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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
of the Quality Control laboratory
WHOPIR

Part 1	**General information**		
Laboratory Details			
Name of the Laboratory	National Institutes for Food and Drug Control (NIFDC) **Institute for Chemical Drug Control** Division of Chemical Drug (Physico-Chemistry activities) Division of Pharmacology (Bacterial endotoxin tests） Division of Antibiotics (for Microbial assay) Division of Narcotic & Psychotropic Drugs (for Optical rotation measurement)		
Address of inspected Laboratory	31 Huatuo Road Daxing District, Beijing China (People's Republic of)		
GPS Coordinates	116.31 E 39.68 N		
Address of corporate office, telephone number, and fax number	Same as above		
Dates of inspection	11-14 December 2023		
Type of inspection	Routine		
Introduction			
Brief description of testing activities	*Type of analysis*	*Finished products*	*Active pharmaceutical ingredients*
	Physical/ Chemical analysis	pH, density, refractometry, viscosity, water content, limit tests, disintegration, dissolution, uniformity of dosage units (mass, content), friability	pH, refractometry, viscosity, loss on drying, water content, heavy metals, acid value, iodine value, limit tests, nitrogen determination specific optical rotation
	Identification	HPLC (UV-Vis, RI detection), GC (FID), TLC, UV-Vis spectrophotometry, FTIR, basic tests	HPLC (UV-Vis, RI detection), GC (FID), TLC, UV-Vis spectrophotometry, FTIR, basic tests

	Assay, impurities, and related substances	HPLC (UV-Vis, RI detection), GC (FID), UV-Vis spectrophotometry, AAS, FTIR, volumetric titrations,	HPLC (UV-Vis, RI detection), GC (FID), UV-Vis spectrophotometry, AAS, FTIR, volumetric titrations
	Micro-biological tests	Microbial assay of antibiotics	Microbial assay of antibiotics
	Bacterial Endotoxin Testing (BET)	Bacterial endotoxin tests (LAL),	Bacterial endotoxin tests (LAL),
General information	The National Institutes for Food and Drug Control (NIFDC), founded in 1950, functions as a subsidiary agency within the National Medical Products Administration (NMPA). NIFDC is the national laboratory responsible for pharmaceutical quality control and the WHO Collaborating Centre for Drug Quality Assurance. Guided by the leadership of NMPA, NIFDC assumes various responsibilities, which include: ✓ Conducting registration testing and post-marketing surveillance for pharmaceutical products, medical devices, health food, cosmetics, pharmaceutical excipients, primary packaging materials, and pharmaceutical containers. ✓ Undertaking or coordinating technical arbitration for pharmaceutical products and medical devices. ✓ Overseeing the batch release of biological products. ✓ Conducting technical evaluations, validations, and the development of standards, technical specifications, and testing methods for pharmaceutical products, medical devices, and food. Additionally, NIFDC is involved in developing and revising technical specifications, practices, and testing methods for health food and cosmetics. ✓ Managing the development, preparation, characterization, distribution, and maintenance of national reference standards for drugs and medical devices. ✓ Providing technical guidance, participating in planning and statistical activities related to food and drug post-market surveillance programs, and organizing training sessions for quality control professionals from research and development institutes, manufacturers, distribution agencies, and healthcare institutions. NMPA relies significantly on NIFDC's testing services for active pharmaceutical ingredients (API) and finished products.		

History	The Laboratory achieved prequalification status on 20 November 2012. In August 2018, it underwent a WHO inspection. During that period, the scope of prequalified Laboratory activities did not encompass microbiology testing.
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 verification of water quality
Restrictions	Documentation was primarily in Chinese, necessitating the use of interpreters for communication and translation purposes.
Out of Scope	Sterility testing – for more details, refer to the list of activities. It is important to note that the inspection only covered relevant divisions of the Institute for Chemical Drug Control that pertain to prequalification status activities.
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
LAL	Limulus Amebocyte Lysate
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
N	Normality

NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
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**

1. Organization and management

The opening meeting provided a comprehensive organization overview. The NIFDC was situated on a campus in Beijing, which served as the location for its operations and activities.

