

To Contribute to a Goal of

JAPAN AS THE BEST PLACE TO LIVE AND AGE

VISION REPORT OF THE INNOVATIVE BIOPHARMACEUTICAL INDUSTRY



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INTRODUCTION

ABOUT OUR VISION

The Innovative Biopharmaceutical Industry is committed to working as a true partner of the Japanese people in order to promote pro-growth and pro-innovation policies for the benefit of Japanese patients and the economy. Our industry works to solve unmet medical needs of patients and families endeavoring to develop new medicines quickly and safely and in doing so provides economic benefits to Japan. We seek to uphold the highest ethical standards and comply with all applicable domestic and foreign laws and regulations, consistent with the trust placed in our industry by patients and the broader society.

We will work together with the Japanese government in order to achieve the best possible health for citizens while maintaining the sustainability of the Universal Health Care Coverage system.

Our industry will contribute to these goals through sustainably advancing innovation underpinned by the best possible evidence to inform decision-making. At the same time, we identify barriers and challenges to achieve this goal and propose recommendations as to how the government might address these issues so together we can deliver better patient outcomes and economic gain.

Patient centricity is at heart of what we do and therefore is the foundation on which our vision is built.

Our vision is based on the three key beliefs of patient centricity:

1. We believe it is crucial to deliver innovative medicines to patients in need, in a safe and timely manner.
2. We believe patient centricity can drive better health outcomes, as well as direct and indirect cost savings.
3. We believe it is crucial to include the patient viewpoint into decision-making about their health care.

PILLAR 1: INNOVATION

ADVANCING INNOVATION WITH A WORLD LEADING REGULATORY ENVIRONMENT TO DELIVER DRUGS TO PATIENTS IN A SAFE AND TIMELY MANNER

Promoting innovative pharmaceutical discovery and translation into medical innovation in Japan.

- Overcoming the ongoing issues in the area of Japanese translational research so that Japan can capitalize on its strengths to become a world leader in medicines discovery and global provision.
- Further harmonizing with international guidelines to enable greater Japanese participation in multi-regional clinical trials.

Improving the competitiveness of Japan as a regional and global leader through regulatory excellence.

- Delivering innovative medicines to patients in the region much earlier through more flexible use of expedited approval pathways.
- Utilizing IT infrastructure to maintain the highest safety standards and streamline the pharmacovigilance and post-marketing surveillance system.

PILLAR 2: SUSTAINABILITY

SECURING TIMELY AND AFFORDABLE PATIENT ACCESS TO NEW INNOVATION IN A SUSTAINABLE UNIVERSAL HEALTH CARE SYSTEM

Delivering innovative medicines and vaccines that contribute to an extension of healthy lifespans under rebalanced NHI that secures timely and affordable patient access to innovation.

- Delivering innovations to Japanese patients that contribute to an extension of healthy lifespans and that help citizens to remain active throughout their lives.
- Maintaining Japan as a priority destination for cutting-edge technology and investment to achieve sustainable promotion of innovation and timely and affordable patient access.

Optimizing expenditure through an increase in efficiency of the off-patent sector and investment in primary and secondary prevention.

- A sustainable pro-innovation environment could be achieved through re-investing some of the savings available through off-patent reforms.
- Developing new policies that encourage and reward primary and secondary prevention measures that contribute to a reduction in the total NHI budget.



PILLAR 3: EVIDENCE

ENSURING POLICY DECISIONS ARE EVIDENCE-BASED AND INCORPORATE A BROAD STAKEHOLDER VOICE

Prioritizing establishment of data infrastructure as a key driver for further optimization of the health care system and resources.

- Building a foundation for health care decision-making of the future through the creation of a comprehensive electronic medical record system and ensuring key stakeholders can access such data whilst protecting patient privacy.

Building a world-leading value assessment framework to ensure predictability and provide a sound process to assess the value of innovation.

- Utilizing a well-designed, evidence-based value assessment framework broadly across health care services, including new technology, to support well-informed, patient-centered health care.
- Including patients, industry, providers and government in early and inclusive dialogue to enable comprehensive evaluation of a therapy's value.

HOW TO REALIZE OUR VISION

INNOVATION

Promoting innovative pharmaceutical discovery and translation into medical innovation in Japan.

1. Overcoming the ongoing issues in the area of Japanese translational research so that Japan can capitalize on its strengths to become a world leader in medicines discovery and global provision.
2. Further harmonizing with international guidelines to enable greater Japanese participation in multi-regional clinical trials.

