

International Pharmaceutical Regulatory Harmonization Strategy

– Regulatory Science Initiative –

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Ministry of Health, Labour and Welfare

I Objective of strategy formulation

- O The Japan Revitalization Strategy (approved by Cabinet on June 14, 2013) refers to the healthcare sector as Japan's global strength and a strategic area for the promise of global market growth. The aim is to boost healthcare-related sectors through development, rapid approval, launch and simultaneous global exporting of first-in-the-world, Japan-origin pharmaceuticals, medical devices, and regenerative medicine products – the core of innovative medical technologies – to create a society formed of a virtuous cycle of ongoing development of Japanese innovative medical technologies.
- O In this respect, the Act on Promotion of Healthcare Policy also clearly states that promotion of overseas expansion is needed for cutting-edge research and creation of new industry development in the health and medical sectors¹ while the Healthcare Policy (approved by Cabinet on July 22, 2014) refers to collaborative activities among Europe, the United States, and Asia to further their understanding of Japan's regulations, standards, etc. concerning clinical trials, regulatory applications, etc., and to establish international harmonization.
- O Strategic and aggressive promotion of international regulatory harmonization and international cooperation, as mentioned above, requires the formulation of a specific strategy that clarifies the medium- to long-term vision and policy priorities with reference to related factors including the characteristics of the respective production sectors for pharmaceuticals, medical devices, and regenerative medicine products, the global harmonization framework, and current status of bilateral cooperation, and also requires coordinated action based on a common public-private appreciation of the issues.
To this end, under the direction of the Minister of Health, Labour and Welfare (MHLW), a project team led by the Councillor of MHLW undertook to formulate the “International Pharmaceutical Regulatory Harmonization Strategy – Regulatory Science Initiative –” following hearings, etc. involving representatives from the pharmaceutical, medical device, and other relevant industries.
- O Coincidentally, in 2015, Japan is serving as chair of the ICH (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use - Japan-US-EU) and of the IMDRF (International Medical Device Regulators Forum); it is also co-chairing the APEC LSIF-RHSC (Asia-Pacific Economic Cooperation Life Sciences Innovation Forum Regulatory Harmonization Steering Committee). These roles call for Japan to demonstrate proactive leadership in the pharmaceutical regulations sector.
- O Over recent years, the level of Japan's regulations on medical products and regulatory science² has been dramatically advancing, as can be seen in reductions in review times, elimination of drug lag, etc.

1 Article 2 of the Act on Promotion of Healthcare Policy

2 “Regulatory science” in the sectors of pharmaceuticals, medical devices, etc. refers to the science of predicting, evaluating, and determining, fairly and promptly, the quality, efficacy, and safety of pharmaceuticals, medical devices, and regenerative medicine products, based on scientific knowledge.

To be able to respond to the future expectations of the global community, establishment of a development environment demonstrating Japan's areas of strength and further promotion of regulatory science under this strategy will enhance Japan's reliability and attractiveness through provision of an infrastructure for approval of first-in-the-world, innovative pharmaceuticals, medical devices, and regenerative medicine products. In addition, international harmonization and cooperation will be proactively promoted through transmission to Asia and other regions of Japan's knowledge of regulations on medical products and regulatory science in order to further contribute to elimination of global drug/medical device lag and promotion of health and hygiene across the global community.

- O In addition, such initiatives will help to boost the attractiveness of the Japanese market and encourage domestic investment in development by both Japanese and foreign manufacturers. Expansion of exporting of excellent products will also boost the pharmaceutical and medical device industries and contribute to domestic growth.

II Current status in the sectors of pharmaceuticals, medical devices, etc. in Japan

- O To more effectively promote initiatives for international harmonization and cooperation in respect of pharmaceutical regulations in Japan, what needs to be done should be considered based on competitive edges and issues in pharmaceutical, medical device, and related sectors.
The principal competitive edges and issues in respect of pharmaceutical, medical device, and related sectors in Japan are as follows:

Competitive edges

- The universal coverage system ensures rapid insurance reimbursement. The system is highly likely to collect clinical data, etc.
- The predictability and speed of pharmaceutical approvals have been improved through structural enhancement, etc. of the Pharmaceuticals and Medical Devices Agency (PMDA).
- Medical technologies and science in Japan are at world-leading levels, providing the technological basis for Japan to be a pioneer in development of pharmaceuticals and medical devices. Japan also has other advantages, such as a greater incentive for engagement in research and development on age-related medical conditions due to the aging society.
- Data on the Japanese population and therapeutic pharmaceuticals developed in Japan can be utilized across Asia in respect of a number of medical conditions that occur with considerable frequency in Asian populations.

