EU - Japan Business Round Table
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Recommendations of the EU-Japan Business Round Table to the Leaders of the European Union and Japan

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Working Party B
Life Sciences and Biotechnologies, Healthcare and Well-being

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List of Abbreviations

Abbreviation	Meaning
ABS	Access and Benefit Sharing
CBD	Convention on Biological Diversity
CE	Conformite Europeenne
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFSA	European Food Safety Authority
EU	European Union
FSC	Food Safety Commission
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HTA	Health Technology Assessment
IFAH	International Federation of Animal Health
iPS	induced Pluripotent Stem
J-PAL	Japanese Pharmaceutical Affairs Law
JPMA	The Japan Pharmaceutical Manufacturers Association
LS & BT	Life sciences and Biotechnologies
MAFF	Ministry of Agriculture, Forestry and Fisheries
MDD	Medical Device Directive
MHLW	Ministry of Health Labor and Welfare
METI	Ministry of Economy, Trade and Industry
MIC	Ministry of Internal Affairs and Communications
MOF	Ministry of Finance
MRA	Mutual Recognition Agreement
NB	Notified Body
NHI	National Health Insurance
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Co-operation Scheme
PMDA	Pharmaceutical and Medical Device Agency
QMS	Quality Management System
VPD	Vaccine Preventable Diseases
WP	Working Party

Introduction

Both, Japan and the EU are facing numerous challenges due to e.g. an aging population, shifting demands in just about all domestic markets and rising costs in many aspects of the welfare system with a need to accelerate and focus on high-end innovations. This particularly in the areas of

- Healthcare
- Plant Protection, and
- Biotechnology.

The enclosed recommendations of WP-B have the clear aim to improve the innovation capabilities of both the EU and Japan through concrete action plans in life sciences and biotechnology, which focus on measures to enhance efficient healthcare practices, food technology / supply and biotechnology.

To highlight priority issues, one asterisk (*) identifies “priority” Recommendations, two asterisks (**) identify “top priority” Recommendations. (e.g. WP B / #07** / EJ to EJ)

Recommendations from both European and Japanese industries

General Issues

WP-B / # 01 / EJ to EJ **Enhancement of bio-venture activities**

In both the EU and Japan, bio-venture activities should be enhanced further and dynamically integrated with each other. BRT members call for governments support to expand these networks of activities through such measures as bio-conferences or the establishment of cluster centres. In addition, strong governmental (METI and MHLW) financial support is essential.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
In the biotechnology-based industries, bio ventures have played an important role to create innovative technologies and products. Bio ventures in the EU and Japan are behind those in the US and need more collaborations or integrations between venture companies. To realize this, expansion and activation of venture networks will be very valuable. Under the current economic situation, it is difficult for ventures to obtain capital from the markets. Some financial support should be considered to vitalize them.

Healthcare

WP-B / # 02 * / EJ to EJ **Regulatory harmonization and MRA for pharmaceuticals**

The regulatory harmonization and further extension of “Mutual Recognition Agreement” should be proceeded in order to avoid redundant inspections of manufacturing facilities. In addition to oral dosage forms, API, Sterile and Bio products are being requested to apply to the MRA. The new initiative of PIC/S> PIC/S stands for "Pharmaceutical Inspection Convention” and “Pharmaceutical Inspection Co-operation Scheme”, it jointly refers to PIC/S". A PIC/S guideline enforces the harmonization of inspections among PIC/S countries. This is an agenda point for the European industry (30 countries), EFPIA, the Japanese industry, JPMA, and PMDA.

<Recent Progress>
Some progress has been seen for this recommendation in that MHLW applied for PIC/S in March 2012. A practical evaluation is planned to start in spring 2013 by PIC/S organization and it is anticipated that Japan’s PIC/S application will be approved within the next three years.

