Pharmacovigilance inspection guidelines

In order to guide the drug regulatory authorities in conducting pharmacovigilance inspections and urge drug marketing authorization holders (hereinafter referred to as holders) to implement pharmacovigilance main responsibilities, these guiding principles are formulated in accordance with the "Measures for the Administration of Drug Inspections (Trial)" and other relevant regulations .

This guiding principle applies to the inspections carried out by drug regulatory authorities at the provincial level and above on pharmacovigilance activities carried out by the holder itself or entrusted by the holder; when conducting pharmacovigilance inspections on drug registration applicants who have been approved to carry out drug clinical trials, they should Combining drug safety characteristics with clinical trial safety information reporting and risk assessment, pharmacovigilance inspections are initiated during clinical trials or before marketing authorization. For specific implementation, please refer to these guiding principles. Regarding the

organization and implementation of inspection work, as well as inspection institutions and personnel, inspection procedures, routine inspections, cause-based inspections, the connection between inspections and audits, cross-regional inspection collaboration, and the processing of inspection results, the relevant work is in accordance with the "State Food and Drug Administration's Notice on Issuance of "Notice of the "Measures for Drug Inspection and Management (Trial)" (SFDA [2021] No. 31) and other relevant requirements shall be implemented.

1. Key considerations for routine inspections

(1) Drug characteristics

1. Safety characteristics of drugs. 2.

Adverse drug reaction monitoring data and occurrence of adverse drug reaction cluster events

condition.

3. Drugs with large sales volume or limited substitute drugs. 4. Drugs

with additional safety conditions when 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 who hold more varieties and larger sales volume. 8. Holders who have not undergone pharmacovigilance inspection. 9. Holders of drug registration certificates obtained in China for the first time. 10. Corporate mergers and acquisitions, organizational structure changes, etc. lead to serious disruptions in the pharmacovigilance system. Holders of major changes or significant impacts on the pharmacovigilance organizational structure.

11. The holder of the commissioned production. 12. The holder entrusted to carry out pharmacovigilance activities.

(3) Other situations

13. Previous pharmacovigilance inspections or other inspections. 14. Other situations where the drug regulatory department deems it necessary to conduct inspections.

2. Key considerations for cause-based inspections

(1) Late reporting, concealment, or underreporting of suspected adverse drug reaction information, poor reporting quality Poor.

(2) Adverse drug reaction monitoring indicates possible safety risks. (3) Failure to discover, assess, control or communicate relevant risks in a timely manner. (4) Suspension of production, sales, use and product recall, but failure to report to the drug regulatory department as required. (5) Failure to carry out post-market safety of drugs in accordance with regulations or requirements of the drug regulatory authorities Comprehensive research, development and implementation of pharmacovigilance plans without providing instructions.

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

(7) Delay in implementation or failure to fully implement corrective measures. (8) Other

situations that require cause-based inspections.

3. Inspection method

Inspection methods include on-site inspection and remote inspection. On-site inspection refers to the inspection carried out by inspectors arriving at the place where the holder carries out pharmacovigilance-related activities. Remote inspection is an inspection carried out by video, telephone, etc. The inspection team

can conduct on-site inspections and/or remote inspections according to work needs.

The holder is required to submit relevant materials required for inspection within the specified time limit.

4. Inspection location

The inspection location is mainly the place where the holder carries out key pharmacovigilance activities. If necessary Extended inspections may be carried out on sites entrusted with pharmacovigilance activities.

5. Defect risk level

The deficiencies discovered during pharmacovigilance inspections are divided into serious deficiencies, major deficiencies and general deficiencies, with their risk levels decreasing in order. 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 items can be judged as serious defects (**), 40 items can be judged as major defects (*), and the remaining 48 items can be judged as general defects (see attachment for details).

6. Evaluation standards

The inspection conclusions and comprehensive assessment conclusions are divided into meeting the requirements, basically meeting the requirements and not meeting the requirements. The inspection team and the dispatched inspection unit can make inspection conclusions and comprehensive assessment conclusions based on the actual inspection situation and the following assessment standards.

(1) No serious defects or major defects were found, and 0 to 9 general defects were found.

Can be assessed as meeting the requirements.

(2) If any of the following conditions is met, it may be assessed as not meeting the requirements:

1. 1 or more serious defects. 2. No serious defects

were found, and there were 10 or more major defects. 3. No serious defects were found, 0 to 9 major

defects were found, and the total defects were 25 or more.

