Guidelines for Pharmacovigilance Testing

In order to guide the drug supervision and administration departments to carry out pharmacovigilance inspection work, and urge drug marketing authorization holders (hereinafter referred to as holders) to implement the main responsibility of pharmacovigilance, these guidelines are formulated in accordance with the "Administrative Measures for Drug Inspection (Trial)" and other relevant regulations. .

These guidelines are applicable to the inspections conducted by the drug regulatory authorities at or above the provincial level on the pharmacovigilance activities carried out by the holders themselves or entrusted by the holders; for drug registration applicants who have been approved to conduct drug clinical trials, they should conduct pharmacovigilance inspections. Combined with drug safety characteristics and clinical trial safety information report and risk assessment, start pharmacovigilance inspection during clinical trial or before marketing authorization, and the specific implementation can refer to this guideline.

The organization and implementation of inspections, as well as inspection agencies and personnel, inspection procedures, routine inspections, causal inspections, connection between inspections and inspections, cross-regional inspection collaboration, and processing of inspection results, etc. The Notice of the "Administrative Measures for Drug Inspection (Trial)" (Suoyao Yaoguan [2021] No. 31) and other relevant requirements shall be implemented.

1. Key factors to consider in routine inspection

(1) Characteristics of drugs

1. The safety characteristics of the drug.

2. Adverse drug reaction monitoring data and the occurrence of adverse drug reaction

aggregation events.

3. Drugs with large sales volume or limited alternative drugs.

4. Drugs with additional safety conditions when they are approved for marketing.

5. Innovative drugs, improved new drugs, and drugs for special groups such as children and pregnant women.

6. Drugs with high social concern.

(2) Characteristics of the holder

7. Holders with more varieties and large sales volume.

8. Holders who have not undergone pharmacovigilance checks.

9. Holders who have obtained the drug registration certificate in China for the first time.

10. Holders who have major changes in the pharmacovigilance system or have a significant impact on the pharmacovigilance organizational structure due to mergers and acquisitions, organizational structure changes, etc.

1 1. Holders of commissioned production.

12. Holders entrusted to carry out pharmacovigilance activities.

(3) Other circumstances

13. Previous pharmacovigilance examination or other examinations.

14. Other situations that the drug regulatory authority deems it necessary to carry out inspection .

2. Key factors to be considered in the cause-based inspection

(1) Late reporting, concealment, or omission of suspected adverse drug reaction information, and the reporting quality is poor.

(2) Monitoring of adverse drug reactions indicates that there may be safety risks.

(3) Failure to discover, assess, control or communicate relevant risks in a timely manner.

(4) Suspending production, sales, use and product recall, and failing to report to the drug supervision and administration department as required.

(5) Failure to conduct post-marketing safety research, formulate and implement a pharmacovigilance plan as required by regulations or the requirements of drug regulatory authorities, and fail to provide explanations.

(6) Failure to provide relevant information on pharmacovigilance as required by the drug regulatory department or the information provided does not meet the requirements .

(7) Delayed implementation or failure to fully implement corrective measures.

(8) Other circumstances that require a cause-based inspection.

3. Inspection method

Inspection methods include on-site inspection and remote inspection. On-site inspections refer to inspections carried out by inspectors at the premises where the holder is carrying out pharmacovigilance-related activities. Remote inspections are inspections carried out by means of video, telephone, etc.

The inspection team may conduct on-site inspection and/or remote inspection according to the work needs, and may require the holder to submit the relevant materials required for the inspection within the specified time limit.

4. Inspection location

The inspection sites are mainly places where the holder conducts key pharmacovigilance activities, and if necessary, extended inspections can be carried out for places entrusted to carry out pharmacovigilance activities.

V. Defect Risk Level

pharmacovigilance inspection are divided into serious defects, major defects and general defects, and their risk levels are decreased in turn. If the defects found in the previous inspection are repeated, the risk level can be upgraded. There are a total of 100 inspection items, of which 12 can be judged as serious defects (**), 40 can be judged as major defects (*) , and the remaining 48 can be judged as general defects (see attachment for details).

