DIA China Advisory Council Young Members

Safety, Pharmacovigilance, and Risk Management Plans in China

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China joining the International Council for Harmonisation (ICH) in 2017, and China's subsequent announcement to follow relevant ICH guidelines such as E2, M1 and M4 in 2018, is continuing to change the conduct of pharmacovigilance in China. Most importantly, to help industry standardize its programs and practices, China's agencies have issued several safety and pharmacovigilance regulations. Necessary and useful, these have also presented challenges to an industry striving for compliance.

Key Takeaways

- New risk management requirements to protect patient safety in clinical trials increase the importance of the Individual Case Safety Report (ICSR) and Drug Safety Update Report (DSUR).
- Although Risk Management Plans (RMPs) are relatively new in China, they are an essential component of the entire product lifecycle; as part of an overall risk management system and strategy, the RMP must be continuously monitored and updated.
- Legally bound to present a drug product's benefit-risk profile accurately, product labeling is one of the most important risk minimization measures to ensure patient safety.

DIA China 2019 presented Safety and Pharmacovigilance sessions that covered multiple aspects of these regulatory changes and resulting industry needs, including the sharing of E2 guidelines (on *ICH Day*), pharmacovigilance methodologies in post-marketing drug surveillance, and using real world data in pharmacovigilance.

IND Safety Requirements

In July 2018, the Center of Drug Evaluation (CDE) of the NMPA issued new Investigational New Drug (IND) application procedures and requirements. These impose more comprehensive risk management, including providing a risk management plan and pharmacovigilance system documents when submitting the IND, to protect the safety of patients in clinical trials. If there is no comment or inquiry from the CDE, sponsors can initiate their clinical trial 60 days after submitting their IND application.

Sponsor challenges and questions remain in building up sufficient pharmacovigilance and risk management system capacity, processing and evaluating ICSRs, and post-market signal detection and aggregate reporting.

Risk Management Plan (RMP)

RMPs in China remain in the development phase. In September 2018, the CDE issued its requirements for the RMP to be submitted as part of the New Drug Application (NDA) package.

Data collected about a drug during clinical trials is generated within very strictly controlled clinical circumstances. However, using that same drug in the real world may present complicated situations that the trials never anticipated or addressed. A well-designed RMP will help minimize these unforeseen potential risks from the first-in-human study (Development RMP, or DRMP) through post-marketing signal detection and evaluation (RMP).

Speakers identified a general RMP process flow:

- Preparation: Identify the risks.
- Draft: Gather data and write draft.
- Review: Review draft with all relevant functional/project stakeholders.
- Communication: Review with regulatory authorities, scientific experts, and other external stakeholders.
- Final refinement and approval.

Patient-Centric Labeling to Minimize Risk

Labeling is one of the most important risk minimization measures for patient safety in China. With China now a member of ICH, simultaneous global product development makes it more important than ever to prepare and maintain accurate product labels as part of risk minimization and safety efforts for prescribing healthcare professionals and their patients.

As a point of reference, Japan has implemented a Drug Guide for Patients to promote proper understanding of prescription drugs among patients and their families and to enable detection of serious adverse reactions at an earlier stage. This Guide presents important information from the product labeling in an easy to understand manner.

More guidelines are anticipated for web labeling, paper labeling, and patient labeling in China. One challenge of paper labeling is that prescribers and patients may only realize that there is a revised label when a new commercial package is distributed, which may be months or even years after regulatory approval. A “patient friendly” version of the label, in language a consumer can easily understand, may reduce the risk of improper product use.

Market globalization will inevitably bring about regulatory globalization. This includes the conduct of safety monitoring and pharmacovigilance in China.