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20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Finished Pharmaceutical Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Guilin Pharmaceutical Co Ltd (FPP-Sterile)**
Corporate address of manufacturer	Shanghai Fosun Pharmaceutical Industrial Development Co., Ltd Building A, No. 1289, Yishan Road, Shanghai, 200233, China
Name & address of inspected manufacturing site if different from that given above	INJ-I, INJ-II & INJ-VI, No 43 Qilidian Road Guilin, Guangxi 541 004 China
Unit / block / workshop number	Building No. 5 (INJ-I & INJ-II) Building No. 19 (INJ-VI)
Dates of inspection	7-11 April 2025
Type of inspection	Routine GMP inspection
Introduction	
Brief description of the manufacturing activities	Guilin Pharmaceutical Co., Ltd. is located at No.43 Qilidian Road, Guilin, Guangxi, 541004, China. It manufactures APIs, tablets, soft capsules, hard capsules, powder for injections, small volume parenteral (SVP) injections, and films. The manufacturing site engages in the following activities:

Name of manufacturing center	Workshop name	Production line	Abbreviation
API manufacturing center	Multi-purpose workshop	Production line of artemisinin-derived APIs	API- I
		Multi-purpose production line	API- II
	Levamisole hydrochloride workshop	Levamisole hydrochloride production line	API- III
OSD manufacturing center	OSD- I workshop	General production line for dosage forms/ preparations	OSD- I
	OSD- II workshop	Lactasin production line	OSD- II
	OSD- III workshop	Soft capsules production line	OSD- III
	OSD- IV workshop	General production line for dosage forms/ preparations (domestic)	OSD- IV
	OSD- V workshop	Films production line	OSD- V
INJ manufacturing center	INJ- I workshop	Production line for Artesunate for injection	INJ- I
	INJ- II workshop	SVP production line	INJ- II
	INJ- VI workshop	SVP production line	INJ- VI
	INJ packaging workshop	Co-package center for Artesunate for injection	INJ-PA
		INJ-VI packaging line	
		Packaging area for Injections of FPP Building (Labelling area of powder for injection and large strength injection)	

The scope of this inspection was limited to the INJ manufacturing center.

General information about the company and site	Guilin Pharma is a pharmaceutical company engaged in R&D, production, and marketing of chemical drugs. Since 2003, Shanghai Fosun Pharmaceutical (Group) Co., Ltd. has become the holding enterprise of Guilin Pharma.
History	The WHO PQ Inspection Services regularly inspects Guilin Pharmaceutical's sterile manufacturing site. The last PQ inspection was conducted from September 18 to 22, 2023.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The following areas were inspected: - Quality management system - Personnel, hygiene, and training - Qualification, media fill, and process validation - Production activities (INJ-II and INJ-I) - Quality control laboratory - Microbiology laboratoryWater for injection and pure steam generation
Restrictions	The inspection was restricted to the products listed in the inspection scope.
Out of scope	All other products and workshops were outside of the inspection scope

WHO products covered by the inspection

1.	MA089	Artesunate Powder for solution for injection 30mg	Prequalified
2.	MA090	Artesunate Powder for solution for injection 120mg/vial	Prequalified
3.	MA051	Artesunate Powder for solution for injection 60mg	Prequalified
4.	MA 168	Artesunate Powder for solution for injection 60mg	Prequalified
5.	MA195	Artesunate Powder for solution for injection 180mg	Prequalified
6.	MA200	Artesunate Powder for solution for injection 120mg	Prequalified
7.	MA201	Artesunate Powder for solution for injection + Arginine/Sodium Bicarbonate Solution for injection 30 mg+20 mg/ml/8.4mg/ml	Under Assessment

Abbreviations	**Meaning**
AHU	Air handling unit
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
APR	Annual product review
APS	Aseptic process simulation
BMR	Batch manufacturing record
BPR	Batch production record
CC	Change control
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis

CpK	Process capability
DQ	Design qualification
EDI	Electronic deionization
EM	Environmental monitoring
FMEA	Failure modes and effects analysis
FPP	Finished pharmaceutical product
FTA	Fault tree analysis
GMP	Good manufacturing practices
GPT	Growth promotion test
HEPA	High efficiency particulate air
HPLC	High performance liquid chromatography (or high performance liquid chromatography equipment)
HVAC	Heating, ventilation and air conditioning
IQ	Installation qualification
LAF	Laminar air flow
LIMS	Laboratory information management system
MB	Microbiology
MBL	Microbiology laboratory
MF	Master formulae
MFT	Media fill Test
MR	Management review
NC	Non conformity
NRA	National regulatory agency
OQ	Operational qualification
PHA	Process hazard analysis
PLC	Programmable logic controller
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
RO	Reverse osmosis
SIP	Sterilization in place
SMF	Site master file
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometer
WFI	Water for injection

Part 2	Summary of the findings and comments

1. Pharmaceutical quality system

Guilin Pharmaceutical Co., Ltd. established a quality management system (QMS) according to the NMPA, WHO, EU, and FDA GMP standards. The QMS was divided into two parts, i.e., quality assurance (QA) and quality control (QC). The quality management and production planning departments operated independently under different leadership and reported directly to the company's president. The logbooks, procedures, and records were manually maintained; no electronic system related to QMS or other functions was implemented on-site. The following QMS elements were reviewed:

Annual Product Quality Review (APQR)

The SMP for APQR of FPP was reviewed. The role of preparing the PQR was that of the QA officer; the subsequent roles of the other teams, including Production and QC, were explained. The review period was reported to be 12 months, and the reports should be prepared within 3 months of the specified review period. There was provision for preparing an APQR even without manufacturing a product in a specified year. There was provision for descriptive statistical analysis, such as standard deviations, control charts, and Cpk. For quantifiable parameters, Cpk (or CpU and CpL) was calculated. According to the SOP, the interpretation was: ≥1.33 capable and robust, 1≤CpK<1.33 consistent, CpK <1 process was variable in meeting its requirements. A detailed description of the number of batches to be considered during calculation was provided, along with the acceptance and rejection criteria outlined in the SOP.

Change control management

The SMP for change control was discussed, and it was noted that the procedure applied to changes in manufacturing processes, quality standards, analytical methods, premises, facilities, equipment, instruments, computer hardware, production, packaging, and testing procedures, among other areas. The change controls were logged in a validated spreadsheet, whereas manual forms were used for assessing change controls. The printed change control log did not provide information on the number of critical, major, or minor changes or their current status.

Quality risk management (QRM)

The SMP for QRM was reviewed, and it was noted that the procedure was applied throughout the product's lifecycle, including the use of raw materials, APIs, excipients, solvents, packaging materials, labels, and all aspects related to drug quality. The risk review was performed once every three years for critical risks and every 3 to 5 years for other risks. It also noted the following:

a) 81 risks assessed in 2023 for the entire facility
b) 141 risks assessed/implemented in 2024 for the entire facility
c) 42 risks assessed/implemented in 2025 for the entire facility

Deviation management

The SOP for handling deviations and its implementation was reviewed.

- Deviation related to a laboratory incident where an abnormal chromatogram was found in a test of related substances of Arginine using HPLC was discussed. The handling of this deviation was thorough, whereas investigation and impact assessment were conducted using proper investigation tools, which considered all aspects of manufacturing.
- Another deviation was observed when handling the invalid result of the endotoxin indicator, including deviation on a frequent regular alarm of the airborne particle monitoring in the sterilizing tunnel.

CAPA management

The SMP for CAPA and several of its implementations across different systems were reviewed. As per the SMP, CAPA may be issued from different root causes, including deviation, change, OOS, OOT, audit results, QRM, gap assessment, etc.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

2. Good manufacturing practices for pharmaceutical products

Artesunate powder for injection was manufactured in a dedicated INJ-I workshop, whereas Sodium Bicarbonate and Arginine solutions were manufactured in the INJ-II workshop. INJ-VI was used to produce diluents such as Sodium Chloride and Sodium Bicarbonate solutions using terminal sterilization and co-packing. The inspection mainly focuses on the variation submitted from INJ-II regarding sodium bicarbonate and arginine solutions.