The organization and management structure of the Institute for Chemical Drug Control, one of the laboratories under NIFDC responsible for prequalification-related activities, including the roles, responsibilities, authority, and interrelationships of personnel, were outlined in the organizational

chart and job descriptions. The laboratory consisted of 13 Service Departments and 14 Management Departments under the leadership of the Director of the Laboratory.

The organization had several deputy directors responsible for quality management across different institutes. This institute was further divided into 10 divisions, with four of them actively engaged in prequalification-related activities:

- Division of Chemical Drug: Responsible for conducting Physico/Chemical testing activities.
- Division of Antibiotics: Involved in performing Microbial assays.
- Division of Narcotic & Psychotropic Drugs: Engaged in tasks related to (Optical rotation).
- Division of Pharmacology: Responsible for conducting LAL Testing.

The Laboratory established measures to guarantee that both its management and personnel remained free from commercial, political, financial, or any other influences or conflicts of interest that could potentially compromise the quality of their work. Additionally, there was a well-defined policy in place to safeguard the confidentiality of information found within marketing authorizations and test reports.

The Laboratory staff worked weekdays from 8:30 am to 4:30 pm with flextime between 9 am and 5 pm.

A dedicated quality manager was appointed to oversee adherence to the quality management system. This designated quality manager had direct access to the highest levels of management, where decisions concerning laboratory policies and resource allocation were made.

To ensure proper communication and coordination when testing the same sample across different units, the staff involved in these activities worked together under the guidance of the Principal Analyst. Furthermore, an effective information channel between the various departments and the QA department was maintained with the assistance of the respective QA representatives of the divisions, who also served as the deputy directors of those divisions.

The observation related to the Organization and management was adequately addressed in the respective CAPA plan.

2. Quality management system

A quality manual defined the quality management system.

In 2002, NIFDC established a quality management system aligned with ISO/IEC 17025, receiving accreditation from CNAS, a member of ILAC and IPLAC. Subsequently, NIFDC made updates to align with certification requirements and customer needs. In 2010, as part of the WHO PQ program, NIFDC integrated WHO-GPCL elements into the quality management system and made the necessary document revisions. The eighth edition of the quality manual was prepared in anticipation of the relocation to the new campus.

NIFDC participated in international proficiency test schemes and was responsible for organizing proficiency tests in the Drug Testing Field. Furthermore, NIFDC held an accreditation certificate under ISO/IEC 17043. A table summarizing proficiency test results from 2019 to 2022, as outlined in the LIF, along with a list of proficiency tests conducted in 2023, was provided during the inspection.

Management Review
A regular management review of quality matters was conducted in compliance with the respective SOP, occurring at least once a year. The most recent review report was dated 3 Feb 2023, and it encompassed:
(a) Reports concerning both internal and external audits or inspections, along with any necessary follow-up actions to address identified deficiencies.
(b) Findings from investigations conducted in response to received complaints, as well as doubtful (atypical) or aberrant results reported in collaborative trials and proficiency tests.
(c) The implementation of corrective actions and preventive measures that resulted from these investigations.

Internal audit
The activities of the Laboratory were systematically and periodically audited internally as outlined in the applicable SOP. The most recent internal audit took place on 11 & 12 May 2023 and involved a team of seven auditors, with leadership provided by an external expert from CNAS. The audit report was issued on 25 Jun 2023.

Change Control
Change control activities were carried out following the respective SOP.

Handling of deviation and implementation of CAPA
Planned deviations were handled in compliance with the applicable SOP. During 2023, no planned deviations were documented.

Non-conformances were addressed following the guidelines outlined in the SOP. A designated report form was used to document both serious and ordinary deviations. The deviations recorded in the respective registry were associated with the internal audit outcomes.

Handling of complaints
The process was carried out in accordance with standard procedures. No complaints were received in 2021, and one complaint was properly handled in 2022.

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

3. Control of documentation

To maintain the quality of testing results, NIFDC implemented a comprehensive document system comprising the Quality Manual, Lab Safety Manual, operational procedures, SOPs, and record forms. These documents underwent drafting, approval, revision, and publication procedures in accordance with SOP for Document Control Procedure. Each SOP had a unique identifier, version number, date of implementation, and reference to the previous version. Additionally, the SOP for QA system document drafting and compilation was in place and regularly reviewed.

