MASTER COPY

SITE MASTER FILE

SOTAC

SOTAC HEALTHCARE PVT. LTD.

(A WHO –GMP CERTIFIED COMPANY)

ADDRESS	Plot No. PF-20, Charal Industrial Estate, Sanand GIDC II, Sanand, Ahmedabad-382110, Gujarat (India)
CONTACT DETAILS	Mobile No.: 9913562852, 9879807120, 9099982396, 9825053462 E-mail: sotachealthcare@gmail.com Website: www.sotacpharma.com
FACILITY	B –LACTAM ANTIBIOTICS FACILITY (TABLETS, CAPSULES AND DRY SYRUP)
DOCUMENT NO.	SMF/SH/01-03
SUPERSEDES	SMF/SH/01-02
EFFECTIVE DATE	22-12-21
REVIEW PERIOD	TWO YEARS OR AS AND WHEN REQUIRED

(Reference Guideline: WHO Technical Report Series, No.961, 2011 .Annex 14 - WHO guidelines for drafting a site master file)

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Note: Above Annexure shall be update as and when required. No need to revise the SMF. Other Annexures shall revise through Change request form

Note: In case of need any above mentioned annexures kindly contact to below mail Id: sotachealthcare@gmail.com

C. Approval of Site Master File:

The site master file accepted as Policy documents by the management of Sotac Healthcare Private Limited. This Site Master File is a master document, which describes the entire facilities and details of the validation & qualification activities, available for the dosage form manufacturing facility of **Sotac Healthcare Pvt. Ltd.,** Plot No. **PF- 20, Charal Industrial Estate, Sanand GIDC II, Sanand, Ahmedabad-382110, Gujarat (India).**

Following have approved this Site Master File:

Prepared by:

Department	Name	Designation	Signature	Date
Quality assurance	Patel Harshal	Manager	Harshal	21/12/22

Review and approved by:

Department	Name	Designation	Signature	Date
Production	Smitesh Shah	Sr. Manager		21/12/21
Quality Control	Laxmi Narayan	Sr. Executive		21/12/21
Engineering	Suresh Sidhu	Manager	Sidhu	21/12/21

Authorized by:

Department	Name	Designation	Signature	Date
Quality assurance	Ramlesh Patel	Head- QA		21/12/21

E.1 General Information:

E.1.1 Brief Information:

SOTAC Healthcare Pvt. Ltd. is a well-established professionally managed pharmaceutical company. It is a manufacturing company with plant located at Sanand GIDC-II.

The facilities are well equipped with latest plant machineries, instruments & equipment's.

Works / Head Office:

Sotac Healthcare Pvt. Ltd.

Plot No. PF- 20, Charal Industrial Estate,

Sanand GIDC II, Sanand, Ahmedabad-382110, Gujarat (India)

E-mail: **sotachealthcare@gmail.com**

Website: **www.sotacpharma.com**

Tel.: 9081993300, 9099982396

The entire project has been designed in such a manner that it complies with the cGMP requirements / guidelines of World Health Organization (WHO), Schedule-M requirements of Indian Drugs & Cosmetics Act and other relevant regulations.

Sotac Healthcare Pvt Ltd is engaged in manufacturing of Beta -Lactum antibiotics types of products: **Tablets, Capsules, Dry Powder Syrups**

E.1.2 Details of Regulatory Inspection and FDA Licensing Activities:

All the Pharmaceutical Manufacturing Activities will be carried out as per Schedule–M of the Indian Drugs & Cosmetics Act 1940 and rules there under.

Sr. No.	Certificate Number / License Number	Validity
1.	Manufacturing License Form 28 : G/28/1755	10 JULY 2020 TO 09 JULY 2025
2.	WHO GMP Certificate TRS No.908 of 2003 Number 21012396	17 JAN 2024

E.1.3 Any Other Manufacturing Activities carried out on the Site:

Apart from manufacturing and trading of human pharmaceutical dosage forms, no other activities or business under taken in the location.

