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 2
Life Sciences and Biotechnologies, Healthcare and Well-being
(Final Version)

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List of Abbreviations

Abbreviation	Meaning
ADI	Acceptable Daily Intake
ARCB	Association of Registered Certification Bodies under J-PMD Act
CE	Conformite Europeenne
CEFP	Council on Economic and Fiscal Policy
CHUIKYO	Central Social Insurance Medical Council
ECPA	European Crop Protection Association
EFPIA	European Federation of Pharmaceutical Industries and Associations
EPA	Economic Partnership Agreement
ESA	European Seed Association
EU	European Union
FQs	Fluoroquinolones
FSC	Food Safety Commission
GCP	Good Clinical Practice
GDP	Good Delivery Practice
GLP	Good Laboratory Practice
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practice
HTA	Health Technology Assessment
IEC	International Electro technical Commission
ISO	International Organization for Standardization
JIS	Japanese Industrial Standards
J-PAL	Japanese Pharmaceutical Affairs Law
J-PMD Act	Japanese Pharmaceutical and Medical Device Act
JVPA	Japan Veterinary Products Association
LLPs	Long-listed products
LS & BT	Life sciences and Biotechnologies
MAFF	Ministry of Agriculture, Forestry and Fisheries
MDD	Medical Device Directive
MDR	Medical Device Regulation
MDSAP	Medical Device Single Audit Program Pilot
METI	Ministry of Economy, Trade and Industry
MHLW	Ministry of Health Labor and Welfare
MNC	Multinational Corporation
MRA	Mutual Recognition Agreement
MRL	Maximum Residue Limits
NB	Notified Body
NHI	National Health Insurance
NVAL	National Veterinary Assay Laboratory
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Co-operation Scheme
PMDA	Pharmaceutical and Medical Device Agency
PPS	Plant Protection Station
QALY	Quality-adjusted life years
QMS	Quality Management System
RMP	Risk Management Plan
TPP	Trans Pacific Partnership
VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
WP	Working Party

Introduction

Japan and the EU face many similar challenges, such as aging populations, shifting demands for products and services, and rising costs in many aspects of the welfare system. Life sciences and biotechnologies offer the possibility of technologies that will help address these challenges.

Working Party 2 focuses on the following sectors:

- Healthcare (pharmaceuticals, medical devices etc)
- Life Science & Industrial Chemicals
- Plant Protection & Biotechnology
- Animal Health

The recommendations of WP-2 have the clear aim to improve the innovation capabilities of both the EU and Japan through concrete action plans in life sciences and biotechnology. The focus is on measures that will enhance efficient healthcare practices, food technology and supply, and biotechnology.

The BRT members are grateful for the actions already taken by the EU and the Japanese governments in these fields. We hope the governments will continue further actions for regulatory harmonisation and collaboration.

An asterisk (*) identifies “priority” recommendations.

Recommendations from both European and Japanese industries

HEALTHCARE

WP-2 / # 01* / EJ to EJ
Mutual Recognition Agreement for Pharmaceuticals GMP should be extended

The EU and Japan should expand their Mutual Recognition Agreement (MRA) on Good Manufacturing Practice (GMP) to various pharmaceutical dosage forms such as ointments, injectables, sterile forms and API, as well as biological products, in order to avoid redundant inspections and testing.

<Recent Progress>
Good progress has been seen. In April 2016, EU and Japan agreed to expand countries subjected by the MRA of the GMP certifications from 15 to 28 EU countries. The EU and Japan also announced that they are considering expanding the MRA subjects, which currently cover only no-sterile oral tablets and capsules, to other medical products.

<Background>
In 2002, the EU and Japan introduced the MRA on the GMP of medical products, but it covered only the then 15 EU countries and its subjects were only non-sterile oral tablets and capsules. In April 2016, the MRA was expanded to cover all the now 28 EU countries, and both the EU and Japan are considering expansion of subjects to other formulations of medical products.

In March 2017, the EU and the US announced they have agreed on MRA of the GMP. Oral tablets, capsules, ointments, injectables, API, and biological products are included in this agreement. Human blood, human plasma, human tissues and organs and veterinary immunologicals are excluded.

Despite Japan being a member of PIC/S, currently only oral solid dosage forms are included within the MRA between Japan and the EU and there are therefore still much redundant inspection and testing 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 integrate the EU and Japan economies more efficiently, standards and guidelines should be harmonised and the MRA expanded. This MRA issue is one of the items of the EPA negotiation between EU and Japan.

