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What is Necessary for the Development of the Medical Device Industry?

~Proposal to Japan Based on Lessons Learned from Successful Examples in the U.S. (Part 1) ~

In 2012, “Medical Creation Fukushima 2012” was held in Koriyama City, Fukushima Prefecture, which was devastated by the Great East Japan Earthquake in March 2011. I had the privilege of speaking about the development of Japan’s medical device industry at the seminar sponsored by the AMDD. The summary is as follows:

Leading U.S. Companies are Acquiring Venture Companies

Looking at the pattern of development in the U.S. medical device industry, most of the medical devices called blockbusters (extremely popular drugs that generate huge sales) did not originate from research and development centers at major companies. In fact, they were produced by a very small number of venture companies. Development of innovative medical devices tends to be accompanied by a risk of failure. Furthermore, it is usually based on out-of-the-box ideas. This is a problem common to both the U.S. and Japan.

Given how much medical technologies have advanced and how cutting-edge medical devices are in demand in the medical front today, few innovative ideas come from the limited resources within major research and development centers alone. That is why the recent trend among major U.S. medical device companies is to look outwards (open innovation), focus only on a few ventures that match their portfolios, and acquire companies that have the best prospects.

However, because venture companies place great importance on speed, many of their medical devices are far from perfect, and their products essentially need to be polished up

for commercialization. Also, as medical devices themselves become complicated, it will be critical to have more rigorous screenings in clinical trials and the manufacturing process, in addition to needing greater funds, so there will be enormous pressure on venture companies to fulfill these needs while continuing development. In short, medical device development in the U.S. is made up of two parts: the first half consists of venture companies starting the development of their ideas, and the second half consists of major companies in charge of the clinical trials, manufacturing and distribution. This arrangement enables great success to be achieved.

Problems with Japanese Medical Device Companies

On the other hand, what about Japan's medical device industry? Many of the leading medical device companies generally have a closed innovation model. Needless to say, a company such as Apple—capable of developing highly innovative products independently—is a world-class winner. Actually, Apple acquires many core technologies through acquisition. This is because innovative ideas hardly come from the limited resources within a company and its research and development center.

Despite a high failure rate in Japan as well as in the U.S., it is desirable to have venture companies willing to take on the challenge of innovative development. There is no reason why we cannot cultivate an arrangement in Japan where major companies acquire ventures, and develop their ideas to the stage of producing products with high accuracy and marketability. Even in Japanese culture—where social and in-house risks are unacceptable—a very attentive development style can be created.

Such venture companies can be compared to laborers risking their lives while mining for rough diamonds. Major companies purchase those rough diamonds from miners and polish them, and after the cutting procedure, they manufacture and distribute diamond jewelry, the pinnacle of all jewelry. There is no doubt that this will surely lead to a generation of many innovative brands.

*To be continued in the next volume (No. 14)



Dr. Fumiaki Ikeno

Senior Research Associate, Division of Cardiovascular Medicine,
Stanford University, U.S.A.

Guest Associate Professor, Department of Cardiology, School of
Medicine, Osaka University

Dr. Ikeno graduated from Jichi Medical University in 1992, and became an internal medicine resident at Shizuoka General Hospital. After working for the cardiovascular department of Yaizu City Hospital, he served as the chief of the Division of Health and Welfare, Department of Health and Welfare, Shizuoka Prefectural Government, and then as the chief doctor of internal medicine at Sakuma Hospital (Hamamatsu City). He assumed the position of research associate at the Division of Cardiovascular Medicine, Stanford University in 2001, and was appointed to his current post of senior research associate at the same division in 2004.

Revisions to the Pharmaceutical Affairs Law are “Passing through a Climactic Point”

Streamlining Regulation and Rapid Implementation of Medical Devices

Medical devices have different characteristics from pharmaceutical products, in that the former are improved and upgraded in order to be supplied to the medical front in short-term cycles, similar to other mechanical products. Therefore, based on the requests from medical device industry organizations including the AMDD, the Pharmaceutical Affairs Law will be revised to take into account the characteristics of medical devices, in order to achieve rapid implementation and streamlined regulations of medical devices. In addition, the following are also under consideration as we revise the PAL: reinforcement of safety measures for pharmaceuticals, and instituting approval applications and post-marketing safety measures for regenerative medicines.

