THE ASIA GROUP

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Japan's Drug Innovation Incentive Policies: Policy Challenges Undermine Desired Goals

Key Takeaways

- The Japanese government is actively working to restore drug discovery capabilities, aiming to create a revitalized ecosystem that can contribute to domestic and global drug development.
- However, these efforts continue to be undermined by remaining constraints on Japan's rewards for innovation in its drug pricing system – even for novel drugs in key areas like rare diseases and pediatrics, where Japan clearly wants more research and development and faster deployment of innovative remedies.
- The Asia Group (TAG) assesses that strict **cost disclosure requirements**, especially the "zero co-factor" rule under the cost-based price calculation method, directly undermine the government's goal of bringing innovative new pharmaceutical products to the Japanese market, including the targets laid out in the Japanese government's five-year plan for the development and approval of pediatric and rare disease drugs.
- The Japanese government **should consider either adjustments to these rules or introducing an entirely new way of pricing and rewarding innovative medicines** to adequately reflect these products' value at launch. Such changes will facilitate innovative medicines' faster entry into Japan, ultimately benefiting patients and contributing to the revitalization of Japan's drug innovation ecosystem.

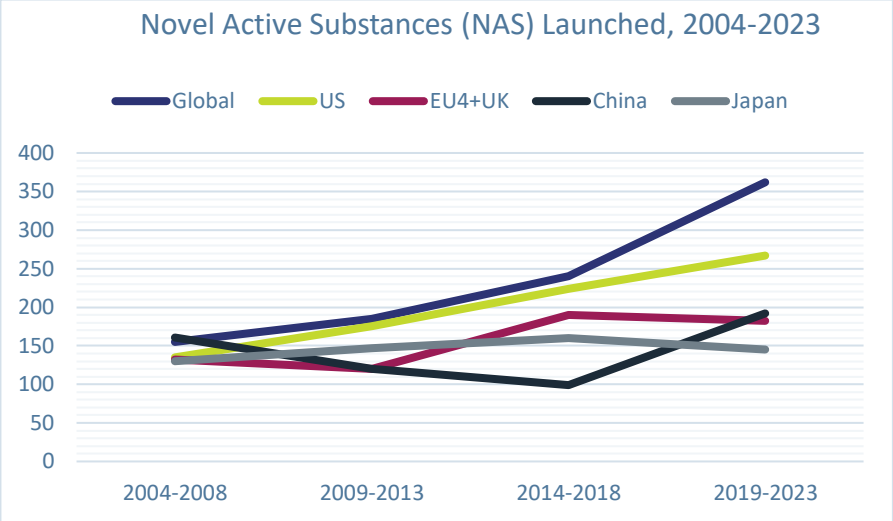
Japan's Lagging Drug Discovery in Focus

Japan remains a key market for many pharmaceutical companies, despite a complex regulatory environment. It is the third largest market behind the United States and European Union, worth about USD 88 billion in 2023 and projected to grow to about USD 91.94 billion by 2029. Despite this projected growth, companies are increasingly considering whether to delay the launch of new products in Japan, due to years of downward pricing pressure coupled with strict regulatory hurdles.

Market reassessment by pharmaceutical companies led to a reemergence of Japan's drug lag problem. That problem was thought to have been overcome in the 2010s, but now we again see a weakening of Japan's drug development ecosystem.

Data shows that Japan is now clearly lagging its competitors in drug discovery. For example, Figure 1 shows the number of novel active substances (NAS) launched by major markets, with Japan having only launched 20 NAS in 2023, the lowest since 2014 and lagging the United States, European Union, and China.

Figure 1: IQVIA Novel Active Substances Analysis



Source: IQVIA

The Japanese government recognizes the need to reform its pharmaceutical policies to better attract innovative drug launches and spur momentum in drug discovery. Legislators, the Ministry of Health, Labor, and Welfare (MHLW), and other critical stakeholders engaged in energetic discussions during 2023 to address the regulations that negatively impact both established pharmaceutical firms and innovative startups, with a goal of reinvigorating the entire system.

These discussions realized positive, long-sought changes in the FY2024 policy reform. Japan's renewed approach to dialogue and transparency among industry stakeholders on issues like regulatory and pricing challenges, investment, research and development (R&D), and the cultivation of human capital, has been a significant and welcome step in reinvigorating the market. However, it will take years to see the real impact of the FY2024 reforms to solve the drug lag problem.