Prioritized items for harmonization between the EU and Japan and with international standards:
- Safety measures
- Clinical development guidelines and biological preparation standards for vaccines
- Minimum requirements for biological products

WP-2 / # 02 / EJ to EJ
Mutual recognition should be improved for Medical Devices

(i) Mutual recognition of quality management audit results for Medical Devices should be established between EU and Japan

The EU and Japanese governments should establish a mutual recognition scheme for Quality Management System (QMS) audit results. In June 2015, the Japanese government announced it would officially join the Medical Device Single Audit Program Pilot (MDSAP), to share QMS audit results between the United States, Canada, Australia and Brazil. We call for a similar regulatory harmonisation approach between the EU and Japan for lower risk medical devices, e.g. those classified as Class II, ARCB under the Japanese Pharmaceutical and Medical Device Act (J-PMD Act).

As a result of the implementation of the J-PMD Act in November 2014, the ISO13485 audit report is accepted for the QMS process in Japan. However, the Japanese original requirement still remains. For a real regulatory harmonization, submission-related formats and standards also need to be harmonized. We request a clear direction towards a product-based and rationalized annual audit.

The EU side requests a complete harmonization by eliminating Japan's deviations on top of ISO13485. As a next step, mutual recognition of Medical Devices products for lower risk classes should be introduced as soon as possible. Further improvements are desirable when introducing a new ISO revision. If the ISO revision differs per country (for example: ISO 60601 rev2 and rev3), the workload for manufacturers is very heavy. Therefore, the introduction schedule of new ISO standards should be harmonized, including a grace period. The EU side would also like to suggest the necessity of disseminating information on QMS ministerial ordinances in English, for the purpose of MDSAP rationalization of investigation pursuant to Chapter 3, Production and Marketing.

<Recent Progress>
Some progress have been seen in this recommendation. Under the Japanese Pharmaceutical and Medical Device Act (J-PMD Act), which came into force in November 2014, the QMS of medical devices in Japan has proceeded towards alignment with international standards. In addition, Japan officially joined the Medical Device Single Audit Program Pilot (MDSAP) to ensure its internationalization. These efforts will lead to international harmonization and realisation of mutual recognition in future.

<Background>
In June 2015, the Japanese government announced it would officially join MDSAP. MDSAP is an international cooperation programme for quality assurance of medical devices by the United States, Canada, Australia and Brazil as members, established in January 2014. Regulatory authorities of the member countries cooperatively evaluate QMS audit agencies and share audit results among member countries. Medical device companies normally have to get a QMS audit in each country. However, under MDSAP a single QMS audit result will be valid among member countries. This programme will reduce the burdens on both companies and

authorities. Although there are issues to be solved to implement this programme, distribution of medical devices will be stimulated between the member countries of MDSAP. A similar scheme between the EU and Japan should be considered.

Based on the Medical Devices Directive (MDD) of the EU and the J-PMD Act, QMS audit results are required for each application for a license to introduce new medical devices into 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. Although Japan has started to accept QMS audit results at a specific manufacturing site for products with the same generic name under certain conditions, a number of RCBs still require submitting QMS audit results for each application. Further alignment is necessary.

(ii) There should be mutual recognition of Medical Devices product licenses

Mutual recognition of Medical Devices product licenses between the EU and Japan should be introduced. Regulations of low risk class II devices are similar in the EU and Japan. Therefore, mutual recognition of this category of products may be realized earlier. PMDA and MHLW should introduce mutual recognition of medical device product licenses with low risk of class II devices by taking the difference of classification of medical devices 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.

The EU will pursue Medical Device Regulation (MDR), but not enough information is communicated to Japan. The EU should communicate with the Japanese government about the new MDR implementation.

<Recent Progress>
There have been some improvements through the implementation of the Pharmaceutical and Medical Device Act (J-PMD Act), which makes Japan accept the audit report ISO13485 issued by the countries. The PMDA's performance has been improved to shorten approval times for medical devices. ISO14155 has been accepted but we request further improvement. Based on the J-PMD Act, some Class II and Class III products will move to "Ninsho" application. In terms of mutual recognition, no progress has been seen.

<Background>
It should be possible to start with lower risk devices. The evaluation schemes between the Medical Devices Directive of the EU and J-PMD Act are quite similar:
- 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, mutual recognition should be easy to implement.

