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

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List of Abbreviations

Abbreviation	Meaning
BRT	Business Round Table
CAS	Chemical Abstracts Service
CEA	Cost Effectiveness Analysis
CGP	Comprehensive Genomic Profiling
EPA	Economic Partnership Agreement
EU	European Union
GCP	Good Clinical Practice
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practice
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
IP	Intellectual Property
ISHL	Industrial Safety and Health Law
ISO	International Organization for Standardization
J-PMD Act	Japanese Pharmaceutical and Medical Device Act
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
MRA	Mutual Recognition Agreement
NHI	National Health Insurance
PBT/vPvB	Persistent, Bioaccumulative and Toxic / very Persistent and very Bioaccumulative
PDSCL	Poisonous and Deleterious Substance Control Law
PHR	Personal Health Records
PMDA	Pharmaceutical and Medical Device Agency
PMP	Price Maintenance Premium
PRTR	Pollutant Release and Transfer Register
QALY	Quality-adjusted life years
QMS	Quality Management System
R&D	Research & Development
REACH	Registration, Evaluation, Authorization, Restriction and Chemicals
RMP	Risk Management Plan
UK	United Kingdom
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 conclusion of the Economic Partnership Agreement was a major achievement for both sides and will bring mutual economic benefit. There is much work to be done to deliver the specific improvements needed to bring our economies closer together.

These once a year meetings are useful, but their value is limited without active follow-up between them. Our Working Party would like to see the creation of working-level government teams, on both the EU and Japan sides, to proactively monitor and drive progress throughout the year. Membership of the teams could perhaps be based on the EPA teams. And these teams should be tasked with developing and delivering on a plan and timelines.

Too many of the recommendations in this report have seen too little progress for too long. Instead of an ending, the EPA should be seen as a beginning. It should be a launch pad: a chance to renew our commitment to removing barriers to business; a chance to find new energy for strengthening our economic relationship; a chance to deliver on the recommendations in this report. Let us take those chances.

In addition, in June 2019, the Japanese government introduced the Bio Strategy 2019, aiming at a sustainable development of the Japanese economy by utilizing and focussing on biotechnology actively. The planning and implementation of specific measures for this bio-strategy allows for an early opportunity to cooperate and collaborate with European stakeholders engaged in the bio-economy promotion and is considered beneficial by the BRT as such early collaboration supports an improvement of the bio-economy in both Europe and Japan.

An asterisk (*) identifies “priority” recommendations.

Recommendations from both European and Japanese industries

COVID-19

WP-2 / # 01 / EJ to EJ
R&D under the new coronavirus situation

The BRT calls on the EU and Japanese Authorities to:

- support the research and development of diagnosis, treatments and vaccines for the new type of coronavirus and related diseases and coordinately promote collaborative actions of companies and/or academia to accelerate their developments, provide appropriate compensation and protection scheme for those treated and providing treatments and
- continuously promote the research and development for other infectious diseases especially for AMR (Antimicrobial Resistance).

The BRT believes that:

- collaborative approach to combat COVID-19 is key for faster realization of solutions for the pandemic. By gathering various expertise of companies and academia and promoting projects in parallel, it is considered that development time can be significantly shortened. Though all the COVID-19 vaccines and therapeutics will undergo rigorous studies on safety and efficacy, health damage may possibly occur with them in some cases. Legislation should be in place to provide speedy, accessible and effective compensation to those suffering health damage resulting from vaccinations and discharge all parties involved in the provision of COVID-19 vaccines and therapeutics from civil liability to facilitate and protect the healthcare provision for COVID-19;
- overcoming the pandemic is the most important issue, but there are also significant challenges in the medium to long term. The number of drug-resistant bacteria is increasing, and if this situation continues, it is predicted that the annual number of deaths worldwide by 2050 due to drug-resistant bacterial infections will rise to approximately 10 million. At the same time, it is necessary to secure resources for solving such problems.

HEALTHCARE

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

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

The BRT calls on the EU and Japanese Authorities to:

- introduce a mutual recognition scheme for Quality Management System (QMS) audit results, preferably through EU accession to the Medical Device Single Audit Program Pilot, or through regulatory harmonization between the EU and Japan,
- harmonize submission-related formats and standards,
- ensure post-approval QMS inspection dates coincide with the renewal of marketing authorization rather than every 5 years in order to simplify and assure proper renewal operation,
- introduce mutual recognition of Medical Devices products for lower risk classes as soon as possible,
- harmonize the introduction schedule for new ISO standards, including a grace period, thereby ensuring they apply the same revision of a particular ISO standard,
- address issues above through the next revision of the J-PMD Act.