6. Evaluation Criteria

The inspection conclusion and the comprehensive assessment conclusion are divided into conforming to the requirements, basically conforming to the requirements and not conforming to the requirements. The inspection team and dispatched inspection units can make inspection conclusions and comprehensive evaluation conclusions with reference to the following evaluation standards according to the actual inspection situation .

(1) No serious defects and major defects are found, and the general defects are 0~9, which can be assessed as meeting the requirements.

(2) Meeting any of the following conditions can be assessed as not meeting the requirements:

1. Serious defect item 1 and above.

2. No serious defects were found, and 10 or more major defects were found.

3. No serious defect items were found, 0~9 major defect items, and 25 or more total defect items.

(3) In other cases, it can be assessed as basically meeting the requirements.

Attachment : Pharmacovigilance Checkpoints

accessories

Pharmacovigilance Checkpoints

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
1. Institutional staff and resources				
PV01	Drug Safety Committee	1.Has the holder established a drug safety committee (**) 2.Whether the responsibilities of the Drug Safety Committee are clear and reasonable 3.Whether the composition of the drug safety committee meets the requirements 4.Whether to establish a reasonable working mechanism and procedures, and to carry out the work according to the procedures (*)	Check the organizational structure of the drug safety committee, including the names of the main members of the committee, position information , etc .; check relevant systems or procedures, including descriptions of the committee's responsibilities, working mechanisms, and work procedures; check the committee's work records, such as meeting minutes, decision-making documents, etc. ; Check whether the implementation and tracking of the decision-making document are consistent with the description; Randomly ask the main personnel of the Drug Safety Committee for their understanding of their job responsibilities and their participation in the work of the committee.	GVP Articles 19, 20, 99, 106
PV02	Pharmacovigilance Unit	5.Does the holder have a dedicated pharmacovigilance unit (**) 6.Whether there are departmental responsibilities and/or job responsibilities, and whether the departmental responsibilities/job responsibilities are comprehensive, clear and reasonable	Check the organization chart of the holder, the organization chart of the pharmacovigilance system (if pharmacovigilance at the group holder level is involved, the relationship with the relevant units in the group should be reflected in the chart); check the documents on the responsibilities and/or job responsibilities of the pharmacovigilance department .	Articles 19, 21, 106 of the GVP, Article 54 of the Vaccine Administration Law
PV03	related department	7.Whether the holder clearly defines the pharmacovigilance responsibilities of each relevant department, which may include drug research and development, registration, production, sales, marketing, quality and other departments	View the Pharmacovigilance System Organization Chart; view the documents covering the responsibilities of the relevant departments.	GVP Articles 19, 22, 106