E.1.4 24 hrs. contacts telephone No$

NAME OF PERSON	CONTACT NUMBER
Mr. Sharad Patel (Managing Director)	Office: 9081993377, Residence: 9913562852,
Mr. Kamlesh Patel (Managing Director)	Office: 9099982396, Residence: 9998176244

E.1.5 Type of Actual Products Manufactured on the Site:

B- Lactam antibiotics type

E.1.5.1 List of proposed Products is attached as **Annexure-I.**

E.1.6 Short Description of the Site:

E.1.6.1 **Location and immediate environment:**

The facility is situated in the center of Pharma zone of Sanand GIDC -II, Ahmedabad.

The production facility is located in a clean area away from polluting industries. The surrounding atmosphere is free from dust & smoke.

E.1.6.2 **Site and Building Description:**

The factory is situated at Sanand GIDC, which is about 25 km from Ahmedabad and well connected with road from Ahmedabad.

The newly constructed Plant having Three Floors Ground Floor (Total Built up area 1343 $M^{2)}$, First floor (Total built up area 1328 M^2) and Second floor (Total Built up area 207 M^2) All floor scattered over the area details given below:

SR. NO.	BLOCK / DEPARTMENT	AREA
1.	Plot Area	2791 Sq. mts.
2.	Production block	680 Sq. mts. Approx.
3.	Quality Assurance & Quality Control.	425 Sq. mts. Approx.
4.	R.M/SPM/FG Stores	403 Sq. mts. Approx.
5.	Administration	95 Sq. mts. Approx.
6.	Utility/Service Floor	680 Sq. mts. Approx.

E.1.7 Employees Engaged in Production, Quality Assurance, Quality Control, Warehouse, Engineering and Personnel & Administration:

E.1.7.1 **No. of Employees:**

List of No. of Employees attached as **Annexure-XIII**

E.1.8 Technical Assistance from Out Side Party(Name & Address)S:

Analytical and calibration assistance is taken from approved analytical testing labs for testing of few specific tests that cannot be carried out at the site. List of Technical Assistance from outside party Annexure –XIV

E.1.8.1 **AMC (Annual Maintenance Contract):S**

List of external laboratory/ external agency as per Annexure – XIV

E.1.9 Quality Management System of the Firm

SOTAC Healthcare Pvt Ltd. Manufacturing drugs under the control of a quality management system as per the guidelines stated in the company quality policy & quality manual.

The purpose of the quality policy is to ensure compliance of quality systems and procedures so that the product meets all the required specifications ensuring the identity, strength, safety & purity of the products.

The quality assurance department is independent from manufacturing & authorized to take appropriate8

decisions on quality matters of raw materials / packing materials / finished products, systems, documentation and validation or any other issues related to quality.

E.1.9.1 **Quality Policy:**

Our quality policy is based on cGMP guidelines, laws and regulations governing the manufacture of pharmaceutical products.

SOTAC Healthcare Pvt. Ltd. being a pharmaceutical company is engaged in **"To create good manufacturing practices to generate quality, which is conceive as process of continual improvement to strive towards excellence and achieve highest standards of quality by implementation of small innovative mechanisms and processes in order to accomplish best quality and customer satisfaction".**

E.2 Organizational Chart:

E.2.1 Organogram:

Organogram shows the structure of an organization and how the various positions are related to each other. It is frequently used to show the chain of command and relative ranking of various positions in an organization or department and may include information such as the job titles, names, and areas of responsibility for the employees.

- The Organogram covering all departments is attached as **Annexure IIA.**
- The list of competent staff is attached as **Annexure IIB.**

E.2.2 Key Personnel: The details of key personnel is described below -

Name	Qualification	Designation	Experience	Responsibilities
Mr. Kamlesh Patel	B. Pharm, MBA	Director	18 Yrs	Quality Assurance
Mr. Chetan Patel	B. Pharm	Director	18 Yrs	Quality control
Mr.Harshal Patel	M.Pharm (Pharmacology)	Manger	5	Quality Assurance
Mr. Suresh Sadhu	BE Mechanical	Manger	6	Engineering
Mr. Narayan Lakum	M.Sc. (Organic)	Manger	4.8 years	Quality control

E.2.3 Key Personnel: The details of key personnel is described below -

Basic and In-service Training and Maintenance of Records:

All the personnel working in the plant and whose job is directly or indirectly associated with product quality are given continuous cGMP training, appropriate to their respective job activities. The Head-QA in consultation with concern department Head develops comprehensive training schedule and programs for employees at all levels.

