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Prequalification Unit Inspection Services
WHO PUBLIC INSPECTION REPORT
Finished Product Manufacturer

Part 1	**General information**
Manufacturers details	
Name of manufacturer	**Ferring International Center SA**
Corporate address of manufacturer	Chemin De la Vergognausaz 50, CH-1162 Saint-Prex, Switzerland
Inspected site	
Name & address of inspected manufacturing site if different from that given above	Ferring Pharmaceuticals (China) Co Ltd No. 6 HuiLing Lu (Ferring Road), National Health Technology Park Zhongshan City, 528437, Guangdong Province, P.R. China Tel: +86 760 88587800 Fax: +86 760 88587801 GPS coordinate, 22· 34'23"N, 113· 30'24'E D-U-N-S number: 52-790-3976
Unit / block / workshop number	Injectable ampoules preparation and filling line along with automatic/manual visual inspection, secondary packaging, and quality control facilities
Inspection details	
Dates of inspection	25 – 29 March 2024
Type of inspection	Initial on-site inspection
Introduction	
Brief description of the manufacturing activities	A number of manufacturing activities were conducted at the site including production, quality control and distribution of granules (powder for oral solution), and small volume parenterals (SVP) as well as secondary packaging of imported bulk tablets, lyophilized powder for injection and small volume parenteral products. The site comprised a production area of 1760 m^2, a warehouse of 1913 m^2, QC laboratories of 553 m^2 and utilities of 3318 m^2. The production area included: (1) an oral solid line, (2) a sterile vial preparation and filling line, (3) a sterile ampoule preparation and filing line, and (4) a secondary packaging area.
General information about the company and site	Ferring Pharmaceuticals (China) Co., Ltd. - Zhongshan manufacturing plant is a subsidiary of Ferring Pharmaceuticals Ltd., which belongs to Ferring Group located in Saint-Prex, Switzerland. Originally founded as Nordiska Hormon Laboratories in 1950, it became Ferring Co. in 1954. Its portfolio includes innovative products in the fields of peptide and protein chemistry including urology, gynaecology & obstetrics, gastroenterology, and endocrinology. The constructions of Ferring Zhongshan manufacturing plant started in March 2003 and were completed in February 2005. The pharmaceutical production comprises of sterile products and non-sterile products manufacturing. The granules (powder for oral solution) are manufactured in the oral solids area and this area is dedicated. The sterile products are manufactured in the sterile preparation production area.

	The site manufactures only pharmaceutical products. Non-pharmaceutical products were not manufactured on-site. Regulatory Affairs dossier submission, Marketing and Export related activities are managed by the Corporate Office according to the information provided by the company.
History	The current inspection was the first on-site inspection by WHO PQ. The ampoule preparation and filling line was subject to regulatory inspections by: – ANVISA, Brazil in November 2019 – NRA, Germany, namely Landesamt Fuer Soziale Dienste Schleswig Holstein in June 2023 with a positive outcome. The focus of the inspection was 0.9% NaCl solvent for injection – NRA Uganda (NDA) in 2023 – NRA Ethiopia (EFDA) in 2024
Brief report of inspection activities undertaken Scope and limitations	
Areas inspected	• Quality management system • Injectable Production Block (ampoule preparation and filling line) • Quality Control laboratories: Physical, chemical and microbiology labs • Utilities including HVAC, water, and nitrogen • Warehouse
Restrictions	The inspection was restricted to the production of the product listed in the inspection scope. Other products and production areas/lines were not covered by this inspection.
Out of scope	All products and production areas/lines, other than those listed under the scope of the inspection, were not covered by this inspection, and were not visited.
WHO products numbers covered by the inspection	RH095 – Carbetocin Solution for injection 100 mcg/ml - glass ampoule 10x1 ml
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
CEHT	Clean Equipment Holding Time
CFU	Colony-forming unit
CIP	Cleaning in place
CoA	Certificate of analysis
CpK	Process capability
DEHT	Dirty Equipment Holding Time
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
NCA	National control authority
NCL	National control laboratory
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

The site quality system and local quality manual and guidelines were derived from the Ferring Global Quality Assurance and were implemented through the site's pharmaceutical quality system. International GMP standards e.g., EU, US FDA, Japanese PMDA, were adopted at the site. Regulations and decrees promulgated by China authorities were implemented.

A formal organizational chart and personnel qualification were available identifying the key positions and names of the appointed staff. The Organogram was authorized. It was noted that QC and Production reported to the Plant Director. The Quality Assurance function was independent from Production. Supply Chain, Engineering, EHS were headed by the Quality Responsible Person who was also appointed as Qualified Person (QP).

