World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Quality Control laboratory
WHOPIR QCL

Part 1	**General information**
Laboratory Details	
Name of the Laboratory	Beijing Institute for Drug Control Department of Antibiotic Testing
Address of inspected Laboratory	No 25 Kexueyuan Road, Changping District Beijing Beijing 102206 China
GPS Coordinates	Latitude: 40.10 E Longitude: 116.3 N
Address of corporate office, telephone number, and fax number	Address as mentioned above. Tel: +8610-52779683 E-mail: guohz@bidc.org.cn
Dates of inspection	5-8 December 2023
Type of inspection	Routine – Follow-up inspection
Introduction	

Brief description of testing activities

Type of analysis	*Finished products*	*Active pharmaceutical ingredients*
Physical/ Chemical analysis	pH, density, water content, limit tests, disintegration, dissolution, uniformity of dosage units (mass, content), friability	pH, refractometry, loss on drying, water content, heavy metals, acid value, limit tests, specific optical rotation
Identification	HPLC (UV-VIS, PDA detector), GC (FID, ECD), TLC, UV-VIS spectrophotometry, FTIR, basic tests	HPLC (UV-VIS, PDA detector), GC (FID, ECD), TLC, UV-VIS spectrophotometry, FTIR, basic tests
Assay, impurities and related substances	HPLC (UV-VIS, PDA detector), GC (FID, ECD), UV-VIS spectrophotometry, volumetric titrations	HPLC (UV-VIS, PDA detector), GC (FID, ECD), UV-VIS spectrophotometry, volumetric titrations

General information	The Laboratory was founded in 1953 and is currently serving as a statutory institution responsible for supervising and testing the quality of drugs. It is an independent legal entity and conducts tests in various fields such as drugs, biological products, food/health food, cosmetics, pharmaceutical packaging materials, clean room environments, and medical devices. Furthermore, the laboratory is involved in carrying out legal testing, which includes registration, supervision, and import testing. Additionally, it engages in scientific research tasks and special assignments. These responsibilities involve tasks such as contributing to the drafting and reviewing of the Chinese Pharmacopoeia, handling assignments from the Ministry of Science and Technology of the People's Republic of China and the Beijing Municipal Science and Technology Commission, conducting national evaluations of test samples, and providing pharmaceutical testing services during large-scale events.
History	A WHO inspection was conducted in August 2018. Following this initial inspection, the inspection team issued a recommendation for a subsequent follow-up inspection. This follow-up inspection aimed to validate the effective implementation of the corresponding Corrective and Preventive Action (CAPA) plan. The Laboratory was audited by the Inspection team of the National Medical Products Administration (NMPA), Beijing Municipal Administration of Market Supervision and Management, and China National Accreditation Service for Conformity Assessment (CNAS). The audit certificates were provided in the submitted LIF.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	Organization and management Quality Management System Personnel Training and Safety Documentation and Records Premises and Equipment Validation – Qualification –Calibration of equipment, including computerized systems Laboratory Practices Reference standards – Reagents, including water qualification
Restrictions	The laboratory documentation was in Chinese, so interpreters were required to facilitate the inspection team's review of the records and practices.
Out of Scope	Refer to the list of activities.

	Furthermore, the laboratory has only strengthened the Department of Antibiotic Testing capabilities to meet WHO-PQ requirements and is committed to testing WHO products in accordance with the applicable standards. It's important to note that other departments of the Laboratory were not within the purview of this inspection.
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
CAPA	Corrective action & Preventive action
DQ	Design qualification
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GC	Gas chromatography or Gas chromatography equipment
GMP	Good manufacturing practices
HPLC	High-performance liquid chromatography (or high-performance liquid chromatography equipment)
IQ	Installation qualification
IR	Infrared spectrophotometry
KF	Karl Fischer titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
N	Normality
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NMPA	National Medical Products Administration “in China”
NRA	National regulatory agency
OOS	Out-of-specifications test result
OQ	Operation qualification
Ph.Eur.	European Pharmacopoeia
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PT	Proficiency testing
PTS	Proficiency testing scheme
PW	Purified water
QA	Quality assurance
QC	Quality control

QCL	Quality control laboratory
QM	Quality manual
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
TLC	Thin layer chromatography
TOC	Total organic carbon
URS	User requirements specifications
USP	United Stated Pharmacopoeia
UV	Ultraviolet-visible spectrophotometry or spectrophotometer
VMP	Validation master plan
VS	Volumetric solution

Part 2	**Summary of findings and recommendations (where applicable)**

1. Organization and management

A comprehensive organizational description was presented during the opening meeting.

