

# AMDD *Vol.19*

## NEWSLETTER

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### Protecting Japan from the Threat of Infectious Diseases

In 2014, a great number of people felt a renewed threat of infection caused by the outbreak of numerous infectious diseases during the year, including Dengue fever in Japan and Ebola hemorrhagic fever in West Africa. Dr. Norio Ohmagari, director of the Disease Control & Prevention Center at the National Center for Global Health and Medicine, spoke about the measures necessary for preventing the threat of infection through a proper understanding of infectious diseases and their backgrounds.

### Various Infectious Diseases From Around the World

#### *Influenza*

In April 2013, patients were discovered to have contracted a strain of avian influenza known as H7N9 in Shanghai, China. Many of the patients were workers at live bird markets and were known to have become infected through their contact with poultry (chickens) suffering from avian influenza. The mortality rate was 27%, and a delay in the administration of anti-influenza drugs is thought to have increased the risk of mortality. Given the dynamic nature of incoming and outgoing traffic to China, there was a distinct possibility of future outbreaks in Japan. It would be essential to deal with any outbreaks rapidly.

#### *Middle East Respiratory Syndrome (MERS)*

2012 saw the emergence of infections of Middle East Respiratory Syndrome (MERS). Camels are known to be carriers of the coronavirus. The main cause of the epidemic in Saudi Arabia was nosocomial infections, and this presented a timely opportunity for health professionals to review their personal protective equipment.

### *Dengue Fever*

The outbreak of dengue fever in Japan last summer is still fresh in our minds. The virus is carried by the Asian tiger mosquito (*Aedes albopictus*). There are few characteristic symptoms during the initial phase, so it is important for medical professionals to gain an understanding of the patient's history, such as if they have traveled lately or been bitten by a mosquito, etc. Some reports noted that dengue fever is a minor infection; however the disease progresses and becomes severe in 5% of patients.

It is important for health professionals not to miss initial symptoms that indicate progression towards severity, such as nausea, vomiting, and severe abdominal pain.

### *Ebola Hemorrhagic Fever*

The incubation period for Ebola hemorrhagic fever is approximately 3 to 12 days, which is comparatively long, and this presents a risk of it being carried into Japan during the incubation period. The symptoms of diarrhea and vomiting resulting in severe dehydration are more apparent than hemorrhaging.

At this stage, the most effective treatment is fluid replacement and blood transfusions to compensate for lost fluid. This is a top priority to prevent organ damage.

## **Protection against the Threat of Infectious Diseases**

The need for medical safety has gained recognition in recent years. Medical institutions must always consider risk management, and it is crucial to introduce a two-person buddy system. In conclusion, Dr. Ohmagari spoke of methods for dealing with a suspected disease encounter. It would not be difficult for general medical institutions to implement the following as fundamental strategies:

1. Keep patients in private rooms.
2. Take measures to prevent bodily contact with patients.
3. Prevent inadvertent close contact with a patient suffering from diarrhea, vomiting, etc.
4. Do not conduct blood sampling if there is a risk of secondary infection.

\* The lecture provided by Dr. Ohmagari was summarized by the editorial desk.



**Dr. Norio Ohmagari**  
Director  
Disease Control & Prevention Center,  
National Center for Global Health and Medicine,  
National Research and Development Agency

Norio Ohmagari graduated from Saga University, Saga Medical School, Faculty of Medicine in 1997. He worked at St. Luke's Hospital in a variety of departments such as the infectious diseases department, pulmonology, and others from 1997 – 2000. He served as a clinical fellow in the infectious diseases department of the University of Texas, Medical School at Houston from 2002. After serving as director of the infectious diseases department at the Shizuoka Cancer Center in 2010, he moved to the National Center for Global Health and Medicine Hospital in 2011 and took his present post of director in 2012. In 2013 he received a master's degree in infectious diseases from the University of London, and in 2015 he received his medical doctorate (M.D.).