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
		(*)		
PV04	Head of Pharmacovigilance	8.Has the holder designated a person in charge of pharmacovigilance to be responsible for the operation and maintenance of the enterprise's pharmacovigilance system (**) 9.Whether the position, professional background, qualifications and work experience of the person in charge of pharmacovigilance meet the relevant requirements, and whether he is familiar with relevant laws and regulations, etc. (*) 10.Whether the responsibilities of the person in charge of pharmacovigilance are comprehensive, clear and reasonable 11.Whether the person in charge of pharmacovigilance is registered in the national adverse drug reaction monitoring system, and whether any changes are updated in time (*)	Check the employment certificate or post certification documents, background and qualification certificates (such as academic and degree certificates, technical titles, job resumes, training certificates, etc.) of the person in charge of pharmacovigilance; check the job responsibilities documents of the person in charge of pharmacovigilance; check the person in charge in the national drug industry Registration in the adverse reaction monitoring system; ask the person in charge about his familiarity with the laws, regulations, and norms related to pharmacovigilance.	GVP Articles 23, 24, 25, 75, 82, 106
PV05	full-time personnel	12.Whether the holder is staffed to meet the needs of pharmacovigilance activities (*) 13.the professional background, knowledge and skills required to carry out pharmacovigilance activities , and whether they are familiar with relevant laws and regulations on pharmacovigilance in China, etc. 14.Whether the full-time staff has received relevant training in pharmacovigilance (*)	Find out the number of full-time staff; check the employment certificate or position certificate of full-time staff, professional background certificate (such as academic degree certificate, work experience, training certificate, etc.); randomly ask the full-time staff to know the degree of familiarity with the laws, regulations and norms related to pharmacovigilance.	Articles 23, 26, 106 of the GVP, Article 54 of the Vaccine Administration Law
PV06	personnel training	15.Whether to develop an annual training plan and carry out the training according to the plan (*) 16.Are all personnel involved in pharmacovigilance activities trained? 17.Whether the training content is reasonable and suitable for pharmacovigilance duties and requirements 18.Whether to evaluate the training effect	View pharmacovigilance training plans, records, and files, including training notices , sign-in forms, training materials, assessment records, training photos, and more.	GVP Articles 26-28
PV07	equipment resource	19.Is the holder equipped with the equipment and resources required to meet pharmacovigilance activities (*) 20.Whether the management and maintenance of equipment resources can continue to meet the requirements of use 21.Whether the pharmacovigilance information system (if any)	Check the office area, office facilities, network environment, data file storage space and equipment; understand the deployment of MedDRA medical dictionary and literature retrieval resources ; check information tools (such as database software for	GVP Articles 29-31, 106

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
		meets the relevant requirements, and whether it has safeguards to realize its security and confidentiality functions	storing and analyzing adverse reaction reports) or information systems (such as Use E2B format reporting system, signal detection or risk early warning system, etc.) to understand whether the information system has a system disaster recovery plan and business emergency plan, etc.; check whether security and confidentiality measures are in place; can request a function demonstration.	
2. Quality management and documentation				
PV08	Quality Management System	22.Does the holder's quality management system include quality management requirements for the pharmacovigilance system and its activities, and whether the pharmacovigilance system and activities are subject to quality management (**) 23.Have pharmacovigilance quality objectives been established and have key pharmacovigilance activities been incorporated into the quality assurance system (*) 24.Are quality control indicators specific, measurable, and cover key pharmacovigilance activities	Understand how the holder conducts quality management of the pharmacovigilance system and activities; check the description of quality management in the master file of the pharmacovigilance system; check the relevant documents of the holder's quality management system, such as systems and procedures, quality system document records, etc.	GVP Articles 6-9, 106
PV09	internal audit	25.Whether an internal audit plan is developed for the pharmacovigilance system and activities, and internal audits are carried out on a regular basis (**) 26.Whether the internal audit is independent, systematic and comprehensive 27.has been formulated before the internal audit, and whether the internal audit records are complete (*) 28.Whether corrective and preventive measures are taken in a timely manner for the problems found in the internal audit, and tracking and evaluation are carried out (*)	Understand how the holder conducts internal audit and review personnel ; view the description of the internal audit of pharmacovigilance in the main file of the pharmacovigilance system; view the internal audit plan, internal audit plan, and internal audit records ; Corrective and preventive actions, understand tracking, assessing the situation.	GVP Articles 11-14, 106
PV10	System and procedure document	29.Are key pharmacovigilance activities covered by institutional and protocol documents (*) 30.Whether the content of the system and procedure documents is compliant, clear and operable 31.Whether the document management operating procedures have been established, and whether the drafting, revision, review, and updating of documents (including the master	View the catalogue of system and regulation documents; review the content and implementation of various system and regulation documents (can be reviewed in conjunction with specific inspection items); check the document management operating procedures and related records.	GVP Articles 100-103, 106