Issues

- The market size in Japan is smaller than that in the United States (global share of the United States is approximately 40% while that of Japan is approximately

10%). In addition, because the scale of key hospitals is smaller than those in other countries, it is necessary to conclude agreements with numerous medical institutions in order to recruit participants in clinical trials. For these reasons, the cost of clinical trials is high, resulting in less incentive for development investment by companies.

- Capability of transmitting information on pharmaceutical regulations in Japan and on know-how and technologies is poor and the global action framework of the MHLW and PMDA is fragile. Requests by the Japanese government and pharmaceutical industry have not been sufficiently conveyed to the governments of other countries.

III Actions required – for Japan to become a “world reference country” –

- Based on the competitive edges and issues in the pharmaceutical, medical device, and related sectors mentioned in the section II, future actions necessary for Japan to be able to contribute as a world reference country³ in such sectors are discussed below.

1 Establishment of infrastructure to facilitate approval of innovative pharmaceuticals, medical devices, and regenerative medicine products in advance of the rest of the world – To improve reliability and attractiveness of Japan –

The initial requirement for Japan to be able to contribute to the pharmaceutical, medical device, and related sectors as a world reference country is to improve its reliability and attractiveness in terms of pharmaceutical approvals and safety measures by establishing conditions whereby significant new pharmaceuticals, medical devices, and regenerative medicine products that are safe to use can be approved in advance of the rest of the world.

To this end, the following initiatives will be promoted.

◆ “SAKIGAKE” Forerunner Review and Designation System and promotion of AMED activities

- Incentives for development of pharmaceuticals, etc. in Japan will be provided through effective implementation of the “SAKIGAKE Review and Designation System” (from fiscal 2015) which is aimed at facilitating rapid commercialization of pharmaceuticals, medical devices, and regenerative medicine products that promise excellent efficacy on the basis of clinical trial data, with support from various agencies (for example, pharmaceuticals and medical devices will be approved within six months, half the normal period) and through promotion of integrated research and development from basic research through commercialization by the Japan Agency for Medical Research and Development (AMED).

3 A country to be referred to by other countries for regulatory system management

◆ **Establishment of development conditions that utilize Japan’s strength**

- To resolve the issue of higher clinical development costs in Japan as compared with those in other countries, new clinical development processes will be developed in Japan’s areas of strength (e.g., cancer, dementia, etc.) within five years through establishment of a clinical development infrastructure utilizing data from disease registries. This will facilitate domestic development as well as attracting overseas manufacturers to develop anticancer drugs, treatment for intractable diseases, biological products, etc. in Japan (concept of “Clinical Innovation Network”). Specifically, a network mainly composed of such organizations as the National Centers for Advanced and Specialized Medical Care (NCs), core clinical research hospitals, PMDA and AMED will be established using the disease registry system created by the NCs and other disease registries, and a clinical trial consortium will be formed based on industry-academia partnerships. Furthermore, corporate utilization of disease registry data accumulated by NCs, etc. will be facilitated through personnel exchanges between hospitals participating in the network and PMDA, and through regulatory science studies on clinical evaluation processes. In addition, this network will be extended across the Asia region to create a framework whereby multinational clinical trials can be facilitated.
- It is assumed that core clinical research hospitals, which have central roles in global-level clinical research or investigator-initiated clinical trials under the Medical Care Act, can recruit many subjects as well as outstanding researchers and other human resources and will receive numerous consultation and study requests from other centers. By approving such hospitals, high-quality clinical research and trials necessary for development, etc. of innovative, Japan-origin pharmaceuticals, medical devices, etc. and of medical technologies will be promoted.