<Background>
As currently only oral solid dosage forms are included within the MRA between Japan and the EU, there are still a lot of redundant inspections of manufacturing facilities. This

is not only a costly process, but it also slows down the launching of new drugs in Japan creating a significant disadvantage for Japanese patients.
In order to eliminate this problem and to integrate EU-Japan economics more efficiently, harmonization of standards/guidelines and expansion of MRA should be conducted under mutual agreements. Below-mentioned are highly prioritized items for harmonization and expansion of MRA.

<Prioritized items for harmonization and MRA>
Harmonization:
- Safety measures from surveillance to vigilance should be harmonized with international standards
- Clinical development guideline and biological preparation standards for Vaccine
- Minimum Requirements for Biological Products
- Sharing knowledge and information of inspections by each regulatory authority through PIC/S

Mutual Recognition Agreement:
- Full support is requested to expand the MRA of GMP to liquids, and sterile forms, API and bio products to avoid redundant inspections and testing

WP-B / # 03* / EJ to EJ Mutual recognition of quality management audit results for medical devices between EU and Japan

Improve mutual recognition of Quality Management System (QMS) audit results for lower risk medical devices, e.g. those classified as Class II, ARCB under the Japanese Pharmaceutical Affairs Law, as a first step.

All industry-related manufacturers request PMDA and MHLW to further harmonize and streamline the QMS audit results. MHLW has notified that RCBs can accept non-Japanese QMS audit results. However, ISO13485 continues to be only one part of the Japanese QMS ministerial ordinance. Hence, part of the Japanese requirements. To resolve this issue, it is recommendable that QMS be evaluated on the basis of ISO13485.

In addition to above, the recognition system of "Application for Accreditation of Foreign Manufacturers" should be considered. Even if QMS is evaluated on ISO13485, all industry-related manufacturers have to be registered and obliged to keep the additional Japanese requirements.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
Based on Medical Devices Directive (MDD) of the EU and the Japanese Pharmaceutical Affairs Law (J-PAL), QMS audit results are required for each application for a license to introduce new medical devices in the market. In Europe the regular annual ISO audit results can be used for all applications during the period in which the ISO audit is valid. Recently, Japan has started to accept QMS audit results at a specific manufacturing site for products with the same generic name under certain conditions.

However, a number of RCBs still require submitting QMS audit results for each application. Further alignment is necessary.

WP-B / # 04 / EJ to EJ **Infrastructure improvement and international harmonization of regulation standards for approval of non-invasive diagnostic medicines and devices**

Both governments should promote infrastructure improvement such as regulatory review process and structures to accelerate simultaneous research and development of therapeutic medicines and accompanying diagnostic medicines and devices (companion diagnostics).

Furthermore, both governments should harmonize each regulation on simultaneous development of therapeutic medicines and companion diagnostics, to support advancing science on personalized healthcare (PHC) based on global genome-cohort research.

<Recent Progress>

Good progress has been seen for this recommendation. Currently, new companion diagnostics' applications have been approved are submitted with therapeutic medicines. PMDA has initiated a working team for this issue.

<Background>

U.S. Food and Drug Administration (FDA) officially announced draft guidance for simultaneous development of therapeutic medicines and companion diagnostics. It requires companies to develop simultaneously new therapeutic medicines and companion diagnostics which are able to stratify efficacy and safety of the new medicine. In EU, the European Medicine Agency (EMA) has already announced a draft for adoption of genome bio-markers in clinical trials. Also in Japan, MHLW officially announced they will draft standards for regulatory approval processes of companion diagnostics by FY2014.

PHC is greatly expected to be of benefit not only for government's healthcare finance but also for society and patients. To support advancing PHC, it is required to harmonize regulatory standards and to promote infrastructure improvement such as regulatory review processes and structures to accelerate simultaneous research and development of therapeutic medicines and companion diagnostics.