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
	management	document of the pharmacovigilance system) are carried out in accordance with the procedures 32. Are policy and procedure documents regularly reviewed and updated in a timely manner 33. Whether documents involving pharmacovigilance activities have been reviewed by the pharmacovigilance unit		
PV11	Pharmacovigilance System Master File	34. Whether to establish the master file of the pharmacovigilance system (*) 35. Whether the content of the master file of the pharmacovigilance system meets the relevant requirements 36. Whether the master file is consistent with the current pharmacovigilance system and activities, and whether it is updated in a timely manner	Check the master file of the pharmacovigilance system; check whether there are any requirements for updating the master file in the relevant systems and procedures; check the update record and content of the master file.	GVP Articles 104-106
PV12	Records and Data Management	37. Are key pharmacovigilance activities documented (**) 38. Are records and data true and accurate (*) 39. Whether records and data are complete and traceable 40. Whether the handwriting of paper records is clear and easy to read and not easy to erase 41. Whether the electronic record system has established business operating procedures, regularly backed up, set permissions, and whether data changes can be tracked and left traces 42. Are there measures in place to keep records and data secure, confidential and free from damage and loss (*) 43. Whether data and record retention years meet the requirements (*) 44. Whether the records generated by the commissioned pharmacovigilance activities meet the requirements 45. Whether the records and data related to pharmacovigilance were obtained when the relevant drug registration certificates of other drug marketing authorization holders were transferred (*)	Check the relevant regulations on record and data management, quality management system documents and ledger records, etc.; review whether various records and data meet the requirements in combination with the inspection items.	GVP Articles 107-115

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
PV13	entrust manage	46.When entrusting pharmacovigilance activities, whether the holder examines the pharmacovigilance conditions and capabilities of the entrusted party, and whether the two parties have signed an agreement or agreed in writing on the corresponding responsibilities and working mechanism within the group (*) 47.entrustment agreement or written agreement meets the relevant requirements 48.Whether the responsibilities of the entrusting parties are clear, whether the mechanism is reasonable, and whether the connection is smooth 49.Whether the entrusted party is regularly audited, and whether corrective and preventive measures have been taken for the audit results and existing problems (*)	Find out whether the holder has a pharmacovigilance entrustment (including entrustment within the group); check the relevant description of the entrustment part in the main document of the pharmacovigilance system; check the entrustment agreement or related documents in written agreement; check the audit results and the correction of the existing problems by the trustee and preventive measures related records; view the trustee training and communication records, etc.	GVP Articles 15-18
PV14	Information registration and update	50.Whether the holder has registered user information and product information in the national adverse drug reaction monitoring system, and whether it has been changed as required (including drug instructions) (*)	View holder user information and product information in the National Adverse Drug Reaction Monitoring System.	Article 10 GVP
3. Monitoring and reporting				
PV15	Information collection methods	51.Has the holder established an independent way to collect information on suspected adverse drug reactions (**) 52.information collection channels and methods are comprehensive, smooth and effective; whether the collection channels include: medical institutions, drug manufacturers, drug dealers , academic literature, post-marketing research , data collection projects, relevant websites, etc. (*) 53.For drugs marketed at home and abroad, whether overseas information collection channels have been established (*)	Knowing the ways and methods of self-collection of the holder's information (including telephone, fax, e-mail, etc.) can verify the validity of the relevant reporting methods and methods; check the description of the sources of information about suspected adverse reactions in the main file of the pharmacovigilance system.	GVP Articles 32-38, 106, Article 54 of the Vaccine Administration Law