◆ **Improvement of predictability and transparency of regulatory approvals, etc. and enhancement of safety measures through intensive promotion of global-level regulatory science**

- To create a reviewing and consultation framework of a high scientific level, a Regulatory Science Center will be established within PMDA in 2018. Corporate development will be promoted through development of new therapeutic evaluation indices and procedures, and drafting guidelines, based on analyses of electronic data on clinical study results, etc., together with utilization of the knowledge of the experts who comprise the Science Committee.
- The Regulatory Science Center will analyze MID-NET⁴ medical data and information contained in the disease registries of NCs and other organizations, promote the use of MID-NET in medical institutions and companies, and enhance safety measures.

4 The MID-NET database currently comprises data on approximately 3 million persons and the intention is to collect medical records and other data on approximately 10 million persons.

- Japan’s presence in the area of safety measures will be enhanced through the exchange of globally advanced safety information with regulatory authorities of the United States and European countries as well as through transmission of safety information on Japan-origin pharmaceuticals. In addition, in order to proactively contribute to improvement of safety measures in Asia and other countries, a system will be established for promptly supplying information on safety assurance measures in Japan, including background information, required for consideration of the need to implement actions in each country, particularly to regulatory authorities in Asia, as well as for responding to consultation requests.
- To improve predictability of medical fee assessments, a system for consultation on pharmaceutical prices and costs of medical materials prior to submission of applications for approval will be established.
- Development of pharmaceutical safety evaluation methods with a high level of predictability using human iPS cells will be promoted through the Health and Labour Sciences Research on regulatory harmonization and evaluation of pharmaceuticals (including promotion of research and development of techniques to evaluate the cardiotoxicity of pharmaceuticals, applying human iPS cell technology, and proposals for global standardization of safety evaluation methods).

2 Proactive information dissemination to the global community

– To distribute Japanese know-how to the world –

In conjunction with the initiatives mentioned in Section 1, global understanding of pharmaceutical regulations in Japan will be promoted through proactive transmission to the global community of information on Japanese know-how on regulatory science, regulatory systems, etc.

◆ Within three years, proactive transmission of information to the global community on Japanese know-how on regulatory science, regulatory systems, etc. will be started.

- To proactively transmit and promote understanding of Japanese know-how on regulatory science, pharmaceutical regulatory systems, etc. to regulatory authority officials in Asia, an Asian Pharmaceuticals and Medical Devices Regulatory Training Center, which will conduct planning, drafting, and arrangements of training for officials of regulatory authorities in Asia, will be established within PMDA. The Center, in cooperation with industry-related associations, will provide effective training opportunities, including training courses to be held in key Asian countries, according to areas in which regulatory authorities in such countries wish to be trained or according to the reviewing and inspection capabilities of Asian regulatory authority officials.
- To appropriately transmit viewpoints of the Japanese government and industries, as well as Japanese know-how on regulatory systems, etc., local frameworks will be

established and effective dialogues with local regulatory authorities will be implemented with the cooperation of industry groups. Specific actions will include mutual dispatch of liaison officers between the PMDA and regulatory authorities in other countries, consideration of establishment of overseas PMDA offices according to progress on international harmonization and cooperation, dispatch of attachés, cooperation with the Japan External Trade Organization (JETRO) and other organizations, and support for organizing local Japanese companies.

- Globally advanced safety information will be exchanged with regulatory authorities of the United States and European countries and safety information on Japan-origin pharmaceuticals will be transmitted. In addition, a system will be established for promptly supplying information on safety assurance measures in Japan, including background information, required for consideration of the need to implement actions in each country, particularly to regulatory authorities in Asia, as well as for responding to consultation requests (as mentioned above).
- Transmission of information in English on Japanese pharmaceutical regulations, including laws and regulations, notifications, review guidelines, review reports, and approval standards for non-proprietary pharmaceuticals, will be stepped up. In addition, transmission of information in English by industry groups, etc. will be promoted on superior Japanese pharmaceuticals, medical devices, regenerative medicine products, and technologies.
- Outcomes of regulatory science research and the content of new pharmaceutical regulations that may also be of value to other countries will be proactively presented in leading scientific journals and medical society forums.

3 Strategic initiatives with specified priorities in each product area – To implement measures more effectively –
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Pharmaceuticals

(1) Strong partnership in the Asia region centered on ASEAN, China, Korea, etc.