WP-B / # 05* / EJ to EJ **Mutual recognition of medical devices product licenses**

Introduce a mutual recognition of medical device product licenses between the EU and Japan. PMDA and MHLW should introduce a mutual recognition of medical device product licenses with low risk of class II devices with taking the difference of classification of medical device between Japan and the EU into account.
By harmonizing QMS and classification it should be possible to introduce new products within the same time frame and in one process. It is desirable that this issue will be solved quickly. Level difference between NBs should also be considered. It should be recognized that the regulatory approval scheme of class II medical devices in Japan is far from that in the EU, i.e. no need to be reviewed by NBs for Conformite Europeenne (CE) marking of class II medical device in the EU but reviewed by NBs in Japan.

<Recent Progress>
No progress and no dialogue have been seen for this recommendation.

<Background>
Mutual recognition of licenses for medical devices in Japan and the EU would make it possible to introduce new products in both the Japanese and European markets within the same time frame and with one process.

As mentioned before, it could be possible to start with lower risk, class II devices.

The evaluation scheme between the Medical Devices Directive of the EU and the Japanese Pharmaceutical Affairs Law are quite similar, with
- Evaluation schemes based on registered 3rd party bodies (Notified Bodies)
- Essentially quite similar requirements
- Based on ISO/IEC or JIS standard compliance
With these similarities, a mutual recognition should be easy to implement.

WP-B / # 06* / EJ to EJ **Mutual recognition of clinical trial results for medical devices**

Introduce a mutual recognition of clinical trial results for medical device development.
Foreign clinical trial data have been accepted as a part of application dossier when; i) standards for conducting medical device clinical trials are set by the regulations of the country or region where the trial was performed, ii) the standards are equivalent or surpass the Japanese medical device GCP, and iii) the clinical trial was conducted in accordance with the standards or considered to have equivalent level of quality.
The GOJ encourages active use of consultation service on individual medical device applications in advance provided by the Pharmaceuticals and Medical Devices Agency (PMDA) to address use of foreign clinical trial data for application of the device.
At present, clinical data are often accepted because the standards of clinical trials in the United States or the EU are seen to be equivalent or sometimes more sophisticated than those required by the Japanese medical device GCP. However, then additional data are required with unclear reasons.

<Recent Progress>
Some progress has been seen in the area of mutual recognition of clinical trial results.

<Background>
Differences in the definition of Good Clinical Practice between Japan and the EU currently prevents the use of non-Japanese clinical trial results in the application for new medical devices in Japan. Mutual recognition of clinical trial results would make it possible to make new products available to patients in Japan and the EU within the same time frame and through one process, ensuring high level of quality while reducing the burden on manufacturers.

Healthcare

WP-B / # 07 / EJ to EJ** **Evaluation of innovation values for pharmaceuticals in prices**

The EU government should reinforce its innovation policy to member states and clarify its healthcare policy, resulting in the appropriate evaluation of the value of pharmaceuticals. In addition, MHLW should initiate the HTA (Health Technology Assessment) dialogue among stakeholders.

<Recent Progress>
No progress has been seen for this recommendation.

<Background>
In the EU, innovation policy is stated by the Lisbon declaration and the G10 group report indicating the importance of innovation in pharmaceuticals. However, each state operates its own healthcare system in different ways, resulting in gaps in survival rates and the QOL of citizens. Under the current economic recession, prices of pharmaceutical products are targeted as a major tool for medical cost containment. BRT members call on the EU and Japan to clarify its healthcare policy and to discuss and totally improve healthcare situations in member states by securing appropriate healthcare budgets, preventing interference with patient access to new medicines and considering the proper utilization of healthcare technology assessment.

Plant Protection & Biotechnology

WP-B / # 08* / EJ to E **Shortening review times of plant protection & biotechnology products**

Shorten review times for new applications/ registrations.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
Research and development of innovative and beneficial Plant Protection & Biotechnology products require high input costs. Therefore, timely access to the markets is crucial for R&D-intensive companies in order to successfully market their products and recover their initial R&D investments, which then again are used to finance further innovations.
Establishment and maintenance of science-based, predictable and timely regulatory systems free from undue political influence and the appropriate protection of proprietary data are therefore key requirements for sustainable and innovative research.