The company conducted a gap analysis to implement WHO TRS 1044, Annex 2, and the results were reported in the interpretation table of regulatory knowledge for EU GMP Annex 1 and WHO TRS 1044, Annex 2.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

3. Sanitation and hygiene

Manufacturing areas were frequently cleaned and disinfected per the defined process and procedure. More than one type of disinfecting agent was used. The sterile IPA used in clean areas, Grades A, B, and C, was sourced from a service provider. The cleaning disinfectants were sterilized before use in Grade A and B areas. The hygiene facilities established on the site appeared acceptable.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

4. Qualification and validation

Aseptic process simulation/APS (media fill)

After the renovation of the INJ-II workshop, Guilin conducted APS tests on three batches of 20 mL and one batch of 1 mL. This protocol relates to 1 mL. One batch of 1 mL was taken to cover the minimum and maximum ranges. The protocol encompassed several key areas, including the number and types of interventions (intrinsic and corrective), maximum personnel, shifts, filling speed, filling time, filling quantity, filling volume, and the selection of TSB (3%), among others. Similarly, the APS protocol for small-volume parenteral products was reviewed, and it was noted that three batches were selected for simulation of the manufacturing process. In general, the protocol and report were deemed adequate.

The process validation protocol for NaHCO3 and Arginine injection was reviewed, which involved three batches. Risk assessment (RA) for $NaHCO_3$ and Arginine solution at INJ-II was performed to determine CPPs and CQAs, which were used to prepare the process validation protocol. A summary report for the process validation lifecycle of NaHCO3-Arginine injection (Stage 1) was discussed. It noted that the CQAs were identified based on the product's QTPP. The experiment related to compounding was performed at Guilin Pharmaceutical prior to the optimization of the manufacturing process. The manufacturing process was developed by a French manufacturer and then transferred to Guilin. Several lab-scale experiments were conducted at Guilin before the manufacturing process was optimized. Similarly, the sterilization process was performed under different conditions using terminal sterilization, which resulted in a spike in the impurity profile. Based on stage one (process design) of the study, it was concluded that aseptic sterilization should be performed instead of terminal sterilization. Stage three, related to continued process verification, was to be implemented after the product's approval and commercialization.

Air visualization study (smoke study)

Upon reviewing the video recording of the smoke study of the filling line and surrounding areas, it was found that a black background banner was used to visualize smoke. A smoke study for a transfer hood was reviewed and noted to be used for transferring sterile materials/components to the filling line. WFI was used to create smoke, and glycol-based foggers were used for Grade A and B areas compared to Grade C and D.

Filter validation

The filter supplier, Millipore, based in Shanghai, China, performed validation of the sterile filter (0.22 µm) for the NaHCO3/Arginine solution. The supplier's tests included a bacterial retention test, a filter compatibility test, a production bubble point test, an API absorption test, and an extractable test. The study was generally adequate, as there were no changes to the formulation, filter type, pore size, supplier, or process parameter.

Filter integrity tester (FIT)

The FIT qualification report for INJ-II was reviewed, and it was noted that the protocol was developed by the supplier and approved by Guilin. The qualifications, which included IQ, OQ, and PQ, were discussed. The IQ included document verification, calibration, physical inspection, component verification, and verification of the utility supply for the FIT. The OQ included power connection, user access, recipe addition, parameter setting confirmation, audit trail, instrument self-inspection, time calculation, printout function, history record backup, cancellation test, and power failure. Access

control was verified as part of the OQ, and four user groups were identified (IT, equipment management, maintenance management, and operator). At the same time, the audit trail was verified to confirm it captured events during the OQ.

Water for injection (WFI)

The WFI system was requalified due to the change in user points for INJ-II. A protocol-based requalification was performed. One user point was added for component washing, whereas the user point was cancelled. The position of the user point was changed. As part of this change, an IQ was performed to verify the correct material installation, welding quality, dead legs, drainability, pipe pressure, cleaning, and passivation, and was subsequently completed. For the OQ, circulation capacity and sterilization capacity were verified. For the PQ, a three-stage sampling plan was established, including Stage 1 (14 days, daily sampling for all user points for full tests), Stage 2 (14 days, daily sampling for all user points for critical tests such as appearance, pH, conductivity, TOC, and endotoxin), and Stage 3 (one-year routine monitoring).