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

Attachment: Key points for pharmacovigilance inspection

appendix

Pharmacovigilance check points

Numbered	items	Inspection items (defect risk recommendation level)	Check method and content	Check basis
1. Institutional Personnel and Resources				
PV01	drug safety committee	1. Whether the holder has 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 a reasonable working mechanism and procedures are established and work is carried out according to the procedures (*)	Check the organizational structure of the Drug Safety Committee, which should include the names and position information of the main members of the committee; check relevant system or procedure documents, which should include descriptions of the committee's responsibilities, working mechanisms, working procedures, etc.; check the committee's work records, such as meeting minutes, decision-making documents, etc. ; Check whether the implementation and tracking of decision-making documents are consistent with what is described; Make random checks to ask key personnel of the Drug Safety Committee about their understanding of their job responsibilities and their participation in committee work.	GVP Articles 19, 20, 99, 106
PV02	pharmacovigilance unit	5. Whether the holder has set up a special pharmacovigilance department (**) 6. Whether there are department responsibilities and/or job responsibilities, and whether the department responsibilities/job responsibilities are comprehensive, clear and reasonable	Check the holder organizational chart and pharmacovigilance system organizational chart (if pharmacovigilance at the group holder level is involved, the chart should reflect the relationship with relevant units in the group); check the pharmacovigilance department responsibilities and/or job responsibilities documents .	GVP Articles 19, 21, 106, Vaccine Administration Law Article 54
PV03	Related departments	7. Whether the holder clearly understands the pharmacovigilance responsibilities of each relevant department, which may include drug research and development, injection Registration, production, sales, marketing, quality and other departments (*)	Review the pharmacovigilance system organizational chart; review documents addressing the responsibilities of relevant departments.	GVP Articles 19, 22, 106
PV04	Pharmacovigilance manager	8. Whether the holder has designated a person in charge of pharmacovigilance to be responsible for the operation and maintenance of the enterprise's pharmacovigilance system ÿ**ÿ 9. Whether the position, professional background, qualifications and work experience of the person in charge of pharmacovigilance meet the relevant requirements? 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 changes are made in a timely manner Update (*) 12.	Check the appointment certificate or position certification documents, background and qualification certificates of the person in charge of pharmacovigilance (such as academic and degree certificates, technical titles, work resumes, training certificates, etc.); Check the job responsibilities document of the person in charge of pharmacovigilance; Check the person in charge's national drug status Registration status in the adverse reaction monitoring system; inquire about the person in charge's familiarity with laws, regulations, norms, etc. related to pharmacovigilance.	GVP No. 23, 24ÿ25ÿ75ÿ 82, 106
PV05	full-time staff	Whether the holder is equipped with full-time personnel to meet the needs of pharmacovigilance activities (*) 13. Whether the full-time personnel have the professional background, knowledge and skills required to carry out pharmacovigilance activities, and whether they are familiar with my country's relevant laws and regulations on pharmacovigilance etc. 14. Whether full-time personnel have received relevant training on	Understand the number of full-time staff; check full-time staff employment certificates or job certification documents, and professional background certificates (such as academic degree certificates, work experience, training certificates, etc.); make random checks to ask full-time staff about their familiarity with pharmacovigilance-related laws, regulations, specifications, etc.	GVP Articles 23, 26, 106, Vaccine Administration Law Article 54
PV06	staff training	pharmacovigilance (*) 15. Whether an annual training plan has been formulated and training carried out as planned (*) 16. Whether all personnel involved in pharmacovigilance activities have received training 17. Whether the training content is reasonable , whether it is compatible with pharmacovigilance responsibilities and requirements 18. Whether the training effect is evaluated	View pharmacovigilance training plans, records and files, including training notices, sign-in sheets, training materials, assessment records, training photos, etc.	GVP Articles 26-28