Animal Health

WP-B / # 09* / EJ to E **Introduction of "1-1-1 concept" for all animal health products**

Introduce 1-1-1 concept for all products (one dossier – one assessment – one decision on marketing authorization applicable to all EU countries). A concept should be worked out between the respective governments / authorities.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
One of the key objectives of the European Union is to create a single market for goods. This goal has yet to be achieved for the animal health industry, with the exception of centrally authorized products. In line with the concepts already existing in the EU (i.e. quality, safety and efficacy described in one single EU dossier as the basis for granting marketing authorizations for veterinary medicinal products, one single assessment of the dossier employing the best expertise, resulting in one decision for marketing authorization) the animal health industry in Europe is seeking a systemic change based on the one, one, one concept ("1-1-1 Concept") for all products. This appears to be the most simple and straightforward way to address all of the major shortcomings of the current system and to finally achieve the goal of a single market for safe and efficacious veterinary medicines.

Healthcare

WP-B / # 10 / EJ to J **Balance between prevention and treatment in healthcare**

Seek balance between prevention and treatment. Thus, confirm inclusion of vaccination programs in the scope of public funding.

<Recent Progress>
Fully implemented and highly appreciated by all members of the WP-B.

<Background>
Disease prevention and diagnostic/ screening procedures are getting a more important position in the healthcare area as they allow to improve the treatment of numerous diseases but also to effectively lower healthcare costs, mid- and long-term. Therefore, vaccines should be in the scope of public funding. The Japanese government allocated special funds to vaccine-preventable diseases, especially cervical cancer and bacterial meningitis. MHLW provided financial support in the amount of 100 Bio Yen for these kinds of vaccines R&D of 4 drug firms in supplementary budget for FY2010.

WP-B / # 11* / EJ to J Nation-wide electronic database for individual health/medical records in Japan

Map out the "grand design" of a nationwide electronically integrated database for individual health/medical records as a basic Japan health policy.

MHLW and MIC started this initiative. One of the hurdles is that there are no single social security numbers and centralized data handling in Japan. A strong project promotion is necessary to safeguard people from potential disasters.

<Recent Progress>

Good progress has been seen regarding the national data base; however, the establishment of the electronic database for individual health/medical records needs to be accelerated. It was planned to be submitted to the 2012's diet. However, this initiative is on hold now. Furthermore, integration of this system and the Citizens ID numbering system should be considered in future.

<Background>

The Japanese government should intend to electronically integrate individual health/medical care related data and information nationwide in order to supply high-quality and patient-suitable medical care, and map out a "grand design" of the systems. The integrated database will also improve the efficiency of medical care by eliminating duplicated examinations or reducing adverse events and treatment for them. Furthermore, the data will be useful for the discovery of new innovative medical treatments and devices. Several European countries have taken the lead on this issue, so Japan may be able to learn much from the experiences of the EU.

WP-B / # 12 / EJ to J Full-fledged implementation of the new drug pricing system and abolishment of market expansion re-pricing**

The premium for new drug creation and elimination of unapproved/off-label use drug (the premium for new drug creation) will be continued until March 2014. It is welcomed as it supports incentives for innovative drug development; however, it is only the continuation of a trial scheme. The Japanese government should finalize the implementation of the new, internationally competitive drug pricing system in Japan based on the industry proposal since in addition to innovation rewards it is also protecting public health. Furthermore, it adds an element of predictability and stability so that the industry can adequately plan, forecast product requirements and effectively manage inventory as well as the distribution of products across Japan.

The abolishment of the market expansion re-pricing was not accepted by the Central Social Insurance Medical Council (Chuikyo) even though industries insisted to eliminate the system. While the agenda for the 2014 NHI pricing discussion between Chuikyo and the industry include topics such as "NHI pricing for long-listed products" and "continuation vs. discontinuation of incentives for innovative drug development" it does not include "abolishment of market expansion re-pricing". We urge to abolish the re-pricing rule by market expansion, which is contrary to the policy of evaluating pharmaceutical innovation.