With Japan being the only East Asian country that is discovering new pharmaceuticals, it is vital to offer Japanese know-how on regulatory science to ASEAN (Association of Southeast Asian Nations), China, Korea, and other countries in the region that are geographically and culturally related, and to proactively contribute to the establishment of pharmaceutical regulations and improvement of hygiene and sanitation in the region. These initiatives are also expected to revitalize the Japanese pharmaceutical industry as Japan-origin pharmaceuticals are rolled out into the Asia region. To this end, the following initiatives will be taken with the aim of forging further partnerships in the Asia region centered on ASEAN, China, Korea, etc.

- ◆ **Within three years, exchanges with key ASEAN countries will be started to promote understanding of pharmaceutical regulations in Japan with the**

aim of achieving a pharmaceuticals approval system that is on a par with those of Europe and the United States, and government-level exchanges of views with China, Korea, etc. will be expedited.

- In conjunction with the initiatives for pharmaceuticals mentioned in Section 2, bilateral cooperation with key ASEAN countries will be proactively advanced to promote understanding of the Japanese regulatory system so that it can be referred to in consolidating the pharmaceutical regulations of those countries. In addition, with the aim of achieving Europe/US-level status, efforts will be made to obtain the understanding of partner countries on matters such as addition of Japan as a country eligible for abbreviated reviews and/or inclusion of the Japanese Pharmacopoeia as a reference pharmacopoeia.
- Government-level exchanges of views with China, Korea, etc. will be accelerated -- for example, convening of a Japan-China-South Korea Directors-General Meeting on Pharmaceutical Affairs, one of which has not been held since 2011, and interchanges through joint symposiums, etc. will be promoted.

◆ Within five years, diffusion of ICH and other guidelines and conduct of joint clinical trials in the Asian region will be promoted.

- The central training facility for multi-regional clinical study projects to be conducted by APEC LSIF-RHSC will be selected from among domestic facilities, and training for officials of regulatory authorities and healthcare professionals, etc. in the Asian region will be discussed with the regulatory authorities in the countries concerned. The aim thereafter is to establish the central training facility as the hub of a global clinical trial network, with reference to progress on the project.
- In joint clinical trials in Asian regions consulted simultaneously with Japan, cooperative clinical trial consultation services will be provided with exchanges of information and views on the content of such with regulatory authorities that can take actions.
- Necessary cooperation will be promoted for utilization of ICH guidelines and clinical evaluation guidelines, etc. in the key Asian countries, targeting ASEAN (in three years), China, Korea, etc. (in five years) and other countries (in 10 years).
- To ensure prompt delivery of innovative pharmaceuticals to Asian populations, initiatives for adoption of the Good Submission Practice standards formulated by the conference of Asian pharmaceutical industries, APAC (Asia Partnership Conference of Pharmaceutical Associations), will be supported.

◆ Within 10 years, cooperation on reviewing, etc. will be promoted in the Asian region.

- Simultaneous launching in Japan and Asia of pharmaceuticals for which applications for approval are concurrently submitted in Japan and other countries will be aimed by promoting cooperation on reviewing with exchanges of information and views on the content during reviewing with the regulatory authorities that can take actions.

- Establishment of the Japanese Pharmacopoeia as the reference pharmacopoeia for each Asian country will be promoted.
- International cooperation, including development of global human resources and regulatory harmonization, will be promoted and, at the same time, in consultation with the countries concerned, the future form of enhanced regulatory authority cooperation through establishment of an Asian Medicines Agency, etc. will be considered.

(2) Leading role in international harmonization as a member of the tripartite entity of Japan, the United States, and Europe

The United States and Europe have mature, large-scale markets and are also the global regulatory leaders. Promoting regulatory harmonization and global cooperation between Japan and US/Europe will also enhance trust in Japanese pharmaceutical regulations. To this end, a global-level regulatory science will be intensively advanced and the following proactive initiatives for regulatory harmonization and global cooperation with the United States and Europe will be continued so as to demonstrate Japan's leading role as a member of the tripartite entity of Japan, the United States, and Europe.

