-The-Counter Drugs

(1) Summary of Revision of Sales System for Over-The-Counter Drugs

The environment surrounding over-the-counter drugs has been drastically changing in recent years, that includes changes in people's consciousness and progress being made in separating dispensing from medical practice. In consideration of above-mentioned situation, the "Law to Amend the Pharmaceutical Affairs Law" (hereinafter referred to as the "Revised Pharmaceutical Affairs Law") was promulgated on June 14, 2006 to revise the entire over-the-counter drug sales system, including categorization of over-the-counter drugs according to the degree of risk.

The revision can be summarized as follows: ① categorize over-the-counter drugs into 3 classes according to the degree of risk and establish an information and consultation system according to the degree of risk, ② establish a system of new type of professionals (registered sales persons) that differ from pharmacists to take a role in sales of over-the-counter drugs, and ③ arrange an environment regarding sales of over-the-counter drugs to enforce on notifications at pharmacy/drug stores and labelling of the degree of risk so that purchasers can make the appropriate choice.

The Revised Pharmaceutical Affairs Law will be enforced entirely within 3 years of the date of promulgation set by the cabinet order. The designation of the risk categories was executed on April 1, 2007 and an examination system regarding registered sales persons implemented in April 1, 2008.

(2) Measures for Enforcement

1) Designation of Risk Categories

A government notice in terms of classification of over-the-counter drugs to be categorized into 3 classes according to their degree of risk was proclaimed on April 1, 2007. The notice calls for efforts to be made in the collection/evaluation of the up-to-date

information on their appropriate use and will be revised as required.

2) Examination System regarding Registered Sales Persons

With regard to examinations for a new type of professionals (registered sales persons) that differ from pharmacists to take a role in the sales of over-the-counter drugs, a “Study Group on Formulation of Guideline to execute Registered Sales Person Examination” was held to discuss the scope of test papers and execution schemes for the examination and compiled a report in June 2007. A Ministry ordinance on the registered sales person examination was proclaimed on January 31, 2008. Registered sales person examinations will be conducted in each prefecture, starting in FY 2008, in accordance with this ordinance.

3) Establishment of System and Environment Related to Sales of Drugs

In preparing for entire enforcement of the Revised Pharmaceutical Affairs Law, “Study Group on Establishment of System and Environment Related to Sales of Drugs” has been held to discuss the system and environment needed to provide appropriate information and consultations from the point of view of consumers and a report is to be compiled.

4) Others

Efforts will be made to publicize the new system and make it well known among related people and the general public as well as to enlighten people on the appropriate use and promote knowledge on drugs and medical devices in cooperation with prefectures and related agencies/ organizations.

4. Recent Development in Blood Business

(1) Promotion of Blood Donations

In recent years, the number of blood donors has been decreasing. With young people in particular the decrease in number of donors is severe. In addition, as restrictions on blood donations were tightened in the spring of 2005, there has been a danger of a shortage of blood required in medical practices due to a further decline in the number of blood donors. And hence the Ministry of Health, Labour and Welfare established a

“Blood Donation Promotion Headquarters” headed by the Minister of Health, Labour and Welfare within the Ministry to implement measures to secure blood donors and promote the proper use of blood products as a united effort between related bureaus and offices. In addition, the Minister of Health, Labour and Welfare has been calling for blood donations at cabinet meetings and on the street and requesting the support of related organizations.

As a result of these measures a stable supply of blood has been secured. However, further efforts that need to include focused enlightenment activities targeting younger generations will continue to be made as the number of blood donors is still decreasing. In addition, a system in which the Japanese Red Cross Society makes compensation available for any health damage to blood donors, with the appropriate participation of the government, was implemented in October 2006 so that people can donate blood without anxiety.

(2) About the Restrictions on Blood Donations

A vCJD (variant Creutfeldt-Jakob disease) patient was discovered in Japan for the first time in February 2005. In order to prevent any outbreaks of vCJD through blood transfusions it was agreed in March 2005 that blood donations from people who had been in the United Kingdom for one day or longer anytime between 1980 and 1996 would be temporarily restricted from giving blood, and was put into effect in June. Best efforts are being made for secure blood donations and promote their appropriate use in cooperation with related institutions to avoid any confusion in medical practices caused by a shortage of blood products due to this restriction.