Numbered	items	Inspection items (defect risk recommendation level)	Check method and content	Check basis
PV07	Equipment resources	19. Whether the holder is 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 usage requirements 21. Whether the pharmacovigilance information system (if any) meets relevant requirements , whether there are safeguard measures to realize its security and confidentiality functions	Check the office area, office facilities, network environment, data file storage space and equipment; Understand the MedDRA medical dictionary and literature retrieval resource allocation; Check the information tools (such as database software for storing and analyzing adverse reaction reports) or information systems (such as Use E2B format reporting system, signal detection or risk 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; you can request a functional demonstration.	GVP Articles 29-31, 106
2. Quality management and documentation				
PV08	Quality management system	22. Whether the holder's quality management system contains quality management requirements for the pharmacovigilance system and its activities? Whether quality management is carried out on the pharmacovigilance system and activities (**) 23. Whether pharmacovigilance quality objectives have been formulated, and whether key pharmacovigilance activities have been included in the quality assurance system Tongzhong (*) 24. Whether the quality control indicators are specific and measurable, and cover the key activities of pharmacovigilance 25. Whether an	Understand how the holder conducts quality management of the pharmacovigilance system and activities; view the description of quality management in the pharmacovigilance system master document; view 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 review	internal audit plan is formulated for the pharmacovigilance system and activities, and internal audits are carried out regularly (**) 26. Whether the internal audit is independent, systematic, and Comprehensive 27. Whether the audit plan is 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, and follow-up and evaluation are carried out for the problems found in	Understand how the holder conducts internal audits and audit personnel; check the description of pharmacovigilance internal audits in the pharmacovigilance system master file; check the internal audit plan, internal audit plan, and internal audit records; check the correction and correction of problems found in the internal audit. Preventive measures, understanding tracking and assessment.	GVP Articles 11-14, 106
PV10	System and procedure document management	the internal audit (*) 29. Whether the system and procedure documents are Cover key pharmacovigilance activities (*) 30. Whether the contents of system and procedure documents are compliant, clear, and operable 31. Whether document management operating procedures have been established, the drafting of documents (including pharmacovigilance system master documents), Whether revisions, reviews, updates, etc. are carried out in accordance with procedures 32. Whether system and procedure documents are regularly reviewed and updated in a timely manner 33. Whether documents involving pharmacovigilance activities are reviewed	View the catalog of system and procedure documents; review the content and implementation of various systems and procedure documents (can be reviewed in conjunction with specific inspection items); view document management operating procedures and related records.	GVP Articles 100-103, 106
PV11	Pharmacovigilance system master file	by the pharmacovigilance department 34. Whether a pharmacovigilance system master document is established (*) 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	Check the master file of the pharmacovigilance system; check whether there are requirements for master file update in relevant systems and procedures; check the master file update record and update content.	GVP Articles 104-106
PV12	Records and data management	system and activities, and whether it is updated in a timely manner 37. Whether there are records of key pharmacovigilance activities (**) 38. Whether the records and data are Authentic and accurate (*) 39. Whether the records and data are complete and traceable 40. Whether the paper records are legible and difficult to erase 41. Whether the electronic recording system has established business operating procedures, regular backups, set permissions, and whether data changes Able to track and leave traces 42. Are there measures to ensure the security, confidentiality, and protection of records and data from damage and loss (*) 43. Whether the retention period of data and records meets the requirements (*) 44. Records generated by entrusted pharmacovigilance activities Whether it meets the requirements 45. When transferring relevant drug registration certificates from other drug marketing authorization holders, whether pharmacovigilance-related records and data are obtained (*)	Check the relevant procedures for records and data management, quality management system documents and ledger records, etc.; review various records and data in conjunction with the inspection items to see if they meet the requirements.	GVP Articles 107-115