It was noted that the General manager was also the Plant Director, and that the Quality Responsible Person was also the QA Manager and Qualified Person. Job descriptions of the Plant Director, Quality Responsible Person, QC Manager and Production Manager were spot-checked.

Annual Product Quality Review

A written procedure for product quality review was established. Product quality review was performed annually (January-December) to evaluate the manufacturing process and quality attributes. PQRs included information on the starting and packaging materials, review of APIs used in production batches, batch analytical data including IPC data, complaints, recalls and returned products, on-going stability data, change control, deviations, CAPA, OOS, ADR, Validation & Qualification, Marketing Authorization, and post-marketing commitments, etc. The PQR was required to be completed as per the PQR schedule which concluded at the end of Q1 of the following year.. The APQRs for Carbetocin Solution for injection 1ml for the period from January to December 2022 and January to December 2023 were reviewed and discussed.

Quality Risk Management (QRM)

A written procedure for Quality Risk Management (QRM) was established which followed the principles of ICH Q9. The general process of QRM included risk assessment, risk control and risk review. Generally, three major tools were used for risk assessment namely Preliminary Hazard Analysis (PHA) Risk Ranking and Filtration (RRF) and Failure mode, Effects and Critically Analysis (FMECA).

Aseptic processing Quality Risk Management addressed all procedures related to sterile products manufacturing. The procedures required involvement of Production, QC, QA, engineering and QP. The requirement was to perform a risk assessment after each major change, recurrent deviation and as part of annual product review. Risk was tracked by using electronic system or templates available in the electronic documents management system (EDMS). A list of risk assessment reports for Carbetocin was available dating since the establishment of the product in 2007. The following risk assessments reports were evaluated:

- Risk assessment upon conducting filtration without pre-rinsing the filter with solution directly following drying post filter integrity testing
- Risk assessment for sampling location of environmental monitoring on ampoule line
- Risk assessment for ampoule production on the shared line

Contamination Control Strategy (CCS)

The SOP on Contamination Control assessment of Sterile product addressed the establishment of the company's policy on CCS. It was presented as a high-level policy document which identified measures for control contamination, monitoring of contamination and types and sources of contamination.

A dedicated document addressed specifically the CCS for the filling line used for Carbetocin Ferring. The CCS was divided in various sections which covered several areas including facility, utilities, personnel and equipment.

Management review (MR)
Managerial responsibilities were specified in the respective SOP. An annual management quality review meeting was conducted with global quality assurance (GQA); however, minutes and attendance list of the meeting were not available. No records of annual site management review meetings were available. Monthly site quality review meetings were attended by site management team, however no indication of which managerial heads were required to attend such a meeting.

Change Control
The change management system was implemented through a well-established SOP. Changes were reported to QA and approved by a Change Committee. A regulatory assessment was performed to determine any regulatory impact. Following the implementation of a change, an evaluation was conducted to confirm that the change objective was achieved. Changes were managed through an electronic system. The CC registers for 2022 and 2023 along with documentation related to several changes were spot-checked.

Deviations
A deviation management system was implemented at the site as per the respective SOP. The procedure described the processes for reporting, assessing, investigating, implementing, and closing of a deviation which occurred during the manufacturing activities or processes that impact on the quality and/or compliance of the product, systems, services, GMP and facility.

The timeline to log a deviation was within 1 working day and reported to senior management which included QA and GQA. If a deviation was not logged within 1 working day, a delay justification was required. Deviations were required to be closed within 30 calendar days from date of initiation. If unable to close, permission was required from QA.

Deviations were classified into critical, major, or minor based on impact on quality and patient safety. If the root cause was not obvious and unknown, root cause investigation was performed using a number of investigational tools. An impact assessment was to be performed and recorded as per a template taking in account the impact on product quality for the given batch and/or other relevant batches/products performed. Appropriate corrective actions and/or preventative actions (CAPAs) were taken in response to the investigations. An electronic system was used to manage the status and progress of the deviation investigation. Monitoring and trending of deviations were conducted and reported monthly at the QA quality meeting including the GQA meeting. The Deviation log for Carbetocin Ferring for 2023 was reviewed and a number of deviations were spot-checked.