Since July 2015, NIFDC established a computerized document control system for drafting, reviewing, approving, online training, releasing, periodically reviewing, and expiring all the quality system documents prepared by NIFDC. Through the system, approved documents were released in electronic form, and formally revised and updated documents were simultaneously released to replace the old versions. The authority to access electronic documents was issued according to the approved scope. For convenience, paper-based documents could be printed from the computerized document control system, and information on the printing operation (such as the operator's name, time of the printing, sequence number of the printed copy, etc.) could be traced. The release of the printed paper copy was recorded, and the version validity was managed by the Division using the document. All records related to document control were stored within the document control system as electronic record forms. The operation and maintenance of the document control system were managed in accordance with SOP for the Management of Computerized Document Control System.

Staff received training on new and updated SOPs. The Quality management system ensured that SOPs were created by the initiator or a person in a corresponding role, reviewed, and approved by the Head of the Institute, and then released by the quality manager (Quality Unit). Appropriate personnel acknowledged their awareness of relevant changes and implementation dates through the electronic Document Management Database.

4. Records

Records were created for analytical tests, encompassing calculations, derived data, method validations/verifications, instrument usage, calibrations, maintenance, and sample receipt. A new version of the respective software application was introduced to document sample receipt and registration, issue analytical worksheets, and record test results. Instrument usage was meticulously logged in respective logbooks, and additionally, each test's instrument utilization was noted in the analytical worksheets.

The records were comprehensive, signed, and included relevant documents such as chromatograms, spectra, and Excel sheets for calculations, which were appended to the test records.

Records were archived in compliance with the respective SOP and the Archive Management Regulations. The documentation was categorized for archiving based on its type, as defined in the SOP.

After completing the test, the analyst would review the documentation. If the documentation was complete, they would assemble all the documents, page number them, and record them into the respective system, creating a table of contents. Once the table of contents was generated, a printed copy was prepared and bound together. Simultaneously, an electronic copy of the content was sent to the archive facility. At the archive facility, a check was performed to ensure the completeness of the documentation. Subsequently, they would mark everything as received in the Archive Management system.

Quality management records consisted of reports from internal audits (and external audits if conducted) and management reviews. These records also included documentation of all complaints and their corresponding investigations, including records related to potential corrective and preventive actions.

To ensure the accuracy of the records, the history of randomly selected samples was reviewed. This review encompassed the receipt log, storage conditions, tests conducted, instruments and standards utilized, results obtained, reporting procedures, and archival processes.

5. Data processing equipment

An inventory of computerized systems was maintained.

The qualification and validation of the selected computerized systems were subject to review to ensure their suitability for use.

As part of the computerized systems validation process, the frequency, roles, and responsibilities were discussed.

Procedures were established and implemented to ensure data integrity, as per the Information Security Management Manual approved on 25 Nov 2016 and reviewed on 5 Dec 2023. It was noted that the document was being revised at the time of inspection. The procedure included measures for ensuring the integrity and confidentiality of data entry or collection, as well as data storage, transmission, and processing, all under the supervision of the Department for Information. Electronic data was required to be protected from unauthorized access, and an audit trail of any alterations was required to be maintained.

Electronic data was backed up at appropriate regular intervals in accordance with a documented procedure for backup and restoration of Information systems & SOP for the respective application operating procedure. The application was employed for networked software systems, including software applications associated with HPLC. External hard drives were utilized for backup purposes for data generated on standalone systems. These hard drives were securely stored, separate from the source data, within the respective department under the supervision of the department's keeper.

For validated spreadsheets (e.g., Excel®), cells containing calculations were secured to prevent accidental overwriting of formulas. Access to cells was restricted, allowing only specific cells to be filled with data. The Excel sheet was validated by a qualified laboratory analyst, and calculation algorithms underwent manual testing by another experienced analyst. This entire process was documented in SOP for the validation of calculation software applications.

A backup process flowchart and an illustration of the organization's IT structure were provided during the inspection.

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

6. Personnel

The laboratory had adequate personnel with the requisite education, training, technical expertise, and experience for their designated roles. After completing training, staff members were evaluated to assess their competency.