At present, the main revisions related to medical devices under consideration are as follows:

◆ Clarification of the positioning of stand-alone programs

In view of the development of information technology in recent years, as well as to achieve consistency with regulations in the U.S. and Europe, we are considering adding a stand-alone program to use for clinical diagnosis of all medical devices, which would also cover regulations for manufacturing and distribution. The U.S. and European regulations and classification for medical devices will be referred to for specific regulating methods.

◆ Simplification and streamlining of authorizations for marketing authorization holders and manufacturers

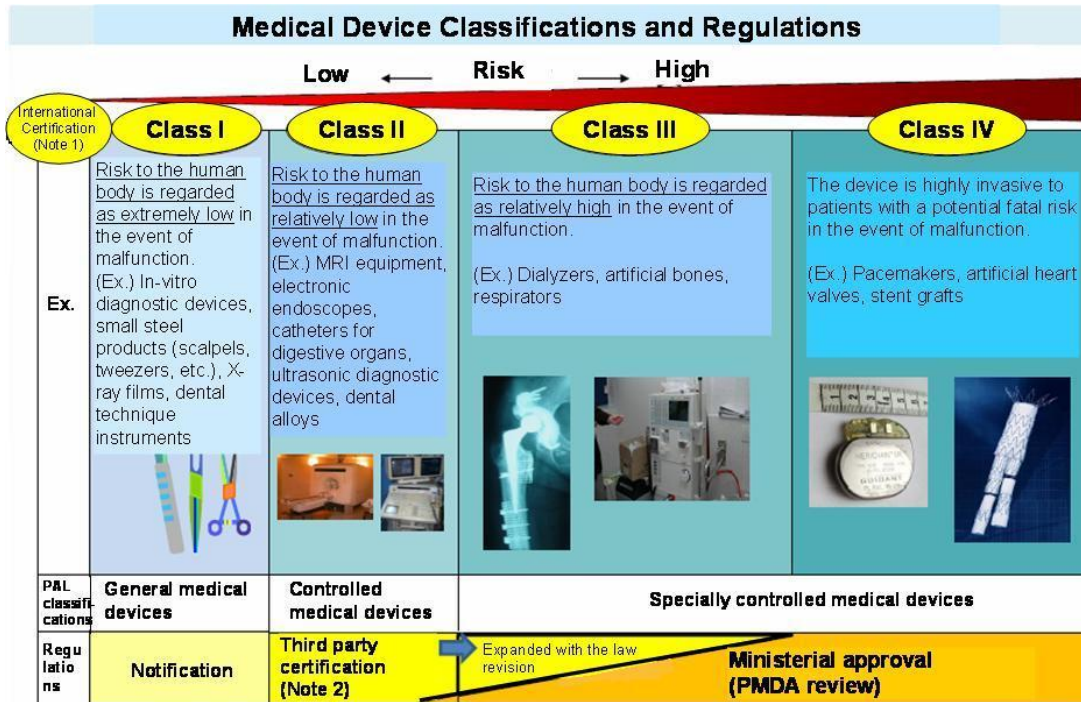
We hope to simplify requirements by replacing the license system with a registration system for the manufacturers of medical devices and in-vitro diagnostics (IVD). In addition, we are considering replacing the accreditation system with the registration system for foreign manufacturers. Also, we are working to integrate the facilities and equipment into the Quality Management System (QMS), which have previously required a permit, and include them in the requirements for approval and certification of product manufacturing and distribution.

◆ Expansion of the coverage and enhancement of supervision for registered certification bodies (See Diagram)

Regarding the manufacturing and distribution of generic medical devices (designated by the Minister of Health, Labour and Welfare based on the standards defined by the Minister) among specially controlled medical devices, we are considering replacing the approval system by the Minister with the certification system by registered certification bodies.

Also, regarding the position of those who are certified as marketing authorization holders for medical devices and IVD, we are aiming to achieve the transfer of approval to successors, merging corporations, and so on with relevant materials. In addition, we are working to have the Pharmaceuticals and Medical Devices Agency (PMDA) engaged in on-site inspections for registered certification bodies.

Furthermore, we are considering stipulating pharmaceuticals in a separate chapter, streamlining QMS surveys, and reviewing reexamination and reevaluation systems.



