



WHO PUBLIC INSPECTION REPORT

(WHOPIR)

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	STRIDES ARCOLAB LIMITED, STERILE PRODUCTS DIVISION
Unit number	NA
Production Block	NA
Physical address	Bilekahalli, OPP. IIM, Bannerghatta Road Bangalore-560076. India
Contact address	Phone: +91-80-66580600 Fax: +91-80-66580606
Date of inspection	23 (pm)-26 February 2009
Type of inspection	Routine inspection, covering all aspects of GMP
Dosage forms(s) included in the inspection	<ul style="list-style-type: none">• Dry powder parenterals in vials• Liquid parenterals in vials and ampoules• Lyophilized parenterals in vials• Pre-filled syringes
WHO product categories covered by the inspection	MA
Summary of the activities performed by the manufacturer	Manufacturing and packaging of sterile parenteral products as well as Penicillin's and Cephalosporin's



Part 2: Summary

General information about the company and site

Strides Arcolab Limited, Sterile Products Division (hereafter referred to as Strides Sterile Products Division), located in Bilekahalli, OPP. IIM, Bannerghatta Road, Bangalore-560076, India, was inspected by a WHO prequalification team on the above mentioned dates. The Strides Sterile Products Division was formed in September 1996. The facility had been renovated and re-started commercial production in September - October 2005.

Besides the sterile product division there were also completely separated penicillin and cephalosporin manufacturing divisions.

At the time of inspection, there were approximately 170 employees working on site, 15 employees were involved in Quality Assurance (QA), 35 in Quality Control (QC) and 88 in production activities.

Sterile products were manufactured in three shifts.

History of WHO and/or regulatory agency inspections

The Strides Sterile Products Division had been inspected and approved by various regulatory authorities, including:

- FDA (USA) – February 2008
- ANVISA (Brazil) – April 2008
- TGA (Australia) - September 2008
- MHRA (UK) – January 2009

Focus of the inspection

The inspection focused on the production and control of solution for injection. The inspection covered all the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

Day 1 - PM	
OPENING MEETING – 13.00 PM	Introductions
	Objectives and scope of the inspection
	Confirmation of the proposed program
	Brief presentation of the factory
	Recent changes & improvements
DOCUMENT REVIEW	Site plan, production block layout indicating the HVAC system and AHU's, material and personnel flow
	HVAC system schematic drawing, pressure cascade
	Purified and water for injection system drawings



	Reduced sampling for starting materials (related to non-sterile products)
Day 2 - AM	
	Validation Master Plan
	Change control and deviation management: SOP's + summary list of changes and deviations (2007-2008)
	Annual product review (2008) for above mentioned products
Day 2 - PM	
DOCUMENT REVIEW	HVAC validation
	WFI validation
	Autoclave validation
	Process validation
	Aseptic process validation
	Cleaning validation
	Ampoule drying oven validation
	Sterility test validation
Day 3- AM	
SITE INSPECTION	Receiving area and stores
	Starting materials, packaging materials and components
	Sampling, dispensing and issuing
INSPECTION OF PRODUCTION ACTIVITIES	Production of solution of injection
DAY 3- PM	
INSPECTION OF PRODUCTION ACTIVITIES	Production of solution of injection - continuation
DAY 3- PM	
INSPECTION OF QC LABORATORY	HVAC system
	PW and WFI system
	Nitrogen generation system
Day 4- AM	
REMAINING DOCUMENTS REVIEW	Complaints: SOP + summary list of complaints of (2007-2008)
	Recalls: SOP + summary list of recalls of (2007-2008)
	BPR
	Supplier qualification
	Deviations
	Change control
	CAPA
	Cleaning
	Other related documents
	Training



DAY 4- PM	Preparation for closing meeting
CLOSING MEETING	4.30 pm

2.1 QUALITY ASSURANCE

A quality assurance system was implemented and maintained.

The QA unit and QC unit were independent from production.

Batch manufacturing and packaging records were checked and approved by the production head and QA head. Certificates of analysis were approved by the head of the Quality Control Laboratory. QA personnel were involved in all the production and quality control activities.

Managerial responsibilities were specified in job descriptions.

A change control procedure and flow chart was available for inspection. Changes were recorded in the register.

A formal system for deviation management was described in writing.

Product quality review (PQR) included all batches manufactured in the calendar year. The PQR was a comprehensive document.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices were implemented and maintained.

Manufacturing processes were clearly defined and reviewed. Manufacturing steps were recorded in Master Formula. The solution for injection Master Formula and Batch Production Records did not specify the filtration time and filling time. The storage and distribution of products ensured batch traceability.

Necessary resources were provided.