◆ Taking the lead in discussions, etc. on the international regulatory harmonization framework as a short-term initiative

- Japan will take a central role in the activities of the ICH, International Coalition of Medicines Regulatory Authorities (ICMRA), OECD, etc. and in formulation of the respective strategies.
 - With representation by regulatory authority officials from Japan, United States, Europe, etc., an agenda including Association for the ICH to draft guidelines for regulatory harmonization of new pharmaceuticals and an increase in the number of participating countries will be discussed; and promotion of establishment of guidelines for new pharmaceuticals and an increase in the number of guideline-applicable countries will be targeted.
 - ICMRA, in which top-level regulatory authorities of the key countries participate, will be officially inaugurated and, as the “control tower” for regulatory global cooperation, will oversee the respective activities of the ICH, APEC, etc. in order to eliminate duplications, establish priorities, etc. In particular, this organization will be the center for prompt international coordination concerning new regulatory issues (e.g. approval of Ebola-related pharmaceuticals)
 - Japan will play a central role through, for example, serving as chair for OECD/GLP activities (including, with participation by regulatory authority officials from OECD member countries, formulation of standards for reliability of nonclinical study data and implementation of mutual acceptance of inter-member GLP inspection results). Through coordination with the related international frameworks, rule-making and development of human resources will be promoted with the aim of expanding this scope of action and increasing the number of mutual data acceptance countries.

- In addition to proactive initiatives for international harmonization of GMP inspection through the PIC/S, expansion of the number of signatory countries to and the category of products covered by the Mutual Recognition Agreement (MRA) on GMP inspection results with Europe will be sought. In addition, penetration of the perspectives of global GMP standards to domestic GMP inspectors (PMDA and prefectures) will be ensured and global standards-compliant GMP regulations will be implemented.
- Global harmonization of the Japanese Pharmacopoeia will be promoted, together with incorporation of the latest quality control measures.

◆ **Within five years, cooperation on reviewing, etc. with the United States, Europe, etc. will be promoted.**

- Cooperation at the clinical trial stage through cooperation on scientific advices based on PMDA clinical trial consultations and similar actions will be sought.
- Cooperation on reviewing with exchanges of information and views on the content of pharmaceutical applications submitted simultaneously in Japan, the United States, and Europe will be promoted among the respective regulatory authorities during reviews.
- Mutual utilization of GMP inspection results from MRA signatory European authorities will be promoted, and the potential for concluding a MRA with regulatory authorities outside of Europe will be considered.
- A forum for global discussion on mutual utilization of GCP inspection results will be considered in Japan, the United States, Europe, etc.

◆ **Within 10 years, diffusion of the ICH guidelines, etc. will be promoted in key regions with the cooperation of the United States, Europe, etc.**

- Necessary cooperation will be promoted for utilization of ICH guidelines, etc. and utilization of current GMP inspection results in BRICs (Brazil, Russia, India, and China) regions, etc., where large-scale market expansion and increasing importance of pharmaceutical regulations are anticipated.

OTC drugs

- Asia-focused actions are vital due to the strong calls for global cooperation concerning OTC (over-the-counter) drugs in the Asian region in particular. Regulatory harmonization and global cooperation in this field will be promoted through pro-active participation by Asian regulatory authority officials in “Self-CARER” (Self-Medication Collaborative Asian Regulator Expert Roundtable), the regulatory harmonization framework for non-proprietary drugs, and reinforcement of international activities such as industry group support for APSMI (Asia-Pacific Self-Medication Industry).

- Mutual understanding of standards for OTC drug approval drafted by individual countries will be promoted and establishment of standards for approvals in each country will be supported.
- In addition, to improve public health and hygiene in Asian countries, industry activities for extending availability of superior OTC drugs, including Japan-specific combination drugs, to Asian countries will be supported.
- As well as sharing Japan's experience with a public health insurance system, awareness of the importance of self-medication will be promoted.

Generic drugs

- Given that overseas distribution of generic drugs is currently at the seminal stage, necessary actions will be taken in line with the characteristics of generic drugs with reference to future industry intentions and the need for overseas expansion.
- First, the Japanese Government will step up the IGDRP (International Generic Drug Regulators Programme) and other global activities carried out by regulatory authority officials worldwide to promote regulatory harmonization and global cooperation on generic drugs.
- Support will be given to industry-based IGPA (International Generic Pharmaceutical Alliance) activities with the aim of improving access to high-quality generic drugs in other countries.
- As with new drugs, submission of applications based on the CTD (Common Technical Document) will be recommended for applications for generic drugs approval.