Corrective and Preventive Actions (CAPA)
A CAPA system was implemented as per a well-established SOP. CAPAs were applied to any quality and GxP non-compliant issues, risks or recommendations for action identified for activities or processes that could impact the quality and/or compliance of products, systems, services, or studies. Corrective actions and/or Preventive actions arose from deviations, inspection observations, customer complaints and strategic quality improvement decisions that were collected by QA and monitored for implementation. CAPA was managed by an electronic system and closed within a defined target date. Any CAPA responses following a regulatory inspection was reviewed by GQA prior to submission. The status of CAPA implementations were reported at monthly Quality Review meetings. A CAPA log register was available and verified and found acceptable.

OOS/OOT investigation
The SOP for investigation and handling of Out of Specifications (OOS) and Out of Trend (OOT) results was reviewed. The initial OOS investigations involved comprehensive laboratory investigations prior to

proceeding to production investigations if needed. The 2023 OOS trending was checked. Any OOS reported by contract laboratories were required to be investigated by Ferring; however, the procedure did not address the investigation of the reported OOS.

Product release

The SOP for batch confirmation/certification and release was established. QA was responsible for the complete review of executed batch records which included batch production records and batch analysis records for intermediates and finished product. The QP was responsible for the final confirmation/certification and release of the batch for sale or distribution. The release of a number of Carbetocin Ferring batches was reviewed.

Electronic data management

The SOP for data integrity was in place. The SOP provided comprehensive guidance on data integrity including data lifecycle, computerized systems (electronic signatures, audit trail, system review, system recovery and system retirement) and data governance along with data integrity breaches. No data integrity risk assessment was performed by the company.

2. Good manufacturing practices for pharmaceutical products

Good manufacturing practices were generally implemented. Necessary human and physical resources with premises, equipment and utilities were provided for the current operational level of Carbetocin Ferring Injection manufacturing activities. The manufacturing processes followed the respective procedures as defined and documented in the BMRs.

3. Sanitation and hygiene

Premises and equipment in the FPP production area were generally maintained at an acceptable level of cleanliness at the time of inspection. Personnel at the site were seen to be performing their duties in an organized and diligent manner. Personal hygiene and sanitation appeared generally satisfactory.

4. Qualification and validation

Validation master plan

The validation and qualification activities at the site were performed according to the validation master plan as well as the SOP for process validation. The VMP was recently updated. In addition, the VMP was updated regularly.

Process validation

The process validation was guided by the respective well-established SOP. Process validation of Carbetocin was established in 2018. Three consecutive batches were considered for establishment of PV. The process was revalidated in 2022. The latter process re-validation considered one single batch. All results of the extensive sampling and testing performed during PV studies were in compliance with the pre-set acceptance criteria and as such the process revalidation was considered well established.

In addition, the sterile filtration process validation was established in 2018. The testing activities included extractables/leachables (using model solution as the drug product would create noise signal which did not enable detection of filter extractables/leachables), bacterial retention, compatibility and absorbability using drug product.

Continuous Process Verification (CPV)

The SOP for PV also provided for guidance on continued process verification (CPV) along with trend analysis and PpK/CpK calculations and interpretation. The CPV report of Carbetocin Ferring solution for injection was reviewed and CPV was well established.

The Aseptic Process Simulation (Media fill) studies

The SOP for aseptic process simulation (Media Fill) was in place. Media fill was performed for the production line of Carbetocin Ferring injection every six months. The worst case scenario of the manufacturing process was considered.

Cleaning validation

A cleaning validation protocol was in place and was executed as per the respective CV report. The cleaning validation was well established as per this executed CV study. The study considered calculation of the MACO based on PDE of Carbetocin (the API with the most stringent PDE on this shared facility). The DEHT and CEHT were also well-established. The cleaning validation study was supported with several other validation studies for detection of Carbetocin residues, microbial recovery and chemical recovery from surfaces. The analytical method validation for detection of Carbetocin was reviewed.

Computerized systems validation

The validation of computerized systems was guided by the respective sections of the VMP which in turn provided reasonable guidance on categorization of computer systems and extent of the necessary validation The list of computerized systems along with validation status was presented and reviewed. In addition, a corporate SOP on commissioning, operation and maintaining the validated state of GxP computer system was in place. As per the corporate SOP and the site SOP, system reviews of computerized systems were performed on an annual basis.

5. Complaints

Customer complaints were reported, categorized, and investigated by QA according to a written procedure. Complaints were divided into critical, major, or minor according to an appropriate definition and were required to be closed within 30 days following feedback to the complainant. Complaints were categorized as Medical or Technical complaints. Complaints were recoded using the respective template and logged into an electronic system prior to initiating the investigation. Complaints were trended and quarterly reviewed by GQA.