(Note 1) The Pharmaceutical Affairs Law adopts the concept of classification into four classes according to the risk levels of medical devices agreed upon in December 2003 at the “Global Harmonization Task Force on Medical Devices (GHTF),” which involved the participation of five areas: Japan, U.S., Europe, Australia, and Canada.

(Note2) The certification system which requires no ministerial approvals for devices with the standards established by the Minister of Health, Labour and Welfare, and allows private third party certification bodies (13 at present) registered by the Minister in advance to certify conformance to the standards

Meeting Between Industry Organizations, Ministry of Health, Labour and Welfare, and PMDA Working-Level Staff

In the current system, we need to aggressively tackle issues that can be addressed through operational improvement of the system by taking into account the characteristics of medical devices. In order to solve these issues, we established the “Task Force on Medical Device Regulatory Systems” (hereafter referred to as Medical Device TF), which has enabled medical device industry organizations, the Ministry, and PMDA working-level staff to meet in January 2012. Since then, we have been engaged in improving operation of the system with cooperation from various sectors, including the AMDD. The main achievements are as follows:

- ◇ The examination method when making changes to approvals of generic medical devices will be reviewed, and the examination would only be conducted on the content necessary to evaluate the changes (notified in February 2012).

- ◇ Procedures were eased regarding accreditation of foreign manufacturers (e.g. the application for reissue of an accreditation certificate in case of loss is no longer required) (notified in July 2012).
- ◇ Among the materials required for a reliability study application, risk analysis materials no longer need to be examined (notified in November 2012).
- ◇ For an approval application, materials attached to certificates of stability testing regarding shelf-lives can be omitted (notified in December 2012).

In addition, through the Medical Devices TF, we will continue to consider issues such as expanding the scope of devices that do not need approval applications when making changes to an approved matter, and utilizing international standards such as ISO and IEC as certification standards.

If We Were in a Marathon, We Have Just Passed the 30-km Point

We are working hard to submit a bill amending the Pharmaceutical Affairs Law to the ordinary Diet session. If we compare this to a marathon, we are passing by the “climactic point,” which is the 30-kilometer point. Yet even after we successfully revise the PAL, we must ensure that it has no flaws, so that it does not just “have the form but not the spirit.”

To that end, not to mention the efforts of the companies and cooperation of the medical frontline, we are determined to strive for further enrichment and streamlining of medical device examinations through post-revision improvement of government ordinance, ministerial ordinance, and notifications, in view of claims pointing out that “actual work of examining medical devices depends on how the examination system and examination work are addressed.”

We would very much appreciate the AMDD’s continued understanding and cooperation.



Dr. Kazunari Asanuma
Director, Office of Medical Devices Evaluation, Pharmaceutical and
Food Safety Bureau, Ministry of Health, Labour and Welfare

After graduating from the Faculty of Medicine at the Jikei University School of Medicine in 1991, Dr. Asanuma started his career at the Ministry of Health and Welfare. After working for Akita Prefecture, Ministry of Health and Welfare, Ministry of Education, Science and Culture, Sasebo City, and Ministry of Health, Labour and Welfare, he became the deputy director of Division of Health and Welfare, Kagoshima Prefectural Government in 2005. He assumed the position of director of the Health Crisis Management Office, Health Science Division, Minister’s Secretariat, Ministry of Health, Labour and Welfare, in 2007. After serving as the director of the Office of Pandemic Influenza Preparedness and Response, Minister’s Secretariat, he was appointed to his current post as director of the Office of Medical Devices Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau from 2011. He is also a visiting professor at the Jikei University School of Medicine.

Patient's Voice

The Unknown Dialysis: CAPD



By Ms. Mamiko Matsumura
President, NPO Kidney Support Association

We are an organization that stands by and supports patients with kidney failure.

First, I would like to start with how this association was founded. At our open civic lecture regarding kidney failure in Sapporo 12 years ago, we had people who, when they developed terminal kidney failure, were only provided information about hemodialysis. As a result, they had no choice but to give up their jobs because of their dialysis treatment, or were forced to move back home to commute to dialysis facilities. They were upset and complained that if they had known there was CAPD (a therapy allowing patients to exchange dialysate by themselves using their own peritoneum), they would not have had to abandon their jobs or move home.

