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# China's Life Sciences and Healthcare-No.2
## —The Good Vigilance Practice rule in China

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## I. China GVP

This article will introduce the drug vigilance activities required by the new Good Vigilance Practice ("GVP"), enacted on May 7, 2021, and come into effect on December 1, 2021. The GVP will be applied to MAHs and NDA applicants conducting clinical trials.

Before the adoption of the GVP, the Administration Measures on Reporting and Monitoring of Drug Failure Reactions (Ministry of Health Order No. 81, effective as of July 1, 2011) and the Public Notice of the State Pharmaceutical Administration on Report of Adverse Drug Reactions (the "No. 66 Notice") issued in 2018 constituted the basic legal framework of monitoring and reporting of adverse drug reactions in China. According to the NMPA's explanation, NMPA will amend the Administration Measures on Reporting and Monitoring of Drug Failure Reactions (Ministry of Health Order No. 81) and apply it to the drug vigilance activities conducted by medical institutions and drug sales companies (wholesale and retail).

## II. Applicable Entity

The GVP applies to MAHs (domestic and overseas) and the applicants for new drug registration authorized to conduct clinical trials. Existing MAHs must register the prescribed information in the National Drug Failure Response Observation System (http://www.adrs.org.cn/) within 60 days of the effective date of the GVP.

## III. The Internal Pharmaceutical Vigilance Department

According to the GVP, the MAH must establish a drug safety committee and a department dedicated to drug alert operations ("PV Department") within the company, which must have clear job responsibilities and a good cooperative relationship with other departments. Usually, the drug safety committee shall be consisted of the legal representative or major management personnel, the drug vigilance officer ("PV Officer"), the head of the quality control department, and the managers of the related departments. The duties of such committee are to handle critical PV matters such as reviewing and deciding on significant risks, handling major or urgent events and determining risk control policies (Articles 19 and 20 of the GVP).

The MAH's legal representative or major management personnel shall, in general, be responsible for PV activities. They shall designate the person(s) responsible for PV, assign sufficient numbers and personnel of commensurate qualifications, provide the necessary resources, and reasonably organize, coordinate, and ensure the effective operation of the PV system and the realization of quality objectives.

Regarding the requirements for personnel related to PV operations, the PV Officer must (a) hold a managerial position, (b) have a professional background in medicine, pharmacy, epidemiology, or a related specialty, (c) have a university degree or higher or a professional technical qualification of intermediate level or higher, (d) have experience in PV related work at least three years and (e) be familiar with the laws, regulations, and technical guidance principles related to drug PV operations in China, as well as knowledge and skills related to PV management operations.

In addition, MAHs should register the PV Officer in the

National Drug Defective Reaction Observation System (If there is a change in the registered information, it must be re-registered within 30 days).

Other personnel in the PV department are not required to have certain years of experience but there must be sufficient staff placed in the department. They must have professional background in medicine, pharmacy, epidemiology, or a related specialty, received PV related training, be familiar with the principles and possess the knowledge and skills which are necessary to handle PV operations (Articles 23, 24, and 26 of the GVP).

Furthermore, MAHs are allowed to outsource PV-related work to domestic companies with the expertise, management systems and resources, and are allowed to outsource work to other MAHs in the same group. But MAHs must sign an outsourcing contract, monitor and inspect the performance of the contractor on a regular basis.

## IV. Internal Audits

MAH shall conduct internal audits ("Internal Audits") regularly to audit the PV systems and company-internal rules and their enforcement and evaluate the PV system's adequacy, sufficiency, and effectiveness. MAHs shall promptly conduct an internal audit whenever there is a significant change in the PV system. MAHs may conduct the internal audit independently, systematically, and comprehensively by designating personnel or outside personnel or experts.

Records of internal audits shall be duly produced and reserved. A written report shall be prepared, including the audit's essential circumstances, contents, and results. For problems discovered by the internal audit, MAHs shall investigate the cause, take appropriate corrective and preventive measures, and track and evaluate the corrective and preventive measures.

## V. Monitoring and Reporting Adverse Drug Reactions

(1) Information collection channels, evaluation, and methods

MAHs must establish channels for collecting information on adverse drug reactions from medical institutions, drug sales companies, patients, other individuals, etc. MAHs must ensure that relevant persons may easily reach to MAH via telephone numbers or e-mails published on the instructions, drug packages, website, etc. And MAHs can collect information through academic literature research, post-marketing safety studies, etc.