The organization and management structure of the Laboratory were specified in the organizational chart. At the time of inspection, the total number of staff, to be attended in the prequalified activities accounted for 57. Although the responsibility, authority, and interrelationship of the personnel were not included in the chart; this information was provided separately in a list in the LIF, along with another list containing complete staff information. The Laboratory comprised 21 offices and departments, including the Office of QA, Department of Instrument Management, and Office of Test Management, as indicated in the organizational chart. The Head of the Laboratory reported to the Beijing Municipal Medical Products Administration (BMMPA). This chart was included in the Laboratory's Quality Manual, approved on 28 November 2023.

The Laboratory obtained accreditation from CNAS (China National Accreditation Service for Conformity Assessment) on 8 September 2021, valid until 19 October 2024, in accordance with ISO/IEC 17025:2017. Additionally, the Lab was certified by CMA (China Inspection Body and Laboratory Mandatory Approval) on 4 November 2021, valid until 22 July 2024.

The Laboratory had established measures to safeguard its management and personnel from potential influences such as commercial, political, financial, and other pressures or conflicts of interest that could compromise the quality of their work. The Laboratory had implemented a policy to guarantee the confidentiality of information within marketing authorizations and test reports included in the Quality Manual. Additionally, a random selection of agreements with staff was reviewed and verified.

A quality manager and their dedicated team were assigned the responsibility of ensuring compliance with the quality management system. The designated quality manager had direct access to the highest level of management, specifically the Laboratory Director, where decisions regarding laboratory policies and resource allocation were made.

Effective communication and coordination were maintained among staff involved in activities that required testing of the same sample in different units. This was facilitated by managing samples, test requests, and the recording of test procedures through the Laboratory Information Management System (LIMS).

Official working hours were noted to be weekdays from 8:30 AM to 4:30 PM.

2. Quality management system

The Quality Management System was established in accordance with the following:

- Competence assessment and general requirements for inspection body and laboratory mandatory approval.
- Mandatory approval conditions for food testing agencies.
- Accreditation criteria for the competence of testing and calibration laboratories (ISO/IEC 17025:2017) and its application guidance in the fields of chemical testing and others.
- WHO Good Practices for Pharmaceutical Control Laboratories.
- Laboratory Testing (LT) & NRA Lot Release (LR) in WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products.

The QMS documentation was structured into four levels, which included the quality manual, procedure documents, operation instructions/testing standards/procedures, and record forms/reports.

A Quality Manual defining the quality management system was available.

Management Review

A management review of quality issues was conducted regularly, at least annually, following the applicable SOP. This review encompassed the following:
(a) Reports on internal and external audits or inspections, along with any necessary follow-up actions to address deficiencies.
(b) Findings from investigations conducted in response to received complaints, as well as the outcomes of proficiency testing.
(c) Implementation of recommendations and preventive measures resulting from these investigations.
The results of the management review were documented using a dedicated form.

Internal audit

The Laboratory's activities were subject to systematic and periodic internal audits, as outlined in SOP for Procedure on Internal Audit.

Recent internal audit reports and the corresponding CAPA plan were accessible and reviewed.

Change Control
Change control activities were conducted in accordance with the applicable SOP.

It's worth noting that various departments within the organization might employ different SOPs than the main SOP for Change Control when handling change control requests. For instance, the Department for Test Management utilized SOP for method change requests.

Handling of deviation and implementation of CAPA
Activities associated with CAPA implementation were executed following the respective SOP. The scope of this SOP was limited to the non-conformities during testing.

In the case of planned deviations, another SOP was adhered to.

For situations where non-conformities were identified during or after testing, the applicable SOP was different.

Handling of complaints
The activities were managed according to the respective SOP.