The personnel and administration department provide induction training to all the new employees for making them acquainted with the company's policies, practices and people, as per induction training schedule. Records of such induction training and the reports are maintained by the head of the department (Personnel and Administration).

E.2.3.1 **Identification of Training Needs:**

Training needs for the individuals are identified at the time of annual performance appraisal by his /

her immediate superior. Training needs are then consolidated by the Head of Department (Personnel and Administration) and submitted to Head–QA. Then Head–QA reviews the identified training needs of the individual and prepares an annual training calendar and gets it approved by Plant Head. The Head-QA organizes training program in accordance with the training schedule and maintain appropriate training records indicating personnel performance and need of improvements after evaluation.

E.2.3.2 **Type of Training:**

Training on GMP is targeted on the different identified groups. The training is mainly divided as GMP training and On-Job training. Job training is also called as In-service training.

GMP training program is conducted & monitored by QA and On-Job training is monitored by QA and conducted by individual dept. Head.

E.2.3.3 **Training Methods:**

The training faculty is drawn from the respective area of work from the line of managers and the senior members from QA / Production along with out side experts (if required) the training program also includes practical training on working site. Following training aids are used for effective training.

- Reading materials-books and notes.
- Video shows.

E.2.3.4 **Training Assessment:**

The training assessment is done from the conducted training program as per the training calendar. The questionnaires are given to the group of employees attending the program. If the score in evaluation is below qualifying range re-training shall be given. Employees are allowed 3 times more for re-training, failing which they shall be transferred to non-critical operations.

E.2.3.5 **Training Record:**

All the records pertaining to the training in prescribed formats are available with Quality Assurance Department. The Quality Assurance Department, maintains the records of cGMP training. Every department maintains the individual training records in case of job training of the employees of their own department

E.2.4 Health Requirements for Personnel Engaged in Production:

E.2.4.1 **Health Checking of Employee – Responsibility:**

All personnel engaged in manufacturing should be free of any contagious disease or severe type of reaction with specific drugs.

The medical examination consists of general examination and eye checkup including color blindness.

E.2.4.2 **Pre-employment Medical Examination:**

All the new employees have to undergo pre-employment medical check ups before joining the organization. Company has authorized doctor, who is a registered medical practitioner, carries out pre-employment check-ups.

E.2.4.3 **Routine Health Checking of Employee:**

There is a well-organized program for all level of staff members and workers for pre-employment & after every year medical and eye checkup to ensure the health of personnel. Independent professional doctor carries out medical examination. Any unusual findings during repeat check up, treatment is

given to recover from reported illness. Rechecking is carried out after prescribed time period and personnel may be granted full rest depending upon the illness. During treatment period, suitable relocation changes are done in employee's job as advised by medical consultant. Ophthalmic checkup for employees is planned after every six months. Routine check up for each employee is planned after every one year.

E.2.4.4 **Reporting of Sickness and Action Taken in Case of Sick Employee:**

All the employees engaged in manufacturing activity has to report to their immediate superior in case of any sickness or if they are in contact with any sick person. Also the employees are advised to report any type of illness observed by them.

E.2.4.5 **System of reporting After Sickness:**
A fitness certificate from registered medical practitioner is to be provided by the employee after recovery from the illness before reporting to his duties.