The pure steam distribution system was requalified after the modification of INJ-II. The location of the autoclave was changed, and two new user points were added. This change triggered the requalification of the PSG. The IQ was similar to WFI, and OQ's operating parameters were verified. For the PQ, condensate sampling and testing of pure steam quality (non-condensable gas, dryness, and overheat) according to EN 285.

Heating, Ventilation, and Air Conditioning (HVAC) system

The HVAC requalification for AHU servicing Grade C areas, and AHU servicing Grade B areas and AHU servicing Grade A for ampule filling was also reviewed. The approach to air recirculation was 90% recirculation and 10% fresh air systems. Air was distributed to every clean room after handling through a primary filter (G4), a medium-efficiency filter (F6), a coil cooler, a pressure blower, a heating section, a humidifier, a secondary filter (F8), and a HEPA Filter (H14). Pressure differentials were monitored across the primary, secondary, and HEPA filters in the AHU. A HEPA filter integrity test was performed annually and replaced every 4 years or as necessary following integrity checks. There was a periodic checking and inspection of duct leakages. All AHUs were requalified annually.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

5. Complaints

The SMP for customer complaint handling and its implementation on complaints was reviewed. The complaint was related to the Artesunate injection combined packaging batch. The investigation was thorough, and no issue was found in the handling and conduct of the investigation.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

6. Product recalls

The company confirmed that there had not been any recalls since the last PQ inspection.

7. Contract production, analysis, and other activities

The company confirmed that no contract production had been undertaken for the WHO-prequalified and under-assessment products. The contracted laboratories carried out some of the tests.

8. Self-inspection, quality audits and suppliers' audits, and approval

The company performed the self-inspection as per the schedule and approved procedure. More details were covered during the inspection of the OSD facility. In addition, the following supplier audits were reviewed:

- The on-site supplier quality audit report for the filter supplier, China, was reviewed. The audit was performed for Tyvek sterilization bags and sterile filters. It was performed using ISO 9001 and Chinese GMP.
- Guilin Pharmaceutical audited a supplier, China, a supplier of 20ml ampoules. It was the first time that the supplier supplied a 20ml ampoule. The audit was performed in accordance with ISO 9001:2015, ISO 15378:2017, USP 660, and USP 1660, as well as national standards.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

9. Personnel

The company has 1063 employees. There were 12 senior engineers, 62 engineers, 170 assistant engineers, and 30 licensed pharmacists. There are 504 personnel in production-relevant departments (OSD/API/INJ), 61 in QA, 108 in QC, and 48 in the warehouse. Others are management staff and staff of supporting departments.

10. Training

The review of the training program focused heavily on assessing the competency of personnel working in aseptic areas and those working as visual inspectors. The company has an SOP for personnel dressing for gowning qualification. Personnel were trained for several SOPs related to working in the cleanroom, including practical training on gowning and cleanliness, and microbiological and aseptic process training. Following the document and practical training, personnel were tested on three successful gowning processes before being allowed to enter the Grade B working area. Afterward, they also participated in a successful aseptic process validation before being allowed to work in aseptic processing. Every six months, personnel must follow the routine gowning qualification. If personnel did not enter the Grade B area within 6 months after the first training, they should undergo a gowning test upon entry. If personnel have not entered the Grade B area in more than 6 months, they should be re-qualified as if they were new employees. The implementation of this SOP was verified by looking at the qualification process of personnel No. XYZ, who was a personnel involved in the latest APS for the INJ-II.

As for the qualification of a visual inspector, the company has an SOP for the qualification of visual inspection personnel. The implementation of the SOP on the qualification of personnel No. F10265 was reviewed. According to the SOP, operators should be qualified in normal working conditions after working for 1 hour with small-volume drug products or 30 minutes with powder injection products.

The qualification was conducted using a mix of good and defective products. The defective goods comprised 10-20% of the sample size, consisting of all severe, general, and minor defects.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

11. Personal hygiene

During the site visit, personnel in the cleanroom area were dressed appropriately as per the cleanroom classification.