The BRT believes that:

- the QMS inspection process remains complicated and burdensome despite Japan now accepting the ISO13485 audit report under the 2014 J-PMD Act.

There should be mutual recognition of Medical Devices product licenses.

The BRT calls on the EU and Japanese Authorities to:

- mutually recognize Medical Devices product licenses. Existing similarities between EU and Japanese regulations on low risk class II devices make mutual recognition on product licenses for this category of products possible.

The BRT calls on the Japanese Authorities to:

- ensure PMDA and MHLW introduce mutual recognition, taking into account the difference of classification of medical devices between Japan and the EU.

The BRT calls on the EU Authorities to:

- improve their communication with the Government of Japan in relation to the new Medical Device Regulation (MDR) implementation,
- monitor whether the switch from the Medical Device Directive to MDR does indeed accelerate the mutual recognition of clinical trials results in Japan.

The BRT believes that:

- harmonizing QMS and classification should allow new products to be introduced in both the EU and Japan within the same time frame and in one process,
- the EU Authorities are communicating insufficient information to Japan about the MDR.

There should be mutual recognition of clinical trial results for Medical Devices.

The BRT calls on the Japanese Authorities to:

- accelerate mutual recognition of clinical trial results in actual operation, where the conformity is currently insufficient due to the existing strict conditions applied when accepting clinical evaluation reports originating outside of Japan,
- provide 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, and
- develop guidelines for effective utilization of clinical evaluation reports soon. The EU industry side requests that the Japanese government responds with specific timelines for this action as this has been a previously listed request with no practical progress.

The BRT believes that:

- although foreign clinical trial data can be accepted in Japan as part of the application dossier under specific circumstances, additional data requirements were sometimes imposed on manufacturers without providing the rational regarding such request,
- the acceleration of mutual recognition of clinical trial results for the development of new Medical Devices would ensure access to new products for patients in Japan and the EU, both within the same timeframe and through one process. This would allow for further reducing the device lag, ensuring a high level of quality whilst minimizing the administrative burden on manufacturers, and
- early disclosure of clinical trial-related guidance would promote the entry of overseas companies to the Japanese market.

PLANT PROTECTION & BIOTECHNOLOGY

WP-2 / # 03 / EJ to EJ
Legal clarity for and appropriate regulation of Plant Protection innovation, including genetic modified plants and gene-edited plants

The BRT calls on the EU and Japanese Authorities to:

- regulate agricultural technologies, including crop protection, genetic modified and gene-edited crops in a science-based and proportionate manner,
- advance and adhere to global harmonization of genetically modified organisms' risk assessments, and support the Global Low Level Presence Initiative,
- provide legal clarity on the status of techniques such as genome editing and corresponding labelling requirements (e.g. for genome edited derived food), and
- work with industry and other stakeholders to increase trust in the regulatory science and gain greater societal acceptance.

The BRT believes that:

- a fact-based platform for dialogue and sharing of information as well as a risk-proportionate, predictable, science-based treatment of new technologies is required,
- taking a science-based and proportionate regulatory approach to agricultural technologies will aid gaining societal acceptance and help weeding out misinformation.

ANIMAL HEALTH

WP-2 / # 04 / EJ to EJ

Ensure mutual recognition of GMP for Animal Health products

The BRT calls on the EU and Japanese Authorities to:

- agree on the mutual recognition of European and Japanese marketing authorizations for veterinary products, starting with mutual recognition of GMP certification of veterinary medicines,
- include veterinary products within the scope of the MRA (Mutual Recognition Agreement).

The BRT believes that:

- mutual recognition of GMP certification for veterinary products between the EU and Japan will provide for faster access to new useful products.

