



Opinion Regarding In Vitro Diagnostics of

The Japan Association of Clinical Reagents Industries, the American Medical Devices and Diagnostics Manufacturers Association and the European Business Council

August 4, 2010 – The Japan Association of Clinical Reagents Industries, the American Medical Devices and Diagnostics Manufacturers Association's In Vitro Diagnostics Committee and the European Business Council's Medical Diagnostics Committee share the following opinion about the regulatory environment of in vitro diagnostic products used for clinical testing in Japan.

Background

Clinical testing is a critical necessity for medical treatment, including the prevention, diagnosis, treatment and follow-up monitoring of treatment. Through clinical testing, it is possible to gather a variety of information about health conditions from things like blood, urine and saliva samples. The medical diagnostic reagents used in clinical tests at medical institutions such as hospitals, physicians' clinics, public health centers, commercial laboratories and blood banks are called pharmaceuticals for use in in vitro diagnostics and require approval under the Pharmaceutical Affairs Law.

The use of medical diagnostic reagents and equipment can provide the basic data that physicians need to diagnose life threatening diseases such as HIV, Hepatitis B and Hepatitis C and can also help diabetes patients manage their condition on their own by monitoring the glucose levels in their blood. Also, by contributing to the early detection of disease, diagnostic testing can make it possible to treat diseases at an earlier stage and help reduce medical costs.

Further, due to the development of in vitro diagnostic reagents and equipment based on the latest technology it also will become possible to discover the cause of a disease at an earlier stage and facilitate the prevention of disease, in addition to the traditional uses of diagnosing disease and monitoring patients' condition after treatment.

It is our industry's role to provide products that help people stay healthy to the medical practitioners in the field. However, it is a reality that many of the latest in vitro diagnostic reagents and equipment already being used in many countries around the world are still not available in Japan. There are situations where Japanese patients cannot undergo tests using in vitro diagnostic reagents and equipment based on the latest technology and as a result cannot undergo the most appropriate treatment based on the most accurate test results. In the areas of pharmaceuticals and medical devices, this problem is called the "drug lag" and "device lag." A similar "diagnostics lag" problem exists for in vitro diagnostic reagents and equipment in Japan (see reference one).

Similar to the situation for pharmaceuticals and medical devices, in order to manufacture, import or sell in vitro diagnostic reagents and equipment in Japan, it is necessary to undergo a review and receive approval based on the Pharmaceutical Affairs Law. Over the past few years, there have been some improvements in the legal and regulatory environment for the in vitro diagnostic reagents and equipment needed for clinical testing. The 2005 revision of the Pharmaceutical Affairs Law was a significant step in the right direction because it included measures like the establishment of a system to quickly supply products to the market through a

new three-level classification system of approval, third-party approval and notification (self certification), based on the level of risk inherent in each product.

Further, it is very encouraging that the topic of in vitro diagnostic reagents and equipment was included in the Ministry of Health, Labour and Welfare's New Medical Device and Health Technology Industry Vision.

Issues

In reality these improvements are still insufficient and the following types of issues can be found particularly for new products that require approval from the Minister of Health, Labour and Welfare. This situation should be improved in a timely manner. As long as rapid improvement of the situation is not seen, the interests of Japanese society (patients) will not be fully served by introduction of the latest in vitro diagnostic reagents and equipment.

1. Need for Improvement in the Review Process for In Vitro Diagnostics

There are a large number of delays in the review of product approval applications submitted by companies to the Pharmaceutical and Medical Devices Agency (PMDA), which is responsible for their review as the first step in the process for having the manufacture, import and sales of in vitro diagnostic reagents and equipment approved by the Minister of Health, Labour and Welfare (see reference two).

The PMDA seeks to review in vitro diagnostic reagents and equipment within a six month review period, but less than half of the approvals are completed within six months and the reality is that many reviews do not conform to this standard review period. As a result, there is a delay in the use of new technology for diagnostic testing and this lag does not serve the interests of the people (patients) of Japan. We have repeatedly requested that the PMDA make improvements that would overcome the current situation, but sufficient improvements have not occurred.

In order to provide the Japanese people the benefit of timely access to testing with the latest technology, we request that the delay in reviews be corrected, such as by establishing a new system and process that would allow the PMDA reviewers to more efficiently conduct product reviews, including measures to improve the review process and to revise the items required for review.