<Recent Progress>

Some progress has been seen for this recommendation, however, the new drug pricing system should be implemented firmly and permanently (not only a 2-year trial). On the other hand, the re-pricing system rule by market expansion can adversely affect innovation in Japan and therefore, should be abolished.

<Background>

The NHI price reform proposed by the industry has been positively reviewed by Chuikyo in December 2009 and the government decided to start a pilot implementation in April 2010. This represented a significant improvement, as it provides price stability for innovative drugs and was seen as a positive signal that the Japanese government is willing to reward innovation in the medical field. The premium for new drugs will be continued until 2014. As a compensation for this new scheme, the government will attach a system that fosters the registration of "unapproved/off-label use drugs". Companies have received requests on developments of many unapproved/off-label use drugs and forwarded those constructively.

Furthermore, companies received additional requests on developments of another hundreds of unapproved/off label use drugs. However, in the draft for FY2012 drug pricing system reform, the premium for new drug creation was determined to continue operation as a trial basis. Therefore, the conclusion brings the industry deep concerns about sustainability for evaluation of innovations. The Japanese government should implement the new premium system for innovative new drugs at the FY2014 drug pricing system revision to evaluate the companies' efforts for elimination of the so-called drug lag in Japan and research and development of innovative new drugs.

WP-B / # 13 / EJ to J **Regulatory transparency and review time by PMDA**

Increase the transparency of evaluation standards, registration process, consistent consultations and shorten review times for pharmaceuticals and medical devices by PMDA. While the review time was shortened, an improvement of the training system and personnel by PMDA is seen as vital. In addition, it is recommended that Japan uses more overseas data in order to further reduce approval time and costs.

Pharmaceuticals showed good progress and a satisfactory level in review times such as 10 months (target is 12 months) for normal products as of October, 2012. This was a big improvement on the initiative of PMDA.

<Recent Progress>

Good progress has been seen for this recommendation and the PMDA should be encouraged to continue on this path.

<Background>

Innovation can contribute to improved quality of life for patients, reduction of social cost and robust industry growth. In order to proceed with the proper evaluation and promote innovation, transparency of evaluation standards and evaluation processes should be guaranteed and improved by both governments. Adoption of health economics/HTA and establishment of a National Data Base for medication/cost are essential for the improvement of transparency.

The increase of staff / personnel at PMDA in 2007, together with an increase of registration fee, has been a welcomed move towards a reduction of review time. It is important to continue to monitor if this will be linked with a significant reduction of review time. Also, it is suggested that Japanese authorities make more extensive use of overseas data, as this would significantly reduce cost and time required to register products in Japan.

WP-B / # 14 / EJ to J **Reinforcement of measures to ensure proper distribution of privately-imported medicines**

Take necessary measures to private imports of a certain or more amount of medicines including unapproved products in Japan.

Japan is not as exposed as less developed countries. There is little parallel trade but private imports of medicines which provide a channel for counterfeits, mostly in OTC non-reimbursed drugs are seen. A similar situation is observed for crop-protection products. Therefore, MHLW is requested to heighten public awareness on this matter.

<Recent Progress>
No progress has been seen for this recommendation.

<Background>
In case of private imports of a certain or more amount of medicines including unapproved products in Japan, a certificate of medicine import is required for custom purposes. Under the current regulations, however, there is a concern it will unintentionally provide distribution channels of counterfeit medicines mainly in OTC and non-prescription medicine fields. Furthermore, there are also problems such as the uncertainty where the responsibility lies or who responsibility has, in case health hazards are unfortunately brought to consumers.

WP-B / # 15* / EJ to J **Appropriate assessment of innovative values of medical devices in prices**

Promote sub-dividing the current functional classification, enhance the premiums for C1 or C2 products and introduce a product-based listing system for new products in order to move towards a product-based, market-oriented reimbursement pricing system in the future.

<Recent Progress>
Insufficient progress has been seen for this recommendation.