HEALTHCARE

WP-2 / # 05 / EJ to E
The UK's withdrawal from the EU should create the minimum of disruption to patients/users and pharmaceutical and cosmetic industries

The BRT calls on the EU to:

- ensure harmonization and continuity around the single regulatory system and maintain a stable EU Regulatory System and smooth functioning of the European Medicines Agency for pharmaceuticals, and

- warrant that there is a single regulatory regime for cosmetics with a single evaluation of the safety of cosmetic ingredients used in products in the EU and the UK. More specifically, the recommendations are:

  - secure ongoing alignment, cooperation and mutual recognition between the UK and the EU regarding the authorization, testing and surveillance of pharmaceuticals and cosmetics,

  - ensure companies can still employ the best talent from around the world, facilitating UK and EU nationals working across Europe after Brexit,

  - maintain scientific research collaboration between the UK and EU even after UK leaves the EU in order to strengthen EU's position in life sciences and attracting global life science investment,

  - ensure that intellectual property (IP) standards and IP incentives continue to be applied in the EU and UK after Brexit.

The BRT believes that:

- retaining the functioning of pharmaceuticals' and cosmetics' supply chains by reaching an agreement with a pharmaceutical/cosmetics protocol, which ensures full alignment between EU and UK legislation is needed to guarantee supply of medicines to patients in Europe or the UK after Brexit.

WP-2 / # 06* / EJ to J

Reform of the pharmaceutical pricing system should provide a stable, predictable environment that rewards innovation

The BRT calls on Japanese Authorities to:

- continuously review the current pricing system to strengthen the reward for innovation, maintain an incentive for companies to develop new drugs, and to bring them rapidly to meet patients' needs in Japan,

- limit the scope of off-cycle price revisions which will be introduced from 2021 onwards. Since drug expenditure has been well controlled by the current pricing system, the scope of off-cycle price revisions must be limited to exceptional cases, such as e.g. the marketed price is significantly lower than the listed price. Innovative patented products should not be subject to off-cycle price cuts,

- expand the Price Maintenance Premium (PMP) system to cover all innovative products, incl. incremental innovations during their patent exclusivity period with the next drug pricing system reform in April 2022,

- further revisit corporate indicators as basis for PMP eligibility; corporate indicators measure the ranking of companies, but are currently unpredictable and do not reflect the degree of innovativeness of individual products, including the tangible benefits provided to the patients,

- expand the reward for innovation for launching an innovative additional indication after initial NHI listing and recognizing real clinical and patient benefit so that it includes real world evidences as well as scientifically validated patient reported outcomes,

- in the middle term, improve the PMP system such as to reflect broader range of values each product provides beyond its price to decide on PMP eligibility, e. g., patient's and healthcare provider's benefit, social contributions in addition to clinical improvements, and

- expand the scope of pricing policy reforms beyond drug costs, as drug costs are only one part of the overall healthcare costs.

The BRT believes that:

- the administrative labour and costs involved in drug price surveys and drug price revisions, which are required to implement annual revisions are a considerable cost driver especially in the midst of the public health emergency and in consequence hinder a sustainable reduction in medical costs. Therefore, in order to improve the return on investment and policy

implications of the off-cycle price revision, it is necessary to limit the revision's scope,

- the reforms to the pharmaceutical pricing system introduced since 2018 could result in a delayed access to the latest treatments for Japanese patients. Unless innovation is properly evaluated, it becomes increasingly challenging for the industry to continuously create innovative drugs to fulfil unmet medical needs. This will not be beneficial for the patients nor for the society,

- in April 2020, minor changes were made to product requirements and company indicators for PMP; as for the product requirements change, the BRT welcomes that products will be eligible for PMP if their additional indications are recognized to be innovative or useful,

- company indicators are evaluation criteria based on past company records and are not directly related to the innovative value of individual products and such products or companies' future contribution to the healthcare system and patients' benefits. It is necessary to verify the effects of this system and to continually review the system,

- expanding the reward for innovative additional indications leads to further access to innovative treatments and additional benefits for patients,

- drug costs are only one part of the overall healthcare costs: a holistic view is needed, and a fundamental reform should not be limited to managing drug prices only. Thus, to ensure long term healthcare system sustainability while securing reward for innovation, future reforms should include a review of all healthcare costs and revenue sources, including medical fees, medical procedures, hospital stays, patient co-payments etc.

WP-2 / # 07 / EJ to J
The 14-day prescription restriction rule for new Pharmaceuticals should be abolished

The BRT calls on the Japanese Authorities to:

- abolish the 14-day prescription restriction rule, or

- extend the prescription limitation to 30 days and shorten the rule application period to 6 months.