12. Premises

The total area for the production district was about 120,000 square meters. The sterile products were manufactured in appropriately cleanrooms, supported by changerooms and airlocks. The component preparation, product preparation, and filling were carried out in Grades D, C, B, and A, respectively. The oRABS were used on the filling line to minimize direct human intervention with the product. The INJ-II facility was recently renovated and has been adequately maintained in terms of finishing, lighting, and cleanliness. Similar was the case for the INJ-I. The inspectors visited INJ-II and INJ-I, observing the operators' aseptic practices during the filling of the Sodium Bicarbonate/Arginine solution and Artesunate powder.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

13. Equipment

The new ampoule filling line was equipped with oRABS and ran appropriately during the inspection. The inspectors raised some concerns related to the extension of LAF, the movement of operators, the transfer hatch, and the use of black gloves for the oRABS.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

14. Materials

During the review of various documents, it was noted that raw and packaging materials were adequately controlled and tested to meet the respective specifications before production. The materials used in the cleanroom were subjected to appropriate sanitization to minimize the generation of particles.

15. Documentation

The company used four levels of documents. The Class 1 documents included the QM, SMF, job description, department responsibility, and organization chart. The Class 2 documents included the quality system management document, process procedures, and specifications. The Class 3 documents included operating procedures in QC and production, equipment verification and maintenance procedures, and batch records. The Class 4 documents included records, confirmation/ verification protocols, and reports. New documents and proposals for change or revision were partially managed using the Document Management System (DMS). Any user who proposed a new document or a revision proposed it using the DMS. Once QA has approved the proposal, the user can edit the file/ document. The proposer then submitted the draft document for QA approval. Once QA has approved,

the document will be sent to the document administrator's account, who will then provide the proposer with access to print the document for training purposes. The training on documents was conducted offline. The proposer would only report the training date to the document administrator so that the document administrator can assign an effective date. Once effective, the document administrator would print the document and distribute it. Return and distribution of the document were conducted offline.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

16. Good practices in production

The inspection team visited the INJ-I area through the separate operator's change room. At the time of the INJ-II inspection, a Sodium Chloride injection was being filled. For the INJ-I line, Artesunate dry powder for injection was filled. During the inspection, no manufacturing activity was observed in the API/lyophilization area, where powder filling was carried out.

Visual inspection was performed manually for the vials, while an automatic inspection machine was used to inspect the ampules. The inspectors visited the visual inspection section, where Artesunate dry powder for injection was inspected. The defects were classified into three categories: critical, major, and minor. The ampoules were manually checked for appearance before the machine inspection. After machine visual inspection, the rejected ampules were checked only for defect classification. All vials rejected by the automatic inspection machine should be rejected, though, without further investigation. Before and after the machine visual inspection, a challenge test was conducted using 10 defective vials: 4 glass foreign matter defects, 1 low fill size defect, 1 empty ampoule defect, 1 color spot defect, 2 fiber defects, and 1 white clot defect. The defect kit used for the challenge test was tested every 6 months.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

17. Good practices in quality control

The inspectors visited the QC laboratory. The QC laboratory was spread on floors 1, 2, and 3, whereas floors 4 and 5 were used for R&D purposes (mainly analytical development, more than process development, which was outsourced). The first floor consisted of a business area for receiving incoming samples, as well as archival and stability chambers. The second floor consisted of physical and chemical testing of APIs, excipients, finished products, water for injection, intermediates, packaging materials, etc. The third floor consisted of a microbiology laboratory, which primarily carried out microbial limit tests, sterility tests, and bacterial endotoxin tests. The retention samples were stored in another building. The laboratory used manual logbooks to record details of the incoming samples. The laboratory had 115 staff, including 45 for physical/chemical analysis, 26 for microbiology testing, including EMP, and 44 for auxiliary testing.

<u>Laboratory samples</u>

Receiving samples in the QC laboratory was governed by the SMP for Lab sample management, which mentioned the timelines for reporting(finalizing) of analysis.

Out of specification (OOS)

A review was conducted on OOS related to the fill volume of Arginine/ sodium chloride injection. The OOS investigation was conducted thoroughly and adequately. The first level of investigation led to the conclusion that there was no obvious error in the analytical method. Further investigation was conducted using a fishbone diagram to identify issues related to personnel, instruments, environment, method, and materials. Still, no obvious error was found by the Laboratory. Therefore, the investigation was continued at the production unit. Based on the investigation, the root cause of the problem was the discrepancy in the correction factor for the equipment between QC and Production, which resulted in a significant difference in the fill volume. A request was raised to revise the related SOP to be more specific. The related batch was finally rejected.

