The JAPAC Drug Development Market

Understanding the regulatory landscape and cultural nuances



There are specific nuances that emerging biotechs and biopharmas (EBPs) need to take note of when navigating the rapidly expanding JAPAC drug development landscape. In this article, we will delve deeper into the regulatory landscape and trends in JAPAC and how to effectively navigate the ever-changing landscape.

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Overview of the JAPAC regulatory landscape

Regulatory authorities are critical to the development and commercialisation of drugs as they govern the safety, efficacy, and quality of pharmaceutical products. For emerging biotech and biopharma companies (EBPs), working with regulatory authorities is crucial to ensure that their products can be brought to market ▶

efficiently and effectively.

The Japan and Asia-Pacific (JAPAC) drug development market is rapidly expanding, with EBPs accounting for around 75 per cent of the total clinical trial volume in the Asia-Pacific region in 2020. However, successful navigation of the JAPAC market requires a unique understanding of its regulatory nuances and safety strategies. In JAPAC countries, multilingual language proficiency is a necessity due to the processing of adverse events in a bilingual database. Additionally, individual case safety reports and other forms must be submitted in the local language throughout a product's lifecycle. There are also specific pharmacovigilance reporting requirements that demand full compliance.

Before trying to navigate the JAPAC regulatory space effectively and efficiently, it is also important to understand how the regulatory trends have evolved.

Priorities of regulatory authorities in this rapidly evolving regulatory landscape

Regulatory authorities in JAPAC are faced with various drug development priorities with the increasing demand for innovative therapies and treatments. They need to develop new guidelines and standards quickly to address an ever-evolving drug development landscape. Hence, the following will be crucial for the development of new drugs:

1. Promote innovation while prioritising patient safety

Regulatory authorities have introduced new guidelines to streamline the regulatory process for EBPs. These guidelines encourage innovation by allowing for flexible and adaptive trial designs, where companies can modify their clinical trials as they evolve, based on new information or feedback from regulators. This can also speed up the drug development process and reduce costs. For instance, Singapore's Health Science Authority (HSA) has established a regulatory sandbox programme that allows companies to test new healthcare products and services in a controlled environment. This helps to identify potential risks and benefits before the products are released to the market. The HSA also offers a priority review scheme for medical devices and drugs that address unmet medical needs.

Such programmes encourage innovation and provide faster pathways to market, while ensuring that rigorous testing and evaluation criteria are met, bringing new and innovative treatments to patients in a timely and safe manner.

2. Refine guidelines to ensure the quality and safety of pharmaceutical products

This involves establishing standards and guidelines for the manufacturing, testing, and distribution of drugs, as well as pharmacovigilance, which focuses on monitoring, evaluating, and preventing adverse effects of drugs. The Pharmaceuticals and Medical Devices Agency (PMDA) and National Medical Products Administration (NMPA), regulatory bodies that oversee the safety, efficacy, and quality of pharmaceuticals and medical devices in Japan and China, respectively, have introduced new guidelines for pharmacovigilance to ensure patient safety.

The PMDA's guidelines emphasise the importance of risk management plans and post-marketing surveillance, while the NMPA's regulations require companies to report adverse events within 24 hours, supporting the establishment of pharmacovigilance standards in drug development and post-marketing surveillance.

> To support industries driving constant innovation and new technology in new drug development, health authorities in JAPAC need to monitor/adapt new global regulatory standards and requirements to address local specific needs to stay aligned with evolving global drug development landscape.

3. Adapt to the post-pandemic landscape

a. Misinformation

Misinformation is a growing concern across industries, and its significant impact has been witnessed since the start of the COVID-19 pandemic. Regulatory bodies in JAPAC recognised the need to tackle this and have been focusing on strengthening public communications. Regulatory bodies, such as HSA, PMDA and South Korea's Ministry of Food and Drug Safety (MFDS), monitor advertising and promotional content to ensure that information is truthful and accurate. In addition, these regulatory bodies are quick to address concerns from healthcare professionals and the public about drugs and medical devices. They have also been collaborating with other organisations to promote accurate information.