At the same time, additional reforms are needed for the pharmaceutical industry ecosystem to recover from years of negative drug price revisions. The Japanese government can build on the FY2024 reforms with additional near-term measures to help move recovery of the ecosystem in a positive direction.

Put simply, as Japan aims to develop its own innovative drug discovery ecosystem and model it after clusters in Boston, Massachusetts, and San Diego, California, it should now assertively identify and address outstanding challenges that create barriers and disadvantages for innovative companies.

In this analysis, The Asia Group will demonstrate that the **challenges that innovative drugs face under the cost-based pricing calculation method continue to burden innovative companies, ultimately undermining government efforts to create a vibrant drug discovery ecosystem.**

Prioritizing Japan's Pharmaceutical Innovation

The FY2024 drug pricing reforms brought the most positive changes to the industry's policy and regulatory landscape seen since 2016, when the government shifted focus toward tougher measures to limit spending on pharmaceuticals. Discussions leading up to the FY2024 reform appeared to be based on the government realizing – especially after the COVID pandemic – that Japan needs a more innovation-friendly stance to rectify the increasing drug lag and drug loss problem.

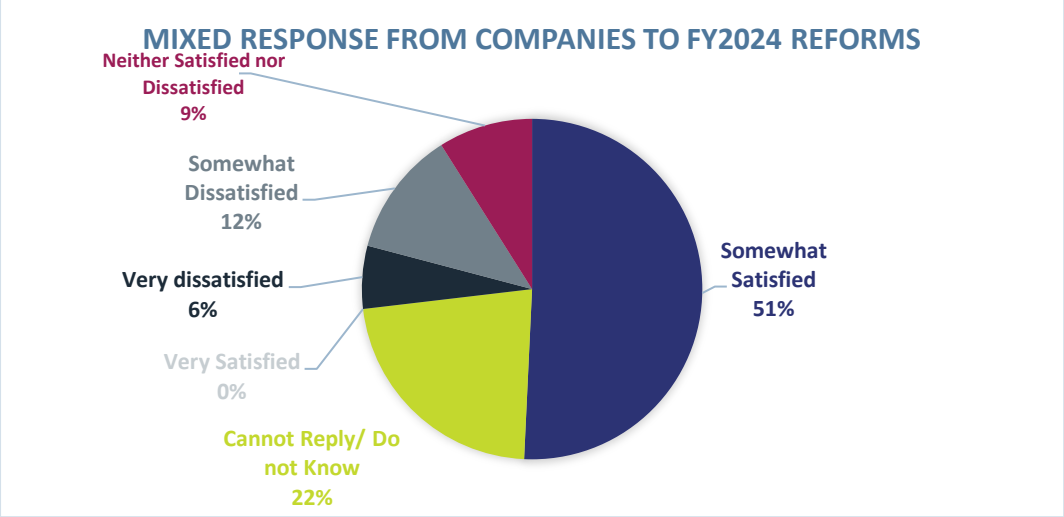
Long sought-after reforms in FY2024 included changes to the price maintenance premium (PMP) and adjustments to the market-expansion re-repricing rule, as well as the addition of new premiums for early launches. All these measures were a welcome reprieve from consecutive years of cost-cutting policies. Moreover, these reforms have been seen as the first step in revitalizing Japan's drug discovery ecosystem, which had begun to lag its global counterparts in innovativeness.

COMPANIES' VIEWS OF THE FY2024 REFORMS

Overall, private companies have welcomed the FY2024 reform measures. A March *Jiho* survey, conducted shortly after the reforms' final details were confirmed, revealed that 51 percent of the 84 companies polled were somewhat satisfied with the reforms. In a separate survey on March 5, a majority of 61 firms who responded strongly supported the updates to the PMP, new evaluation items for the usefulness premium, and the addition of the new early launch premium.

While there was clear support for the FY2024 reforms, surveyed companies also expressed disappointment that they did not address major outstanding challenges such as the zero-co factor rule or propose any alternative evaluation method for setting prices for products without using inappropriate comparators.