E.2.5 **Personal Hygiene Requirement:**

E.2.5.1 **Washing, Changing and Rest Areas:**

Every person engaged in manufacturing activities has to comply with requirements of personal cleanliness and hygiene conditions to protect himself and the product. Suitable changing rooms and washing facilities are provided before entering the manufacturing area. Lockers are provided in change rooms for keeping clothes, foot wear and employee's belongings. The employees remove street footwear and keep them in the lockers provided. Employees (Operators & workman) remove the street clothes and keep them in the locker provided. Other employee (Staff) and visitors wear the dresses/coat over their street cloths by changing the street footwear by factory foot wear. All employees wear Plant uniform and cross the step over bench while wearing factory foot ware and enter the plant to proceed to their respective work place through the airlock. Employees required to enter process area has to wear another foot wear in the second change room. Employees sanitize their hands, before entering the process area corridor to proceed to their respective work place (s).

E.2.5.2 **Description of Clothing:**

Appropriate lint free clothing is provided to the employees depending upon nature of their work. Staffs are provided Factory full dress with cap and factory footwear. Masks for covering mouth and nose also provided where-ever necessary. Hand gloves are provided for employee coming direct contact with products.

E.2.5.3 **Change of Clothing:**
Gowning and de gowning instructions in the form of SOPs are kept in each of the change rooms. The person involved in manufacturing shall change his cloth daily. The persons working in Q.C shall change their cloths weekly. The person involved working in microbiology laboratory shall change their cloths daily. The in house laundry facility is available for washing of used company garments.

E.3 **Premises and Equipment:**

E.3.1 **Premises:**

Premises have been designed, keeping cGMP, safety and manufacturing capacity in consideration. Premises and equipment are located, designed, constructed, adapted and maintained to suit the operators to be carried out. The layout and design is in such a way that it is aimed to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, any adverse effect on the quality of products.

E.3.1.1 **Legibility of Plan:**

A plan of production facility with indication of scale and names of the area is attached as **Annexure-III.**

A plan of quality control department with indication of scale and names of the area is also attached as **Annexure-III.**

E.3.2 **Nature of Construction and Finishes:**

The building is made of Reinforced Concrete Cement (RCC), and designed such, that no beams or columns are visible in the manufacturing and testing areas. The walls of the plant are constructed of brick and plastered to provide a hard smooth finish, with minimized recesses. They are further painted with epoxy paint. Wherever possible, all floor and ceiling joints are "coved" to avoid any sharp edges, right angles. All the windows between process and non-process area are fixed in a fashion that no window projection is toward process area. From process to process area, the windows are fixed in centre of wall with proper slope on both side to provide easy cleanable surface, thereby eliminating dust accumulation. The Production, Quality Control / Assurance, Warehouse and the inter-connecting corridors - Kota stone has been used. PVC roofing has been used anywhere. Walls, floors and ceiling are constructed of hard non porous non-shredding material using best quality of cement and concrete. These surfaces are able to withstand repeated hot water and detergent cleaning operations. All the surfaces are free from any holes or cracks. All surfaces of walls are flat and do not have any projecting features. All surfaces are finished with smooth non-pealing paints

Pest Control: Termite treatment is done during construction to column and various grids / footings.

Painting: Three types of painting have been done. External paint is cement based water repellent paint. Internal Poly Urethane paint is applied in Production and stores area. In QC & Administration Plastic & water proof Paint is used.

Door & Windows: All doors are made of Galvanized M.S. sheet heaving PU paint coating with flushed door having flush glazed view panels.

Electrical Wiring: Conceal

E.3.3 Equipments: HVAC System

The critical areas like processing and primary packaging areas where products are directly exposed are provided with HEPA filters of 0.3μ Rating with 99.99% efficiency. The Air Handling Systems are designed to maintain the temperature below 23 ± 2°C and humidity below 30 % RH in LOW RH production areas.

The areas of different criticality levels are provided with minimum 15-pascal pressure differential. The air flows from clean corridor to the cubicles having dust-generating activities. The processing areas have been provided with minimum of 20 air changes/hour. The rest of the air changes are due to re-

circulated air.