(iii) There should be mutual recognition of clinical trial results for Medical Devices

Mutual recognition of clinical trial results for the development of new Medical Devices should be accelerated. This would make it possible to make new products available to patients in Japan and the EU within the same timeframe and through one process, ensuring a high level of quality, while reducing the burden on manufacturers.

At present, the standards of clinical trials in the United States, EU and Japan are seen to be almost equivalent and there are several cases where clinical trial results are already mutually recognized between the EU and Japan. EU-Japan BRT members request that both the EU and Japan accelerate mutual recognition of clinical trial results by increasing the number of such cases and showing clinical trial conductors implementing guidelines.

More specifically, Japan GCP (J-GCP) has been harmonized with ISO14155, but the EU side requests Japan to improve the actual operation of J-GCP. The clinical trials performed in EU countries according to ISO14155 should be easily accepted and if not accepted, an explanation with a scientific background is a must. In addition, the Japanese government should prepare a clear definition for accepting and preparing clinical trial reports.

Furthermore, we hope for early disclosure of a clear guidance for judgment on the need for clinical studies, conditions for acceptance, etc. in order to make the actual operation of GCP smoother. Early disclosure of clinical trial-related guidance would promote the entry of overseas companies to the Japanese market. Regarding the guidance for the preparation of the Clinical Evaluation Report, we request the Japanese Government to issue the guidance as early as possible.

<Recent Progress>
A certain level of progress has been seen for this recommendation. We expect that the Japanese Government will publish guidelines for creating clinical evaluation reports as soon as possible. In June 2016, the EU published the fourth revision of guidance 'Clinical evaluation: A Guide for Manufacturers and Notified Bodies under Directives 93/42/EEC and 90/385/EEC (MEDDEV 2.7/1 revision 4)'. The guidance focuses much more on the applicability of the clinical data rather than its origin. In general foreign clinical data is accepted in the EU for conformity assessment by Notified Bodies if certain criteria are met, such as e.g. an analysis whether data generated outside the EU are transferable to the EU population.

<Background>
Differences in the definition of GCP between Japan and the EU currently prevent the general use of non-Japanese clinical trial results in the application for new medical devices in Japan. However, foreign clinical trial data has been accepted in Japan as a part of the 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 standards or considered to have an equivalent level of quality. Even in these cases, additional data has sometimes been required with unclear reasons.

More positively, the Japanese government encourages active use of the advance consultation service provided by the Pharmaceuticals and Medical Devices Agency (PMDA) on individual medical device applications, to address the use of foreign clinical trial data for the application of a device. A similar situation exists in Europe, where there is no general ability to use Japanese clinical data but some cases where clinical trial results acquired in Japan have been applied to the new medical device applications in the EU.

With regards to the procedure between the United States and Japan, mutual recognition of clinical trial results is already being practiced under the clinical trials by comprehensive and simultaneous processes, such as “Harmonization By Doing (HBD)” by both regulatory authorities in the United States and Japan.

PLANT PROTECTION & BIOTECHNOLOGY

WP-2 / # 03* / EJ to EJ
Acceleration and dissemination of scientific knowledge on new plant technologies by both the governments and the private sector

The governments and the private sector should implement concrete actions in order to increase public awareness and societal acceptance on the benefit and contribution of new technologies in the Plant Protection & Biotechnology area, including GMOs, to the sustainable supply of safety foods. To achieve these objectives the Japanese and European biotechnology and bio-industry associations should work closely with other sectorial organisations and their respective authorities. Specifically:

- Both the EU and Japan should advance and adhere to global harmonization on GMO risk assessments, and support the Global Low Level Presence Initiative.
- Both the EU and Japan should provide legal clarity on the status of new plant breeding techniques such as genome editing, preferably in a harmonized manner.

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

<Background>
While Plant Protection & Biotechnology significantly contribute to the sustainable food production for an ever growing population, the contribution of new technologies has never been well recognized. Moreover, the benefit of improved quality traits on imported seeds has not been fully addressed. Considering the possible limitation of future access on foods and feeds as a consequence of limited arable land and global competition on limited foods, new technologies bringing higher productivity are required.

It is therefore necessary to increase the societal acceptance of new technologies in Plant Protection & Biotechnology, including GMOs, as an option to increase and sustain the agricultural productivity in the world through awareness-building on the benefit of this technology to better life.