## **International Strategy of the PMDA**

### **Introduction**

As the development and distribution of pharmaceuticals and medical devices continues to globalize, international cooperation is required for the rapid provision and safe use of them. The Pharmaceuticals and Medical Devices Agency (PMDA) promotes international harmonization as one of its principles of conduct<sup>1</sup>, and states that it will play an active role on the global stage. As an organization, the PMDA undertakes planned and systematic promotion of international activities, such as the formulation of an international strategy, vision, and a vision roadmap. In this paper, we will outline the international activities of the PMDA.

### **The PMDA and International Business**

The PMDA regulates the pharmaceuticals and medical devices of international corporations, and helps to improve the health and safety of Japanese citizens as well as administrative efficiency in Japan using foreign regulatory information. The agency has become integral and inseparable as a go-between for domestic and international businesses concerning international cooperation on safety measures and GMP inspections.

Regarding domestic businesses, if each function of the safety triangle (for example, the quality and speed of approval) does not reach international standards, there will be no increase in the resultant cooperation with international bodies. The efforts of the PMDA allow domestic and international businesses to mutually reinforce each other, and further enhances the already excellent regulatory affairs of Japan (approval, safety measures, etc.). At the same time, these efforts also contribute to enhancing the international status of the PMDA.

### **The PMDA International Strategy**

The PMDA undertakes negotiations with the Ministry of Health, Labor and Welfare regarding how to proceed with international activities in the field of pharmaceuticals and medical devices, and established the “PMDA International Strategic Plan”<sup>2</sup> on February 6, 2009 detailing the targets and basic policies to be achieved during their second five-year plan (2009 – 2013). In accordance with this strategy, the PMDA is able to accurately meet the needs of Japanese citizens for pharmaceuticals and medical devices, as well as the needs of people around the world through proactive international activities and better planned/systematic promotional activities.

The strategy contains the following three items as targets to achieve during the second five-year plan period:

1. Strengthen cooperation and build cooperative relationships with Western and Asian countries as well as other international organizations.
2. Proactive participation and a greater number of contributions to international harmonization activities.
3. Enhance and strengthen the dissemination of information to the international community.

With the end of the 2014 fiscal year, the beginning of the third five-year plan period (2014 – 2018) has begun thereby ending the period of the aforementioned international strategy;

however the concepts and content, including the international vision and vision roadmap as well as the plan for the third period, will continue as described below.

### **PMDA International Vision**

In November 2011, approximately 2.5 years after the implementation of the “PMDA International Strategic Plan”, the PMDA achieved the strategy goals, and created the “PMDA International Vision”<sup>3</sup> clarifying the goals for the upcoming 5 – 10 year period. Following the development of the PMDA International Strategic Plan, there were changes in international circumstances, such as the increase in the relative importance of countries other than ICH founder countries, so the PMDA gained experience through various international activities. The International Vision will see the PMDA establish its international status as part of the three top level international regulators including Japan, the USA, and Europe, and not simply as a regulatory authority buried in the Asian region. Specifically, as one of these three top level regulatory authorities standing shoulder to shoulder with both Europe and the USA, the International Vision lists the following three goals: Maintain the world’s top level talent, hold close partnerships with Asian countries, and make a positive contribution to international harmonization.

### **Roadmap for the PMDA International Vision**

In recognizing the construction of a system to realize the PMDA International Vision as an urgent issue, the following five areas of focus for international activities were formulated in April 2013, resulting in the “Roadmap for the PMDA International Vision.”<sup>4</sup>

- (1). Response to advanced science and technology
- (2). Improvement of international operation basis
- (3). Dissemination of English information on regulatory review of medicinal products, especially publication of review reports in English
- (4). Dissemination of information and international cooperation on safety measures
- (5). Increase of the leverage of Japanese Pharmacopoeia (JP)

It should be noted that, for each item of the roadmap the “importance” of its creation as well as “concrete policies and the time to achieve goals” in order to achieve “the ideal situation” should be clarified and specified.