The laboratory maintained current job descriptions for personnel involved in tests, calibrations, validations, and verifications. Additionally, records detailing technical personnel's qualifications, training, and experience were kept. A competency assessment system, managed by an electronic tool, was in place. The relevant SOP was available.

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

7. Premises

The premises consisted of multiple buildings within the NIFDC campus. A floor plan specifically allocated to premises related to prequalification-related activities in Building 3 was provided, with rooms marked in pink designated for prequalification-related activities.

The laboratory facilities were appropriately sized and designed to accommodate their functions and conduct the necessary operations.

Separate storage facilities were in place for secure storage, including samples, retained samples, reagents, laboratory accessories, and reference substances. The environmental conditions of these rooms were continually monitored and controlled using digital monitoring systems. The laboratory also provided a separate storage facility for solvents used for interim storage.

Gases were stored in a dedicated, secure cabinet within a designated area. Access to the laboratory facilities was limited to authorized personnel using keycards. Special precautions were implemented, including using a separate and dedicated unit or equipment (such as a laminar flow workbench) for handling, weighing, and manipulating highly toxic substances, including genotoxic substances. Strict procedures were in place to prevent any potential exposure and contamination. Safe removal of types

of waste, including toxic waste (chemical and biological), reagents, samples, solvents, and air filters, was carried out following the applicable procedures by a contract partner with official authorization.

For microbiology testing activities, the Laboratory requested qualification specifically for Microbiology assay and LAL testing. Therefore, only the facilities dedicated to these activities were visited. Microbiology assay is a technique used to determine the concentration or potency of a substance, typically a pharmaceutical product, by measuring its effects on microorganisms. This method involves cultivating specific microorganisms under controlled conditions and then exposing them to the substance being tested. The extent of growth or inhibition of the microorganisms is used to quantify the substance's concentration or potency. Microbiological assay testing was conducted in a designated laboratory unit equipped with a laminar airflow hood (LAF). Laboratory activities, including sample preparation, media and equipment preparation, and enumeration of microorganisms, were physically separated to minimize the risk of cross-contamination.

8. Equipment, instruments, and other devices

During the inspection, the relevant documentation on the randomly selected test equipment, instruments, and other devices used for activities within the scope of the inspection was examined to verify the correct performance of tests, calibrations, validations, and verifications. Information on the purchase, installation, operational qualification, and performance qualification of the equipment was provided by SOP for Instrument and Equipment Management.

The volumetric equipment and flasks were adequately verified.

For more details, refer to Section 12.

9. Contracts

The laboratory had a procedure established for selecting and procuring services and supplies. Suppliers providing critical consumables, supplies, and services that had an impact on the quality of testing were subject to evaluation. Records of these assessments and lists of approved suppliers were maintained to substantiate their suitability with respect to the laboratory's requirements.

The laboratory did not subcontract any testing services.

10. Reagents

The reagents employed met the requisite quality standards and were accurately labeled. The labels on the reagent containers included information such as content, manufacturer, date of receipt, date of opening, concentration (if applicable), storage conditions, expiry date, and retest date.

Reagent solutions were required to be prepared in accordance with published pharmacopeial or other standards where available. Records of the preparation and standardization of volumetric solutions were kept.

Volumetric solutions prepared in the laboratory were required to be labeled by the name, molarity, date of preparation, date of standardization, technician initials, and standardization factor.

The water quality was regularly verified to ensure the purified water met the appropriate specifications.

Toxic or flammable reagents were handled with the necessary precautions in accordance with SOP. These reagents were stored in dedicated, separate cabinets. Additionally, small quantities of acids, bases, and solvents were temporarily stored within the laboratory's interim storage area. However, the primary stocks of these substances were stored in a separate facility outside the laboratory building.

Reagents subject to poison regulations or controls related to narcotic and psychotropic substances were appropriately marked in accordance with national legislation. These reagents were to be stored separately from other substances within locked cabinets. A designated staff member was responsible for maintaining a register of these substances. Additionally, the head of each unit assumed personal responsibility for ensuring the safe storage of any such reagents within the workplace.