Figure 2: Mixed Response from Companies to FY2024 Reforms (March 2024)

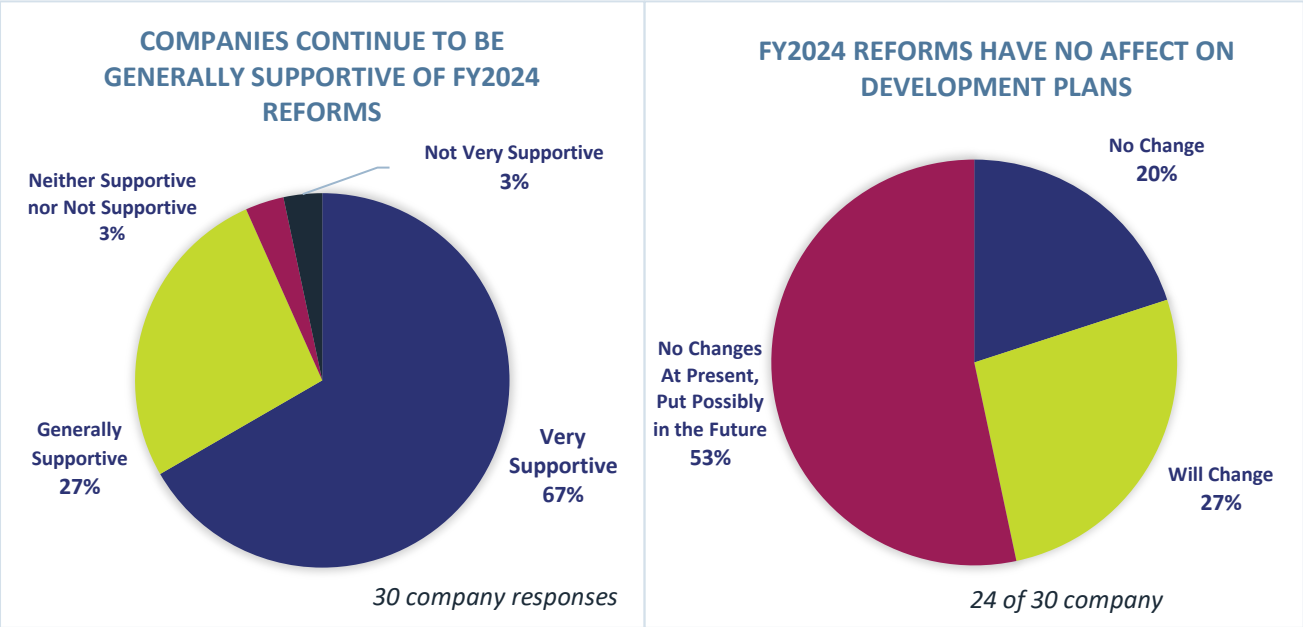


Source: Jiho Survey, March 2024

An August 2024 survey of 30 companies by the Japan Pharmaceutical Manufacturers Association (JPMA), the Pharmaceutical Research and Manufacturers of America (PhRMA), and the European Federation of Pharmaceutical Industries and Associations (EFPIA) also showed strong interest in further reform. Responding companies viewed the FY2024 changes positively but indicated skepticism that they will produce the kind of immediate-term results – including changes in company behavior – expected by government officials.

Of the 30 companies surveyed, 18 responded that the level of priority they place on Japan as an investment destination "could increase" due to the FY2024 reforms, while 12 said it "has not changed." Furthermore, eight companies said that the reforms have positively affected their development plans in Japan, while 16 responded that they have "not at the moment, but maybe in the near future."

Figure 3: Joint Survey Company Responses to FY2024 Reforms (August 2024)



Source: JPMA, PhRMA, EFPIA Joint Survey, August

Given that the reforms were implemented starting in April 2024, the government needs to have reasonable expectations for their sustained impact on company decision-making after years of more adverse policies. It appears that further positive changes are needed to incentivize company decisions to launch in Japan and achieve broader government objectives.

SHIFTING GOVERNMENT PRIORITIES

After the 2024 reforms were implemented, the Japanese government now appears to have shifted its primary focus from pricing reform to supporting innovation and growth in the industry, especially among startups. This support has come from the highest levels of government, demonstrating an unprecedented commitment to addressing the challenges identified by industry leaders.

Officials have driven forward substantive, high-level dialogue on these challenges, including through a Cabinet-level council formerly led by Deputy Chief Cabinet Secretary Hideki Murai as chair and deputy chair Ichiro Kamoshita as vice chair (the "Council of the Concept for Early Prevalence of the Novel Drugs to Patients by Improving Drug Discovery Capabilities"). There was also a more expansive focus on innovation promotion in the 2024 Basic Policy on Economic and Fiscal Management and Reform (*Honebuto*), compared to previous years.