Proficiency Testing
Participation in proficiency testing was conducted following SOP for Procedure on Proficiency Testing or Interlaboratory/Intra-laboratory Comparison. Subsequently, the results underwent thorough analysis and evaluation, serving as input for the management review, as outlined in SOP for Procedure on Management Review. A comprehensive list of the laboratory's participation in chemical drug proficiency testing over the past three years, as well as pertinent information regarding proficiency tests for the year 2022, was supplied within the submitted LIF. In 2023, the laboratory actively participated in a total of 15 tests related to WHO PQ inspections, with the attendance list for these proficiency tests being provided in an Excel sheet. It's noteworthy that the PT organization, NIFDC (National Institutes for Food and Drug Control), holds certification from the CNAS, granted through the Proficiency Testing Provider Accreditation certificate, which remains valid from 8 Oct 2018 to 7 Oct 2024.

Observations related to the Quality Management System were adequately addressed in the respective CAPA plan.

3. Control of documentation

The Laboratory had established a comprehensive system to manage Standard Operating Procedures, covering their preparation, revision, distribution, return, and archiving. This system was facilitated through an application that comprised various modules and included a designated form for requesting SOP revisions from respective departments.

Each SOP within this system was uniquely identified and included essential information such as an identifier, version number, revision number, date of implementation, and reference to the previous version. The QA department maintained a list of SOPs, in addition to the list within the document management system, which was regularly reviewed for revision purposes. The procedures for this process were outlined in the respective SOP for document management. Currently, the system does not generate notifications for SOP revision due dates.

Staff underwent training on both new and revised SOPs as part of the personnel training process. Relevant staff members acknowledged their training by signing off before the implementation of any new or revised SOP. The training documentation for the Out-of-Specification (OOS) SOP, following its recent revision, was thoroughly reviewed to ensure compliance with the procedure.

The Laboratory also had specific SOPs in place for managing SOPs themselves. Additionally, a general SOP for document control was available. These SOPs were reviewed and discussed as part of the ongoing quality management process. It was recommended that all Quality Management System (QMS) documentation be treated as controlled documents, complete with version numbers and evidence of authorization.

The observation related to the controlled documentation was sufficiently addressed in the respective CAPA plan.

4. Records

The Laboratory maintained records in both electronic and paper forms as follows:

- Analytical records were documented either directly in the eLIMS (for simple tests such as identification using UV-visible), or the analyst could use test record templates designed by the QA department and incorporated into a designated software application with an ID number. The analyst recorded the test steps on this template and uploaded the complete template into the eLIMS.
- The usage of instruments and equipment was recorded and documented in the respective logbooks or templates. The ID number of the instrument used was also documented in the eLIMS.
- Calculations were made using validated Excel sheets incorporated into the eLIMS (a recently implemented practice), and the Excel sheets with the results were uploaded to the eLIMS for each sample testing.
- The use of instruments was recorded in the respective logbook or designated form.
- Calibration and qualification records were kept with the Department for Instrument Management.
- Information about the receipt of samples was documented in the eLIMS.
- Data from HPLC, UV-VIS, and GC were automatically transferred to the eLIMS, where the respective results were calculated.

The records were electronically signed within the eLIMS, and alterations should be captured in the audit trail. Additionally, “pdf” files of chromatograms and spectra records were uploaded into the same system.

All paper records were maintained in an archive in compliance with the applicable SOP, outlining procedures for document retrieval for a minimum of six years, depending on the document type. Access to the archive was restricted to authorized personnel, and continuous monitoring of temperature, humidity, and pest control was conducted. Fire detectors were installed in the facility with ample space and efficient arrangement.

Quality management records encompassed reports from both internal and, if applicable, external audits, as well as management reviews. Furthermore, records of all complaints and their investigations, including those related to possible corrective and preventive actions, were included.

The history of the randomly selected samples was checked (receipt log, storage conditions, tests, instruments and standards used, results, reporting, and archive) to verify the records' accuracy.

5. Data processing equipment

An inventory of computerized systems belonging to analytical equipment with data processing functions was presented during the inspection, containing details such as Name, Version, Purpose, Validation Date, Next Validation Date, and their associated instruments.

The qualification and validation of the selected computerized systems based on a risk-based approach were reviewed to confirm that each system had been adequately validated or verified for its intended use.

Procedures were implemented to safeguard the data's integrity, in line with SOP for Procedures to guarantee data integrity within the information systems. These SOPs encompassed measures to secure the integrity and confidentiality of data during entry, collection, storage, transmission, and processing. Electronic data remained protected against unauthorized access, and an audit trail of any changes was meticulously maintained.