Medical devices

(1) Proactive involvement in the International Medical Device Regulators Forum (IMDRF) and other multilateral activities to promote international harmonization of medical device regulations

Medical device regulations in Japan include the European-style certification system for relatively low-risk items and the American-style approval system (global mainstream) for relatively high-risk items and, consequently, can assume a hub function in international harmonization. To achieve global harmonization of medical devices, the activities of the IMDRF, the forum for international harmonization with participation by Brazil, Russia, China, etc. as well as the United States and Europe, and of the ISO (International Organization for Standardization) and IEC (International Electrotechnical Commission), which draft the international standards for the engineering and electricity sectors, are crucial. Taking these factors into consideration, the following initiatives will be promoted.

◆ Taking the lead in discussions, etc. on the international regulatory harmonization framework as a short-term initiative

- A medium- to long-term action plan for the IMDRF will be developed at the Kyoto Conference to be held in September 2015 while Japan is serving as chair of IMDRF in 2015. Japan will also proactively contribute to the drafting of guidelines in the IMDRF.
- Quality management will be promoted through official participation in the MDSAP Pilot (trial initiative in which the regulatory authorities of Australia, Brazil, Canada and the United States are participating for applying the outcomes of QMS inspections conducted by an assessed audit organization).
- As with pharmaceuticals, Japan will serve as chair for OECD/GLP activities or take a similar central role and, in coordination with the respective international framework, rule-making and development of human resources will be promoted with the aim of expanding this scope of action and increasing the number of mutual data acceptance countries.
- To advance international regulatory harmonization in Asian countries, opportunities will be provided at APEC LSIF-RHSC to proactively share both information on IMDRF activities and Japan's knowledge and experience.
- In addition, greater transparency in medical device regulations in Japan will be brought about through clarification of the scope where application for partial change approval is required and of the criteria for determining the need for clinical trials, together with a review of further global harmonization of Japan's QMS.

◆ Diffusion of global adoption of IMDRF guidelines, etc. through cooperation with IMDRF members as a long-term initiative

- In cooperation with IMDRF members, the cooperation necessary to promote utilization of the IMDRF and other guidelines by other countries and regions will be promoted, and efforts will be made to obtain an understanding for utilization the MDSAP Pilot and PMDA QMS inspection results.
- International standardization of Japan-origin specifications and specifications reflecting Japanese views will be promoted through active participation in ISO/IEC activities that are vital in the medical devices field.

(2) Focused bilateral cooperation based on trust relationships gained through multilateral international contributions

A stronger cooperative relationship with the United States, a country with a large-scale market and high-level reviews, etc., should be fostered. In addition, it is vital to share Japan's knowledge and experience based on the IMDRF and other multilateral international activities, with Brazil, Russia, and China, where their regulatory systems for medical devices have recently been amended and the future management is in the spotlight, and with countries including India, where system amendment is scheduled. Prioritized and focused bilateral cooperation is conducted as shown below.

◆ **Mutual understanding, establishment of cooperative relationships, and specific cooperation projects will be promoted with the United States, BRICs, key ASEAN countries, etc.**

- Further mutual understanding with the United States, Brazil, Malaysia, and other countries that have already initiated cooperative activities will be promoted.
- Dialogues will be held for mutual understanding and establishment of cooperative relationships with BRICs and key ASEAN countries, utilizing the opportunities of IMDRF, etc.; and utilization of IMDRF results and understanding of Japan's pre-market review system will be promoted in order to contribute to effective operation of medical device regulations among the regulatory authorities.
- Activities including cooperation in clinical trial scientific advices and pre-market reviews, which is already underway with the United States, will be promoted in regulatory authorities with which Japan has already advanced mutual understanding and cooperative relationships:
 - (1) Cooperation at the clinical trial stage, such as scientific advices based on PMDA clinical trial consultations
 - (2) Cooperation on pre-market reviews of medical devices for which applications for approval have been submitted simultaneously in Japan and the respective countries, through exchanges of information and views on the content of the respective medical device applications among regulatory authorities during reviews
 - (3) Efficient implementation of the QMS system through mutual utilization of QMS inspection results

