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Why many global drugs never reach Japan

By Tamra Sami, Staff Writer

For years, Japan's "drug lag" was shorthand for slow regulatory reviews and delayed approvals compared with the U.S. and Europe. But even as regulatory timelines have shortened, review capacity has expanded and international alignment has improved, Japanese patients still face gaps in access to innovative drugs.

Mayumi Hasegawa, vice president of drug development solutions, Certara Consulting

"When we talk about drug lag in Japan today, it is less about slow regulatory review and more about whether drugs ever enter development or submission in Japan at all," Mayumi Hasegawa, vice president of drug development solutions at Certara Consulting, told *BioWorld*.

For example, the U.S. FDA and the EMA approved 243 new drugs between 2016 and 2020, but about 70% of these drugs are not available in Japan.

As previously reported by *BioWorld*, among the top 300 bestselling drugs in 1991, 53 originated in Japan, but that number dropped to 24 in 2021 and is expected to drop further by 2026.

There is no disputing the scientific fundamentals in Japan, said 1004 Venture Partners General Partner Soyoung Park during the 2025 Bio Japan conference, pointing to the Nobel Prize in Physiology or Medicine awarded to Shimon Sakaguchi for his discovery of a subtype of CD4-expressing T cells that affect the immune response.

"That strength is beyond top notch, [but] now it's time to think about business. We want to see how you can bring this science to the society, to the patient," Park said.

Increasingly, drugs approved in Western markets are never developed, submitted or launched in Japan, creating an access gap even when approvals elsewhere proceed smoothly, said Hasegawa, who previously held roles at Bristol Myers Squibb Co. (BMS) as senior investigator for Pharmacometrics and Clinical Pharmacology and a leadership role in the Japan Medical and Development team.

That shift reframes drug lag not as a downstream regulatory bottleneck, but as an upstream strategic decision. Choices around trial design, data generation and global development strategies are often made years before a filing reaches Japan's Pharmaceuticals and Medical Devices Agency (PMDA). Those early decisions, she said, frequently determine whether Japanese patients will ever see a therapy.

Historically, Japan's drug lag stemmed from requirements for local clinical data, expectations for additional studies in Japanese patients, pricing pressures and the absence of a local development footprint for many multinational companies. Together, these barriers discouraged companies from including Japan in global drug development programs.

Over time, many of those hurdles have eased. Regulatory processes have become more streamlined, English documentation is increasingly accepted, and participation in international clinical trials has expanded. The PMDA has strengthened its review capacity, added reviewers and invested in digital tools.

"These steps have helped improve efficiency during the review phase," Hasegawa said, but faster reviews only address part of the problem.

Local challenges remain

"Challenges remain, particularly for companies without a local footprint or for therapies targeting rare diseases or pediatric

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populations where small patient numbers and development costs still influence decision making," she said, noting that many drug loss cases occur because development programs stall earlier, and formal regulatory reviews are not initiated.

Japan's PMDA has actively encouraged early dialogue with sponsors, and quantitative approaches such as model-informed drug development (MIDD) are increasingly embedded in Japanese submissions. These tools can help address uncertainty and reduce knowledge gaps without requiring large, Japan-specific trials.

Even so, applying global data to Japan-specific contexts, especially for small populations or novel modalities, continues to be an area of uncertainty, and sponsors often struggle to predict how their evidence packages will be assessed locally, which can discourage early inclusion.

Japan has made a concerted push to attract first-in-human (FIH) studies through policy initiatives and investing in infrastructure. These efforts signal a desire to participate earlier in development rather than waiting for late-stage data generated elsewhere.

But whether this "positive momentum" leads to lasting change depends on how easily sponsors can integrate Japan into early phase strategies, Hasegawa said. Tools that support dose selection, safety assessment and cross-population understanding can make early inclusion more practical, but uncertainty remains a deterrent.

"Early phase work requires confidence that development decisions made today will not create barriers later," she said, and concerns around data expectations, patient recruitment and pricing still weigh heavily on those calculations.

For rare and pediatric indications, barriers are even higher. Small patient populations, ethical considerations and recruitment challenges make conventional trial designs difficult. Without alternative evidence strategies, sponsors may deprioritize Japan despite clear unmet medical need.

Japan's clinical trial networks have improved recruitment in areas such as pediatrics and oncology, but gaps persist. Digital tools are not yet widely implemented at local clinics, and universal health insurance also shapes patient behavior, with Japanese patients (particularly parents) reluctant to participate in trials when standard care is already accessible.

Programs such as the Sakigake designation and the conditional early approval (CEA) pathway were designed to speed access to innovative therapies, and although they signal regulatory flexibility and a willingness to adapt pathways for high unmet needs, uptake has been lower than expected. Hasegawa pointed to the need for clearer, more predictable development strategies that align regulatory, clinical and commercial considerations. Greater clarity around evidence expectations and broader use of quantitative methods could make these pathways more accessible.

Regenerative medicine offers blueprint

Japan's experience with regenerative medicine offers a blueprint for reducing drug lag in other areas. Flexible frameworks, early engagement, adaptive evidence strategies, real-world data and openness to alternative endpoints have all helped accelerate access while maintaining scientific rigor. Those principles are equally relevant to oncology, rare diseases, and emerging modalities.

Global companies, however, still tend to prioritize the U.S. and Europe, with Japan often treated as a second-wave market, especially by smaller firms without a local presence. Changing that perception will require making early inclusion less burdensome and less risky.

When asked to name the most impactful reforms, Hasegawa highlighted earlier integration of Japan into global development programs, broader acceptance of model-informed approaches when data are limited, and closer coordination between regulatory approval and reimbursement.

Even when PMDA approval is efficient, reimbursement decisions can introduce additional delays: "Approval does not always translate into timely patient access," Hasegawa said, arguing that drug lag should now be viewed as a system-level issue rather than a purely regulatory one. Better coordination across regulatory and access pathways will be essential to prevent drug loss.

As previously reported by *BioWorld*, Japan's pricing scheme has gotten more complicated. Traditionally, Japan has instituted biennial price cuts that were based on the difference between reimbursement prices and acquisition prices. That earlier biennial pricing policy was more mechanical, and companies came to expect their drugs' prices would be reduced by about 2% every two years. But that changed with the approval of Gilead Sciences Inc.'s hepatitis C (HCV) drug, Sovaldi (sofosbuvir), which put considerable pressure on the country's National Health Insurance (NHI) despite the potential of the drug to cure HCV.

As a result, Japan introduced the ultra-expensive drug repricing rule in early 2016, which targeted drugs that far exceeded the revenue forecasts provided by manufacturers at the time of pricing.