Electronic data was backed up as outlined in the respective SOP. Superseded software versions were archived or retired in compliance with the applicable SOP. These archived versions were stored for a defined period in a retrievable and readable electronic format. The restoration process for the relevant software applications was detailed in an SOP, and the evidence of the most recent restoration was both accessible and reviewed. Electronic data produced by standalone instruments in the laboratories were overseen by the Department for Instrument Management, following an applicable SOP. The data were backed up either on a server or a hard disk, depending on the software and the associated instrument. The organization’s IT structure map was accessible and subject to review. It was advised that the map be incorporated into the relevant SOP or issued as a controlled document.

Regarding spreadsheets, Excel®, all cells including calculations, were locked to prevent accidental overwriting of formulas. Unrestricted access was only granted to cells designated for data input. Calculation algorithms were rigorously tested using a separate calculator, and a recognized dataset

was employed for software verification. The spreadsheets were made accessible within the LIMS, following the procedures outlined in the SOP for validating Excel spreadsheets. This practice has been in effect since November 2023.

While validating computerized systems, the frequency, roles, and responsibilities for reviewing original records, including audit trails, were determined following a documented and justified risk assessment. The risk assessment for one of the software applications was thoroughly examined and reviewed to validate the procedure.

Observations related to Data processing management were adequately addressed in the respective CAPA plan.

6. Personnel

The laboratory ensured it had an adequate number of personnel with the required education, training, technical knowledge, and experience for their assigned roles. The training was evaluated upon its completion.

The department had a competency list detailing the skills relevant to each individual's job. Tests and activities were assigned based on these competency lists. It was noted that the list was not issued in a controlled manner. SOP training was delivered to personnel through both the document management system and manual training sessions in a designated training room, with attendees signing an attendance sheet.

The Laboratory maintained current job descriptions for personnel involved in tests, calibrations, validations, and verifications, along with records describing their qualifications, training, and experience. Randomly selected CVs, job descriptions, and qualifications were reviewed to confirm adherence to the procedure.

Personnel training was conducted in accordance with the SOP for the personal training procedure, which was reviewed and discussed. When a new employee was hired, a change control request was raised to include their training and education.

Training records related to the use of selected software systems were available and reviewed.

7. Premises

The Laboratory facilities were appropriately sized and designed to accommodate their intended functions and operations.

Separate storage facilities were in place to securely store samples, retained samples, reagents, laboratory accessories, and reference substances as necessary. These storage areas included refrigeration units (2-8°C) and freezers, and environmental conditions were regularly monitored and

controlled. Additionally, the laboratory provided separate metal cabinets specifically designed for the safe storage of flammable substances.

Access to the laboratory facilities was restricted to authorized personnel.

Stringent precautions were implemented, including the use of dedicated equipment, such as laminar flow workbenches, for handling, weighing, and manipulating highly toxic substances, including genotoxic substances. Procedures were established to minimize the risk of exposure and contamination.

The proper disposal of various types of waste, including toxic waste (both chemical and biological), reagents, samples, solvents, and air filters, was conducted in accordance with the applicable SOP.

8. Equipment, instruments, and other devices

Throughout the inspection, the inspection team checked the requisite test equipment, instruments, and other devices utilized in activities falling within the scope of the inspection and examined the pertinent documentation associated with them. The objective was to validate that these instruments were performing tests, calibrations, validations, and verifications accurately. For further information, please consult Section 12.

The volumetric equipment and flasks underwent verification, and their certifications were uploaded into the eLIMS system.

9. Contracts

The Laboratory had established a procedure for the selection and procurement of services and supplies. Suppliers of critical consumables, supplies, and services that could impact the quality of testing underwent an annual evaluation, including the completion of an appraisal form. Records of these evaluations, as well as lists of approved suppliers, were diligently maintained to demonstrate their compliance with the Laboratory's quality requirements.

The Laboratory did not subcontract any tasks related to WHO products.

Contracts were executed to outline the contracted work and assign responsibilities to each party involved. The contract with the waste management service provider was available and subjected to discussion.

10. Reagents

In the laboratory, reagents of appropriate quality were utilized and correctly labelled. The labels on reagent containers included essential information such as content, manufacturer, date of receipt, date of container opening, concentration (if applicable), recommended storage conditions, expiry date, and retest date.

Reagent solutions were prepared following established pharmacopeial or other relevant standards whenever available. Records were maintained documenting the preparation and standardization of volumetric solutions. Reagent solutions prepared in the laboratory were labeled with the reagent's name, date of preparation, initials of the responsible technician or analyst, expiry date (if applicable), retest date (as justified), and concentration (if applicable).