6. Product recalls

Recalls were controlled by QA and the Quality Review Board, and centrally coordinated and managed by GQA. The respective SOP was reviewed and found to be acceptable. Communication was directly with the Market Authorization Holder who was responsible for informing the relevant Health Authority of the country on the proposed recall. Recalls were classified as Class I, Class II or Class III with the depth of a recall described as Class A (entire distribution chain), Class B (Retail level) and Class C (Wholesale level). A template for a recall notification was available however was not referenced in the SOP. Destruction of recalled product was executed at country level with a copy of the destruction certificate submitted to GQA.

A mock recall was performed every year with the latest mock recall performed in July 2023. The mock recall was closed out as successful. Until the date of the inspection no recall of any product manufactured at Ferring (China) had taken place.

7. Contract production, analysis and other activities

Contract production, analysis and any other activity covered by GMP were defined, agreed and controlled.

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

Self- Inspection

A self-inspection plan and SOP were in place. Self-inspections were conducted twice a year ± 7 days from the tentative date in the schedule and performed by internal Quality Assurance or GQA. A predetermined inspection schedule was available with an Internal Audit Plan for 2023.

The QA Head identified experienced and qualified auditors. Self-inspections were conducted using a checklist for a specific department with the inspection observations recorded on a template. The necessary CAPAs were initiated as required and effectiveness checks were performed. An Internal Auditor should be qualified and certified. In case of external auditors, a written agreement should be signed. A self-inspection team was selected based on knowledge and experience. CAPA were required within 2 weeks. The annual audit plan was approved by the Site Manager. The 2023 self-inspection audits were confirmed. The 2024 audit plan for Ferring (China) was available and was verified.

Supplier qualification and approval

Suppliers were assessed and qualified through a combination of qualification testing, vendor questionnaires and, for suppliers of critical materials, site audits. For drug substance, container and closure suppliers, supplier qualification testing and ongoing documented evidence (e.g., certificates of analysis) of conformance to predetermined quality specifications were required. Suppliers were re-evaluated on a periodic basis according to a risk assessment. The corporate vendors were qualified at global level while the local vendors were assessed by the local QA together with related departments. Ferring Pharmaceuticals (China) Co., Ltd. was responsible for the final approval of suppliers used. A list of approved suppliers was prepared and maintained by QA Ferring (China).

9. Personnel

There was an adequate number of personnel suitably qualified by education to perform and supervise the manufacture of sterile FPPs. The personnel met during the inspection appeared to be knowledgeable about GMP. At the time of the inspection, 120 staff was employed at the site. A formal organizational Chart and personnel qualification SOP was available, identifying the key positions and names of the appointed staff.

10. Training

GMP training system was implemented and coordinated by QA. Training covered basic GMP knowledge including quality management, sanitation and hygiene, documentation practice, material and personnel flow, and others for all employees with on-the-job training conducted by each function. A training program was created for new employees. The introduction training for new employees was provided by QA and HR department, while on-the-job training (e.g. mandatory SOPs) was provided by each department. The training program for new staff were required to be completed within 3 months following the onboarding of the new employee. Training effectiveness was assessed using a questionnaire, oral, observations by trainer, online test, and internal audits. The Learning Management System (LMS) was also utilized at the site.

A training plan for 2024 was available which included training for each quarter of the year. The training plan was found acceptable. Training records including effectiveness evaluation were spot-checked for a number of employees.

11. Personal hygiene

New employees underwent a health check / medical examination as per the respective SOP prior to starting work, and all personnel underwent annual physical examination which included X-ray, Liver function, Blood pressure, Vision test etc.

12. Premises

In general, the premises were located, designed, constructed, adapted, and maintained to suit the preparation, filling and further processing of injectable ampoules, for the production of non-sterile and sterile products. The pharmaceutical production areas were situated on the ground floor and were physically separated into the following zones:

- Oral solids (powder for oral solution)
- Vial filling line
- Ampoule filling line – preparation (including compounding and ampoule washing)
- Ampoule filling line-filling
- Secondary packaging for non-sterile products
- Secondary packaging for injectable products

The ampoule filling area comprises rooms for unloading of autoclave, aseptic filling of ampoules, disinfectant receiving and a changing and airlock for personnel. The air characteristics in the sterile areas fulfil the requirements of grade B and local laminar flow of grade A (RABS).