CULTURE MEDIA

The laboratory purchased media from approved and qualified vendors. Prior to each sample testing, growth promotion tests and, if applicable, other relevant performance assessments were conducted on all media. The adequacy of culture media performance was verified in accordance with the respective SOP.

The washing procedure underwent validation following the relevant SOP. Media repackaging after sterilization was executed under controlled conditions to minimize the risk of environmental contamination, including the cooling of media. The shelf-life of prepared media, under defined storage conditions, was determined and verified, and it is recommended that the laboratory include the practice in the respective SOP.

11. Reference substances and reference materials

a) Reference substances and reference materials

Reference substances were stored and utilized in a manner that preserved their quality.

Official pharmacopeial standards, prepared at NIFDC or provided by the applicant, were employed for the purposes outlined in the respective specifications. In-house reference standards underwent testing to establish, determine, and continuously monitor their identity, purity, and traceability to primary standards, as appropriate within a different department of the organization.

The information, including the material's name and description, batch or control/identification number, source, date of receipt or preparation, intended use, date of the first opening of the container, use of the reference substance, expiry date or retest date, storage location and conditions, certificate/batch validity statement of compendial reference substances, testing results (CoA), and

assigned content, as well as safety data sheets, was documented on the labels of reference substances and/or the accompanying documentation, as deemed appropriate.

The analytical worksheets included the respective identification number whenever a reference substance was utilized. Furthermore, a comprehensive register of all reference substances was maintained.

b) Reference cultures

Reference cultures were essential for establishing the acceptable performance of media, including test kits, validating methods, verifying the suitability of test methods, and assessing ongoing performance. Management of reference cultures followed the procedures for the recovery, storage, and disposal of reference cultures.

Traceability was maintained by utilizing reference strains of microorganisms directly sourced from a recognized national supplier.

The laboratory received the strains in lyophilized form. These cultures were reconstituted by transferring them into a broth. Subsequently, they were stained onto agar culture media to form slants. A small portion was taken from the slants and transferred into a culture flask. Afterward, a washing step with purified water was performed to create a suspension of bacteria. Upon obtaining this suspension, it was divided into three groups labeled A, B, and C. Prior to this division, thorough verification was conducted to ensure the viability and activity of the bacteria. Working stocks were then prepared using these suspensions. Working cultures were derived from the reference stock by diluting it into the appropriate working solutions. This entire process was detailed in the respective SOP.

Working stocks were not subjected to subculturing. Subculturing was limited to a maximum of five generations (or passages) from the original reference strain, as defined by a standardized method or supported by laboratory documentation confirming the absence of changes in any relevant properties. In compliance with the Chinese Pharmacopoeia, commercial derivatives of reference strains were exclusively utilized as working cultures. This procedure was executed in accordance with the applicable SOP.

A test verification was additionally conducted to assess the appropriateness of the Microbial Assay test method.

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

Each instrument was uniquely identified. Labels indicated the status of the calibration and the date when recalibration was due. The equipment was calibrated by external providers.

The frequency of calibration and performance verification was determined by:

- National Metrology law
- Pharmacopeia
- The usage of equipment and the Laboratory's assessment

Balances were checked daily using internal calibration and regularly with suitable test weights. Requalification was conducted annually by three different entities. pH meters were verified routinely and before each use.

The respective documentation verification was reviewed to determine if the laboratory conducted sufficient calibration/qualification to confirm the stability of temperature, uniformity of temperature distribution, and the time required to reach equilibrium conditions in incubators, water baths, and temperature-controlled rooms.

Sensors employed for controlling or monitoring the operating cycles of autoclaves required calibration, and the performance of timers had to undergo checks. The timer was also validated using a calibrated device. In addition to directly monitoring an autoclave's temperature, the effectiveness of its operation during each cycle was assessed using biological indicators for sterilization or decontamination purposes. The laboratory utilized a dedicated autoclave for decontamination, and this process was duly documented.

Records and logbooks were maintained for equipment items. Additionally, the logbooks included records of the instrument's usage. Information regarding maintenance activities, history of damage, modifications, or repairs was also diligently recorded.

The documentation for the selected equipment was reviewed to verify that it was qualified according to the applicable SOP and suitable for its intended use.

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

13. Traceability

Test results were ensured to be traceable, when applicable, back to primary reference substances.