The laboratory routinely verified the quality of water to ensure it met the specified standards for different grades of water, as outlined in the Chinese Pharmacopoeia and USP.

Toxic or flammable reagents were stored and handled with necessary precautions, utilizing dedicated separate cabinets (located in separate rooms). Small quantities of acids, bases, and solvents were stored in the laboratory store, while the primary stocks of these items were kept in a separate storage area outside the laboratory facility.

11. Reference substances and reference materials

Reference substances were supplied by the applicant or procured from NIFDC. These reference substances were carefully stored and utilized to ensure their quality remained intact. Desiccators were made accessible in the laboratory for the storage of hygroscopic substances when the need arose.

Reference standards, sourced either from the applicant or acquired from NIFDC, fulfilled the specific requirements outlined in the corresponding monographs. Details, including the material's name and description, batch or control/identification number, source, date of receipt, intended use, method of using the reference substance, expiry date or retest date, location of storage, and specific storage conditions, were systematically documented on the test record, when applicable.

The HPLC test record form included the relevant identification number and details of the reference substance (RS), which were subsequently uploaded into the eLIMS. This practice represented a recent addition to their procedures. Each set of records was accompanied by a batch validity statement. It's noteworthy that, in the past, the Certificate of Analysis (CoA) for reference substances was not requested from the supplier, but the Laboratory has now implemented this practice. Previously, the registration of reference substance receipts was not applicable, and records of these substances were solely accessible through the test requests received from the applicant. At present, the Laboratory employs uncontrolled forms to document the receipt and usage of reference substances. The inspection team was informed that a new practice of using the eLIMS module for reference substances and chemical registry has recently been initiated. It's worth noting that this module was validated in 2020.

The laboratory utilized the RS only once, and any remaining portion was subsequently disposed of. In the event of unassigned OOS results, a new bottle of the RS from the same batch would be opened for the repeat test.

The observation related to Reference Standards was adequately addressed in the respective CAPA plan.

12. Calibration, verification of performance, and qualification of equipment, instruments, and other devices

Each instrument was assigned a unique identifier, and labels were affixed to them to indicate the status of their calibration and the date when recalibration was required.

The qualification documentation of the following equipment underwent a review to ascertain whether they were qualified in accordance with the applicable SOP and were suitable for their intended use:

- HPLC instruments
- UV-VIS instruments
- Balance
- Friability apparatus
- Karl Fischer titrator

Balances were checked daily using internal calibration and regularly using suitable test weights. Requalification was performed annually using certified reference weights.

Records/logbooks were kept for items of equipment with information to identify the device, current location, and any respective maintenance. History of damage, malfunction, modification, or repair was recorded in the designated module in the eLIMS. The use of the instrument was also recorded.

For each equipment, there was an SOP outlining the procedures for qualification and performance verification of the instrument. The equipment underwent periodic verification in accordance with the respective SOPs to ensure their continued qualification. A designated service provider was chosen to conduct these verification activities, and the Department of Instrument Management oversaw and verified the completion of these tasks.

Observations related to Equipment were adequately addressed in the respective CAPA plan.

13. Traceability

Test results were traceable, as applicable, back to primary reference substances.

Moreover, all calibrations or qualifications of instruments were systematically traceable to certified reference materials and the International System of Units (SI), thereby ensuring metrological traceability.

In addition to this, the traceability of the sample was meticulously maintained from the moment of receipt through every testing stage until the generation of the analytical test report.

14. Incoming samples

Sample receipt procedures adhered to the guidelines outlined in the SOP for Procedure on Testing Sample Handling. Additionally, a dedicated sampling office was responsible for collecting samples

exclusively for import products, in accordance with SOP for Sampling of imported drugs. Samples from other sources were typically received directly from manufacturers, dealers, or the NMPA. Hence, the laboratory served clients from both government departments and commercial organizations.

Upon receipt, the sample custodian visually inspected each sample to verify that the labeling matched the information in the test request. Any observations were meticulously documented, including the date and signature. If any discrepancies or obvious damage were identified, this information was recorded on the test request form, and any queries were communicated to the sample provider.