Education and awareness campaigns can also help to counter misinformation in drug development. For instance, the PMDA has launched campaigns to raise awareness of the risks of over-the-counter painkillers and encourage proper disposal of unused medications. It also shares educational content with healthcare professionals on topics such as drug interactions and adverse events.

b. Emphasis on Patient-Centred Drug Development (PCDD)

Drug development is traditionally focused on developing safe and effective treatments for patients. However, there has been a growing emphasis on proactive patient involvement during the drug development process to meet patients' needs.

With this shift, new guidelines and regulations are being developed to promote patient participation in clinical trials and other aspects of drug development. Industry organisations, such as the International Society for Medical Publication Professionals (ISMPP), have created guidelines to ensure that patients are provided with accurate and reliable information about the drugs.

In JAPAC, regulatory authorities such as the NMPA, HSA, PMDA and MFDS dictate that patients must be fully informed about the purpose of the trial, the risks and benefits of participation, and their right to withdraw at any time. The guidelines also require patients to be given adequate time to consider their participation and that they provide informed consent before participating. The guidelines also encourage the recruitment of a diverse patient population, including women, minorities, and elderly patients, per Good Clinical Practice (GCP) standards.

c. Increased adoption of virtual and digital approaches

The pandemic has pushed the biopharmaceutical industry to adapt to new ways of working, with the biggest shift being the adoption of virtual and digital technologies in clinical trials. This has resulted in the development of new regulations and guidelines to ensure patient safety and data integrity. PMDA, NMPA, MFDS, Australia's Therapeutic Goods Administration (TGA) and HSA have issued guidance to ensure data quality and integrity when using electronic data capture and other digital technologies during virtual and remote clinical trials.

As the drug development landscape in JAPAC mirrors the rapid changes in global trends, regulatory authorities have had to pivot quickly to ensure that patients have access to safe and effective healthcare products, while also promoting innovation in the EBP industries.

The adoption of ICH guidelines in China and evolution of ICH guidelines in Japan

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an international non-profit association, brings together regulatory authorities and the pharmaceutical industry to coordinate scientific and technical aspects of drug registration to ensure the safety, efficacy, and quality of pharmaceutical products. Japan is one of the founding regulatory members, while South Korea, China and Singapore are members of the ICH.

> The adoption of ICH guidelines has helped China and Japan to join global clinical program more actively minimising drug lag time and eventually accelerating the launch of innovative drugs locally. It is paramount for regulatory authorities in JAPAC to explore various ways to streamline the drug registration process to help patients in need of new innovative treatments.

International collaboration through the ICH has been at the forefront of global drug development, especially in the post-pandemic era. Both China and Japan have adopted ICH guidelines, which have accelerated the launch of innovative drugs locally.

A deeper dive into the adoption of ICH guidelines in China

China entered ICH regulatory membership in 2017 with a pledge to gradually transform its regulatory science ecosystem. As of December 2023, China has implemented 62 out of 63 ICH guidelines .

The NMPA in China actively participates in the coordination and implementation of the ICH guidelines. Clinical trial design guidance, electronic data capture guidelines, inspection and auditing, and training and education are just a few examples of how the NMPA has implemented the ICH guidelines in China. The adoption of ICH guidelines has accelerated drug development growth in China and globally, promoting the alignment of technical requirements with global standards, which support:

- Multinational companies to introduce early-stage research and development into China; and
- Global drug development with new drugs that are developed by local pharmaceuticals.

The impact of ICH guideline adoption in China can be seen in the significantly reduced review and approval timelines for Investigational New Drug (IND) Application, Biologics License Applications (BLA) and New Drug Application (NDA).

IND application approvals have been shortened to 60 days from 27 months, while BLA and NDA applications have been cut from 26 months to 60 days and 12 to 18 months respectively. In addition, the time lag between China and the United States for innovative drug development was between 5 to 7 years in 2015 but is being gradually synchronised.

The adoption of the ICH guideline has therefore made it easier for sponsors to conduct clinical trials in China and seek approval for their drugs. This has led to increased investment in the country's biopharmaceutical industry, which has the potential to drive economic growth and improve public health.

Ongoing development of the evolution of ICH guidelines in Japan

The evolution of Japan's Multi-Regional Clinical Trials (MRCTs) has been significant.