The BRT believes that:

- the 14-day rule is no longer required because the safety of new drugs in Japan is now underpinned by the post marketing surveillance system and

the introduction of a Risk Management Plan (RMP),

- abolishing the rule would provide better patient access to innovative new drugs.

WP-2 / # 08 / EJ to J
The environment for innovative Medical Devices should be improved in Japan

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

The BRT calls on the Japanese Authorities to:

- revise the reimbursement pricing scheme bringing it closer to a product-oriented system,
- improve the reward for innovation by sub-dividing current functional classifications, and
- set the reimbursement price for old products separately from the reimbursement price for new products.

The BRT believes that:

- it would be sensible to allow a certain period-of-time prior to conclusive assessment, because it often takes time for effectiveness of new products to become apparent and safety and efficacy to be adequately addressed.

Japan should abolish the foreign price reference system for Medical Devices

The BRT calls on the Japanese Authorities to:

- abolish the foreign price reference system for Medical Devices since the average price in Japan is already only 80% of foreign prices.

The BRT believes that:

- when comparing foreign prices with Japanese prices, it should be acknowledged that Japanese prices include wholesalers' and hospitals' margins as well as distribution costs.

Health insurance environment for cancer genome profiling (CGP) testing should be improved for patients to get early access to indicated testing

The BRT calls on the Japanese Authorities to:

- enable patients to conduct CGP testing and receive their results at optimal timings using public insurance system.

The BRT believes that:

- CGP testing which comprehensively detects cancer-related genes has been covered by national health insurance and reimbursed as a medical device since June 2019, but there is a restriction that they are reimbursed only if CGP testing are performed at the end of the standard of care when patients already get drug resistance or are in worse general status. An environment is socially demanded where each patient can get access to CGP testing at early and optimal timings.

WP-2 / # 09* / EJ to J
Careful introduction of Health Technology Assessment (HTA)

Health Technology Assessment (HTA) for Pharmaceuticals should be introduced with caution so that it does not become a barrier for patient access

The BRT calls on the Japanese Authorities to:

- keep refining the system of using HTA and Cost Effectiveness Analysis (CEA) for Pharmaceuticals, and

- refrain from using CEA in making reimbursement decisions.

The BRT believes that:

- CEA/HTA should be positioned as being supplemental to the current drug pricing system, and that

- the scheme introduced in April 2019 relies on a single measure such as the Incremental Cost Effectiveness Ratio (ICER), but this indicator does not reflect the full value of a medicine and its value varies widely depending on the choices of data, assumptions and models. Disease severity, unmet need, ethical and societal considerations should be considered as additional factors in evaluating the true value of drugs. Through this approach Japan should establish a more balanced HTA system,

- all stakeholders, including experts from the industry, should fully participate in the discussion of refining the newly introduced system to ensure that the

experiences and failures of other countries are duly evaluated and considered.

HTA for Medical Devices should be introduced with caution

The BRT calls on the Japanese Authorities to:

- be prudent in the introduction of HTA (Health Technology Assessment) systems for Medical Devices taking into account the following factors:
  - QALY, an indicator often used in HTA evaluation for pharmaceutical products is difficult to 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.

The BRT believes that:

- 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 adding human resources). Such outcomes would delay patient access to cutting-edge medical technologies. To avoid this, there should be a clear distinction and balance between assessment and appraisal. There should be no inappropriate use of the ICER measure.

WP-2 / #10* / EJ to J
A harmonized approach for integration of health-related data and construction of data health infrastructures

The BRT calls on the Japanese Authorities to:

- foster a harmonized approach for integration of health-related data and strongly promote construction of data health infrastructures in Japan,
- accelerate the integration according to the grand design under cross-ministerial guidance.

The BRT believes that:

- personal health records (PHR) will directly contribute to individual patients' choice of personalised treatments,

- the integrated health data will promote evidence-based policy making in health areas to improve efficiency of healthcare, medical services and nursing care,

- utilization of the big data by academia and industries will lead to new products and services.

Plant Protection & Biotechnology

WP-2 / # 11* / EJ to J
Reviewing period for Plant Protection & Biotechnology products should be shortened

The BRT calls on the Japanese Authorities to:

- further shorten reviewing period through harmonization in data requirement for plant protection product and biotechnology products as well as dossier on human & environment safety, and through acceptance of summaries in English, as well as

- take advantage of the evaluation results from foreign countries in order to reduce the resource burden on the Japanese authorities,

- expand the scope of the biotechnology products for which local confined field testing may be excluded to genetically modified soybean and other crops based on accumulated evidences and scientific justification by leveraging data from foreign countries.