Improving the competitiveness of Japan as a regional and global leader through regulatory excellence

3. Delivering innovative medicines to patients in the region much earlier through more flexible use of expedited approval pathways.
4. Utilizing IT infrastructure to maintain the highest safety standards and streamline the pharmacovigilance and post-marketing surveillance system.

SUSTAINABILITY

Delivering innovative medicines and vaccines that contribute to an extension of healthy lifespans under rebalanced NHI that secures timely and affordable patient access to innovation.

5. Delivering innovations to Japanese patients that contribute to an extension of healthy lifespans and that help citizens to remain active throughout their lives.
6. Maintaining Japan as a priority destination for cutting-edge technology and investment to achieve sustainable promotion of innovation and timely and affordable patient access.

Optimizing expenditure through an increase in efficiency of the off-patent sector and investment in primary and secondary prevention.

7. A sustainable pro-innovation environment could be achieved through re-investing some of the savings available through off-patent reforms.
8. Developing new policies that encourage and reward primary and secondary prevention measures that contribute to a reduction in the total NHI budget.

EVIDENCE

Prioritizing establishment of data infrastructure as a key driver for further optimization of the health care system and resources.

9. Building a foundation for health care decision-making of the future through the creation of a comprehensive electronic medical record system and ensuring key stakeholders can access such data whilst protecting patient privacy.

Building a world-leading value assessment framework to ensure predictability and provide a sound process to assess the value of innovation.

10. Utilizing a well-designed, evidence-based value assessment framework broadly across health care services, including new technology, to support well-informed, patient-centered health care.
11. Including patients, industry, providers and government in early and inclusive dialogue to enable comprehensive evaluation of a therapy's value.

Overcoming the ongoing issues in the area of Japanese translational research so that Japan can capitalize on its strengths to become a world leader in medicines discovery and global provision.

Japan is one of only a handful of countries that has the scientific capability, regulatory rigor and manufacturing expertise to be able to undertake the entire process of drug development from basic research through clinical development to commercialization. While Japan has a large pharmaceutical industry, including some global leaders, much of this industry is focused on servicing the domestic market. In addition, given world leading levels of basic research, there are issues for the bridge between Japanese basic research and pharmaceutical commercialization; therefore, strengthened translational research is necessary to fill the gap.

At the same time, innovation may represent the best bet for Japan to manage the challenge of being the world's most rapidly aging population and, if viewed as an investment rather than solely as a cost, to use innovation to reduce overall health care costs and increase productivity.

Discovery and translation to clinical practice of new medicines is a high risk activity¹



Recommendation

We recommend the further establishment of a public-private collaboration between AMED, academia, bio-ventures and the pharmaceutical industries in Japan to tackle barriers to translational research in Japan and to accelerate research and development of new medicines to address both Japan's specific health needs as well as to improve global health.

Our Contribution

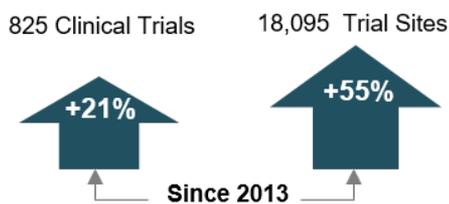
The innovative industry is contributing by promoting awareness of translational research in Japan, growing the abilities of young researchers and expanding the opportunities for research collaboration. Our activities include support of the Mansfield-PhRMA Research Scholars Program, Researcher Fly-ins and co-hosting of the Young Scientists Symposium.

Further harmonizing with international guidelines to enable greater Japanese participation in multi-regional clinical trials.

Japan has increasingly been included in global development programs that reflect the positive incentives resulting from pro-innovation government policies over the last decade. However, clinical trials in Japan tend to take longer and are more costly than in other countries, which acts as a significant disincentive to including Japan in multi-regional clinical trials.

Through further harmonization with international guidelines, Japan should become considerably more competitive for multi-regional clinical trials, especially given the size of the market. In turn, this would provide positive benefits for Japanese patients who would receive new medicines earlier than at present.

Number of PhRMA and EFPIA company sponsored clinical trials in Japan, 2015²



Clinical Trials Cost More in Japan³



Recommendation

To achieve this vision, we recommend rapid implementation of international guidelines, especially ICH-E17⁴, in order to promote more multi-regional clinical trials including Japan. Implementation of ICH-E17 will set the pre-conditions for Japan’s inclusion in more multi-regional clinical trials. To help achieve this goal, we suggest greater engagement in international capacity building workshops on ICH E17 principles, such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and Asia-Pacific Economic Cooperation (APEC) programs. As part of this implementation, we would suggest ensuring that current high cost and time-consuming aspects are addressed to further increase Japan’s competitiveness compared with other countries that are competing for multi-regional clinical trials.