MAH shall evaluate the reports based on the following items.

(i) Transmitting the original records: whether the documents' truthfulness, completeness, and traceability have been maintained in transferring the original forms.

(ii) Follow-up: follow-up on missing information regarding reporting severe or unanticipated adverse reactions.

(iii) Assessment of predictability: MAHs must evaluate the predictability of adverse drug reactions. An adverse reaction shall be deemed as unpredictable if the characteristics, severity, or outcome of the negative response is not inconsistent with the drug attachments description.

(iv) Assessment of severity: an adverse reaction shall be deemed as severe if any of the following occurs: death, life-threatening, requiring hospitalization or prolonged hospitalization, permanent or significant disability/function, those with congenital anomalies or congenital disabilities, other medically substantial events.

(v) Assessment of relevance: assessment of the relevance relationship between the suspect drug and the reaction that occurred in the patient in accordance with the criteria for assessing the relevance classification class of drug adverse reactions published by the National Drug Failure Reaction Monitoring Center.

(2) Reporting of adverse reaction

Report of adverse reaction shall contain adverse reactions related to quality problems of the drug, prescribing over indications, over dosages and contraindications.

MAHs should submit a report to the regulatory authority about severe adverse reactions within 15 days at the latest and non-serious adverse reactions within 30 days. In the case of a severe adverse reaction to a drug used outside of the country, the MAHs must submit a report to the regulatory authority about each adverse reaction. If the MAHs need to suspend the sale or use of the product or remove the product from the market outside of the country due to a defective reaction, MAHs must submit a report within 24 hours.

(3) Identification and evaluation of safety risks (detection and evaluation of signals)

The GVP newly defines the concept of signal detection and requires that signals must be detected by appropriate methods, such as review and inspection of individual drug

adverse reaction report, case series evaluation, human detection methods such as case report summary and analysis, and computer-assisted detection methods such as data mining. It also stipulates the frequency of detection of signals, the types of signals to be focused on, the factors to be considered when decide the priority, the principles of signal evaluation, and the procedures to be taken when clustered signals are detected (however, as the content of GVP about the evaluation of signals is only a set of principles, detailed regulations are expected to be issued later).

(4) Post-marketing safety studies of pharmaceutical products

The GVP requires that post-marketing safety research on pharmaceutical products should be conducted in compliance with GCP (if applicable), and the post-marketing safety research (which is needed by NMPA), the research plan, and the result report must be submitted as required by the regulatory authority.

(5) Risk communication and PV plan

The GVP states that MAHs must communicate drug safety information to healthcare professionals, patients, and the public and conduct risk communication for drugs, such as publishing documents for healthcare professionals and drug guides for patients and holding presentations.

The PV plan must include an overview of drug safety, drug alert activities, and a description of planned risk management measures, timing, a cycle of implementation, etc. The PV Officer must review and confirm the plan and report to the MAH's drug safety committee for review and confirmation.

(6) Documents, records, and data management

MAHs must establish a well-developed system for vigilance management. Regarding the management of relevant documents, records, and data, MAHs shall establish rules about a retention period (at least ten years from the expiration of the drug registration certificate for drug alert data and records) and procedures for their management and maintain a master file, which shall be updated from time to time to reflect current conditions. The drug alert master file shall include at least the following.

(i) Organizational structure: describes the organizational structure, responsibilities, and interrelationships as they relate to PV activities.
(ii) Basic information on the PV Officer: including an area of residence, contact information, biography, responsibilities, etc.
(iii) Deployment status of full-time staff: including the number of full-time staff, their professional backgrounds, responsibilities, etc.
(iv) Sources of information on suspected adverse drug reactions: the main channels and methods of collecting data on suspected adverse drug reactions.
(v) Information tools or systems: the information about tools or systems used in the PV activities.
(vi) Management system and regulations: An overview explanation of the PV management system, an inventory of PV management systems and rules.
(vii) Operational status of the PV management system: describes the situation of monitoring and reporting of adverse drug reactions, identification, evaluation, and control of drug risks, etc.
(viii) Outsourcing of drug alert activities: Provide a list of outsourcing contracts, details of outsourcing, deadlines, contractors, etc.
(ix) Quality control: Explain the quality control situation of PV. Include quality objectives, quality assurance system, quality control indicators, internal audits, etc.
(x) Appendix: Include system and operating rule documents, drug list, contractor agreement, internal audit report, revision history of the master file, etc.

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