Physicians must provide proper explanation on the options of hemodialysis, CAPD, and kidney transplants as alternative therapies for terminal kidney failure. However, many hemodialysis facilities often fail to explain CAPD.

As the result, CAPD patients account for less than 4percent –approximately 10,000 out of 300,000 dialysis patients in Japan. This figure is much smaller than that of other developed countries.

While Japan actually boasts the leading hemodialysis technology in the world, CAPD is more suitable for children or for people with jobs. Also, although home hemodialysis – in which a machine is installed at a patient's house – is excellent in improving patients' QOL, there were only 100 patients under this treatment 12 years ago. In fact, the treatment is still not widely used, with the current number of patients being 300.

It is truly obvious which is less stressful for the body: blood purification for four hours, three times a week; injection and discharge of 1—1.5 liters of dialysate into/out of the peritoneum to remove waste matter three to four times every day; or dialysis all night long.

Kidneys not only produce urine but also secrete hormones. Therefore, to live a longer life, it is most ideal to maintain the residual kidney function for as long as possible, choose CAPD to keep excreting urine at the time of introducing dialysis, then shift to hemodialysis when peritoneal fatigue occurs. In such cases, home hemodialysis, which allows patients to perform treatment by themselves for a shorter period of time every day, is preferable, but the reality is that it has not spread in Japan.

Instead of being solely committed to hemodialysis at facilities, our association continues to strive to keep the public informed of a variety of therapies to improve patients' QOL.

NPO Kidney Support Association:
<http://www.kidneydirections.ne.jp/>

Medical Journalist Viewpoint Lessons Learned from Israel



By Mr. Tatsushi Fujioka
Reporter, Medical Products and Devices Group, Editorial Office,
The Chemical Daily Co., Ltd.

A capsule endoscope which enables observation of the lining of the gastrointestinal tract once swallowed, mapping technology which facilitates catheter ablation for arrhythmia, and devices for transcatheter aortal valve replacement to treat cardiac disease without thoracotomy—these advanced medical technologies were invented by Israeli medical device ventures. It is estimated that one-third of new medical devices currently used worldwide come from Israel.

In a small country of 7.1 million people, with a total land area equivalent to Shikoku and with few natural resources, why were high-tech venture companies—including those for medical devices—starting up one after another? Why does innovation take place there? The book *Why do Apple, Google, and Microsoft Want Israeli Companies?* (published by Diamond, Inc.; original title: *START-UP NATION*) answers these questions.

Israel is the world's runaway leader in venture capital investment, the number of startups, and the number of scientists and engineers per capita. In the field of medical devices, the number of venture companies tops 500, and the country boasts the largest number of patents obtained in the world. Global medical device manufacturers, as well as the IT companies mentioned in the book title, have their research and development centers located in Israel in order to maintain their in-house innovation.

The book makes a multifaceted analysis of why the entrepreneur culture was formed in Israel, examining it from various angles, such as its history, human resources, education, and industrial policies. What is intriguing is that the book points out the association between immigrants and conscription, and the entrepreneurial spirit. An influx of capable Jewish researchers, educators, and doctors—as immigrants from the Soviet Union and Eastern European nations in the 1990's after the collapse of the Soviet Union—contributed to the development of science and technology in Israel. Many Israelis find business partners during the time of their military service, when people from different areas of specialization gather together. It is often said that “innovation is generated by ‘connecting’ the heterogeneity,” and it is the State of Israel that plays this part as connector.

Meanwhile, how about the situation in Japan? Although it has excellent technological seeds and production technologies, Japan fails to produce innovations. This book helps readers understand that these are necessary conditions, but not sufficient ones. In order to generate medical innovations in Japan, it is necessary to accept heterogeneity and build a mechanism to connect it as Israel does.

4th AMDD New Year's Party Held

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) held the 4th New Year's party on January 18, 2013 at the Imperial Hotel. In the opening address, Mr. Takashi Shimada, Chairman of the AMDD (President, Medtronic Japan Co., Ltd.) expressed his hope for the new Abe administration, which launched in December of last year, saying, "I hope that revisions to the Pharmaceutical Affairs Law will lead to division into different chapters. We thank PMDA's cooperation every day in approval of new products, and under the mission of the AMDD to deliver more innovative and new products and therapies to Japanese patients, I hope that all of us will join hands to exert our efforts through this year."