Our Contribution

The innovative industry stands ready to work with the PMDA to implement ICH-E17 in a manner that is aligned with implementation in the U.S. and Europe. Implementation of ICH-E17 by Japan will stimulate industry to include Japan in more multi-regional clinical trials.

Delivering innovative medicines to patients in the region much earlier through more flexible use of expedited approval pathways.

Over the past ten years, the PMDA has made very significant advances in improving its review processes. This has led to a dramatic acceleration in review times and PMDA regulatory reviews are now among the fastest in the world.

The PMDA has implemented expedited approval pathways for first-in-class innovative medicines. However, at present, the “conditional early approval system” and *Sakigake* (“Pioneer”) Designation are under-utilized in promoting domestic R&D and clinical innovation.

It is important for patients with unmet needs to have timely access to promising new medicines that can offer substantial benefits over existing standards of care. New expedited pathways in the U.S. and EU are enabling accelerated clinical development and review for such medicines. Therefore, we consider that the PMDA needs to ensure sufficient regulatory flexibility to allow rapid patient access to medicines undergoing expedited approval pathways.

Recommendation

To achieve this vision, we recommend that the *Sakigake* designation system should be formally implemented from the current trial basis as soon as possible, and to designate all innovative drugs that meet the requirements. Additionally, the conditional early approval system should be equivalent to the U.S. and EU systems in terms of the eligible products and number of designated products. This will assure the global competitiveness of the Japanese early approval system compared with U.S. and European expedited approval pathways such as Breakthrough Designation, PRIME and Accelerated Approval, and enable early access of innovative drugs to Japanese patients.

Our Contribution

The innovative industry is willing to work closely with the PMDA through sharing U.S. and European regulatory best practices and experiences in order to help improve the Japanese system further.

Utilizing IT infrastructure to maintain the highest safety standards and streamline the pharmacovigilance and post-marketing surveillance system.

A common position between industry, the government, physicians and patients is that safety is paramount. Japan has a broad pharmacovigilance and post-marketing surveillance system in order to ensure patient safety. However, much of this system is unique to Japan and has evolved slowly over time with a result that the current system is cumbersome, very expensive to maintain and includes elements that could be refined or are redundant.

The industry believes that Japan needs to modernize its pharmacovigilance and post-marketing surveillance system in order to improve safety standards through using all the data potentially available and to improve the existing system with a more efficient and effective approach that aligns to international standards.

The approach also has the potential to increase the early detection of possible safety signals in medicines being launched in Japan under expedited approval pathways such as *Sakigake* or other pathways.

Recommendation

To achieve this vision, we recommend that the Government of Japan leads the establishment of data infrastructure and conducts necessary change of related regulations. We believe the government should integrate the National Database (e.g. MID-NET) and similar large-scale medical information databases utilizing ICT (Information and Communication Technology) to help evolve the current systems uniquely developed in Japan into the global standard method incorporating signal management.

Our Contribution

The innovative industry supports the highest safety standards for our medicines. We are willing to support the creation of a new system and engage with the Government of Japan on the creation of this system.

Delivering innovations to Japanese patients that contribute to an extension of healthy lifespans and that help citizens to remain active throughout their lives.

The long-term sustainability of Japan’s world leading health care system is threatened by the growing demographic burden of a rapidly aging society. The number of elderly are forecast to represent 35.3% of the population by 2040 while the number of working-age people supporting each elderly person will have dropped from 7.4 in 1980 to two by 2020⁵. In general, the elderly have a higher demand for care, with per-capita direct medical care expenditure approximately four times that of younger patients⁶. Indirect costs are also significant. To help address this demographic challenge, the government has set a policy goal of extension of healthy lifespans, including a focus on prevention of chronic diseases from worsening and preventing people from being forced to prematurely leave their jobs.

In an aging society, medicines represent an excellent option to improve healthier lifespans while reducing expensive downstream health-related costs. Medicines are transforming the treatment of many difficult chronic diseases including cancer, cardiovascular disease, diabetes and rheumatoid arthritis. Continuous development and diffusion of innovative medicines and vaccines that improve health outcomes relating to the diseases and conditions of the elderly will be essential to support the government’s goal of healthy lifespan extension.