The Ministry of Health, Labor, and Welfare and former MHLW Minister Keizo Takemi have driven forward much of the recent reform efforts, as well as initiatives to revitalize Japan's pharmaceutical ecosystem, and expanded engagement with the industry. Minister Takemi's work has positioned the pharmaceutical sector as core to the Japanese economy and rallied support for its growth from the highest levels of the government, culminating in the July 30 "Gate Opening Summit for Innovative Drug Discovery" hosted by former Prime Minister Fumio Kishida. The event showcased the Kishida government's direct backing of the industry in terms of innovation promotion and investment in Japan.

Kishida pledged that "by positioning the pharmaceutical industry as a growth and core sector, we will secure the budget necessary to develop a system for attracting further private sector investments and work all-out as the government to make tangible progress on the proposal made by the [Murai and Kamoshita] council." The government will leverage a five-year plan to promote drug discovery, key targets presented at the Summit, and guidance from the private-public dialogue to be launched in 2025 to achieve its goal of developing the drug discovery ecosystem.

FURTHER PRICING DIALOGUE NEEDED

These commitments reflect an acknowledgment that Japan needs a dynamic and innovative pharmaceutical ecosystem to ensure the health and well-being of its population and see the economic benefits of a globally competitive pharmaceutical sector. However, these efforts will be undermined if Japan's pricing system cannot be reformed to appropriately award innovation.

Despite the progress made, however, punitive pricing policies continue to impact companies' abilities and decisions to launch products – especially novel products – in the market. These problems could perpetuate Japan's drug loss and drug lag trends.

Self-Contradictory Innovation Incentives

Japan's efforts to revitalize its drug discovery ecosystem are centered around the discovery and commercialization of innovative products – especially in pediatric and rare disease medicines, which have been identified as major drug lag and loss areas.

The first pillar of government's newly released five-year plan indicates specific targets under its goal of "promptly deliver[ing] the latest medicines to people." The government aims to promote development in several therapy areas between FY2024 and FY2028, including: 1) 50 development plans to be formulated for pediatric medicines, and 2) 150 orphan drug approvals.

However, most innovative and novel drugs (including many pediatric and orphan drugs) are **priced by the cost-based method**. This method's current rules will continue to impede Japan's efforts if changes are not made to the mechanism.

COST-BASED PRICING METHOD

The cost-based method – also known as the cost calculation method – is used to determine the prices of products when no comparator drugs exist in the Japanese market at the time of launch. The method requires companies to disclose information regarding the costs of manufacturing, R&D, sales, operations, and distribution, as well as its estimated consumption tax. Premiums are then added based on certain criteria including innovativeness, usefulness, marketability, and designation for *sakigake* review and, as of April 2024, an early launch criterion.

The cost-based method has some useful aspects, and some important drawbacks.

Figure 4: Pros and Cons of the Cost-Based Method

	PROS	CONS
Cost-Based Method: Zero Co-Factor Rule	• The system encourages greater transparency in overall costs submitted by the manufacturer aiming to secure premiums. • A graduated scoring system allows for some variability in cost disclosure.	• In many cases, unsatisfactory cost disclosure rates are unavoidable due to the difficulty of determining the cost of materials within complex supply chains and operations. • The zero-co factor rule completely cancels out premiums awarded for innovation in pricing, ***including new rewards introduced in the FY2024 reform.*** • The loss of approved premiums affects startup companies attempting to enter the Japanese market the most.

Overall Challenges: Novel products reaching the Japanese market face common challenges with the cost-based method, as it is the only pricing method available for innovative drugs. The method calculations do not, for example, take into account the costs of drug discovery activities conducted overseas, such as R&D costs, clinical trial costs, and the cost of stepwise development cycles outside of Japan that failed but provided useful information. Therefore, the final price does not accurately reflect true total costs invested in new product development. The complexities of supply chains, and of defining costs associated with development in Japan at all stages of a product's lifecycle – from development to commercialization – make the use of this pricing method a challenge for companies and regulators alike.

Companies have in the past also referenced the prices of their products overseas (transfer prices). However, MHLW officials have argued that a lack of visibility into pricing methods overseas makes it difficult to use transfer prices to justify the application of evaluated and approved premiums.