Numbered	items	Inspection items (defect risk recommendation level)	Check method and content	Check basis
PV13	entrusted management	46. When entrusting pharmacovigilance activities, does the holder examine the pharmacovigilance conditions and capabilities of the entrusted party, and whether both parties sign an agreement or agree in writing on the corresponding responsibilities and working mechanisms within the group (*) 47. Whether the entrustment agreement or written agreement complies with Relevant requirements 48. Whether the work responsibilities of both parties are clear, the mechanism is reasonable, and the connection is smooth. 49. Whether the trustee conducts regular audits, and whether corrections and precautions are taken to audit results and existing problems. Precautions (*)	Understand whether the holder has a pharmacovigilance entrustment (including intra-group entrustment); check the relevant description of the entrustment part in the main document of the pharmacovigilance system; check the entrustment agreement or relevant documents agreed in writing; check the trustee's correction of the audit results and existing problems and preventive measures related records; check the trustee's 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? Changes as required (including drug instructions) (*)	Check the holder user information and product information in the National Adverse Drug Reaction Monitoring System.	GVP Article 10
3. Monitoring and reporting				
PV15	Information collection methods	51. Whether the holder has established an independent channel for collecting information on suspected adverse drug reactions (**) 52. Whether the information collection channels and methods are comprehensive, smooth, and effective; whether the collection channels include: medical institutions, drug manufacturers, and drug operating companies , academic literature, post-marketing research, data collection projects, related websites, etc. (*) 53. For drugs that are marketed both domestically and abroad, has an overseas information collection channel been established (*)	Understand the ways and methods for the holder's independent collection of information (including telephone, fax, email, etc.) to verify the effectiveness of relevant reporting ways and methods; check the description of the source of information on suspected adverse reactions in the pharmacovigilance system master file.	GVP Articles 32-38, 106, Vaccine Administration Law Article 54
PV16	information processing	54. Whether there are original records for information collection (*) 55. Whether the records maintain the authenticity, accuracy, completeness and traceability of the information during the transmission process; original record form Is the design of the grid (if any) reasonable? 56. Missing information in serious adverse reaction reports (including death case reports) and unexpected adverse reaction reports Whether follow-up is carried out, 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 downloaded regularly and processed as required (*) 58. Whether it cooperates with the investigation of adverse drug reactions and vaccine AEFI. 59. For For drugs that are marketed both domestically and abroad, whether sales of the drug has been suspended overseas due to safety reasons have been reported in a timely manner information on sale, use or withdrawal from the market	Understand the processes 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 departments, and understand the analysis, evaluation, and reporting of feedback data.	GVP Articles 40-42 and 51, AEFI Plan 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 severity, predictability and relevance of adverse drug reactions are evaluated scientifically and compliantly 62. Whether the reporting scope and reporting time limit are compliant (*) 63. Whether the original records and follow-up records are traceable 64. Whether the vaccine holder reports the discovered vaccine AEFI to the county-level disease prevention and control agency where the recipient is located in accordance with his duties	Randomly check the suspected adverse drug reaction/AEFI report forms of different categories (general, serious, and fatal) to check the completion and evaluation status of the report form; trace the original records and follow-up records to check whether the report content is consistent with the original records; check whether the reporting time limit is in compliance.	GVP Articles 43-54 AEFI Plan Three "Report" and Seven "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 attention, Whether the holder has strengthened monitoring based on the safety characteristics of the variety 66. Whether the monitoring method is appropriate 67. Whether the monitoring results have been analyzed and utilized	Understand the innovative drugs and improved new drugs that the holder has approved in the past five years, as well as the varieties that the regulatory authorities or adverse reaction monitoring agencies require attention; check relevant information for strengthening monitoring, such as plans, records, reports, etc.	GVP Article 39