Incremental innovation allows patient to continue to contribute to society⁷

Step by step, we are beating cancer. Today, 3 out of 5 Japanese with cancer survive at least 5 years



81% of cancer patients return to work within 12 months of their initial sick leave

Investment in new innovations that address social cost is needed⁸

Societal cost of dementia is already huge and will grow as the population ages



50% of care cost borne by families
100,000 people per year leave work to provide care

Recommendation

To realize our vision, it is necessary that the government and stakeholders recognize the value of innovation as a key investment in achieving a healthy and productive society. In order to achieve this goal, we recommend that all stakeholders should work to build a social health care system that values and properly uses innovative medicines and vaccines.

Our Contribution

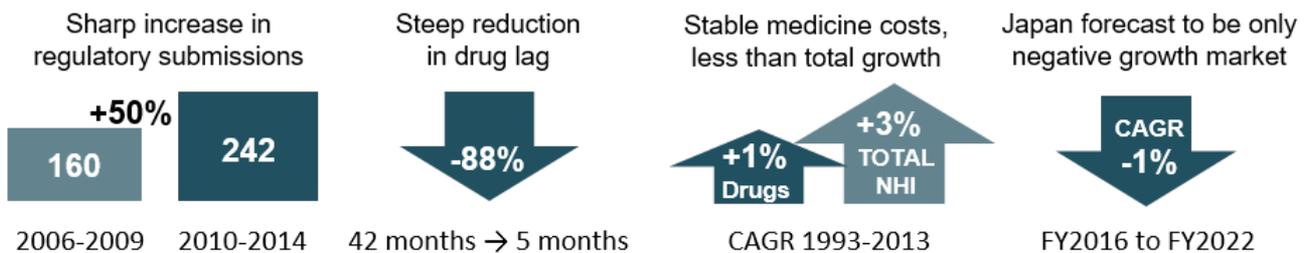
In addition to discovering new medicines, the innovative industry is contributing by providing the best possible evidence to allow our medicines to be appropriately valued and utilized. Under a health care system that values innovation, the industry will be incentivized to continue to develop and diffuse innovative medicines and vaccines that contribute to an extension of healthy lifespans and that help citizens to remain active throughout their lives.

Maintaining Japan as a priority destination for cutting-edge technology and investment to achieve sustainable promotion of innovation and timely and affordable patient access.

Prior to 2010, Japanese patients experienced significant delays, often in years, in accessing cutting edge innovations that were available in the U.S. and Europe. The delay was caused by a combination of clinical trial barriers, long regulatory review times and an unfavorable reimbursement environment, including regular price cuts of medicines while on-patent. Between 2010 to 2015, pro-innovation government policies encouraged a rapid decline of the drug lag and catch-up with medicines that had been available in other markets. From industry’s perspective, two improvements were key: reforms to the PMDA review process and the introduction of the so-called Price Maintenance Premium (PMP)⁹.

In the 2018 pricing reform package, GOJ stated that the balance between “sustainability of NHI” and “promotion of innovation” had been achieved. However, in our view, the reforms targeting innovative medicines have gone too far while alternative approaches could have achieved the same cost-saving objective without damaging pro-innovation policies.

From 2010, pro-innovation policies achieved a significant increase in new drug approvals and a dramatic reduction to the drug lag, all the while keeping costs under control¹⁰



Recommendation

A drastic review of the pricing reforms implemented in 2018 is necessary. In order to maintain Japan as a global leader, we believe that pro-innovation policies need to be restored, including meaningful consultation with industry in advance of future policy changes and fair and predictable rules that appropriately reward innovation while still ensuring the sustainability of the NHI.

Our Contribution

In order for Japan to remain a global leader, it must maintain or restore pro-innovation policies. Both the NHI and industry need a predictable, fair and stable environment. To the extent that reforms are required, industry stands ready to work with the MHLW to find constructive solutions.

A sustainable pro-innovation environment could be achieved through re-investing some of the savings available through off-patent reforms.

Japanese policymakers are facing a challenge in ensuring the long-term sustainability of universal coverage. Industry acknowledges that we have a role to play in helping reduce the fiscal burden of the NHI on the Japanese population while also providing innovations that help reduce the burden on the overall system through improving the health of society.

Despite the government's own data, showing that expenditure on medicines was well controlled, in recent years, policy has shifted from supporting pro-innovation to imposition of cost-containment measures. Over 80% of the 440 billion yen reduction target for social security expenditure from 2016-2018 was raised by drug price reduction. The government's focus on suppression of social security expenses primarily through NHI drug price reform is an unbalanced response that does not address the actual drivers of the total NHI increase.