"Zero Co-Factor Rule": In FY2018, a new rule to encourage transparency was introduced, applying a co-factor of 1, 0.8 or 0.2 multiplier based on cost disclosure rates in order to reduce premiums granted for innovation in cases of low cost transparency. In an attempt to further improve price transparency and capture the most appropriate pricing level, in FY2022 the lowest co-factor was **further reduced from 0.2 to zero** for cost disclosure ratios of less than 50 percent.

While premiums could be slashed up to 80 percent under the previous framework, partial rewards remained for innovative products. However, since FY2022, the co-factor has canceled out all premiums granted to innovative products if the minimum cost disclosure is not met, even if the premiums were recognized via the successful and well-received *sakigake* program (for products developed in Japan) or under the FY2024 reforms (including the early introduction premium).

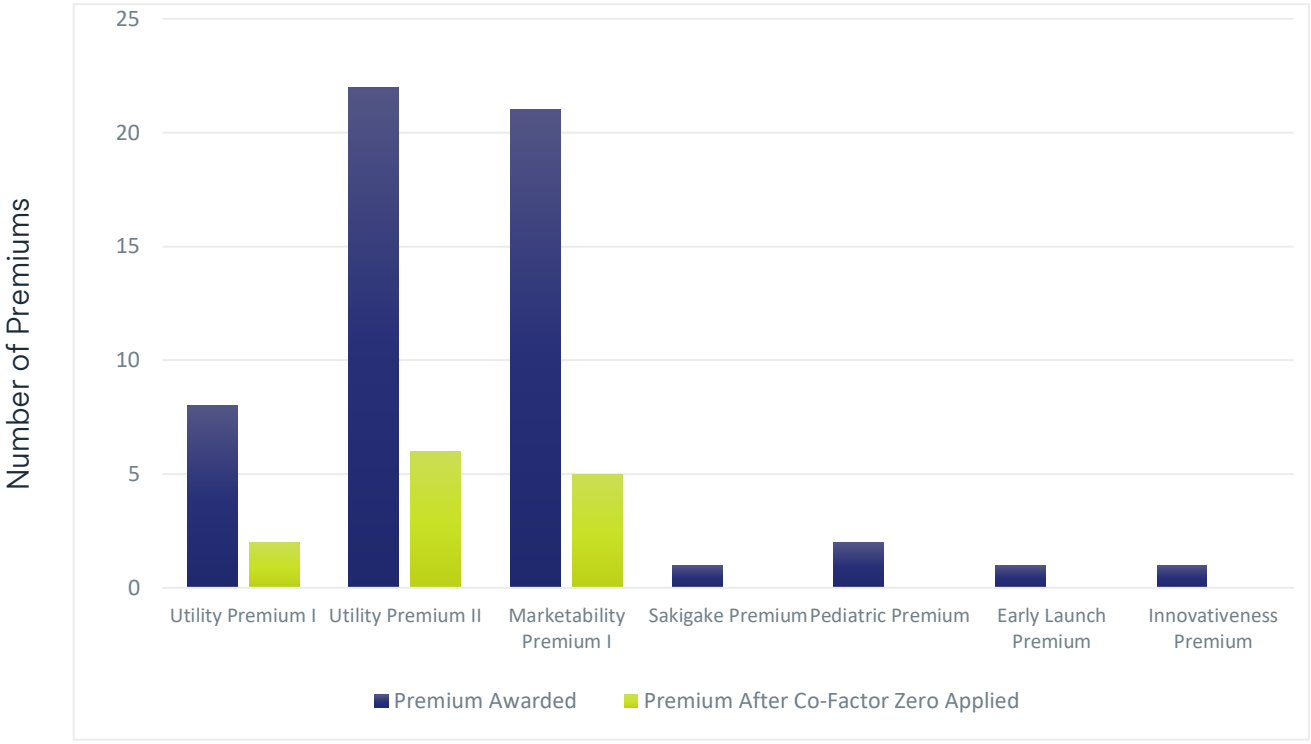
The 2022 implementation of the zero-co factor rule has so far been applied in the case of 23 products.

- From April to November 2022, 13 products were priced using the cost-based method, of which 10 products were assessed as eligible for launch premiums ranging from 5 to 30 percent (Figure 5). However, the zero co-factor rule was applied to all ten of those products, eliminating all innovation premiums. This included Sanofi's Xenpozyme, which saw the co-factor cancel out three types of premiums it was eligible for, including the *sakigake* premium.
- In 2023, there were ten drugs that gained a launch premium, and eight of these lost their premiums due to the rule.
- So far in 2024, 12 drugs have been priced by the cost-based method. Four received full premiums and three received 60 percent of their total premiums,

but five have been affected by the zero-co factor rule. These included products from U.S.-based Alexion Pharmaceutical and Japan-headquartered Nobelpharma. The former saw the co-factor nullify the benefit of the new FY2024 early launch premium, while the latter lost the rare innovation premium and breakthrough premium (awarded for the first time in six years).