ANIMAL HEALTH

WP-2 / # 04* / EJ to EJ
There should be mutual recognition of GMP and marketing authorization for Animal Health products

Mutual recognition of EU and Japanese marketing authorizations and recognition of GMP certification for veterinary products is important to promote trade and

investment. MAFF and the European agency should accept the GMP certification of the other party where the GMP requirements are similar or equivalent.

<Recent Progress> EU side will revise
MAFF revised regulations to issue accreditation licenses written in both Japanese and English in December 2014. However, since then there has been no further progress, and there remain no examples of mutual recognition at the product level.

<Background>
Overseas production facilities that are involved in manufacturing 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. The EU-Japan Economic Partnership Agreement should aim for mutual recognition of European and Japanese marketing authorizatiosn for veterinary products, starting with mutual recognition of GMP certification of veterinary medicines where the GMP requirements are similar or equivalent.

HEALTHCARE

WP-2 / # 05 / EJ to E
Maintain the UK within the current EU regulatory and research framework on medicines

With UK exit from the EU likely in 2019, there is a strong need to support the harmonization and continuity of EU legislation relevant for life sciences, to ensure that patients in both the UK and the EU do not suffer reduced access to innovative medicines. There is a particular need for harmonization and continuity around the single regulatory system, in order to maintain a stable EU Regulatory System and smooth functioning of the European Medicines Agency.

It is important to maintain across the UK and EU the current research funding for life sciences, as well as common standards in terms of intellectual property and patent requirements, which are essential for innovative and research-based companies. In addition, additional barriers resulting from tariffs and a reduction in free movement of people should be avoided.

<Recent Progress>
New recommendation

<Background>
In June 2016, the citizens of the United Kingdom voted in a referendum to leave the European Union. Since then, the new British Prime Minister Theresa May and her cabinet have been working on a strategy for the so-called “Brexit”.

For the pharmaceutical industry, there is considerable uncertainty regarding the implications of Brexit on research, development, approval and uptake of new drugs, from both a UK and European perspective, as well as on commercial and trade related questions.

PLANT PROTECTION & BIOTECHNOLOGY

WP-2 / # 06 / EJ to E
Regulations governing import Maximum Residue Limits (MRLs) into the EU should be clarified so as to allow free trade of food commodities

There is potential contradiction between REGULATION (EC) NO 396/2005, which governs import MRLs, and REGULATION (EC) NO 1107/2009, which governs market authorization of plant protection products in Europe. BRT members are concerned that the latter regulation is influencing import MRLs, as it introduced hazard cut-off criteria which can eliminate substances from the market. There may be cases where an import MRL regulated under REGULATION (EC) NO 396/2005, is beyond the cut-off level established under REGULATION (EC) NO 1107/2009, and substances which have been assessed as safe under the first regulation might be banned by the second. The regulations should be clarified, based on sound science, so as to facilitate free trade.

<Recent Progress>
No progress has yet been seen: decisions in Europe on import MRLs have not been made. An evaluation process of the pesticides legislation (Regulation (EC) No 1107/2009 and Regulation (EC) No 396/2005) is planned in 2017 and will tackle this issue.

<Background>
In the absence of necessary import MRLs, food commodities containing the residue of the active substance are prohibited for importation even though the said substance is approved in the exporting country and the residue does not cause any harmful effect on human health. Excessive protection measures for food safety should be avoided in order to facilitate international trade. The delay of review for import approval on agricultural commodities, including the establishment of import MRLs, may limit the access to innovative technology in exporting markets due to trade barriers in the importing countries.

HEALTHCARE

WP-2 / # 07* / EJ to J
Reform of the pharmaceutical pricing system should provide a stable, predictable environment that rewards innovation

The Basic Policy for “drastic” drug pricing system reform was issued by the government at the end of 2016, and the Central Social Insurance Medical Council (Chuikyo) is now discussing possible changes, with implementation of the revised system from April 2018.

The EU-Japan BRT members strongly call for this review to lead to a system which appropriately values and rewards innovation, maintaining an incentive for companies to develop new drugs and bring them rapidly to Japan and thereby giving Japanese patients early access to the latest treatments.

Specifically, the price maintenance innovation premium should be expanded to allow all new innovative products to keep their initial price level for the duration of their period of exclusivity. This strengthened reward for innovation could be funded by savings made on non-innovative products, with annual price revision for long-listed products (LLPs) and generics that discount from the NHL list price beyond a certain percentage. In addition, repricing rules related to market expansion should not become deterrents to investment.