For efficient sample management, a registry, specifically the eLIMS software system, was available to maintain comprehensive records of all incoming samples. This system generated unique sample numbers, produced accompanying documents, and documented information related to the receipt, distribution, and monitoring of sample consignments to specific units. The electronic register was systematically updated to include the following crucial details:

- The unique registration number assigned to each sample.
- The precise date of sample receipt.
- The specific unit to which the sample was subsequently dispatched.

Every test conducted was initiated after the formal receipt of the corresponding test request.

A test application accompanied each sample submitted to the laboratory before the products were received. This application included essential information, including but not limited to:

- A description of the sample.
- Specifications to be utilized for testing.
- Required storage conditions.

The laboratory conducted a thorough review of these test requests to ascertain its capacity to fulfill them and to ensure that the selected tests/methods aligned with the customers' specific requirements.

Upon receipt, the samples were divided into three approximately equal portions:

- Immediate testing
- Confirmation of testing if required
- For retention in case of dispute (Refer to Section 20).

The part of the sample that required immediate testing would be sent to the lab within 24 hours. The remaining portions of the sample, which would be used for retesting (when applicable), were kept in the sample room. The access to the sample room was restricted by a face scanner and key, and the samples were stored according to the prescribed storage conditions. The sample labels included provisions to indicate whether the sample was undergoing testing, had testing completed, or was being retained. The responsible person would transport the samples to the specific unit for testing, along with the flow sheet. The samples were then distributed for analysis based on a competency matrix.

The samples were stored while taking into account the required storage conditions. The laboratory used a manual thermometer to monitor temperature and humidity, with readings recorded once a day in a dedicated logbook. Entry and exit information were also documented in a separate logbook for this purpose.

If the storage conditions were expected to be below ambient conditions, the shipment condition was monitored using a datalogger.

The observation related to the Sample handling was adequately addressed in the respective CAPA plan.

15. Analytical worksheet

Information about samples, test procedures, calculations, and results was recorded in analytical records integrated into the Laboratory's eLIMS application system. The source documents for measurements were not provided to be kept alongside the analytical results. Since November 2023, the Laboratory has improved its system to include information about reagents and reference standard details in the eLIMS, along with the test procedures. Before this update, these details were not available in the system. Furthermore, the Laboratory has provided validated Excel sheets within the system for use by analysts in their calculations.

The eLIMS test records included the following information:

- The dates when the analysis commenced and concluded.
- References to specifications, a comprehensive description of the testing methods applied to the sample, including specified limits, identification of the testing equipment utilized, reference substances, reagents, and solvents used.
- Interpretation of the results.
- The determination of whether the sample conformed to the specified requirements or not.

All values obtained from each test, including blank results, were recorded on the analytical record templates, and then they were either uploaded into the eLIMS or directly inputted into the eLIMS, depending on the type of test. All graphical data, whether acquired from recording instruments or manually plotted, were uploaded as PDF or other image files into the LIMS system, ensuring traceability to the electronic record or document where the data was originally sourced.

The completed analytical records were initially signed by the responsible analyst and then verified by a second qualified analyst. Following this, they were approved, signed by the supervisor (Lab chief), and authorized by the BIDC - authorized signatory.

In case corrections were required, outdated information was rectified in the system in accordance with the respective SOP by submitting a change request. The system's audit trail maintained a record of all changes made.

The specifications necessary for sample assessment were defined within the test, either in the form of NMPA specifications, in Chinese Pharmacopeia, or USP standards.

16. Validation of analytical procedures

The SOP on Analytical Method Verification, Transfer, and Validation was reviewed and discussed. This SOP was applicable to the analytical method verification, transfer, and validation of drugs. Methods that needed verification, transfer, or validation included identification tests, impurity determination (limit or quantitative tests), assay, and characteristics (including dissolution and drug release).

When the standard method was used for the first time, the laboratory carried out technical verification, and the applied method was considered the initial testing of samples from the new enterprise.

System suitability tests were conducted before the chromatography tests.

The observation related to the Validation of analytical procedures was addressed in the respective CAPA plan.

17. Testing

The samples were tested in accordance with the product's test specifications, which were uploaded in the eLIMS following the completion of the preliminary procedures, as outlined in the SOP for Testing Procedure.

Guidance on official requirements was typically provided in the product specification form by NMPA. If this information was not available, reference was made to the national pharmacopeia or other official instructions in line with the test request. The product specification form detailed the respective test procedures comprehensively, furnishing ample information for appropriately trained analysts to conduct the analysis reliably.