(3) System to Provide Vaccines

Vaccines contribute to public health as a means of preventing infectious diseases in Japan. It has become necessary, however, to establish a system for developing and providing vaccines that includes risk management to cope with the new threats to public health which have emerged in recent years, such as the new types influenza and re-emerging infectious diseases. In the meantime, internationalization has progressed as seen in vaccines produced abroad also being used in addition to those made in Japan in response to medical demands. Under such circumstances it is necessary to secure a stable supply of vaccines while maintaining their quality, in consideration of the fact that it is difficult to increase production of vaccines in response to demands in a short period of

time, unlike general chemical drugs.

In light of this various issues with developing and securing the stable supply of vaccines required in Japan were published in March 2007 as the “Vision for Vaccine Industry”. The “Vision of the Vaccine Industry Promotion Committee” has also met with discussions being made on promoting the measures provided in the vision.

5. Improving the Quality of Pharmacists and Enhancing the Role of Pharmacy

(1) Improving the Quality of Pharmacists

It has become necessary to foster high-quality pharmacists in order to meet social demands being made in recent years such as promoting appropriate use of drugs in terms of the advance of medical technologies and the progress in separation of dispensing from medical practice.

Accordingly, the education course at universities fostering pharmacists was extended from 4 years to 6 years so that they can foster practical abilities related to clinical affairs. As a result, graduates that have completed the 6-year school education course are qualified to take the National Examination for Pharmacists in 2006.

Discussions on the National Examination for Pharmacists started in FY 2007 in responding to the revision of the educational curriculum due to the introduction of the 6-year pharmacy education system. In addition, discussions have also commenced on the future trends in the supply and demand of pharmacists in estimating the effect of an increase in the number of pharmacy students, which may arise from the increase in the number of Schools of Pharmacy and Faculties of Pharmaceutical Sciences in addition to the further specialization of pharmacy students and changes in workplaces due to the introduction of the 6-year course.

While new training focused on the fields of medical pharmacy and practical training that had not been taken in the 4-year course has been conducted. It has been started to improve the quality of pharmacists that had completed the 4-year course before introduction of the 6 year-course since FY2007. In addition, specific field training on cancer drug therapy has been conducted since FY2006 in order to train pharmacists specialized in cancer with advanced knowledge and skills.

(2) Enhancement of Roles of Pharmacies and Promotion of Separation of Dispensing from Medical Practice

The Pharmacists Law was amended by the "Law to Amend the Medical Care Law for Establishment of the System to Provide High Quality Medical Care" enacted in 2006 to enhance the functions of pharmacies so that pharmacies can further contribute to community medical care. In April 2007 pharmacies were positioned as medical care provision facilities in taking the role as bases for supplying pharmaceuticals. In addition, a pharmacy information system has been established to contribute to patients'/residents' choices as well as an environment for facilitating in-home medical care. Furthermore, re-education training for pharmacists punished administratively has been obligated and the names of those pharmacists has been disclosed to public.

In addition, efforts are being made to promote the separation of dispensing from medical practice with aim of ensuring the appropriate use of drugs. In FY 2006, the number of prescriptions issued by external pharmacies was approximately 660 million. The rate of separation was estimated at 55.8%, of which increase of 1.7% from the previous year (according to the Japan Pharmaceutical Association).

It is necessary to promote a high quality system in a systematic manner according to the actualities of respective regions so that the people can realize the merits of the system. Therefore efforts will be made to improve the quality of separation of dispensing from medical practice through creating/providing enlightenment materials on the appropriate use of pharmaceuticals.

6. Measures for Preventing Drug Abuse

(1) Measures against Narcotics and Stimulants

The number of drug offenders arrested reached approximately 15,100 in 2007. And the number of methanphetamine offenders was 12,200, and increased compared to previous year. The number of cannabis and synthetic narcotics, such as MDMA offenders is still high level and the situation of drug abuse in young generation especially those in their twenties appeared rampant and continued grave situation.