In comparison with peer markets, in general Japan pays comparatively less for innovation across the on-patent period and considerably more for off-patent medicines. If Japan were to reinvest part of the savings available through off-patent reforms to promote innovation, we can achieve a sustainable pro-innovation environment.

Recommendation

Further reforms of the off-patent sector could release savings to support the broader health care budget, cover pro-innovation policies and remove the need for additional cost-cutting measures.

Our Contribution

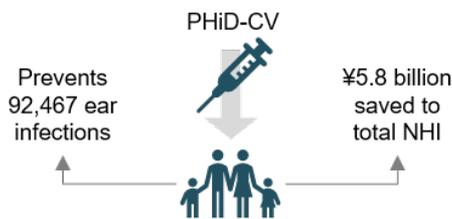
Innovative companies are willing to contribute further savings from their off-patent portfolios provided that a portion of such savings are used to support innovation in an integrated manner.

Developing new policies that encourage and reward primary and secondary prevention measures that contribute to a reduction in the total NHI budget.

The Japanese government’s goal of promoting healthier lifespans is a prevention strategy aimed at reducing the rate of increase in health care expenditure as the population ages. In comparison to some other mature health care markets, Japanese prevention strategies are relatively undeveloped which leads to unnecessary downstream costs in the system.

Significant medical and social costs can be avoided or mitigated through improved use of preventive medicines and strategies, such as smoking prevention. Medicines and vaccines for primary prevention can avert or slow disease progress in its earliest stages. Medicines for secondary prevention can prevent or delay disease progression or the emergence of complications, and can substantially reduce subsequent morbidity and mortality.

Preventing more cases of illness benefits patients and can result in NHI savings¹¹



Prevention of expensive complications can achieve a high return on investment¹²

	Prevention of diabetic aggravation	Dialysis
		
Number of patients:	2,000,000	100,000
Annual medical cost (per patient):	¥400,000	¥5,800,000

Recommendation

To realize a goal of achieving healthier lifespans through prevention, we believe that the government should adopt pro-vaccination policies and give greater recognition to the value of incremental innovation relating to prevention. Of particular importance would be policies that incentivize innovations where their acquisition cost is less than cost-savings for the total health system and to the broader economy.

Our Contribution

The industry wants to bring innovations that contribute to primary or secondary prevention to Japan. Our industry also wants to help ensure that these medicines have the best possible beneficial impact and would like to help address patient needs through improvement of delivery devices and utilization of ICT (Information and communication technologies), for example to help achieve high levels of adherence.

Building a foundation for health care decision-making of the future through the creation of a comprehensive electronic medical record system and ensuring key stakeholders can access such data whilst protecting patient privacy.

To support the optimal use of health care services in order to derive the best treatment for the patient and also to utilize available resources in the most efficient way, a strong data system and infrastructure needs to be put in place. Japan's current use of electronic health care records is limited and the collection, linkage and analysis of health data is relatively undeveloped¹³.

The foundation of evidence-based medicine, and indeed all health care policy, is use of quality data from a range of sources. In a patient-centered health care system, it is important to have integrated data across a patient's entire treatment journey in order to better understand physician and patient behavior and to optimize the entire care pathway. Quality data in health care can be leveraged by different stakeholders and improve medical treatment for patients overall. Key areas for potential data-driven improvements include:

- Identification and targeting of unmet medical needs: ranging from identification of under-treated populations in Japan through to optimizing trial design.
- Study the benefits of health care options: including the benefits of different treatment practices or technologies based on a range of patient-reported outcomes and acceleration of detection and response to safety issues.
- Manage delivery: including optimizing supply chain operations, improving care coordination and utilization, improving adherence, reduction of waste¹⁴ and optimization of procurement.

Recommendation

To achieve this vision, we believe the government should integrate the National Database (e.g. MID-NET) and similar large-scale medical information databases utilizing ICT (Information and Communication Technology). We recommend that the government should set a goal for the entire population to have electronic medical records and all hospitals and physicians to utilize digitized health data. The integrated database should include information covering a patient's entire treatment journey so that health care is tailored to the needs of each patient while providing access to de-identified data to qualified stakeholders in industry, government, and academia. Safeguards should be put in place to ensure patient privacy, protection of commercially sensitive information including intellectual property, and responsible use of the database, following global standards.