Instructions and procedures were written in a clear and unambiguous language

2.3 SANITATION AND HYGIENE

The site's sanitation and hygiene program covered personnel, equipment, materials and premises. The sanitation and hygiene measures in place at the time of the inspection were generally found to be sufficient to assure the prevention of contamination of the premises and product.

Operators and technical staff who worked in sterile product division were not allowed to enter Penicillin's and Cephalosporin's production divisions and opposite. Different colours garments were used in production divisions.

2.4 QUALIFICATION AND VALIDATION



The key elements of a qualification and validation program were defined and documented in the Validation Master Plan.

Generally, validations were considered to be appropriately performed.

For cleaning validation, a matrix had been set up. This matrix was based on the assessment of the solubility and the toxicity of the active pharmaceutical ingredient in order to select some of the more toxic and the less soluble active substances as the worst case products (product chosen).

2.5 COMPLAINTS

Complaints and other information concerning potentially defective products were reviewed according to a written procedure and corrective/preventive actions were taken.

2.6 PRODUCT RECALLS

Recalls were handled in accordance with a written procedure. The recall procedure was regularly reviewed and updated. A mock recall was initiated every 2 years. Recalls were classified as Class I, II and III recalls.

2.7 CONTRACT PRODUCTION AND ANALYSIS

No manufacturing was contracted out.

Analytical technical assistance was contracted out to one analytical laboratory. A written contract with that laboratory was available. The contract laboratory was audited and audit reports were available for inspection. A re-audit of the laboratory was scheduled for 2009.

2.8 SELF INSPECTION AND QUALITY AUDIT

Self-inspection was performed in accordance with a written procedure. The procedure included questionnaires on GMP requirements and all essential GMP items were covered. After completion of each self inspection, a self inspection report was drawn up and necessary CAPA's were initiated. The self inspection schedule was available for inspection. Self inspections were carried out every 6 months. The self inspection team was properly trained. Self inspection observations were classified and self inspection trends were evaluated.

Vendor audits, vendor approval procedure and flow chart were available for inspection. Vendors were included in the approved vendor's list based on review of the vendor's surveillance form and other supporting documents. When necessary, audits were performed by an audit team that was composed of corporate staff and site representative. The re-audit criterion was 3 yearly. An approved vendor's list was available.

2.9 PERSONNEL

The personnel met during the audit were experienced, skilful and conscientious.



An organization chart was available. Key personnel responsibilities were specified in job descriptions. The production and quality control responsibilities were independent and in line with GMP requirements.

2.10 TRAINING

Training issues were covered in a written SOP. A training needs matrix was set up for each employee and the matrix was reviewed every 2 years. The company provided induction training for new employees, GMP training for all employees, on the job training and training by external organizations. Comprehension of training content was assessed by discussions and observation of performed activities, as well as written examinations. The training plan and program for the year 2009 was available. Training records were maintained in the employees personal files. The training file contained the following information:

- Job description
- Training records
- Training assessment
- External training
- Attendance certificates

A qualification record and competency list was available for each analyst. The performance of each analyst was re-evaluated every two years.

Reviewed training files were considered to be comprehensive.

2.11 PERSONAL HYGIENE

All personnel prior and during employment were required to undergo medical examinations. Persons with illness and/or open lesions were not allowed to work in areas where open products were exposed to the environment.

The level of hygiene observed and the measures taken to manage this were considered sufficient. All changing rooms were provided with photos describing the gowning procedures.

2.12 PREMISES

The sterile product division was completely separated from the penicillin and cephalosporin production divisions. All three production divisions had separate canteens, HVAC, compressed air systems, Nitrogen, PW and WFI systems.

Buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance, and production operations. Facilities were designed to minimize potential contamination; production areas had adequate space for the placement of equipment and materials to prevent mix-ups and contamination. There was also sufficient space for the movement of materials and personnel.

There were separate personnel and material entrances. Temperature, relative humidity and pressure differentials were regularly monitored and recorded.

In general the buildings were well maintained and clean.



Storage areas

The receiving and dispatch areas protected materials and products from the weather.

Quarantined, rejected, recalled and returned materials and products were stored separately and securely.

Temperature mapping of storage areas was carried out and reports were available for inspection. The retention store for finished products was extremely overloaded.

Sampling areas

There was one sampling room for all materials.

Weighing and Dispensing areas

All materials used in production were dispensed in one room.

Production areas

In general, facilities were smooth, free from cracks and open joints and permitted effective cleaning. Facilities were designed and maintained to minimize the risk of cross-contamination and contamination. Production areas were effectively ventilated.

Quality Control (QC) areas

QC laboratories were separated from the production areas. Adequate space was provided for the storage of samples, laboratory reagents and reference standards, solvents, reagents and records. Separate rooms were provided for instruments such as HPLC and IR.