Stability programme

The SOP for the stability test was reviewed. Stability samples were stored in a walk-in stability chamber. Temperature and humidity mapping were conducted annually and monitored electronically, with temperature and relative humidity recorded every 5 minutes. Stability chambers were equipped with alarm systems that were tested during the requalification process. One batch of product was placed on a stability program annually. It was noted that stability samples of finished products were placed in the stability chamber in their primary packaging material. The protocol for Sodium bicarbonate and arginine injection was reviewed.

Microbiology laboratory

The microbiology areas consisted of two microbial limit test (MLT) areas, a sterilized article area, two sterilization areas, preparation areas for microbial limit tests, preparation areas for sterility tests, a preparation area for microbial limit tests, an autoclave room, a BET test room, a wash bay, incubation rooms, and a sterility area. The primary gowning was required before entry into the general passage. The procedure for growth promotion tests/GPT of the media was available. The GPT used Pseudomonas Aeruginosa, Bacillus Subtilis, E. coli, S. aureus, C. Albicans, and C. sporogenesis. The certificate of analysis for the ATCC reference cultures was available, and passage two indicated subculturing. The criteria used to choose isolates for growth promotion and APS were described in the APS isolate selection report.

In-house environmental isolates

A list of environmental isolates for the year 2024 was available. There were 1824 entries of identified microorganisms. Microorganisms identified through various sampling methods included the following: settle plates (104 isolates), viable microorganisms (42), room and equipment surfaces (4), personnel surfaces (3), water systems (17), and bioburden testing samples (31). There was no OOS result in 2024. Trend reports on the library were performed, and there were reduced isolates compared to 2023.

Trend Analysis

A trend analysis for environmental monitoring was presented. Some microorganisms identified through various sampling methods in the environment were tracked. The trend analysis included data from the water analysis results. The TAMC, online and analytical testing for all PW and WFI systems, were within specifications. The trend analysis concluded that cleaning, decontamination, water sanitization, and personnel hygiene were under control, as evidenced by a decline in the number of isolated microorganisms in 2024 compared to 2023.

Reconstitution study

The inspector visited the quality control laboratory and witnessed the reconstitution study for Artesunate 60mg and $NaHCO_3$/Arginine solution. The analyst followed the approved SOP for Artesunate for injection.

The deficiencies raised in this section have been adequately addressed and will be verified during future PQ inspections.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Guilin Pharmaceutical Co., Ltd,*** located at ***No.43 Qilidian Road, Qixing District, Guilin, China,*** was considered to be operating at an acceptable level of compliance with WHO GMP Guidelines.

All non-compliances observed during the inspection, as listed in the full report and reflected in the WHOPIR, were addressed by the manufacturer 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 manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   https://digicollections.net/medicinedocs/documents/s21467en/s21467en.pdf

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
   untitled (digicollections.net)

3. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-sixth Report. Geneva, World Health Organization, 2022 ***(WHO Technical Report Series, No. 1044), Annex 2.***
   TRS 1044 - Annex 2: WHO good manufacturing practices for sterile pharmaceutical products

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   9789240020900-eng.pdf (who.int)

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   https://digicollections.net/medicinedocs/documents/s21440en/s21440en.pdf

6. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
   https://digicollections.net/medicinedocs/documents/s23455en/s23455en.pdf

7. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4
   https://digicollections.net/medicinedocs/documents/s20108en/s20108en.pdf

8. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-seventh Report. Geneva, World Health Organization, 2024 (WHO Technical Report Series, No. 1052, Annex 4.
   Short name: WHO TRS No. 1052, Annex 4
   TRS 1052 - Annex 4: WHO good practices for pharmaceutical quality control laboratories

9. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://digicollections.net/medicinedocs/documents/s22358en/s22358en.pdf

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
    Short name: WHO TRS No. 961, Annex 7
    https://digicollections.net/medicinedocs/documents/s18677en/s18677en.pdf

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9***
    https://digicollections.net/medicinedocs/documents/s18683en/s18683en.pdf

12. General guidelines for the establishment, maintenance, and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
    https://digicollections.net/medicinedocs/#d/s21438en

13. 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://digicollections.net/medicinedocs/documents/s18682en/s18682en.pdf

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
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