In Order to reach class 100,000 in clean levels, the number of air changes shall be related to the size of the equipment & the personnel present in the room

The requirement & limit for the area shall depend on the nature of operation carried out.

Type of Operations to be carried out of the Various Grades for Clean Preparations

CLASSIFIED AREA	TYPE OF OPERATIONS
1,00,000 (Grade D)	Dispensing Area with Reverse Laminar Air Flow Production Primary Packing,

Air Changes are designed according to the nature of operation in different areas.(Annexure-XV)$

E.3.4 Filter Design Efficiency and Alarms:

The supply line plenums are provided with a series of filters of rating 10μ and 3μ . The filters in production areas are HEPA filters of 0.3μ Rating and 99.99% efficiency. The return air risers are provided with filters of 10μ rating. The Micro-weave filters are changed in any of the following events: Choking of filters and CFMs out of limit.

Special Areas For Handling Highly Toxic, Hazardous And Sensitising Materials#

E.3.5 Details of PAO Introduction Points:

PAO (Poly alpha olefin) Test is done at the time of validation of HEPA filters. All the filters of air handling system, laminar flows etc. are validated 12 months.

E.3.6 Frequency of Revalidation of the System:

The HVAC system is revalidated as per respective SOP..$

The system performance is routinely monitored through monitoring of pressure differentials, temperature / humidity conditions and pressure differentials across filters and microbiological monitoring of the environment.

E.3.7 Design Criteria of Ventilation:

For Solid dosage forms, the class of air in core processing area meets the requirement of Grade-D. Pressure differentials are maintained as per the specified Guidelines for then respective dosage forms. Temperature in all areas is NMT 25°C. Relative humidity in the different sections is as mentioned below.

SECTION	RELATIVE HUMIDITY (%)
Tablet areas	NMT 60
Capsule areas	Between 45 to 50
Dry Powder Syrup areas	NMT 30
Low RH	NMT 30

E.3.8 **Brief Description of Water System:**

Schematic diagram of water system is as per the **Annexure- IX.**

Raw Water:

GIDC treated water is used & Raw water is mainly used for toilets and miscellaneous activities.

Soft Water:

This water is prepared using softner is transferred to soft water storage tank. From soft water storage tank it is transferred to ultra-filtration storage tank through ultra-filter system. Finally, water from ultrafiltration storage tank is transferred to RO permeate water tank through RO-EDI system. The loops are made up of S.S. 316 material having facilities of sanitization.

The Purified water is stored and continuously circulated at ambient Temp, to the point of use.

Specifications of Purified Water:

Purified Water meets the specifications laid down in the IP, BP. Samples are drawn every day, for analysis, from predefined sampling points.$

The purified water meets the following microbiological specifications (Annexure-XVI)

The purified water is sampled to check the conformance of laid down specifications from the various sampling points. The locations of sampling point and the testing frequency is well defined in its SOP.

E.3.9 **Description of ETP:**

Entire effluent is treated in a suitably designed effluent treatment plant and the treated effluent is recycled for usage in garden and tree plantation activities. No waste is discharged in the surrounding area.

E.3.10 **Preventive Maintenance of Equipment:**

The preventive maintenance is carried out as per the predefined frequency using duly Approved written procedures.

The preventive maintenance program comprises of daily, weekly, fortnightly/monthly, quarterly and yearly overhauling checks including inspection of lubrication ports, all drives, sensing and recording systems, wear and tear of moving parts etc.

Apart from above mentioned areas, preventive maintenance of water system includes inspection of system and joints for absence of leakages, inspection and lubrication of Flow Diversion Valves, cleaning of filters and testing and verification of set points, alarms and other controls.

The preventive maintenance of HVAC system includes monitoring of pressure differential across pre-filters & Fine filters & cleaning of these filters apart from the above mentioned general checks.

The preventive maintenance of AHU system includes monitoring of pressure differentials across pre-filters and Micro-weave fine filters and cleaning of these filters apart from the above mentioned general checks.