<Background>
Different from pharmaceutical brand-oriented pricing systems, about 300,000 medical devices are classified into about 700 functional classes in Japan and one reimbursement price is set for one functional class, based on structure, intended use, effectiveness and so on.
Currently, various old and new products, having various realized prices, have the same reimbursement price within one functional class, which means that the price drop of old products influences the reimbursement price of new ones on the revision of the

reimbursement price. This is the reason why the introduction of a product-based reimbursement pricing system is desired. In Japan's 2012 price revisions, the government's efforts to progress forward the assessment of innovative values can be seen, such as implementation of the device lag reduction premium and expansion of the improvement premium. However, further government's efforts are still required.

Plant Protection & Biotechnology

WP-B / # 16* / EJ to EJ Acceleration and dissemination of scientific knowledge on GMOs by both the governments and the private sector

Governments and the private sector should speed up research in Plant Protection & Biotechnology and inform populations regularly and accurately about the state of play on GMOs, based on sound scientific knowledge.

To that effect Japanese and European biotechnology and bio-industry associations should work closely with other sectorial organisations and their respective Authorities.

<Recent Progress>
This is a new recommendation.

<Background>
A stable supply of food is an urgent requirement. While world population keeps growing, the limits of enhancing conventional culture on existing farmlands are being reached. GMOs offer the hope of breaking these limits, but remaining doubts about their safety hamper the development of their utilisation. Considering this situation, it is an urgent matter to speed up research on GMOs and inform people regularly and accurately about the state of play of that research.

WP-B / # 17* / EJ to J Support research in Plant Protection & specifically Biotechnology

Support research in Plant Protection & Biotechnology.

<Recent Progress>
No progress has been seen for this recommendation.

<Background>
Overall in Japan the cooperation between governmental institutes and MNC is limited. Applied science is widely done for instance by PPS (Plant Protection Stations) in all prefectures, however, this is not basic research. Also agricultural universities in Japan do some research on an independent basis.
MAFF is spending around 400 Mio. Yen for residue trials on substances used for rice to confirm the level of the residue in rice for feed and the transfer into livestock (cow and chicken) but the ownership is with the government or some independent institutes. The project is motivated by the policy to increase food sufficiency rate.
In biotechnology, considerable money is spent on plant molecular biological research but the budget is recently decreasing and no GM products are developed in Japan. In the past, the rice genome project was supported by the government but the project has

been finalized, a smaller post genome project is still running. The outcome of the project is only contribution to develop a marker assisting the breeding of rice. From such research where a considerable amount of Japanese tax payers' money is invested, yielding practical applications is desirable through co-operations among governmental institutes, universities, Japanese domestic companies and MNC.

Recommendations from European industry

Animal Health

WP-B / # 18* / E to EJ **Regulatory harmonization for animal health products**

The food animal product registration process is particularly cumbersome, involving a sequential review by MAFF followed by the FSC and the MHLW. Decision criteria and timelines for the following stages of the review process are not provided, resulting in extended review times and often different conclusions from regulators in other countries.

We propose to harmonize and streamline regulatory requirements for product registration of animal health products. MAFF should start harmonization with related countries as this is the path to the 1-1-1 concept recommended previously.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
While such global new veterinary medicinal products go already through rigorous review processes in Europe and the USA prior to registration, it requires substantial additional testing in Japan under the Pharmaceutical Affairs Law before an approval is granted. Restrictions on withdrawal period for innovative oil-adjuvant vaccines are especially stringent in Japan, and therefore, a product which is readily available to veterinarians and animal owners in Europe cannot be used in Japan. Increased harmonization of regulatory requirements would certainly improve access of animals and animal owners to innovative animal health products.

An additional important aspect is the negative impact on animal welfare: since the regulatory requirements are not harmonized, the companies are required to repeat some tests on animals in Japan, even though results of identical tests are already available and are fully compliant with stringent frameworks like GLP or VICH.