### **Conclusion**

On April 13, 2015 the third Government Industry dialogue was held concerning the creation of innovative pharmaceuticals and medical devices. The Ministry of Health, Labor and Welfare announced the creation of an “International Regulatory Harmonization Strategy — Regulatory Science Initiative —“ (tentative name).<sup>5,6</sup>

The PMDA will move forward to achieve further internationalization and is expected to actively proceed with international regulatory harmonization in the field of pharmaceuticals and medical devices and will continue to make contributions to the international community.

1. PMDA Philosophy  
<https://www.pmda.go.jp/about-pmda/outline/0003.html>
2. PMDA International Strategic Plan  
<https://www.pmda.go.jp/int-activities/outline/0002.html>
3. PMDA International Vision  
<https://www.pmda.go.jp/int-activities/outline/0003.html>
4. Roadmap for the PMDA International Vision  
<https://www.pmda.go.jp/int-activities/outline/0004.html>

5. International Regulatory Harmonization Strategy (tentative name) — Regulatory Science Initiative — <http://www.mhlw.go.jp/file/05-Shingikai-10801000-Iseikyoku-Soumuka/0000082665.pdf>
6. The Third Government Industry Dialogue for the Creation of Innovative Pharmaceuticals and Medical Devices  
<http://www.mhlw.go.jp/stf/shingi/other-isci.html?tid=127362>



### **Teruyoshi Ehara**

Office Director of the Office of International Programs,  
Pharmaceuticals and Medical Devices Agency (PMDA)

Mr. Ehara earned his master degree at the Graduate School of Pharmaceutical Sciences, Chiba University and previous to joining the Ministry of Health, Labor and Welfare in 1993. He studied as a graduate student at the Center for Drug Development Science at Georgetown University, United States of America in 1998. He has been in his current position since September 2014 and is responsible for enhancing PMDA's overall international affairs, including communication and cooperation with foreign counterparts and international organizations

## **Patient's Voice** **The Hopes of ALS Patients**



Japan Amyotrophic Lateral Sclerosis Association (JALSA)

ALS (amyotrophic lateral sclerosis) is a disease in which the activity of the motor neurons is impaired. It occurs at a rate of 2-6 in 100,000 people, of which 10% is caused by hereditary factors. As the symptoms of the disease progress, assistance is required for all aspects of a person's life due to the weakening of muscles in the extremities. Furthermore, there is a progression in dysphagia, language disorders, and respiratory dysfunction, ultimately leading to the necessity of a gastric feeding tube, special equipment for communication, or a tracheotomy/ventilator.

Because these choices are forced on a patient in order to maintain life as well as a social life, ALS has been known as “the most difficult of incurable diseases” since the term *nanbyo* (incurable disease) was defined. In Japan there are currently approximately 9,000 patients who have applied for an incurable disease medical care certificate.

JALSA was established in 1986 as a gathering of patients and families, bereaved families, medical staff and specialists, and volunteers struggling to deal with ALS. It is a nonprofit organization established for the purpose of ALS patient recuperation and to find a cure for the disease. It does not belong to a specific religion or political organization. There are 41 nationwide branches with approximately 5,000 members of which 40%, approximately 2,000 people, are patients or family members.

The root cause of ALS has still not been discovered. The “ALS Fund” was established in 1992 through the support of donations from patients, family members, and other supporters, and each year they donate money to ALS research. In addition, they carry out medical assistance activities, including ALS consultations, a business which lends communication equipment, and ALS care seminars.

Further development is expected in the area of assistive devices supporting the activities of daily life, especially in the development of new robotic technology that is useful in assisting communication. However, the search for the fundamental cause of and treatment for ALS and its loss of physical functionality is the prime wish of patients who are still lucid. Currently, studies are underway to discover the causative gene of familial ALS. It is hoped that this discovery will lead to a breakthrough in treatment for all patients suffering from ALS.