E.3.10.1 **Written Procedures and Recording forms:**

All activities related to planned Preventive maintenance are recorded on log books indicating the activity, date and time of carrying out the activity, the details of the checks carried out, significant observation and any action taken, record of spare parts replaced, repair and any modifications to the system. Wherever required, the modifications are done to the system after proper change control.

E.3.10.2 **The key responsibilities are:**

To provide uninterrupted support of utilities like power, chilled & D.M. water for manufacturing operation.

To carry out planned preventive maintenance of all equipment's.

To attend to breakdown & carry out repair jobs.

To prepare Equipment history card for each equipment.

To calibrate measuring devices like pressure gauge, humidity tester & temperature recorder daily.

To clean & change filter of A.H.U. System periodically as per SOP.

E.3.10.3 **Preventive Maintenance of Premises:**

The house keeping team is given the charge to make the premises clean and tidy. An experienced supervisor takes the lead with his experience and makes sure that the premises is always clean. The same team takes care of Pest control on regular basis and keeps the cleaning records as per the procedure mentioned in the SOP. The house keeping staffs are given training in regular intervals as per the cGMP norms.

E.3.11 Qualification, Validation and Calibration:

E.3.11.1 **Validation Policy:**

All major equipment's are qualified as per the written installation, operational and performance (wherever applicable) qualification protocols before taking them in actual operation, test data sheets are filled. Equipment's are re-qualified after major repair, change in functions or shifted to other location

Following is the approach of the organization for Qualification / Validation:

- **Design Qualification (DQ):**

Demonstrates that the proposed design of the facility, utility equipment, control system and selected components are suitable for intended purpose. It is the first element of the validation of new facilities, system or equipment

- **Installation Qualification (IQ):**

The documented verification that the facilities, utility, control systems and equipment as installed or modified, comply with the approved design and manufacturer's recommendations. This provides documented evidence that all key aspects of the installation are adhered to the design intentions and that all equipment manufacturer's recommendations have been suitably considered.

- **Operational Qualification (OQ):**

The documented verification that the facilities, utility, control systems and equipments, as installed or modified, perform as intended throughout the anticipated operating ranges. This provides documented verification that the facility, utility, equipment, and other control systems perform as intended throughout its operating ranges.

- **Performance Qualification (PQ):**

The documented verification that the facilities, utility, control systems and equipments, as connected together, can perform effectively and reproducibly based on the approved process method and product specification.

This stage is related to system performance in the production mode, using actual processing materials or data (for computers). Critical equipments undergo extensive validation studies to ensure consistent performance depending on approved validation protocol

➢ **Re-Validation Policy:**

This provides the documented verification by re-ensuring of the equipment that it is working in accordance with qualification status.

The re-qualification period may depend upon the equipment functionality.

Following guidelines should be used for re-qualification.

- ✓ Once in five years.
- ✓ After major modification in equipment.
- ✓ After relocation of equipment.

E.3.11.3 **Process Validation:**

It is the objective of the organization to make all product of consistent and reliable quality.

Process validation ensures and provides documented evidence that the processes are capable of repeatedly and reliably producing a finished product of the required quality meeting approved specification operated within established parameters.

Documentation describing the process parameters to be achieved shall be developed by the Validation Team based on manufacturing data and documentation available.

Process qualification and validations shall be performed in the following situations:

- ➢ New product
- ➢ New equipment (only process validation to be done). In case of deletion or addition of equipment only the critical stage to be monitored.
- ➢ Change in batch size
- ➢ Change in critical parameters of processing. e.g. Change in method of granulation from wet granulation to dry granulation & Transfer of product from one site to another.

E.3.11.4 **Prospective process validation:**

Prospective process validation shall be carried out before routine production of products intended for sale and after new master formula and the manufacturing process have been established, as demonstrated by process optimization batches.

E.3.11.5 **Concurrent process validation:**

Concurrent Validation shall be carried out for establishing documented evidence that a facility and process do what they purport to do, based on information generated during actual imputation of the process.

Concurrent validation can be conducted when, Data from replicate production runs are unavailable because only a limited number of batches have been produced.