Some form of Health Technology Assessment (HTA) is likely to be introduced. To ensure that such a system does not become a barrier to access for patients, an open, transparent process is needed, where stakeholders such as the industry and patient groups can contribute and share experience of HTA from European counties. Any new system should be based on the following:

- Assessment based largely or entirely on cost per QALY (quality-adjusted life years) thresholds risks becoming a major barrier to access. Multi-criteria decision analysis has more flexibility and hence is more appropriate.
- The number of products assessed should be limited. Japan does not yet have a well-established HTA infrastructure, so cannot assess a large number of products. The focus should be on products with a large budget impact and in receipt of a significant price premium.
- Any assessment should be post-launch, e.g. two years after market entry. If the assessment will be conducted before launch, the system should not hinder patients' access to new drugs.

<Recent Progress>
The situation has been getting worse. At the 2016 drug price revision, an unexpected rule was suddenly introduced and prices of innovative and huge-selling drugs were cut drastically. And in 2017, an innovative drug with large forecast sales was hit with a price cut of 50%, based on a suddenly introduced new rule. At the end of 2016, the Cabinet issued the basic policy for the drastic drug pricing system reforms and Chuikyo is discussing revision of the pricing system, to be introduced in 2018.

<Background>
The cost of researching and developing a new drug has increased, at the same time as the success rate of products in development has declined. According to research at Tufts University, $2.5 billion is now necessary to launch one new drug. If innovative drugs cannot get appropriate evaluation in their prices, it becomes difficult to continue R&D for new drug creation and patients will lose the benefit of new innovation.

Since highly effective but expensive drugs such as Harvoni (ledipasvir/sofosbuvir combination tablet) and Opdivo (nivolumab) have come onto the market in the past two years, prompting an intensification of the discussion about finding an appropriate balance between the appropriate evaluation of innovative drugs and limited health finances. At the drug price revision in 2016, a new drug price cut rule, an "extra repricing for huge seller drugs", was suddenly introduced and prices of drugs with annual sales over 100 billion yen were drastically cut. Harvoni was one of four drugs subject to this rule. On top of that, the price of Opdivo was unpredictably reduced by

50% based on a discussion at the Council on Economic and Fiscal Policy (CEFP) at the cabinet office in 2017.

Although Chuikyo generally leads on the discussion about reimbursement policies including drug pricing, the CEFP, a higher level of council than Chuikyo, has become the center stage for discussions on the drug pricing system reforms recently. The CEFP has concerns that the current drug pricing system had been unable to respond flexibly to problems that raise concerns about the sustainability of health finances, and believes that the system needed to be drastically changed. As a result, in December 2016 the Japanese government issued its Basic Policy for drastic drug pricing system reform, based on suggestions from experts on the council.

The Basic Policy highlights the importance of balancing "the sustainability of universal healthcare" and "the promotion of innovation," while "alleviating burdens on people" and "improving the quality of healthcare." Specific policy proposals include:

- review of national health insurance (NHI) drugs prices four times each year, at the timing of new drug listings, in order to swiftly respond to sales expansions beyond a certain level resulting from indication additions.
- annual drug price revision, in contrast to the current biennial revision.
- the system maintaining innovative drug prices during patent protected periods will be fundamentally reviewed on a zero basis.
- HTA, which could not only reduce but also raise potential the NHI prices of cost-effective drugs, will be fully introduced.

It is still unclear if the drastic pricing system reforms proposed by the Basic Policy could truly realize the appropriate evaluation for innovation.

WP-2 / # 08 / EJ to J
<u>The 14-day prescription rule for Pharmaceuticals should be abolished</u>

Japan should abolish the 14-day prescription rule, which has been superseded by more recent and more robust safety measures. However, although this recommendation was in line with the 2015 recommendation of the government's own Regulatory Reform Council, Chuikyo concluded that this rule is necessary and the government announced rejection of this recommendation in July 2016. In April 2017, the Regulatory Reform Council requested again to discuss this agenda at Chuikyo. The BRT members continue to recommend abolition of this rule for better patient access to innovative new drugs.

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

<Background>
Despite the government's policies to promote new drug development, patient access to innovative drugs is hindered by the 14-day prescription rule, which restricts the prescription length to a maximum of 14 days for all new drugs in the first year after their launch. In practice this means a delay of one year in patient access to drugs which are already in extensive use abroad. The safety of new drugs in Japan is now underpinned by the post-marketing surveillance system, and by the introduction of a Risk Management Plan (RMP) in 2013, and hence the 14-day rule is no longer necessary.