The BRT believes that:

- delivering novel and safe plant protection products and seeds is vital for meeting the needs for food of the growing world population. While R&D-intensive companies are continuously and heavily investing in new technologies, the innovation will not contribute to food production without their governmental approval. Hence, early market access to novel plant protection products is crucially important,

- a delayed market access of novel products will cause technology gaps, resulting in unnecessary disadvantages for farmers due to limited access to innovative products,

- further progress in shortening the reviewing period would bring Japan much closer to international best practice standards,

- harmonizing international data requirements will enable the industry to avoid duplicated investment for market access in the respective area. Currently only China and Japan request local confined field testing for GMO crops for import use, while other import countries like EU, Korea and Taiwan etc. leverage the field data collected in cultivation countries for safety assessment.

Recommendations from European industries

HEALTHCARE

WP-2 / # 12 / E to J
Requirements for Japanese versions of the clinical trial protocol and investigator's brochure should be relaxed

The BRT calls on the Japanese Authorities to:

- accept clinical trial protocols and investigator's brochures as well as applications, which are written only in English.

The BRT believes that:

- acceptance of English-only protocols and investigator's brochures would reduce costs and make innovative drugs earlier available to patients in Japan,

- the requirement for translation of the original English version of a clinical trial notification is delaying the start of patients' enrolment in Japan.

LIFE SCIENCE & INDUSTRIAL CHEMICALS

WP-2 / # 13 / E to J
English translations for issued regulations

The BRT calls on the Japanese Authorities to:

- provide English translations of all issued regulations from METI (Ministry of Economy, Trade and Industry) & MHLW (Ministry of Health, Labour and Welfare) at the same time as, or shortly after, the announcement in Japanese.

The BRT believes that:

- Japan's regulating authorities should provide English translations of issued regulations, adapting to global practice and thereby enhancing Japan's presence in the world market.

WP-2 / # 14 / E to J
Provide a reference to CAS numbers in regulations for Chemical substances

The BRT calls on the Japanese Authorities to:

- indicate CAS (Chemical Abstract Services) numbers in addition to chemical compound names in regulations issued by authorities, as has become a global practice.

The BRT believes that:

- if METI and MHLW regulations would refer to Chemical Abstracts Service (CAS) numbers in addition to chemical compound names, risks of differing interpretations and varying degrees of regulatory compliance can be avoided. In addition, swift and accurate internal alignment of concerned companies could be ensured.

WP-2 / # 15 / E to J
Align naming requirements for product labels of chemicals with the names used in Japanese law

The BRT calls on the Japanese Authorities to:

- revise the labelling requirement of the Poisonous and Deleterious Substance Control Law (PDSCL) to indicate chemicals in accordance with the naming used in Japanese law instead of stating the specific names of the included substance.

The BRT believes that:

- a harmonization of the labelling requirement regulations (PDSCL, ISHL and PRTR) to list the contained chemical "as regulated by the Japanese law" on the label would allow users to quickly assess the toxicity and regulatory relevance of the materials they handle,

- the discrepancies between naming in Japanese regulations and product labelling requirements poses a risk that substances are used without a clear understanding of the regulations they relate to. This should be avoided.

Recommendations from Japanese industries

INDUSTRIAL CHEMICALS

WP-2 / # 16 / J to E
The draft regulations on microplastics for cosmetics in EU under REACH (regulation for chemicals) should be reconsidered

The BRT calls on the EU Authorities to:

- reconsider the definition of microplastics. Only small plastics with environmental risks should be defined as microplastics,
- derogate all wiped-off cosmetic products (make-up, lip and nail products) from the restriction of microplastics.

The BRT believes that:

- restriction of microplastics only by persistency is not consistent with the principles of existing regulatory framework,
- polymers and microplastics should not be regarded as the same category of chemical substances since they are two different chemical terms with fundamental compositional differences,
- microplastic emission from make-up, lip and nail cosmetic products to the aquatic environment is insignificant, because they are wiped-off after their use and, in addition, they are trapped at sewage treatment systems. Restriction of make-up, lip and nail cosmetic products does not contribute to reducing the environmental impact.

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