In 2007, the PMDA developed a "Basic Principles on Global Clinical Trials (GCTs)" guideline that stated the requirements for conducting an MRCT in Japan. In 2012, they expanded it to offer points of consideration for countries in East Asia looking to conduct MRCT , covering jurisdictions of China, Japan, and South Korea. The "Basic Principles for Conducting Phase 1 Trials in the Japanese Population Prior to GCTs " guidance was subsequently released in 2014 to address the requirements of phase 1 clinical trials in Japan on the Japanese population. This has increased MRCTs conducted in Japan. ▶

As an ICH Rapporteur of the E17 Guideline, which provides guidance on the design, conduct, and analysis of clinical trials that are conducted in multiple regions of the world, Japan has been in a transition phase to achieve complete implementation of ICH E17 since 2018 . The E17 guideline is intended to help ensure that trials conducted are scientifically valid and ethically sound, while also taking into account the cultural and regulatory differences in different regions. The ICH E17 guideline provides recommendations on the trial design, trial conduct, data analysis and ethical considerations related to MRCTs.

An analysis done across 167 MRCTs of 130 drugs found that more than 75 per cent of MRCTs are well-considered in GCP compliance. However, there are several areas which are less adequately addressed, such as the use of relevant guidelines for disease and primary endpoint definitions, standardisation of efficacy/safety information, sample size allocation, and the training/validation on subject selection and primary endpoint.

For future MRCTs, it is recommended that the analysis strategy for consistency evaluation, including the use of pooled regions or subpopulations, is pre-specified. More clinical experiences and data will be necessary to pool Asia as a single region for efficient clinical development and appropriate consistency assessment in treatment effects.

South Korea's regulatory update

In line with other countries' efforts to speed up the regulatory process, Korea introduced the Global Innovative Product on Fast Track (GIFT) in 2020. GIFT is a supporting programme for accelerating the regulatory review of "global innovative products", aimed at facilitating the market launch of innovative products intended for life-threatening or serious diseases to ensure faster access for patients. With GIFT, the regulatory review process can be shortened by 75 per cent when compared to the standard review cycle.

Since 2020, GIFT has conducted expedited review designation on 23 products and expedited review after designation on 17 products. Anti-cancer products account for the largest portion of products designated for expedited review, followed by COVID-19 vaccines.

Navigating the regulatory landscape in JAPAC: A China case study

How can EBPs navigate the diverse regulatory landscape in JAPAC? Some of the major nuances in the JAPAC market that EBPs should be aware of include language barriers and differing regulatory guidelines. For instance, when adopting ICH guidelines in China, EBPs should note the additional requirements when conducting stability studies for formulations that are prone to phase separation, reduced viscosity, precipitation, or aggregation. Furthermore, consideration should be given to low temperature or freeze-thaw testing. Additionally, there are minor differences between Chinese Pharmacopoeia requirements and ICH Q4 (Pharmacopoeias). Chinese Pharmacopoeia places more emphasis on traditional Chinese medicine (TCM) than ICH Q4 as TCM is an important part of the healthcare system in China, and many drugs derived from TCM are regulated under the Chinese Pharmacopoeia.

Another factor to consider is the Ethnic Factors (E5) in the ICH guideline , which states that EBPs need to ensure that bridging clinical studies include Chinese population data, even if there is clinical data from outside of China as the data might prove insensitive to ethnic factors. However, products for critical diseases, rare diseases, paediatrics, and the products listed in the "Marketed overseas and urgently needed in China" are exempted. In compliance with ICH E5 3.2.2, the regulatory authorities may still request a bridging study for approval even for compounds insensitive to ethnic factors for regions with little experience with registration based on foreign clinical data.

Understanding these requirements can be challenging, but leveraging strategic tools and technology can simplify the process. Bilingual safety databases, robotic process automation, workflow management tools, and automated narrative tools are some examples that can help EBPs navigate the JAPAC regulatory landscape.

The best way forward in JAPAC

For EBPs looking to enter JPAC, they need to understand the regulatory environment, acknowledge cultural nuances when conducting preclinical and clinical studies, and prepare high-quality submissions in local languages.

They can also consider partnering with a company that has the expertise and experience to navigate the drug regulatory landscape in JAPAC. New technology could also help expedite the drug approval process, especially around data collection and submission preparations.

As the biopharmaceutical industry continues to evolve, it is essential to stay alert and understand the latest regulations and guidelines to ensure compliance and patient safety. ■

AUTHOR BIO



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