Quality control laboratories, on the other side, consisted of a chemical laboratory, microbiological laboratory, stability room, and sample retention room. QC premises were separated from production areas. Chemistry Laboratory was located on the 1st floor adjacent to the Microbiology laboratory. Separate entrances to Chemical and Micro laboratory were available.

HVAC system

The production areas were equipped with 19 air handling units (AHUs) and 5 pre-Cooling air unit (PAUs) including 2 PAUs used for non-GMP area for clean area, QC, warehouse, and office building. The sterile and non-sterile manufacturing areas, packaging area, warehouse, sampling room, QC laboratories, and adjacent facilities had their own HVAC system with separate air handling units. The AHU fans were equipped with built-in air flow measuring devices which facilitate monitoring of delivered air. The entire system was controlled by the building management system (BMS). The temperature, relative humidity, and differential room pressures were continuously monitored, and recorded with alarms in place in case of being out of pre-set limits.

The validation status of HVAC was well maintained by routine preventative maintenance, clean area environment monitoring and periodic requalification. Among other regular qualification criteria, the HEPA filters integrity test was performed for grade A/B clean room every six months and grade C/D clean room once per year.

Quality of air supplied to production areas was regularly monitored through a well-established environmental monitoring programme and data was trended on a regular basis using several limits (specification, action, and alert limits). The sampling locations for environmental monitoring was risk based.

Compresses air system

The quality of the compressed air was regularly monitored (once every 6 months) or in case of changes. The compressed air system was subjected to review on an annual basis. The annual review of compressed air system 2023 was verified and the quality of the compressed air system appeared well established and maintained.

Nitrogen system

There was no nitrogen generation system at the site. Commercialized nitrogen cylinders were used to supply nitrogen to the production area. The general logbook for instrument/equipment (usage record of nitrogen gas) was reviewed. The used nitrogen system was subjected to annual review. The annual review of nitrogen system 2023 was verified and the quality of the nitrogen system appeared to be well established and

maintained. Nitrogen cylinders were handled as incoming materials with electronic segregation and issue through the ERP system. Nitrogen cylinders were securely stored outside in a separate storage area close to the point where nitrogen gas was supplied/pumped to production areas.

Water System

The water system including PW and WFI was renovated in 2021. The qualifications were commissioned in 2021 for PW and WFI and were completed (phase 3 PQ) in December 2022 and June 2023 respectively. The quality of the water system was monitored through online and offline testing against the respective specifications. The sampling and testing procedure for the water system was in place. The cumulative data for these testing activities were regularly evaluated and interpreted as per a well-established process for trend analysis.

13. Equipment

In general, the equipment at the site were located, designed, constructed, adapted, and maintained to suit the production and quality control operations. The layout and design of equipment permitted effective cleaning and maintenance with avoidance of cross-contamination, build-up of dust or dirt. Logbooks were available and suitably placed to record use, cleaning, and maintenance of equipment as needed.

Equipment maintenance

The SOP for plant maintenance was in place. The SOP provided for preventive maintenance plan, calibration plan, repairs, alarm handling, among others. The 2024 preventive maintenance plan (a validated excel sheet controlled by QA department) was reviewed, and some activities were verified including preventive maintenance of the ampoule washing machine and depyrogenation tunnel during March 2024, as reflected in the respective logbooks.

Equipment calibration and qualification program

A detailed procedure was in place for metrology management. The SOP provided for calibration management including calibration categories, range, reports, certificates, delays, and other related subjects. The inventory and verification/calibration plan for measuring instruments in 2024 was reviewed. Calibrations of some devices were verified including pressure gauges of the depyrogenation tunnel. It was noted that some calibration activities were undertaken internally by the site using standard equipment/devices. Another dedicated SOP was in place for laboratory instrument management and calibration which provided for a standalone calibration plan of laboratory instrument.

14. Materials Management

Materials were properly managed at the site including receipt, quarantine, storage, QC testing, release, and dispatch. A unique Ferring batch number was assigned to each batch of material received. When each batch of incoming material was received, they were checked if they come from QA approved suppliers, each container was identified on its label, the number of containers was verified according to the purchase order, the package was checked for any potential damage, and warehouse staff confirmed receipt in the respective electronic system. Rejected materials were stored in a separate, dedicated, locked and clearly identified area. All areas at the warehouse were utilized for storage of different materials and products using electronic segregation system through the established computerized systems.