Whenever system suitability criteria were specified within the method, they were met.

18. Evaluation of test results and OOS investigation

Test reports were automatically generated through eLIMS using the original data.

An SOP outlined the procedures for investigating test results. When a doubtful or suspected OOS result was identified, both the supervisor and the analyst conducted a thorough review of the procedures used during the testing process.

The records of randomly selected samples underwent a comprehensive review to ensure accuracy in recording, qualifications of analysts and equipment, preparation of reagent solutions, adequacy of reference standards, completeness of analytical records, traceability, evaluation of test results, information on the CoA, and investigation of out-of-specification results. Doubtful results were

accepted only if an identifiable error was found. In cases where the investigation yielded inconclusive results, the SOP provided guidance on conducting retests. Once an error was identified, corrective and preventive measures were documented and put into practice. A designated form was used during the investigation of OOS, and individual results, along with their acceptance criteria, were reported.

Samples randomly selected from the Laboratory's list of samples spanning from 1 Jan 2021, to 8 Nov 2023, encompassing FPP and API, were subject to review.

The test reports also included the following information:
- Background and testing objectives.
- References to the specifications and methods employed.
- Comprehensive results of all tests conducted (or numerical results along with the standard deviation of all tests performed).
- A statement indicating whether the sample met the specified requirements.

The respective CAPA plan adequately addressed the observation related to the result investigation.

19. Certificate of analysis

There was an SOP in place that outlined the use of LIMS for CoA preparation within testing activities. The LIMS system automatically generated the analytical report using the original data. Any modifications made were traceable within the system. However, it's important to note that final results could not be altered under any circumstances. In the event that modifications were deemed necessary, a formal request was raised to initiate an investigation and make changes in accordance with the SOP for reporting testing results.

A Certificate of Analysis was prepared for each sample or batch of a substance or product, encompassing a range of information, including but not limited to data derived from the test report generated in the eLIMS. The laboratory printed the test report along with an accompanying cover page.

This Certificate of Analysis included:
- Comprehensive results of the tests conducted, compared against the specified limits.
- A definitive conclusion indicating whether the sample fell within the defined specification limits.
- The date when the tests were concluded, denoted as the “Date of Test Authorization”.

20. Retained samples

Samples were stored for one year in compliance with the relevant legislation, as outlined in the SOP for Retained Samples. A sufficient quantity of retained samples was maintained, ensuring the possibility of conducting at least two re-analyses. These retained samples were stored in their original packaging.

The specific quantity required for each portion was determined as per the guidelines provided in the applicable SOP, which covered general product testing quantities.

21. Safety

During the laboratory inspection, it was evident that safety was a priority within the facility. Staff members had access to both general and specific safety instructions. These instructions were communicated through various means, including written materials, poster displays, and occasional seminars. Staff had received training in fire-fighting equipment usage, including fire extinguishers, fire blankets, and gas masks.

In terms of personal protection, staff members wore laboratory coats and eye protection, with special precautions taken when handling highly potent, infectious, or volatile substances. Safety showers were readily available for immediate use in case of emergencies. Safety data sheets were provided prior to testing activities, and first-aid kit was available.

Chemical containers within the laboratory were appropriately labelled, including clear warnings such as "flammable" when necessary. Electrical safety was upheld with adequate insulation and spark-proofing measures for electrical wiring and equipment, including refrigerators.

Moreover, the laboratory had established safe disposal practices for unwanted corrosive or hazardous products, implementing techniques such as neutralization or deactivation.

Part 3 – Conclusion / Inspection outcome

Based on the areas inspected, the people met, and the documents reviewed, including the CAPA plan provided for the observations listed in the Inspection Report ***Beijing Institute for Drug Control - Department of Antibiotic Testing***, located at ***No 25 Kexueyuan Road, Changping District, Beijing, Beijing 102206; China,*** is considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

All the non-compliances observed during the inspection that were listed in the full report, as well as those reflected in the WHOPIR, were addressed by the Laboratory to a satisfactory level prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 4	List of WHO Guidelines referenced in the inspection report

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1.
   Short name: WHO GPPQCL Guidelines or ***TRS No. 957, Annex 1***

https://www.who.int/publications/m/item/trs957-annex1

2. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
   Short name: WHO TRS No. 961, Annex 2
   https://www.who.int/publications/m/item/trs961-annex2

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