As the government, as a whole, to address the problem, a "headquarters for the promotion of countermeasures to drug abuse" headed by the Prime Minister formulated a "New 5-Year Strategy to Prevent Drug Abuse" in July 2003, and the Ministry of Health,

Labour and Welfare has been promoting comprehensive measures in close cooperation with related ministries and agencies.

Regarding the control of drug offences, the Narcotics Control Departments in Regional Bureaus of Health and Welfare have strengthened their structure by increasing narcotic control agents, while efforts are also being made to control drug trafficking organizations made up of foreigners as well as trafficking over the internet. As measures to prevent drug-abuse, consultation programs for drug abusers themselves and their families are provided in health centers and local mental and welfare centers. In addition, national campaigns like the "'No, Absolutely No!' public awareness Promotion Campaign" has been taken place and "caravan cars for drug abuse prevention" used as effective public awareness activities in schools all over Japan.

Regarding the promotion of proper use on narcotics in medical field, efforts are being made to establish a system where narcotics used for pain relief are properly and smoothly made available and guidance and supervision given to narcotic handlers.

(2) Measures against Substances of Abuse not-controlled under the Narcotic Control Law and other legislation for drug control

Substances of abuse not-controlled under the Narcotic Control Law and other legislation for drug control not only damage the health of abusers but also cause harm to public health as they can lead to narcotics or other illicit drugs being abused. Hence enlightenment campaign on preventing any substance abuse are being conducted through distributing leaflets on the harmful effects and danger of such substances. In addition, surveillance and crackdown on their products as a violation of the Pharmaceutical Affairs Law are being carried out, including procurement investigations and monitoring the internet.

Those with a high probability of hallucinatogenic, stimulative or sedative effects on human central nerve system are being controlled more rigorously under the Pharmaceutical Affairs Law, since April 2007. With the legislation, manufacture, import, and sale of designated substances and their products other than for medical use are prohibited (33 substances had been designated as of December 2007). Also, efforts are being made to impose further rigorous controls under the Narcotic Control Law, designating substances of narcotic as soon as they have been scientifically validated to have dependency and other psychotoxicity .

7. Security Measures for Chemicals

(1) Acquisition of Safety Information on Chemicals

In accordance with the “Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc.” (hereinafter refferd as the “Chemical Substances Control Law”), the government regulates production, import, etc. of new chemicals which have not been produced or imported before. The regulation is based on toxicity of a new chemical, and the toxicity is reviewed before the chemical is produced or imported. Regarding the safety of existing chemicals, the government evaluates toxicity of those chemicals. In addition, information on the safety of high production volume chemicals have been collected through a joint program among the private and the public sectors for collecting and releasing safety information of Japan HPV existing chemicals (hereinafter refferd as the "Japan Challenge Program"), which started in cooperation with the Organisation for Economic Co-operation and Development (OECD) and industries.

In recent years, the international environment regarding the management of chemicals has been drastically changing; for instance, new regulations on chemicals have been established in Europe. In consideration of these circumstances, the Ministry of Health, Labour and Welfare started discussions to revise the “Chemical Substances Control Law” with the Ministry of Economy, Trade and Industry and the Ministry of the Environment in January 2008. In order to establish a more effective and efficient chemical management system, these Ministries have been discussing risk assessment, in which not only toxic information but also exposure information, such as production volume, is assessed.

(2) Safety Measures for Household Products

In order to prevent health damages caused by chemical substances used in household products, regulatory standards have been set for textile products, cleaning agents, and timber for gardening in accordance with the “Law for the Control of Household Products Containing Harmful Substances ”(as of the end of FY2007 standards had been set for 20 substances). In addition, health damage report system in relation to household products has been implemented.

(3) Safety Measures for Poisonous and Deleterious Substances

Chemical substances, which are strongly poisonous or deleterious from the viewpoint of acute toxicity, are designated as poisonous or deleterious substances under the “Poisonous and Deleterious Substances Control Law” to regulate their manufacture, import and sales from the viewpoint of public health and hygiene. As of the end of FY2007 101 items had been designated as poisonous substances and 360 items as deleterious substances in accordance with the law.