15. Documentation

A hybrid documentation approach was in use which included both paper based and electronic based systems. Documentation was controlled by the QA department. Three levels of documentation were available: Corporate Documents, Site Management documents and Site Records/reports. Documents were reviewed and distributed according to a documented procedure. Documents were reviewed every 3 years. Review was driven by the implemented EDMS system. Superseded documents were stamped as obsolete and archived.

Batch records, control records and lab records were archived for 1 year after product expiry. Validation records, master documents etc. were archived as per the product lifecycle plus 1 year following expiry date of the last manufactured product. Archiving of documents was in different locations at the site.

16. Good practices in production

The manufacturing processes were performed and recorded according to instructions in the batch production records. The production of Carbetocin Ferring was in operation during the week of the inspection.

The commercial production of Carbetocin at this site started in 2021. The Master formula for Carbetocin Ferring Solution for injection was reviewed.

17. Good practices in quality control

The QC function was independent of other departments. The QC laboratory was separated from production areas. The chemical laboratory was located on the 1st floor in a separate block of the facility. The QC laboratory was well equipped with HPLCs, GC and other testing instruments.

Physico-chemical Laboratory

The identity, content, and impurities of Carbetocin were performed using HPLC. The test instruction of Carbetocin Ferring was in place and provided comprehensive guidance on test methods, sampling plan, calculations, and other related subjects.

The analytical method was originally established and validated at Ferring Germany. The method was subsequently transferred to Ferring China through an intermediary site. The original method validation report was reviewed and the validation parameters included specificity, linearity, recovery, repeatability, intermediate precision, robustness, LOD and LOQ. The SOP on transfer of analytical procedures was in place and guided the transfer of the analytical method to Ferring China. An SOP was in place for validation and lifecycle management of analytical test methods. Technical transfer of the HPLC analytical method for identity, content, and impurities of Carbetocin was in place with the criteria for analytical method transfer being met.

The SOP for chromatographic analysis was reviewed. The SOP provided for set up, system suitability, sample analysis, integration and interpretation, audit trail and column maintenance, among others.

Reference standard supplied by the API manufacturer was used by the site for analytical testing. An SOP for management of reference standard and reference standard solution was in place. The SOP provided for selection and source of reference standard, purchase and reception, calibration, storage and handling, expiry, and other related subjects.

The SOP for reference and retention samples was in place. The SOP guided on definitions, sample size, sample storage, sample usage, periodical inspection.

The procedure for stability test was reviewed. The procedure provided for selection of batches, study protocols, storage conditions, test methods, testing frequency. In addition, the SOP provided for notification of relevant competent authorities in case of potential failure in the stability test results based on trend analysis. At least one batch per year was included in the stability testing programme. The 2024 stability test plan was reviewed. The ongoing stability report of Carbetocin Ferring – Y2023 was reviewed.

Microbiology Laboratory

The Microbiology laboratory was separate from the physico-chemical laboratory. Access was restricted to authorized personnel only. Microbiologists reported to the Microbiology Team Leader, who in turn reported to the QC Laboratory Supervisor, who in turn reported to the QC Laboratory Manager.

The laboratory activities, such as media preparation, equipment preparation, testing and enumeration of microorganisms were segregated. There were appropriate entry and exit procedures, including gowning procedures. Sterility testing was performed in a separate area with appropriate gowning and a separate access.

Laboratory equipment and glassware were not used outside of the microbiology laboratory.

Commercialized sterile media were brought in and stored under appropriate conditions as recommended by the manufacturer. Growth promotion testing was done on all media on every batch. The performance of the media was checked against recovery of the target organisms. Reference cultures were used for establishing acceptable performance of all media according to the respective culture management procedures.

There was an autoclave sterilizer for the sterilization of equipment and garments. A separate sterilizer was used for decontamination purposes.

An environmental monitoring program was in place.

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, ***Ferring Pharmaceuticals (China) Co Ltd*** located at ***No. 6 HuiLing Lu (Ferring Road), National Health Technology Park Zhongshan City, 528437, Guangdong Province, P.R. China*** was considered to be operating at an acceptable level of compliance with WHO GMP 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 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 GMP 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-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

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
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
Short name: WHO TRS 1010, Annex 9
https://www.who.int/publications/m/item/trs1010-annex9

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
https://www.who.int/publications/m/item/annex-3-trs-1033

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://www.who.int/publications/m/item/annex-4-trs-929

6. 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
https://www.who.int/publications/m/item/who-good-practices-for-pharmaceutical-quality-control-laboratories

7. 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://www.who.int/publications/m/item/trs957-annex3

8. 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.
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