Japan Amyotrophic Lateral Sclerosis Association (JALSA): <http://www.alsjapan.org/>

## **Voice from the Local Government Toward the Development of Market Oriented Medical Devices - Initiatives of Mie Life Innovation’s Comprehensive Special Zone -**



Yasushi Takamura  
Life Innovation Section Chief,  
Mie Prefectural Health and Welfare Department

The value of manufactured goods shipped from Mie Prefecture totals approximately 10.35 trillion Yen, ranking it 9th in Japan (2013 Industrial Statistics Survey Results (Preliminary Report)). 67% of this comes from three industries; transportation equipment, electric and electronic products, and petrochemicals. This makes the value of manufactured goods shipped from Mie Prefecture on a single resident per capita basis No. 1 in Japan.

However, because these industries are sensitive to economic factors, it has become necessary to shift to a more potent and diverse industrial structure by promoting medical, health, and welfare industries which are less subject to economic fluctuations, and will better serve the increasing needs of an aging society.

To achieve this, Mie Prefecture started the “Mie Medical Valley Project” in FY2002 with the aim of industrial development in those three manufacturing fields. This project saw the participation of 123 medical institutions in the creation of the “Mie Investigational Medical Network”, in addition to cooperation between industry, government, academia, and the citizens of Mie Prefecture to establish a manufacturing base.

In addition, after the designation of the “Mie Life Innovation’s Comprehensive Special Zone” by the national government in 2012, they are advancing initiatives towards the creation of innovative pharmaceuticals and medical devices through the consolidation and





use of medical information from research and development support institutions in seven locations across Mie Prefecture as well as other medical institutions in Mie.

The total value of medical devices manufactured in Mie Prefecture ranks a low 39th in Japan (2013 Pharmaceutical Industry Manufacturing and Production Survey). To raise this rank, Mie Prefecture is assisting companies in different business fields from across the Prefecture which possess a high level of manufacturing technology to enter the three business areas of medical, health, and welfare, which have high growth potential.

In order to assist the entry of these companies coming from different fields in the difficult job of developing contacts with workers from the medical and welfare fields as well as the development of sales channels, they are creating match-making opportunities with medical device manufacturers and manufacturing companies in Mie Prefecture, and advancing the development of products which incorporate the know-how and networks of medical device manufacturers.

Currently, in cooperation with the “Commercial and Industrial Association, Japan Medical Industry Association” of the Tokyo Hongo district they are holding an exhibition to introduce the products and technologies of Mie’s manufacturing companies in the Hongo district. This has resulted in numerous achievements, such as new business deals between medical device manufacturers from the two regions and the start of joint development projects between them.

Mie Prefecture has worked closely with industry support organizations in this match-making for companies, such as the Mie Prefecture Industrial Research Institute, the Mie Industry and Enterprise Support Center (Public Interest Incorporated Foundation), and Mie University, and this has boosted product development by placing professionals who are familiar with the development of medical devices in contact with manufacturers.

We are also interested in promoting the development of the medical device industry in Mie to international companies and research institutions, and would like to promote collaboration with medical device manufacturers from North America and other regions around the world. Moving forward, in collaboration with everyone at AMDD, Mie Prefecture hopes manufacturers will take advantage of the research and development system in Mie with its superior manufacturing technology as well as its industry, government, academia, and citizens in the development of medical devices.

## **AMDD and its Participation in Government Industry Dialogue**

The American Medical Devices and Diagnostics Manufacturers’ Association (AMDD) participated in the third “Government Industry Dialogue for the Creation of Innovative Pharmaceuticals and Medical Devices” on April 13, 2015. This dialogue was held for the purpose of carrying out a lively exchange of opinions between government and industry officials. Participants included: Mr. Yasuhisa Shiozaki, the Minister of Health, Labor and Welfare (MHLW), and other officials from the Ministry of Economy, Trade and Industry (METI), Ministry of Education, Culture, Sports, Science and Technologies (MEXT), the Cabinet Office and the Cabinet Secretariat from the government side and the respective representatives of pharmaceutical and medical device related organizations from the

industry side. From AMDD, Chairman Takashi Shimada (President/CEO, Medtronic Japan Co., Ltd.) participated as a member of a medical device related organization, along with The Japan Federation of Medical Devices Associations and the European Business Council in Japan.