WP-2 / # 09 / EJ to J
Japan should improve its environment for innovative Medical Devices

(i) Japan should further sub-divide the current functional classification for Medical Devices

Japan should further sub-divide the current functional classifications in order to improve the reward for innovation. Currently, the various products within a functional class, which may have varying market prices, all have the same reimbursement price. This results in price reductions for old products influencing the reimbursement price of new products. In order to appropriately reward innovation in Medical Devices, the reimbursement price of new products should be set separately from the price of old products. The reimbursement pricing system should be revised so that it is closer to a product-oriented system.

<Recent Progress>
Minor progress. At the revision of medical service fees in 2016, the functional classifications wer reviewed and 852 classes were set, up from 844 classes. The exceptional rule of the functional classification remains.

<Background>
Different from pharmaceutical pricing systems, about 280,000 Medical Devices are classified into about 900 functional classes in Japan, and one reimbursement price is then set for one functional class, based on structure, intended use, effectiveness etc.

(ii) Japan should abolish the foreign price reference system for Medical Devices

The foreign price reference system for Medical Devices in Japan should be abolished because: (i) the average price in Japan is already only 80 per cent of foreign prices, according to MHLW documents; and (ii) the upper limit of the price variance between foreign countries and Japan no longer makes sense in reality.

<Recent Progress>
No major progress has been seen. At the medical service fee revision in 2016, the government determined to lower the upper limit of reimbursement price variance between foreign countries and Japan from the current level 1.5 times to 1.3 times.

<Background>
As one of a series of medical expenditure containment policies, at the medical service fee revision in 2016 the Japanese government determined to lower the upper limit of reimbursement price variance between foreign countries and Japan to 1.3 times so that the shrinkage of the price variance of medical devices can be achieved. It is required that the reimbursement pricing system should be revised by considering the special characteristics in Japan, such as the necessity to support wholesalers' distribution costs (a very important role was played by wholesalers when disaster hit Japan) and medical institutions because the patients are highly decentralized in Japan.

(iii) HTA for Medical Devices should be introduced with caution

Japan should be cautious in the introduction of HTA (health technology assessment) systems for Medical Devices, taking into account the following factors:

- QALY, a sort of HTA evaluation index for pharmaceutical products, cannot be applied for evaluation of medical devices
- users' skills and techniques of each medical device can affect the evaluation
- medical devices have a shorter improvement cycle than pharmaceuticals

It is important that HTA systems do not hinder the creation of innovative products, delay the listing for medical insurance reimbursement, or impose an excessive burden on the industry (e.g. development of databases or human resources). Such outcomes would delay patient access to cutting-edge medical technologies.

<Recent Progress>
Five medical device products have been under trial assessment of cost effectiveness since 2016. Detail method of application of the results is under discussion at CHUIKYO.

<Background>
In April 2016, the Japanese government launched a trial HTA system that included assessment of some Medical Devices.

PLANT PROTECTION & BIOTECHNOLOGY

WP-2 / # 10* / EJ to J
Review times for Plant Protection & Biotechnology products should be shortened

The introduction of parallel review by MAFF (Ministry of Agriculture, Forestry and Fisheries) and the FSC (Food Safety Commission) in 2016 offers the potential for a major improvement in the time taken to review and approve new products. The first priority should be to assess if the new process is working as intended in practice.

There may be other possible ways to shorten review times:

- Further harmonization of the dossier on human safety and acceptance of summaries in English.
- Opportunistic use of the evaluation results from foreign countries in order to reduce the resource burden on the Japanese authorities.
- Association and synchronization of review for domestic registration with that for import MRLs.
- Parallel review by MHLW.

<Recent Progress>
Major progress. Parallel review by MAFF and the FSC was introduced in 2016, and has the potential to reduce the registration process by 150 days.

<Background>

Delivering novel and safe Plant Protection products and seeds is very important if the needs of the growing world population for high quality foods and feeds are to be met. While R&D-intensive companies are continuously and heavily investing in new technologies, the innovation will not contribute to the food production without governmental approval. Therefore, early market access of novel Plant Protection products is crucially important not only for R&D companies but also for farmers who have to be competitive on their agricultural production, as well as consumers whose living is dependent on the sustainability of food production. The delay of market access of novel products will cause technology gaps, resulting in unnecessary disadvantage to farmers due to the limited access to innovative products which are safer and more effective.