The microbiological laboratory, which was separated from the chemical laboratory, was quite cramped.

2.13 EQUIPMENT

Process equipment was installed and maintained in a way that minimizes risk of error and contamination.

A preventive maintenance program was in place and was followed. Cleaning SOP's and records were available. Production and quality control equipment was identified as to content and cleanliness status and appropriately indicated by labels.

Equipment calibration schedule was established on annual basis and the calibration was performed accordingly.

2.14 MATERIALS

The procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing and approval or rejection of materials were available. Materials in the warehouse were handled by the SAP system.

Incoming goods and finished products were quarantined until tested and released by QC. Materials and products were generally stored in a proper manner.



Damage to containers was reported to QC. Containers under quarantine and approved containers were appropriately labeled.

Lists of approved vendors of the raw materials and packaging materials were available.

Each container of starting material was sampled for identity test purpose.

Culture media were prepared and controlled according to written procedures. The pH of media was checked before and after sterilization.

Positive and negative controls and growth promotion tests were performed. For the sterility test, a stasis test was carried out for all products. The isolates from the environment was used for growth identification.

The autoclave for media sterilization was regularly checked and the sterilization processes were validated.

Reference and working standards were stored appropriately.

Disinfectants were approved by QA and prepared according to written procedures. In the aseptic processing area, sterile isopropyl alcohol (IPA) was used for disinfection. The IPA was sterilized by filtration and held in a pre-sterilized plastic squeeze bottles.

2.15 DOCUMENTATION

In general, the documentation system was well established and maintained.

Documents were designed, prepared, reviewed and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons.

Documents had unambiguous contents, were laid out in an orderly fashion and were easy to check.

Documents were regularly reviewed and kept up to date. The review period for documents was specified as 2 years.

2.16 GOOD PRACTICES IN PRODUCTION

Production operations were carried out following clearly defined procedures.

Operations on different products were not carried out simultaneously or consecutively in the same room.

During processing, materials, bulk containers, major items of equipment, and the rooms and used packaging lines were labeled and indicated the products being processed, its strength and the batch number.



Access to the production premises was restricted. All doors leading to the production areas were appropriately interlocked.

An environmental monitoring program was established and followed. Aseptic processing was monitored continuously by exposing settle plates. Settle plates were exposed for four hours; this exposure time had been validated. Contact plates were used for monitoring surfaces. Non viable particles were monitored according to a written procedure. An appropriate operator monitoring system was in place. Trending of environmental monitoring results was reviewed and found to be appropriate. Alert and action limits for environmental monitoring was set up, and no alert limits were exceeded.

Line clearance was performed and recorded before processing operations were started.

2.17 GOOD PRACTICES IN QUALITY CONTROL

In general, good practice in Quality Control was implemented and maintained.

The quality control functions were independent of other departments.

Adequate facilities, trained personnel and approved procedures were available for all relevant activities.

Batches of products were released for sale or supply only after certification by the authorized person or designated persons.

Sufficient samples of starting materials and products were retained to permit future examination of the product.

Quality control personnel had access to production areas.

Each “out of specification” (OOS) was appropriately evaluated and investigated in accordance with a written procedure.

The expiry dates for dry chemicals and solutions were 3 and 2 years respectively, and had been set up based on company experience.

Utilities

The HVAC system

HEPA filters were installed for the penicillin and cephalosporin production divisions' HVAC systems. Exhaust air quality checks were regularly carried out.

The sterile products division HVAC system was designed to avoid possible contamination and cross contamination. Incoming air quality checks were regularly carried out.

The HVAC system was designed in a way that production corridors were in negative pressure with respect to production rooms.

A preventive maintenance program for HVAC was in place and was followed.



Purified Water (PW) and Water for Injection (WFI) System

PW was produced by reverse osmosis. Utilities were located in a separate building. Water was kept in continuous circulation.

WFI was produced by multicolumn distillation. WFI was kept in continuous circulation at 80 °C. The water systems were sanitized as per written procedures. The WFI system was sanitized on a monthly basis using steam at 100 °C for 15 minutes.

A sampling plan was established for routine monitoring of PW and WFI. The final user points were monitored with suitable frequency.

WFI system welding and welders certificates were available.

Trends for WFI monitoring were reviewed. Alert and action limits were set up, and no alert limits were exceeded.

Part 3: Conclusion

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, as well as the corrective actions taken and planned, STRIDES ARCOLAB LIMITED, STERILE PRODUCTS DIVISION, Bilekahalli, OPP. IIM, Bannerghatta Road, Bangalore-560076, India 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.