Regenerative medicine products

Actions for commercializing regenerative medicine products are accelerating in Japan through measures such as introduction of the pre-market approval with conditions and time-limit schemes and advances in the field of iPS cells and other clinical researches. For regenerative medicine products, too, establishment of a framework for international industry-government-academia communication to facilitate global development of regenerative medicine products based on Japanese technologies and institutional strengths will therefore be sought, to which the following initiatives will be promoted:

◆ **Becoming a global leader with an established cutting-edge technologies and regulatory structure**

- An operation and knowledge regarding pre-market reviews in Japan, post-marketing safety measures, etc. will be built up based on the newly introduced regulations.
- International symposiums will be hosted with participation by industry-government-academia representatives to promote mutual understanding among the respective parties.

- A framework for international dialogues with countries, including Europe, the United States, etc., will be established with the aims of, for example, establishing common international ground on the minimum study data required for pre-market reviews of regenerative medicine products, and of forming a basic common viewpoint on product quality assurance.
- Cooperative relationships will be established with key ASEAN countries, etc. for the purpose of sharing information on the Japanese regulatory system, its operation and Japanese knowledge.

“Dangerous drugs”, SSFFC medicines, etc.

With the spread of the Internet, cross-border circulation of “dangerous drugs” (New Psychoactive Substances), SSFFC (Substandard, Spurious, Falsely labelled, Falsified and Counterfeit) medicines, etc. has become a global issue in recent years, and internationally coordinated action is called for. Accordingly, to help prevent circulation of “dangerous drugs”, and SSFFC medicines, etc., the following initiatives will be promoted.

◆ Promotion of international coordination to help prevent circulation of “dangerous drugs”, SSFFC medicines, etc.

- Globally circulating substances used in the formulation of “dangerous drugs”, etc. will be analyzed and prompt controls will be imposed following toxicity data-gathering. Furthermore, online purchasing surveys will be conducted to identify circulation of SSFFC medicines that are purchasable online from other countries. In addition, internationally coordinated border controls will be reinforced through promotion of measures such as sharing of Japanese regulatory information and information on exporters, etc. with countries from which influxes to Japan of “dangerous drugs” and SSFFC medicines, etc. originate, and through intensive exchange of information by overseas dispatching of narcotics agents.
- Active surveillance of overseas online sales sites advertising unapproved and unlicensed drugs including “dangerous drugs” and SSFFC medicines will be conducted (with requests for registrars to suspend such online sales websites, as known as Internet patrol). In particular, internationally coordinated online selling controls will be stepped up through measures such as sharing of information on the respective unlawful sites with countries in which these sites are domiciled.
- International frameworks for information exchange concerning “dangerous drugs”, SSFFC medicines, etc. will be proactively participated in (e.g. the Global Synthetics Monitoring: Analyses, Reporting and Trends Programme [SMART Programme] of UNODC [United Nations Office on Drugs and Crime] and the WHO Meeting of the Member State mechanism on SSFFC medical products), and such forums will be used to play a proactive role in promoting the international coordination of the border controls and online selling controls referred to above.

4 Promotion of international regulatory harmonization and cooperation in an ongoing and consistent manner
– To take leadership in international society –

To promote international regulatory harmonization and cooperation in an ongoing and consistent manner, the global action frameworks of the MHLW and PMDA will be reinforced as described below. In addition, periodic progress control and necessary reviews will be conducted.

◆ Establishment of global units within the MHLW and PMDA and introduction of a managerial system per country and region

- Global action units will be newly established within the MHLW and PMDA. While the MHLW will promote development of global human resources as well as undertaking a “control tower” function for global strategy, the PMDA will conduct analyses for centralized management of local information in other countries and tactical global cooperation. In addition, a managerial system for each country and region will be introduced and its teams will cover major countries.

◆ Periodic progress control and reviews of the International Pharmaceutical Regulatory Harmonization Strategy

- The global unit within MHLW will undertake periodic progress control of the implementation of the International Pharmaceutical Regulatory Harmonization Strategy and conduct necessary reviews with reference to specific progress and the latest international situation, based on exchanges of views with the industry.