2. Proposal to Create a Guideline on Clinical Efficacy Testing of In Vitro Diagnostic Reagents and Equipment

Because there currently are no guidelines on clinical efficacy testing of in vitro diagnostic reagents and equipment, the rules on how to test new products are not clear and there is no consistency on how various medical institutions handle clinical efficacy testing. As a result, we believe that the creation of guidelines with clear instructions on how to implement clinical efficacy testing of new in vitro diagnostic equipment is necessary.

Through the creation of guidelines on clinical efficacy testing of in vitro diagnostic equipment, it will be possible to implement clinical efficacy testing in an appropriate manner and respect will be shown for people that participate in the testing more consistently. As a result, this would not only help rationalize the new product review process but it would also contribute to the development of the field of medicine by providing in vitro diagnostics to the people of Japan in a faster and more scientifically rational manner.

3. Need for New Rules and Review and Approval Standards for Companion Diagnostics

Before administering medicine, there are an increasing number of cases in Japan, especially in the area of cancer, where things like patient biomarkers, including genes and proteins, are researched in order to choose the most appropriate medicine for each patient, to determine the most appropriate administration method, to confirm efficacy and to avoid side effects. This is called personalized medicine (or order made medicine, tailor made medicine), an area that is expected to become more and more common because it allows the provision of medicine and treatment methods that are most appropriate for each patient.

In personalized medicine, just having medicines and treatment methodologies is not enough. It is also necessary to conduct tests to select the most appropriate medicines and

treatment methodologies. The in vitro diagnostics used to select medicines and treatment methodologies are called companion diagnostics.

For the promotion of personalized medicine, it is necessary to simultaneously develop new medicines and treatment methodologies and to improve the environment for using companion diagnostics. However, there are many cases where the provision of companion diagnostics are falling far behind because the standards for reviewing and approving companion diagnostics in a timely and appropriate manner are not clear.

In order to accommodate the rapidly expanding area of personalized medicine and to create an environment where the most appropriate health care can be provided to each and every patient (the Japanese people) in a timely manner, it is important to create new approval and review standards and rules for in vitro diagnostics.

Reference

- 1) 2008 Device Lag Study (ACCJ Medical Device and IVD Subcommittee)
- 2) 2009 Research of the Japan Association of Clinical Reagents Industries

About the Japan Association of Clinical Reagents Industries

The Japan Association of Clinical Reagents Industries is an organization composed of the enterprises that contribute to medical care and welfare of the nation by developing and manufacturing (importing) in vitro diagnostics for sale to medical institutions primarily through wholesale in Japan and export to the world at large. The purpose of the Association is to ensure the sound growth of the clinical diagnostics industry and to broaden its activity range. True to this mission, the Association has engaged in efforts to widen the scope of business activities by joining the Federation of Pharmaceutical Manufacturers' Associations of Japan which represent the pharmaceutical industry of Japan, shed light on the various problems of the clinical diagnostics sector both at home and abroad so as to contribute to the expansion of business and the future prospect of the industry through the appointment special committees. For more information, please visit: www.jacr.or.jp

About the American Medical Devices and Diagnostics Manufacturers' Association

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) was established on April 1, 2009 to represent the Japanese operations of 65 U.S.-based companies that provide medical devices, including heart pacemakers, ICDs, catheters such as PCI and stent grafts, orthopedics such as artificial joints, and artificial ocular lenses, imaging diagnostic equipment, in vitro diagnostics and other advanced medical technologies to patients and healthcare providers in Japan. The Association's member companies account for approximately 13,000 jobs in Japan and generate approximately \$8.5 billion in sales, representing 40% of the Japanese medical technology market. For more information, please visit: www.amdd.jp

About the European Business Council

The European Business Council (EBC) is the trade policy arm of 17 European National Chamber of Commerce and Business Associations in Japan and has been working to improve the trade and investment environment for European companies in Japan since 1972. The EBC was registered with the Ministry of Economy, Trade and Industry (METI) in 2008 as the European (EU) Chamber of Commerce in Japan. The EBC currently represents over 2,500 local European companies and individuals who are affiliated with the EBC through their respective national chamber of commerce. Some 300 of these companies participate directly in one or more of the EBC's 29 industry committees, whose work covers a wide variety of economic sectors. The EBC works closely with the Delegation of the European Commission in Japan, the national European Embassies, and other business organisations to co-ordinate policy proposals and make suggestions to the Japanese Government on how to create an open environment for trade and investment in Japan. For more information, please visit: www.ebc-jp.com