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Navigating An Ever Evolving Regulatory And Pharmacovigilance Landscape

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The growing trend toward globalization in the pharmaceutical industry, whether through offshoring of research and development or worldwide product launches, has brought numerous benefits to companies, health systems and patients. Globalization of R&D enables companies to access larger, more diverse patient populations while reducing development costs, enhancing efficiency and expanding their commercial footprint into untapped markets.

Global launch programs reduce companies' reliance on mature markets for pharmaceuticals, unlocking new sources of growth. Patients and health systems gain a wider range of innovative treatment options, whether through clinical development or at launch, in countries where these options may otherwise be limited.

Asia has been a prime beneficiary of these trends. It offers both established markets, such as Japan, with advanced regulations and a developed, globally active pharmaceutical industry, and fast-emerging territories, such as China or India, where immense populations, unmet needs and commercial potential collide with limited resources and the continuing evolution of regulatory frameworks. The Asian region also exemplifies the challenges that come with accelerated globalization of the pharmaceutical market.

Prominent among these is ensuring that drug safety and pharmacovigilance (PV) keep pace with the widening pool of ever more diverse patients exposed to new medicines through clinical trials or market entry. In reality, provisions for PV in Asia can vary substantially from market to market, whether in terms of local capacity and capabilities, or of implementing nominally harmonized international standards.

HIGHLY EVOLVED

Japan, for example, already has highly evolved pharmacovigilance procedures, partly as a by-product of its commitment to ensuring that patients have early access to innovative medicines. The need to offset conditional approvals with scrupulous real-world drug monitoring is reflected in provisions such as the Pharmaceutical and Medical Devices Agency (PMDA)'s re-evaluation scheme for launched medicines, including its requirement for marketing authorization holders (MAHs) to submit periodic safety update reports.

In India, on the other hand, successive attempts over more than 30 years to establish nationwide monitoring programs for adverse drug reactions (ADRs) have repeatedly fallen short. A rekindled Pharmacovigilance Program for India was launched in 2010[1]. Last year, the Central Drugs Standard Control Organization proposed adopting a four-year cycle for routine pharmacovigilance inspections, mirroring the risk-based procedures followed by the European Medicines Agency since 2009[2].

Somewhere between these two scenarios sits China. Recently approved revisions to the country's drug-administration law include not only support for drug innovation but also new responsibilities for MAHs, such as analyzing and reporting ADRs, post-approval studies, risk-management planning and establishing a robust pharmacovigilance system to ensure whole life-cycle safety surveillance. The amendments also include a commitment to establishing a drug-recall system in China and full traceability for marketed medicines[3].

These types of variations extend across Asia. A recent survey of pharmacovigilance agencies in 21 member countries of the Asia-Pacific Economic Cooperation (APEC) region found harmonization of laws and regulations for general PV and risk-management systems. But it also highlighted discrepancies in PV infrastructures and processes, such as sources of ADR reports and reporting of medication errors[4]. Further complications included cultural diversity in medical practices across Asia; barriers of language, education and awareness; different reporting structures and timelines for ADRs; deficits in relevant expertise as well as financial and human resources; lack of government support; and poor-quality and/or sporadic PV reporting[1]. With more clinical trials and postmarketing activity being conducted in the Asian continent, there is an immense need to understand pharmacovigilance and implement it to a higher, more consistent standard.

GLOBAL VARIATIONS

Variations between PV systems and procedures across Asia mirror global discrepancies that present significant challenges to the pharmaceutical industry in maintaining and monitoring drug safety. Companies need to keep pace with regulatory change while harmonizing and streamlining their worldwide pharmacovigilance operations, ensuring both patient safety and protection

against warning letters, site inspections, financial penalties or drug withdrawals that can result from suboptimal compliance.

This is all the more difficult where moves toward global consistency of PV procedures, through organizations such as the International Conference on Harmonization (ICH), not only impose technical challenges for industry but also remain at different stages of implementation from market to market. One such example is the new ICH E2B (R3) format for electronic transmission of Individual Case Safety Reports (ICSRs), which improves the granularity of ICSR data but also gives countries and regions leeway to add their own locally specific requirements.

Another hurdle for companies is making sure they are aware of all pertinent legal and regulatory documents around pharmacovigilance, both at a global and a national level. Many countries or regions rely on multiple regulations and directives, laws, guidance, letters and notices. Moreover, existing regulations may include overlapping and/or contradictory requirements, or may not cover all aspects of a particular process. Securing all the relevant information from Competent Authorities (CA) can be time-consuming and complex, if CA resources are limited or relationships with these agencies only tentative.

Once legal requirements are understood, companies need to conduct a comprehensive impact assessment covering the whole spectrum from serious adverse event (SAE) collection through to case assessment and expedited distribution. Then the challenge is to operationalize requirements. That brings into consideration a range of functional issues geared to process efficiency, such as submission routes for SAE reporting, local presence, language constraints and confirmation of delivery, as well as testing and resource requirements.

In an ever-evolving landscape, new regulatory updates can often emerge just as everything is in place to meet legal requirements. It is therefore imperative that companies maintain a flexible and holistic PV system, capable of responding rapidly to unexpected developments. Clearly defined procedures for the collation of regulatory intelligence are a crucial prerequisite for drug-safety compliance throughout the product life cycle.

CAN AUTOMATION HELP?

To stay on top of these challenges, companies need multilingual pharmacovigilance-intelligence specialists who can identify and analyze legal requirements through ongoing review of regulations and guidelines, whether by scrutinizing local CA webpages or through direct contact with regulatory bodies. Regulatory intelligence must extend to enabling readiness when legislative changes have a wider impact, or to initiating cross-functional regulatory change-management processes if necessary.

These processes are burdensome, but can be eased significantly by applying advanced automation to pharmacovigilance. A cloud-based PV solution will ensure compliance with pharmacovigilance requirements while providing full visibility of a medicine's safety profile, during clinical development and throughout the life cycle.

Using regulatory intelligence from countries across the globe, these systems can be configured with date-stamped decision rules. That way, any required safety information is distributed automatically to stakeholders, including trial sites, ethics committees and CAs, within the stipulated timelines. Information is submitted in mandated formats, and with a fully auditable distribution trail. Also important is the ability to generate reports and dashboards showing individual submissions and aggregate safety reports over time and across clinical-trial portfolios, further enhancing transparency for effective real-time PV monitoring and management.

With ever-more complex medicines entering the market, and growing scrutiny of drug safety as regulators embrace accelerated or conditional approval procedures to facilitate patient access to innovation, companies simply cannot afford to skimp on pharmacovigilance. Nor can they take anything less than a 360° view of the drug-safety landscape, whether across Asia or around the world. With the help of regulatory expertise and automated tools, companies can rise to the many challenges of PV in a global marketplace, delivering higher-quality, more exhaustive safety data on time, in the right format and across a multitude of national or regional contexts.

In conclusion, there are clear variations in the structures, processes and outcomes of pharmacovigilance status among Asian countries, with many diversities and complexities. Taking into consideration the latest drug-administration law from China's National Medical Products Administration (NMPA), as well as E2B (R3) implementation in the near future by Korea's Ministry of Food and Drug Safety, we do see a general trend toward a more stringent regulatory environment in Asia.

To reduce variations in PV administration based on various regulatory requirements, drug safety reporting must look to rule-based automation and robotic process automation, so that it can leverage pharmacovigilance expertise, maximize human capital, ensure regulatory compliance and ultimately protect the patient.

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