The next speaker was Mr. Yasuo Otani, Vice-Minister for Policy Coordination, Ministry of Health, Labour and Welfare. He delivered a congratulatory speech, saying, "Revisions to various systems including the Pharmaceutical Affairs Law and medical fees are scheduled this year, and this will bring a significant change to the environment surrounding medical devices. Also, we hope to promote development of medical devices, prompt implementation of clinical trials, speedy pharmaceutical approvals, and early introduction to the Japanese market, including the application of appropriate insurance. In order to achieve these, we would appreciate support from the industry."

Mr. Andrew Wylegala, Minister-Counselor for Commercial Affairs at the U.S. Embassy, then noted that the AMDD is now a core organization responsible for important tasks in the medical device industry, despite its short history of only four years since its establishment, saying, "This industry has the capability to bring innovation and generate economic growth, as well as to make the society healthier. I hope that the AMDD will exert its value more than ever, and look forward to the continued great performance of the member companies."

Lastly, Mr. Koji Nakao, Chairman of the Japan Medical Devices Manufacturers Association (Chairman of Terumo Corporation) cited three points as highlights of this year: revisions to the Pharmaceutical Affairs Law, fair evaluation of innovations, and the tax system. "As there is not enough evaluation of medical devices, we need to penetrate the general public with the awareness that they represent important technologies."



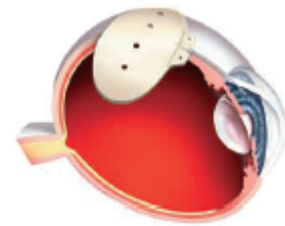
Mr. Takashi Shimada, Chairman of AMDD

The Value of Medical Technology (Ophthalmic Materials) Glaucoma Implant

Glaucoma is a disease characterized by progressive damage to the optic nerve cells of retina resulting from factors such as elevated intraocular pressure. The loss of vision occurs gradually, and advancement of the disease leads to blindness. According to the epidemiological survey conducted by the Japan Glaucoma Society (the Tajimi Study), it is estimated to be prevalent in about 5 percent of Japanese people age 40 or older, which is not unusual.

Currently, the only evidence-based treatment for glaucoma is to lower intraocular pressure, and medication or non-invasive laser treatment is the first-line choice. However, failure of such therapy leads to indication for an open surgery.

One of the open surgeries is the tube-shunt surgery (see diagram). Although glaucoma implants used in this surgery had not been approved for a long period of time in Japan, they were recognized by the “Study Group on Early Introduction of Medical Devices with High Medical Needs,” of the Ministry of Health, Labour and Welfare in 2009, as medical devices whose early introduction was awaited, later approved, and are now covered by insurance. If an additional option of the tube-shunt surgery offers a “ray of hope” to patients battling the fear of blindness, nothing could give me greater pleasure than this as someone engaged in the medical device industry.



(By Mayumi Kurihara, AMO Japan K.K.)

AMDD Supported and Participated in “Medical Creation Fukushima 2012”

The American Medical Devices and Diagnostics Manufacturers’ Association (AMDD) supported and participated in the 8th “Medical Creation Fukushima 2012” in Koriyama City, Fukushima Prefecture on November 28–29, 2012.

This event has been held since 2005, and holds seminars along with exhibits of manufacturing technologies and medical device makers’ products. Amid the increasing focus on the medical device industry, AMDD’s participation in this “Medical Creation Fukushima” marked the initial step toward activities contributing to the development of Japan’s medical care and medical device industry by providing advanced medical technologies.

The AMDD booth displayed panels introducing the development history of advanced medical devices, as well as AMDD’s activities and its support for areas afflicted by the Great East Japan Earthquake. It also provided hands-on demonstrations of medical devices. Furthermore, at the “AMDD Seminar,” Dr. Fumiaki Ikeno, Senior Research Associate, Division of Cardiovascular Medicine, Stanford University, and Mr. Susumu Nozawa from AdvaMed gave lectures under the theme of “Proposal to Small and Medium Sized Enterprises Aiming to Expand into the Medical Device Industry.”

(A summary of Dr. Ikeno’s lecture is on Page 1.)



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.