The medical device industry requested reasonable implementation and application of the Pharmaceuticals and Medical Devices Act enacted last year, and development and expansion of the innovation evaluation system to further activate the medical device industry which is currently positioned as a growth industry under “Abenomics”. Chairman Shimada also requested, in light of his international business experience, the promotion of regulations for international harmonization, and as the chairman of the AMDD, he would like to see the previously requested abolition of the foreign price reference (FAP)/recalculation system.

Minister Shiozaki mentioned that “because Abenomics is progressing rapidly, a government industry dialogue held only once a year is too infrequent” and asked if it was possible to increase the frequency. He also said that the public and private sectors are now in a place to hold meaningful discussions for both sides.



Left: Mr. Takashi Shimada, Chairman, AMDD

Right: Mr. Yasuhisa Shiozaki, Minister of Health, Labor and Welfare

## Value of Medical Technology <Diagnostic and Treatment Devices>

### The Widespread Use of Low-Flow Anesthesia

“Hopes for Global Warming Counter-Measures and the Reduction of Medical Costs”

At present, in the area of anesthetics, the issue of “low-flow anesthesia” from the viewpoint of reducing medical costs and environmental issues has not been covered. Low-flow anesthesia makes it possible to suppress the amount of anesthetic and oxygen in inhalational anesthetics to a minimum, and reduce the amount of the greenhouse gas CO<sub>2</sub> which has an effect on global warming.



So, how much of a reduction are we talking about?

In the provision of general anesthesia, using an anesthesia apparatus a carrier gas is necessary to supply the inhalational anesthetic to a patient. A vaporizer is used to vaporize the inhalational anesthetic, and this adjusts the concentration of the anesthetic which controls the depth of the anesthetic sleep. The technique of increasing the amount of re-inhaled anesthetic to



more than the regular amount by suppressing the amount of carrier gas to a minimum is known as “low-flow anesthesia”.

The widespread use of low-flow anesthesia can reduce the amount of inhalational anesthetic used on a nationwide scale. This has the potential of saving several hundred million to several billion Yen.

On the other hand, there are safety issues with low-flow anesthesia that rely on the skill of the doctor. However, the safety issue is being resolved through the use of EtC (End-tidal Control), which is similar to the autopilot function of an aircraft, mounted to the anesthesia apparatus. It is hoped that the widespread use of low-flow anesthesia will result in global warming counter-measures and a reduction in medical costs.  
(Takeyasu Hosonami, GE Healthcare Japan)

## **AMDD and JACRI Collaborate on Media Event - Protecting Japan from the Threat of Infectious Diseases -**

The American Medical Devices and Diagnostic Manufacturers’ Association (AMDD) held the 4th joint media seminar in Tokyo co-sponsored by the Japan Association of Clinical Reagents Industries (JACRI) on April 14, 2015.

At the seminar, Dr. Norio Ohmagari, director of the Disease Control & Prevention Center at the National Center for Global Health and Medicine, one of the three designated institutions which handles specific infectious diseases in Japan, gave a lecture regarding the pathology, background, counter-measures, and future challenges involved in the emergence and re-emergence of the infectious diseases Avian influenza, Middle East Respiratory Syndrome (MERS), Dengue fever, and Ebola hemorrhagic fever.

In closing, AMDD director Mr. Haruyoshi Sakamoto (President/CEO of Abbott Japan Co., Ltd), revisited portions of Dr. Ohmagari’s talk in addition to news coverage during the event, and touched on the importance of the communication of timely accurate information. He also mentioned that, as a person who earns his livelihood delivering the value of inspections, he would like to provide opportunities through seminars like this to discuss the latest accurate information from professional educators.



View of the JACRI/AMDD joint seminar

### **Value of Medical Technology**

Our mission is to make more people understand the unlimited potential of advanced medical technology and its contribution to the reformation of the Japanese medical care system

Note: All opinions in this newsletter are the personal opinions of the authors, and do not necessarily represent the opinions and activities of AMDD.