Japan still requires local clinical trials, which are not only scientifically unnecessary but also problematic from an animal welfare point of view, as the efficacy and safety of the products would have been proven already by trials in the EU and / or the USA. Animal breeds are largely the same worldwide in both livestock and pet animals and so is their feed. Japanese regulations do not stipulate the use of breeds particular to Japan, so there is no conceivable benefit in additional testing.

WP-B / # 19* / E to EJ **Mutual recognition of GMP and marketing authorization for animal health products**

Mutual recognition of European and Japanese marketing authorizations and recognition of GMP certification for veterinary products. MAFF should work out harmonized regulations leading to the 1-1-1 concept.

The resources freed in MAFF could probably be diverted to speeding up the processing of dossiers in general, where MAFF has a severe lack of resources adding to the delay in

drug availability as described in #25. However, no indication is found that MAFF is planning to make changes.

<Recent Progress>
Some progress has been seen for this recommendation. However, further strong efforts are required to reach mutual recognition of GMP.

<Background>
While laboratory testing is largely acceptable if conducted under GLP and according to VICH standards, Japan still requires local clinical trials as there is no mutual recognition of Good Manufacturing Practice (GMP) for veterinary medicinal products. Moreover, any overseas production facilities that are involved in manufacture of veterinary medicinal products imported into Japan have to be accredited by MAFF even though their GMP status is authorized by European authorities. This process involves a large amount of administrative work.
In order to improve decreased speed, predictability and quality of the registration process in Japan, which were pointed out in the benchmark surveys conducted by the International Federation of Animal Health in 2007, several new steps were taken by MAFF with some progress. However, there are still delays in review process of some product segments. An EU – Japan Economic Integration Agreement should aim for mutual recognition of European and Japanese marketing authorization for veterinary products by starting off with mutual recognition of GMP certification of veterinary medicines. Harmonized regulations on animal vaccines should also be addressed under such an agreement.

WP-B / # 20* / E to EJ **<u>Responsible use of antibiotics in animal health</u>**

MAFF should promote responsible use of antibiotics in animal health.
Furthermore, the establishment of a cascading system, prioritizing the use of approved drugs and formulations where they exist, rather than other available products lacking such claims, would be a method promoting responsible use of all drugs in animal health.

<Recent Progress>
Some progress has been seen for this recommendation. However, no activities by MAFF are known or have been seen over the last 12 months in this regard.

<Background>
In common with the rest of the world, Europeans and Japanese are concerned by the development of resistance to antibiotic medicines used in human health and the potential threat that the use of antibiotics in animal health will accelerate this process.
The use of antibiotics as growth promoters has been prohibited in EU since 2006.

As a responsible industry, the animal health industry seeks to work with veterinarians, farmers and the feed industry to dispel the myths about the use of antibiotics in animals and promote their responsible use.

Healthcare

WP-B / # 21 / E to J Application of GMP on medicinal gases (manufacture of medicinal gases) in Japan

Reinforce the regulation for GMP on medicinal gases in Japan. MHLW has started these initiatives along with industries. But industries are protective to non-GMP facilities because of financial implications.

<Recent Progress>

Some progress has been seen for this recommendation. In February 2012, MHLW noticed to medical gas suppliers to obey voluntary standard by the industry. This standard is almost compatible to GMP standard.

<Background>

Medicinal gases are drugs or medicinal devices and have to be compliant with governmental regulations. Main regulations are national Pharmacopeia, GMP (Good Manufacturing Practices), and GDP (Good Delivery Practices). Annex 6 describes GMP and GDP for medical gases: production and distribution. The currently loose interpretation of GMP in Japan along with relatively low standards of Japanese Pharmacopeia is of lower standards as compared to those applicable in Europe or the US. We would like to suggest a reinforcement of regulations on GMP for medical gases in Japan.

WP-B / # 22* / E to J Requirement of Japanese version of the clinical trial protocol and investigators brochure

The Japanese health authority requires a clinical trial protocol and investigator's brochure in Japanese. Translation from English is required for clinical trial notification in Japan. The acceptance of English-only materials for global clinical trials performed in Japan requires further English language education of Japanese regulators. However, if applications could be made in English-only, it would substantially accelerate the process and make innovative drugs available to patients earlier in Japan.