Numbered	items	Inspection items (defect risk recommendation level)	Check method and content	Check basis
4. Risk identification and assessment				
PV19	Signal Detection	68. Whether the holder has carried out signal detection on suspected adverse drug reaction information collected through various channels (**) 69. Whether the method and frequency of signal detection are scientific and appropriate (*) 70. Signal determination (such as the determination of concern signals , invalid signal determination, priority determination) whether the principle	Understand the coverage of the included signal detection varieties; check the progress of signal detection work and view signal detection records; understand the methods, frequency, and procedures of signal detection; understand the principles and standards of signal determination; check whether there are detected signals and focus on signals (Including signals showing clustering	GVP Articles 55-59
PV20	Signal Analysis Evaluation	Reasonable 71. Whether the detected signals have been evaluated (**) 72. Whether the evaluation is comprehensive and reasonable evaluation opinions have been put forward 73. Whether the detected signals showing clustering characteristics have been analyzed and investigated in a timely manner (*)	characteristics). Check the signal evaluation records or reports to understand the evaluation process, results and suggestions; check the case analysis and situation investigation data showing clustered signals; check whether any new drug risks have been discovered through signal detection and evaluation.	GVP Article 60
PV21	risk assessment	74. Whether the new drug safety risks have been assessed, and there are records or reports of the risk assessment (*) 75. Whether the content of the assessment is comprehensive and scientific 76. Whether reasonable assessment opinions have been put forward 77. Whether the risks have been identified as required and report the risks discovered during the assessment process	View risk assessment records or reports to understand the assessment content, results and risk management recommendations.	GVP Articles 62-68
PV22	Post-marketing safety studies	(*) 78. Whether post-marketing safety research on drugs is carried out in accordance with the requirements of the drug regulatory authorities at the provincial level and above ÿ**ÿ 79. Whether post-marketing safety research of drugs is actively carried out based on the risk profile of the drug. 80. Whether the research plan is formulated by personnel with appropriate disciplinary background and practical experience, and reviewed or approved by the person in charge of pharmacovigilance. 81. Whether the findings discovered during the research are reviewed as required. New information and drug safety issues are assessed or reported (*)	Randomly check post-marketing safety research cases, including research plans, research reports, information reported to the drug regulatory authorities, etc.	GVP Articles 69-78, Vaccine Administration Law Article 57
PV23	Periodic Security Update Report/ Periodic Benefit-Risk Assessment Report	82. Whether the writing format and content comply with the "Specifications for Writing Periodic Safety Update Reports for Drugs" or the relevant guidelines of the International Conference on Technical Coordination of Registration of Drugs for Human Use (*) 83. Whether the data coverage period is complete and continuous 84. Whether the report complies with regulations The frequency and time limit required for submission (*) 85. Whether the report has been approved by the person in charge of pharmacovigilance 86. Whether the review opinions of the submitted report are processed in a timely manner or responded to as required (*)	Check the regular safety update report/periodic benefit-risk assessment report submitted by the holder to the national adverse drug reaction monitoring system, check the report coverage period, submission time and frequency; check whether all varieties that should be reported are covered; spot check the recent Submit regular safety update reports/regular benefit-risk assessment reports, check the format and content of the report, and verify whether the safety information included in the report includes all sources of information; for those with relevant requirements in the review opinions of the drug regulatory department , check whether it is handled or responded to in a timely manner.	GVP Articles 79-86
5. Risk Control				
PV24	Risk Management	87. Whether appropriate risk management measures are taken for identified risks and potential risks based on the risk assessment results (**) 88. Whether a pharmacovigilance plan has been developed for important risks (*)	Learn about the risk management measures taken by the holder, 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 to prove that it has taken risk management measures, such as revision or filing of drug instructions Applications, pharmacovigilance plans, post-marketing studies and enhanced	GVP Articles 66, 87, 97, Vaccine Administration Law Articles 54, 59
PV25	Risk control measures	89. Whether appropriate risk control measures have been taken (*) 90. Whether the effectiveness of the control measures has been evaluated or an evaluation plan has been formulated 91. Whether the risk control measures have been reported to the local provincial drug regulatory authorities as required and informed to relevant authorities unit(*)	surveillance plans, reports, etc. Check the pharmacovigilance plan and other relevant information; check the letters, leaflets, receipts and other supporting documents in which the holder reports to the drug regulatory authorities and informs relevant units; understands the varieties for which risk control is required by the drug regulatory authorities (such as revising and improving instructions), check whether the holder has carried out or completed the corresponding work as required.	GVP Articles 87-90, Vaccine Administration Law Article 73

Numbered	items	Inspection items (defect risk recommendation level)	Check method and content	Check basis
PV26	risk communication	92. Whether risk communication has been carried out? 93. Whether risk communication is timely and whether the method, content and tools are appropriate? 94. When an emergency occurs, whether risk communication is carried out urgently as required	Understand whether the holder has conducted risk communication and when; understand the methods and tools of risk communication; check the risk communication content of tools such as letters to medical staff and patient safety medication reminders; understand the emergency risk communication status of the holder; Regarding the addition of warnings, serious adverse reactions, restricted user groups, etc. in the revision of the instructions, understand whether the holder has carried out risk communication and the specific situation.	GVP Articles 91-95
PV27	pharmacovigilance plan	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 the awareness of risks	Review the pharmacovigilance plan and related materials demonstrating its implementation.	GVP Articles 96-99, Vaccine Administration Law Article 57
PV28	Investigation and handling of cluster incidents	98. Whether the cluster events of adverse drug reactions were investigated and handled in a timely manner (**) 99. Whether appropriate risk control measures were taken (*) 100. Whether the investigation and handling status and results were reported as required (*)	Understand whether the holder has discovered or learned about cluster events of adverse drug reactions; understand the investigation and handling of cluster events; check investigation reports, follow-up reports, and summary reports; check documents or records proving that the company has carried out relevant risk control measures.	GVP Articles 61, 89, 132

Note: 1. The relevant information required from the holder is generally within three years, or the information formed between the last inspection and this inspection.

2. In this table, GVP refers to the "Pharmacovigilance Quality Management Practices" and AEFI scheme refers to the "National Suspected Abnormal Vaccination Reaction Monitoring Program".