Our Contribution

The innovative industry has been supporting the PMDA's MIHARI project and MID-NET, actively contributes to government discussions on IT infrastructure and has a common view with the government regarding the future system architecture. We support strong protection for personal data and would be willing to work with the government to ensure consistency with the best international privacy standards.

Utilizing a well-designed, evidence-based value assessment framework broadly across health care services, including new technology, to support well-informed, patient-centered health care.

Industry supports the use of sound evidence for informed decision-making in health care and recognizes the interest of the government in adopting Health Technology Assessment (HTA) for Japan.

HTA is a complex process and at present there is considerable diversity in how countries have implemented HTA. Most HTA systems have shortcomings in recognizing value or can lack objectivity due to focusing overly on cost-containment. Such issues can lead to delays in patient access to needed medicines and misalignment between the HTA and overall health system goals. Many countries are evolving their systems in response to shortcomings, which may help Japan to avoid the unintended consequences of a new system as some problems take time to identify.

Overseas experience has demonstrated that critical elements to developing a quality HTA framework include (i) development of a sound process that has clear data requirements, methodology and decision rationale; (ii) inclusiveness of patient and clinician input; (iii) a system-wide perspective through examination of the full range of evidence and broad outcomes; and (iv) that places value on the continued step-wise nature of scientific and medical progress.

Recommendation

To achieve this vision, we recommend that Japan continue to develop its approach to HTA to ensure that the evaluation is patient-centered and ensures that incentives remain for needed therapies. In order to achieve a high-quality, evidence-based outcome that is predictable, fair and transparent, we recommend that value assessment should deliver reliable, relevant information using rigorous methods that rely on the full range of evidence.

Our Contribution

The innovative industry supports evidence-based decision-making that is designed to ensure that patients receive the most appropriate treatments to meet their needs. Industry has experience with many different approaches to HTA and is willing to work with the government in designing an appropriate HTA system for Japan that aligns with the current pricing system while avoiding many of the unintended problems that have occurred in HTA systems elsewhere.

Including patients, industry, providers and government in early and inclusive dialogue to enable comprehensive evaluation of a therapy's value.

The understanding of the value that a given innovative technology provides can vary considerably across stakeholders due to differences in perspective, including the relative weighting of clinical, social, and economic factors. Therefore, it is crucial to involve broad stakeholder input, especially from clinical experts, patients and the manufacturer.

We believe that the evaluation of a therapy's value needs to be patient-centered, which would require substantive patient input. In order to achieve patient-centered care, health care systems should identify and promote health technologies that are of value to patients, and allow for patient participation in the evaluation process—including a permanent role of patients in decision-making. Many countries are already adopting this approach.

Furthermore, biopharmaceutical developers need to understand what authorities expect in terms of therapeutic added benefit and what benefit they judge worth paying for—this will require dialogue between industry and authorities prior to marketing authorization. Dialogue should focus on determining benefits that are particularly relevant to patients and health care providers.

Recommendation

To achieve this vision, we recommend that the government meaningfully include broad stakeholder input into all phases of technology valuation. We believe that the government should consider how to support training patients and related organizations on how to provide relevant and objective input in the health care decision-making process. We suggest further platforms for regular policy dialogue between all stakeholders as equal partners. In addition, we recommend establishment of an early advice process following the successful models used in other countries.

Our Contribution

The innovative industry helps to support patient-centered inputs through clinical assessments (PROs, etc.) and via supporting initiatives to enable patient groups to provide their non-clinical experiences in an unbiased way.

NOTES

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7. Endo et al., 2015, "Returning to work after sick leave due to cancer: a 365-day cohort study of Japanese cancer survivors," Journal of Cancer Survivorship. Note: Return to work includes full-time and part-time work.
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13. OECD Reviews of Health Care Quality: Japan 2015.
14. Here 'waste' means wasteful medical expenditure and can result from non-adherence, over prescription, prescription error. Refer: National Institute for Research Advancement, 2015, "Towards fully-fledged reform of Japan's medical care system, My Vision."

ABOUT PhRMA

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the United States' leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested more than \$600 billion in the search for new treatments and cures, including an estimated \$65.5 billion in 2016 alone.

ABOUT PhRMA in Japan

Since its opening in January 1987, PhRMA's Japan office has actively developed various activities on behalf of its member companies in Japan. We promote activities focusing on direct dialogue with all concerned parties such as administrative officials, medical policy officers, doctors and other medical staff, media parties and patient organizations. PhRMA cooperates with the Japan Pharmaceutical Federation, the Japan Pharmaceutical Industry Association, and the European Pharmaceutical Federation to develop activities.

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