All instrument calibrations or qualifications were established with traceability to certified reference materials and SI units (metrological traceability).

The sample's traceability was maintained from receipt through all testing stages up to the final completion of the analytical test report.

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

14. Incoming samples

The NIFDC was responsible for testing new drugs and generic drugs. Depending on the applicants' location, samples were submitted to the Laboratory. The Laboratory conducted approximately 2000 batches of tests annually. However, the number of Microbiology assay tests conducted was relatively low, with no such tests performed since May 2022. The Laboratory did not participate in product sampling.

The Laboratory received samples from various sources, including:
- Manufacturers
- Regulatory agencies
- Research institutes

The sample received was visually inspected by the sample custodian at the reception area to ensure that the labeling conformed with the information contained in the test request. Before submission of the test request, communication took place between the applicant, the office of administration, and the laboratory to ensure that adequate resources were available to perform the test.

In the applicable software system, a registry was in place to electronically maintain records of all incoming samples and accompanying documents. It documented information regarding the receipt, distribution, and supervision of the consignment of the samples to specific units.

A test request was entered into the aforementioned system prior to shipping the sample to the laboratory. This request included, among others, the following information:
- Description of the sample
- Specifications for testing
- Required storage conditions

All delivered samples and accompanying documents were assigned a registration number by the system, and a barcode was generated. The electronic register recorded the following information:
- Sample registration number
- Date of receipt
- Unit to which the sample was forwarded

All tests were conducted following the receipt of the test request.

Prior to testing, the samples were securely stored in accordance with their specified storage conditions. Subsequently, they were dispatched for testing to the designated unit. The test request was available in the system and accessible to the respective laboratory, where it was assigned to an analyst with the requisite competency as determined by a competency evaluation.

The samples were divided into three portions for submission to the laboratory and for storage of retained samples. The retained portion was a quantity required for full testing in accordance with the applicable SOP:

- Immediate testing
- Confirmation of testing, if necessary
- Reserved in case of disputes

15. Analytical worksheet

The analysts meticulously documented information related to samples, test procedures, calculations, and results in analytical worksheets, which included raw data. These analytical worksheets were assembled from different units but pertaining to the same sample. The analyst responsible for the test activity printed these analytical worksheets using the eLIMS. Templates for these analytical worksheets were initially prepared and approved within the digital document management system and then electronically transferred to the eLIMS for use by the assigned analysts. All the steps involved in exporting or printing the relevant template for the analytical worksheet, electronically recording data within the worksheet or test record, and finalizing the report were diligently documented within the system and/or in the system's audit trails.

The worksheets included the following essential information:

- The commencement and completion dates of the analysis.
- References to specifications and comprehensive descriptions of the test methods used to analyze the sample, including defined limits; identification of the test equipment utilized; references to substances, reagents, and solvents employed.
- Interpretation of the results.
- The determination of whether the sample met the specified requirements.
- Any deviations from the prescribed procedures, which were duly approved and reported.

All values obtained from each test, including blank results, were promptly recorded on the analytical worksheet. Additionally, all graphical data, whether generated by recording instruments or plotted by hand, were attached or linked to the electronic record file or document where the data was stored.

The completed analytical worksheets underwent a thorough review process. They were initially signed by the responsible analyst, then subjected to a second review, and finally verified, approved, and signed by the Division director. Authorization for the Certificate of Analysis (CoA) was granted by the Authorized Signatory of the institute.

In the case of corrections, the existing information was not erased or rendered illegible; instead, a single line was drawn through it. The individual making the corrections signed the alteration, and the date of the change was noted. Additionally, a clear reason for the change was provided. Any modifications within the eLIMS system could be traced through the system's audit trail.

The specifications necessary for assessing the sample were defined in the test request. Any uncertainties or ambiguities were addressed through communication between the Laboratory and the applicant.

16. Validation of analytical procedures

The procedures used for testing were selected based on their suitability for the intended purpose, as confirmed through either validation or verification of the method or method transfer, as deemed appropriate.

Validation or verification processes followed a defined protocol, which included the verification of performance characteristics specific to various analytical procedures. The respective SOP outlined a list of typical characteristics that should be considered during this process.