If it works as planned, the new approval system should bring Japan much closer to international best practice, with an expected average approval time of 21 to 27 months (versus 27 to 36 months before the 2016 change). However, in the US and Korea the time taken for review is 18 to 24 months, so it may be possible to make further progress.

Recommendations from European industry

HEALTHCARE

WP-2 / # 11 / E to J
Requirements for Japanese versions of the clinical trial protocol and investigators brochure should be relaxed

In Japan, the clinical trial protocol and investigator's brochure is required in Japanese, and translation from English is therefore required for clinical trial notification in Japan. This raises the cost and delays the timelines for clinical trials in Japan.

The acceptance of English-only materials for global clinical trials performed in Japan would require 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 earlier to patients in Japan.

<Recent Progress>
No progress has been seen for this recommendation, but currently an English application format is being positively discussed.

<Background>
The requirement for translation from the original English version for clinical trial notification of global trials in Japan is considered to be a cause of delay to the start of patients' enrolment in Japan.

LIFE SCIENCE & INDUSTRIAL CHEMICALS

WP-2 / # 12 / E to J
English translations for issued regulations

METI (Ministry of Economy, Trade and Industry) & MHLW (Ministry of Health, Labour and Welfare) should provide English translations for issued regulations.

<Recent Progress>
This is a new recommendation.

<Background>
Currently, METI and MHLW provide English translations of issued regulations only in limited cases. This holds true for new laws, enforcement ordinances, enforcement regulations, official notices, guidelines and similar communication published by the ministries. Consequently, to ensure regulatory compliance, companies with activities outside Japan need to translate by themselves such regulations to be able to align internally with non-Japanese-speaking stakeholders. This results not only in additional efforts in each company, but also creates a risk of differing interpretations by each company based on their own translations.

In other Asian countries, such as Korea, regulating authorities provide English translations at the same time as, or shortly after, announcements in the local language. Japan should adopt a similar approach, thereby ensuring consistent compliance with regulations and enhancing Japan's presence in the global marketplace.

WP-2 / # 13 / E to J
Provide a reference to CAS numbers in regulations for Chemical substances

METI and MHLW regulations should refer to CAS numbers in addition to chemical compound names.

<Recent Progress>
This is a new recommendation.

<Background>
CAS provides a unique identifier for chemical substances and is nowadays used by most companies in their internal processes to ensure regulatory compliance. However, the regulations in Japan currently only list the names of concerned chemical substances without indicating respective CAS numbers. These include the Poisonous and Deleterious Substance Control Law (PDSCL), the Industrial Safety and Health Law (ISHL) and the Pollutant Release and Transfer Register (PRTR).

As a result, in order to assess the relevance of any new regulation, each company needs to individually map CAS numbers to the chemicals listed in published regulations. This results not only in additional efforts by each company, but also induces risk of differing interpretations by each company and consequently varying degrees of regulatory compliance.

It has become standard for authorities in the EU and US to indicate CAS numbers in issued regulations. Also in other Asian countries, such as Korea, China and Taiwan, regulating authorities already reference CAS numbers in their announcements. Japan should adopt the global practice of indicating CAS numbers in issued regulations to ensure swift and accurate internal alignment of concerned companies.

WP-2 / # 14 / E to J
Align naming requirements for product labels of chemicals with the names used in Japanese law

MHLW should revise PDSCL labelling requirements to indicate chemicals in accordance with the naming used in Japanese law.

<Recent Progress>
This is a new recommendation.

<Background>
Japanese law regulates chemical substances mostly by chemical group and only in exceptional cases by specific name. Regulations such as ISHL and PRTR require

that labels for products containing chemical substances name these substances “as regulated by the Japanese law”. However, only the PDSCL requires that labels of products containing related chemical substances always state the specific names of the included chemical substances. From a user perspective, it is easier to work with descriptions such as “Organic Cyanide Compound” (chemical group name) than “2-Methyl-6-oxo-1,6-dihydro-3,4'-bipyridine-5-carbonitrile” (specific name of the chemical substance). Discrepancies between naming in Japanese regulations and product labelling requirements creates a risk that substances are used without a clear understanding of the regulations they relate to.

Japan should renew the PDSCL so that product labels must list contained chemicals in the naming “as regulated by the Japanese law” instead of “by specific chemical substance name”. This would allow users to quickly assess the toxicity and regulatory relevance of the materials they handle.

(Document ends)