As noted above, the most notable cases since the implementation of the zero co-factor rule include Sanofi's Xenpozyme, which saw the co-factor wipe out its sakigake premium upon listing in 2022. This was a significant upset for the industry considering the additional requirements companies take to gain the *sakigake* designation and reward. Nobelpharma's Sargmalin losing its rewards was also particularly noteworthy given that it was the first Japanese company to receive the latter premium in six years, and only the sixth to receive it at any time, but it still saw its value wiped away. Alexion Pharmaceutical's Voydeya was the first product to receive the new FY2024 premium after the reforms were implemented but subsequently lost it due to the co-factor rule.

Figure 5: Premiums Awarded Under Cost-Based Pricing Method (2022-2024)



Source: MHLW Drug Pricing Lists

The disappearance of these premiums suggests that the current pricing system undermines the efficacy of the FY2024 reforms, the government's stated desire to promote growth and innovation in the industry, and the purpose of rewarding companies that are focusing on developing rare disease and pediatric products – a core focus of the government. The rule has simultaneously had little success in

achieving transparency, as the number of companies willing or able to comply remains low.

The Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ) has pointed to frequent cases where low disclosure rates are inevitable because of difficulties in obtaining detailed cost information on a wide variety of business transactions, manufacturing and operational costs, and import processes.

At a December 2022 meeting of MHLW's expert panel on pharmaceutical reform, Takuma Sugahara, a professor of economics at Hosei University, argued that the current pricing mechanism does not fit the current state of the industry due to the complexity of the pharmaceutical value chains. According to *Pharma Japan*, industry representatives have expressed concern that the rule "would completely prevent innovation from being reflected in NHI prices and interfere with efforts to increase disclosure."

Most recently, officials within MHLW and the Central Social Insurance Medical Council (Chuikyo) are taking a closer look at the rule given its impact on innovation premiums.

It is understandable that officials want to incentivize cost transparency, but continuing to use this method to penalize companies for factors often out of their control will only hold back Japan's push to bring more innovative medicines to the market. This recognition is leading officials to consider how the rule might be reformed.

Conclusion and Recommendations

The Asia Group assesses that the cost-based method and the zero-co factor rule will continue to impede the Japanese government's efforts to develop a vibrant ecosystem and attract development of critical medicines in areas of unmet needs. The zero co-factor rule is not actually increasing transparency, given the reality of complex supply chains, and instead is penalizing companies for their integration into the global system.

Especially for startups looking to launch in Japan, the cost-based pricing method creates a disincentivizing and penalizing environment that makes market entry even more difficult for companies that cannot afford to be commercially unsuccessful in case of early product introduction into Japan. Such companies must be successful in Japan to enable further innovation and launches in the market. If this pattern continues, Japan will fall further in the global rankings as companies prioritize launching new medicines and treatments elsewhere.

The Asia Group recommends the following menu of actions – with options for immediate change/immediate impact and long-term change/long-term impact -

for the Japanese government to consider that can address issues linked to the cost-based method has caused and to create a more inviting and rewarding ecosystem.

RECOMMENDATIONS:	
IMMEDIATE CHANGE / IMMEDIATE IMPACT	**LONG-TERM CHANGE / LONG-TERM IMPACT**
• Fully eliminate the co-efficient system to ensure that products receive the entire premium amount for which they are eligible. • Broaden the scope of products that can be priced under comparator methods instead of the cost-based method. • For products priced under the cost-based method, immediately start to exempt products from the cost transparency rules if those products qualify for innovation premiums.	• Set a target date to develop a new pricing method to replace the cost-based method for the pricing of products based on international research and development. ○ Such a method should take into account important non-Japan cost factors such as R&D costs, clinical trial costs, and the cost of failed but informative and iterative development cycles outside of Japan.

Such changes, if implemented, would not cost Japan heavily in terms of overall health expenditure. But these changes would greatly ease the process and rate of success for market entry by new players. This will in turn stimulate growth and foster a more dynamic innovation ecosystem for Japanese healthcare more generally.