Prior to conducting analytical tests, system suitability tests were appropriately implemented. These tests were designed to verify the suitability of pharmacopeial methods and/or validated analytical procedures.

17. Testing

Following the completion of preliminary procedures, the sample was analyzed/tested in accordance with the official specifications.

Guidance regarding official pharmacopeial requirements was typically found in the pharmacopeia's general notices and specific monographs. These monographs contained detailed descriptions of the respective test procedures, and applicants were responsible for supplying sufficient information along with their submissions.

In cases where system suitability criteria were specified within the method, they were diligently met. Any deviations from the prescribed test procedure were subject to approval and thorough documentation in accordance with the applicable SOP.

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

18. Evaluation of test results and OOS investigation

The OOS investigations were managed in accordance with the respective SOPs:

- For Physicochemical test
- For Dissolution, release checks, content uniformity, weight variation, loading variation, sterility, pyrogens, and bacterial endotoxins, the laboratory only performs the first phase of investigation according to the respective SOP. For the second phase of the investigation, the laboratory followed the specifications implemented in the pharmacopeia.
- For OOS handling in Microbiology tests of drugs - bioassay
- For LAL testing

SOPs were in place to outline the procedures for handling OOS test results. When a doubtful or suspected OOS result was identified, both the supervisor and the analyst reviewed the procedures used during the testing process.

If the investigation yielded inconclusive results, the SOP provided clear guidance on the permissible number of retests, as determined by statistical principles. Upon identifying an error, corrective and preventive measures were documented and put into effect. All individual results, including those meeting acceptance criteria, were reported. Subsequent test repetitions were carried out by a second (senior) analyst.

The laboratory generated analytical test reports using data recorded in analytical worksheets. These test reports contained the following information:

- The background and purpose of the testing.
- References to the specifications and methods employed.
- The results of all tests conducted (including numerical results with the standard deviation for all tests).
- A statement indicating whether the sample met the specified requirements.

The records of the randomly selected samples were examined to confirm the accuracy of records, assess analyst qualifications and equipment readiness, evaluate the preparation of reagent solutions, verify the adequacy of reference standards, scrutinize analytical worksheets, ensure traceability, assess the evaluation of test results, review information on the Certificate of Analysis (CoA), and investigate any out-of-specification results, if applicable.

19. Certificate of analysis

A Certificate of Analysis (CoA) was generated for every sample or batch of a substance or product, encompassing a range of information, including:

- The outcomes of the tests conducted within the specified limits.
- A determination regarding whether the sample fell within the specification limits.
- The date of completion of the tests.

20. Retained samples

Samples were retained in compliance with local legislation, as outlined in the SOP for Sample Management. A quantity of retained samples was maintained to facilitate a minimum of two re-analyses. These retained samples were stored in their original packaging.

21. Safety

General and specific safety instructions, addressing identified risks, were made accessible to all staff members. The laboratory had a dedicated department responsible for safety measures.

Staff members were required to wear laboratory coats and eye protection. Precautions were implemented when handling highly potent, infectious, or volatile substances. Safety cabinets were used for highly toxic and/or genotoxic samples. Safety showers were installed, and safety data sheets were made available prior to testing.

Chemical containers were fully labelled, with clear warnings such as "flammable" when applicable. Guidelines for the safe handling of compressed gas cylinders were established, and they were stored in dedicated cabinets. Warning signs were prominently displayed throughout the premises.

Adequate insulation and spark-proofing measures were implemented for electrical wiring and equipment, including refrigerators.

Procedures for the safe disposal of unwanted corrosive or hazardous products through neutralization or deactivation were in place, emphasizing the necessity for the safe and complete disposal of mercury and its salts.

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

Miscellaneous	
Assessment of the Laboratory Information File	An English translation of the laboratory's LIF was submitted before the inspection and was subsequently reviewed.
Annexes attached	N/A

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***, the National Institutes for Food and Drug Control (NIFDC), Institute for Chemical Drug Control, located at 31 Huatuo Road, Daxing District, Beijing, China,*** is considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

The laboratory addressed all the non-compliances observed during the inspection listed in the full report and those reflected in the WHOPIR 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. 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***
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