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
PV16	information dispose of	54.Is there an original record of information collection (*) 55.Whether the records keep the information true, accurate, complete and traceable during the transmission process; whether the original record form (if any) is reasonably designed 56.Whether the information missing in the serious adverse reaction report (including death case report) and unexpected adverse reaction report is followed up, whether the follow-up is timely, and whether there is a follow-up record 57.Whether the data information fed back by the supervision and management department is regularly downloaded and disposed of as required (*) 58.Whether to cooperate with the investigation of adverse drug reactions and vaccine AEFI 59.For drugs that are marketed at home and abroad, whether the information such as the suspension of sales, use or withdrawal of drugs overseas due to safety reasons has been reported in a timely manner	Understand the process of recording, transmission, verification, follow-up, and investigation of information from different sources; spot-check original records, follow-up records, and investigation reports; view the download records of feedback data from the supervision and management department, and understand the analysis, evaluation and reporting of feedback data.	GVP Articles 40-42 , 51, AEFI Program 4 "Investigation and Diagnosis", 7 "Responsibilities "
PV17	Evaluation and Reporting	60.Whether the filling in the report form is true, complete, accurate and standardized, and meets the relevant filling requirements (*) 61.Whether the evaluation of the severity, anticipation and relevance of adverse drug reactions is scientific and compliant 62.Whether the reporting scope and reporting time limit are compliant (*) 63.Whether original records and follow-up records are traceable 64.vaccine holder responsible for reporting the vaccine AEFI found to the county CDC where the vaccine is located ?	drug reaction/AEFI report form of different categories (general, serious, death) , check the filling and evaluation of the report form; trace the original record and follow-up record, check whether the content of the report is consistent with the original record; check whether the time limit of the report is compliant.	GVP Articles 43-54 AEFI Plan 3 "Report", 7 "Responsibilities"
PV18	Strengthen post-market surveillance of drugs	65.For innovative drugs, improved new drugs, and varieties that regulatory agencies or adverse reaction monitoring agencies require to pay attention to, whether the holder has carried out enhanced monitoring in combination with the safety characteristics of the varieties 66.Is the monitoring method appropriate? 67.Have the monitoring results been analyzed and utilized?	Learn about the innovative drugs and improved new drugs that have been approved by the holder in the past five years, as well as the varieties that the supervision and management department or the adverse reaction monitoring agency requires attention; check the relevant information on strengthening monitoring, such as plans, records, reports, etc.	Article 39 GVP

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
4. Risk identification and assessment				
PV19	Signal detect	68.holder has carried out signal detection for the suspected adverse drug reaction information collected through various channels (**) 69.Whether the method and frequency of signal detection are scientific and appropriate (*) 70.of signal judgment (such as the judgment of concerned signals, the judgment of invalid signals, and the judgment of priority) is reasonable	Understand the coverage of signal detection varieties; check the development of signal detection work , check signal detection records; understand the method, frequency, and procedure of signal detection; understand the principles and standards of signal judgment; check whether there are detected signals and focus signals (including signals exhibiting aggregated features).	GVP Articles 55-59
PV20	Signal Analysis Evaluation	71.Is the detected signal evaluated (**) 72.Whether the evaluation is comprehensive and whether reasonable evaluation opinions are put forward 73.Whether the detected signals exhibiting the characteristics of clustering are timely for case analysis and situation investigation (*)	View signal evaluation records or reports to understand the evaluation process, results and recommendations; view case analysis and situation investigation data showing aggregated signals; check whether new drug risks are discovered through signal detection and evaluation .	Article 60 GVP
PV21	risk Evaluate	74.Are new drug safety risks assessed, and risk assessments documented or reported (*) 75.Whether the content of the assessment is comprehensive and scientific 76.Whether to provide a reasonable assessment opinion 77.Are the risks identified during the risk identification and assessment process reported as required (*)	View risk assessment records or reports for assessment content, results and risk management recommendations.	GVP Articles 62-68
PV22	Post marketing Safety Studies	78.Whether to conduct post-marketing safety research on drugs in accordance with the requirements of the provincial and above drug regulatory authorities (**) 79.Whether to take the initiative to conduct post-marketing safety research based on the risk of the drug 80.Whether the study protocol was developed by persons with appropriate disciplinary background and practical experience, reviewed or approved by the head of pharmacovigilance 81.Are new information and drug safety issues identified in the study assessed or reported as required (*)	Randomly check post-marketing safety research cases, including research plans, research reports, and information reported to drug regulatory authorities.	Articles 69-78 of the GVP, Article 57 of the Vaccine Administration Law
PV23	Periodic Safety	82.Whether the writing format and content comply with the requirements of the Guidelines for Writing Periodic Drug Safety Update Reports or the relevant guidelines of the International Technical Harmonization for Registration of	Check the periodic safety update report/periodic benefit-risk assessment report submitted by the holder to the National Adverse Drug Reaction Monitoring System, check the report coverage	GVP Articles 79-86