MAFF, MHLW and FSC should start harmonized ways to shorten review times.

<Recent Progress>

No progress has been seen for this recommendation.

<Background>

The Japanese health authority requires a clinical trial protocol and investigator's brochure in Japanese. Translation from the original English version is required for clinical trial notification of global trials in Japan. Therefore, the requirement is considered to be a cause for delay of the start for patients' enrolment in Japan.

WP-B / # 23* / E to J **Shorten or eliminate national tests for hemophilia-derived products and vaccines**

For imported hemophilia-derived products and vaccines, national tests in both Japan and manufacturing sites have been conducted (for more than 20 years in some cases). National tests for hemophilia-derived products and vaccines should be eliminated or reduced to an absolute minimum.

<Recent Progress>
Some progress has been seen for this recommendation.

<Background>
For a long time, there have been no critical quality issues in Albumins or Immunoglobulins. In addition, production is done according to GMP and PMDA periodical audits of production sites. Concerning the national test results which are published by MOU (memorandum of understanding), manufacturing countries should be accepted by the Japanese authority and the national tests for imported haemophilia-derived products and vaccines in Japan should be eliminated or reduced to an absolute minimum.

Animal Health

WP-B / # 24* / E to J **Shortening review times for animal health products**

Shorten review times for new product applications. MAFF, MHLW and FSC should start harmonization to shorten review times. The process is complicated in addition to a review period that already for pet animal products (not requiring ADI and MRL) is among the longest in the world. A lot of questions are asked in the process that might be academically interesting but are not necessarily safety or efficacy related.

<Recent Progress>
No change or improvement was seen for this recommendation.

<Background>
In Japan, marketing authorization of a veterinary medicinal product is granted by the Ministry of Agriculture, Forestry and Fisheries (MAFF). For an animal drug intended for use in food-producing animals, the Food Safety Commission (FSC) and the Ministry of Health, Labour and Welfare (MHLW) are also involved in establishing the acceptable daily intake and maximum residue limit, respectively. The review process, involving three different authorities, is rather complex and certainly has some room for efficiency improvement. Also, the review can take an extremely long time to be completed. Hence, delaying the access of animal owners and animals to innovative animal health products.

WP-B / # 25* / E to J **Japanese customs clearance's (cc) rule for investigational drugs and related materials does not allow efficient investigational drug supply**

MAFF should harmonize with VICH guidelines.

<Recent Progress>

Some progress has been seen for this recommendation.

<Background>

To import investigational drugs either 1) the Original Clinical Trial Notification sealed by both sponsor and PMDA or 2) YAKKAN is necessary. Recent clinical trials require frequent investigational drug delivery from overseas investigational drug warehouse to study sites. Since both 1) and 2) should be archived by the sponsor and CC agents do not keep those, frequent and timely CC is not possible. If a certified copy of 1) or 2) (certified by sponsor and kept by CC agent) is accepted by the custom, investigational drug delivery will become efficient.

Recommendations from Japanese Industry

Healthcare

WP-B / # 26* / J to E **Shorten the approval time to register new micro-organism and introduce new technology for producing seasonings and amino acids**

Shortening the approval time needed for registration of new materials and introduction of new technologies which aim for product expansion, cost reduction, environmental concerns or diversification of the fermentation material. Clarification of the approval process is also requested.

<Recent Progress>

Some progress has been seen for this recommendation. Shortening the approval time and clarification of the approval process are accelerated in EU countries.

<Background>

The long term process for approving a set of safety evaluation such as the bacteria manufacturing process, test products and co-products, delays the enhancement of production and consequently, competitiveness in the EU market. The slow approval process makes companies hesitate to invest in the EU market. On the other hand, it also weakens the export competitiveness of EU companies. For information: US companies are introducing new technologies aggressively. In a typical case, one application takes 30 month-long review time to complete approval processes by regulatory authority in EU, EFSA.