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
	Update Report / Periodic Benefit-Risk Assessment Report	Pharmaceuticals for Human Use (*) 83.Whether the data coverage period is complete and continuous 84.Whether the report is submitted according to the required frequency and time limit (*) 85.Is the report approved by the Pharmacovigilance Officer? 86.Whether the review comments submitted to the report are processed in a timely manner or responded to as required (*)	period, submission time and frequency; check whether all the varieties that should be submitted for report are covered, etc.; The reported periodic safety update report/periodic benefit-risk assessment report, the format and content of the inspection report, and whether the safety information included in the verification report includes all sources of information; for those with relevant requirements in the review opinions of the drug regulatory authority , to check whether it is processed or responded in a timely manner .	
V. Risk Control				
PV24	risk manage	87.Whether to take appropriate risk management measures for the identified risks and potential risks according to the risk assessment results (**) 88.Is there a pharmacovigilance plan for important risks (*)	Understand the relevant situation of the holder's risk management measures, such as risk control measures, post-marketing research, strengthening post-marketing monitoring of drugs, etc.; check the relevant information and evidence that the holder has taken risk management measures, such as the revision or filing of drug instructions Applications, pharmacovigilance programs, post-marketing studies and enhanced surveillance programs, reports, etc.	Articles 66, 87, 97 of the GVP, Articles 54 and 59 of the Vaccine Administration Law
PV25	Risk Control Measures	89.Are appropriate risk control measures in place (*) 90.Has the effectiveness of the control measures been assessed or an assessment programme developed 91.Whether the risk control measures are reported to the local provincial drug supervision and administration department and inform the relevant units as required (*)	Check the pharmacovigilance plan and other related materials; check the supporting documents, such as letters, leaflets, and receipts that the holder reports to the drug regulatory department and inform the relevant units ;), check that the holder has carried out or completed the corresponding work as required.	Articles 87-90 of the GVP, Article 73 of the Vaccine Administration Law
PV26	risk communicate	92.risk communication has been carried out 93.risk communication is timely , and whether the methods, content and tools are appropriate 94.In the event of an emergency, is risk communication carried	Understand whether the holder has carried out risk communication and when; understand the methods and tools of risk communication; check the risk communication content of the letter to medical staff	GVP Articles 91-95

Numbering	project	Inspection items (defect risk recommendation level)	Inspection method and content	Inspection basis
		out urgently as required?	and patient safety medication reminders ; understand the emergency risk communication carried out by the holder; In view of the addition of warnings, serious adverse reactions, and restricted groups of users in the revision of the instruction manual, it is necessary to know whether the holder has carried out risk communication and the specific situation.	
PV27	Pharmacovigilance Program	95.Whether the pharmacovigilance plan has been reviewed by the Drug Safety Committee and whether the relevant content meets the writing requirements 96.Whether the pharmacovigilance plan is implemented (*) 97.Whether the pharmacovigilance plan is updated in a timely manner based on perceptions of risk	Review the pharmacovigilance plan and related materials that demonstrate its implementation.	Articles 96-99 of the GVP, Article 57 of the Vaccine Administration Law
PV28	Cluster incident investigation and handling	98.Whether the clustering events of adverse drug reactions were investigated and handled in a timely manner (**) 99.Whether appropriate risk control measures are taken (*) 100.Whether investigation disposition and results are reported as required (*)	Find out whether the holder has discovered or been informed of aggregated adverse drug reaction events; understand the investigation and handling of aggregated events; view investigation reports, follow-up reports, and summary reports; and view documents or records that prove that the enterprise has carried out relevant risk control measures.	GVP Articles 61, 89, 132

Note: 1. The relevant information required by the holder is generally within three years, or the information formed during the period from the last inspection to this inspection.

2. In this table, GVP refers to the "Quality Management Practice for Pharmacovigilance", and the AEFI program refers to the "National Monitoring Program for Abnormal Responses to Suspected Vaccinations".