Batches are produced routinely by a validated process that has been modified.

Prior to the completion of concurrent validation, batches can be released for commercial distribution based on thorough monitoring and testing of the batches.

Concurrent validation to be performed on three consecutive production batches.

E.3.11.6 **Retrospective process validation:**

Validation of a process for a product which has been marketed based upon accumulated manufacturing testing and control batch data.

Retrospective validation is historical trending of results of testing and evaluation on established products to demonstrate that:

- Critical quality attributes and critical process parameters are still valid as they give consistency in results & in process controls are appropriate for given product.
- Majority of the batches meeting the equipment, process and timing, manufacturing environment and the operators re demonstrating consistency to specifications.

An exception can be made for retrospective validation for well-established processes that have been used without significant changes to finished product quality due to change in material, equipment, system, facilities or the production process.

Batches selected for retrospective validation should be representative of all the batches made during the review period, including any batches that failed to meet specifications, and should be sufficient in number to demonstrate process consistency.

E.3.11.7 **Re-Validation:**

Revalidation is done to evaluate the impact of changes in process, procedure, equipment, raw material and primary packing material, environment.

The re-validation process is intended to ensure that validated systems continue to perform in accordance with the parameters defined during the original validation.

All systems subject to validation should be revalidated within a pre-specified period of time. The re-validation frequency will be determined upon completion of the initial validation of a system.

Re-validation frequency requirement shall be evaluated based on impact analysis study carried out during Change control procedure.

Revalidation is of two types:

- Revalidation after changes to evaluate impact on product quality.
- Revalidation after change is done in the following circumstances:
- Major changes in processing steps, equipment size, design and material.
- Major change in area and support system.
- Major change in Quality Control Analytical Methods.
- Major change in Computer – Software and Hardware.
- Periodic Re-validation at scheduled intervals.

Periodic Re-validation is done to evaluate consistency in operations, equipment wears and tear, processing steps, In-process standards and overall product quality.

Note: The extent and frequency of re-validation will depend on the nature and significance of the changes.

E.3.11.8 **Release for Sale or Supply of Development and Validation Batches:**

The batch on which prospective validation is done is not release for sale.

The batches on which concurrent validation is done is release for sale after getting reports from quality control and approval from quality assurance department.

E.3.11.9 All measuring instruments and gauges like pressure, temperature, vacuum gauges, temperature

indicators, temperature controllers, recorders etc. are calibrated against reference standard periodically and instrumentation department maintains record regularly.

E.3.12 Sanitation:

E.3.12.1 **Procedures for Cleaning:**

Each area in production undergoes cleaning as per the standard operating procedures on cleaning. The SOPs clearly specify the type of detergents to be used and the sanitizing agents with their concentration and frequency.

All the equipment's are cleaned after use as per their cleaning procedure. The cleaning procedures are validated as per their protocol. The cleaning of equipment is evaluated based on the rinse water / swab analysis collected.

The water lines are cleaned as per the standard operating procedure.

The air handling system is cleaned as per the standard operating procedures. Pre-filter and fine filters are cleaned as per Standard Operating Procedure. HEPA filters are evaluated periodically and if found damaged they are replaced. The ducts are cleaned with vacuum cleaner, as per the frequency in the standard operating procedures. Dust extraction systems are vacuum cleaned as per the standard operating procedures.

E.3.12.2 **Change of Cleaning Agents:**

Cleaning agents shall be changed as per "SOP on disinfectant usage policy".

E.3.12.3 **Validation of Cleaning Procedures:**

Specific validated cleaning procedures for production equipment is included as part of the batch documentation and these procedures cover both between-batch and between-product cleaning.

The operators keep machinery and equipment clean during use. The operators are also responsible for cleaning. Machinery and ancillary equipment are kept in a clean condition even when not in use.

Cleaning procedures for equipment are regularly validated and methods are monitored routinely by chemical and microbiological methods.

In case of a product change over, the rinse water/swab sample is analyzed by Quality Control Department to ensure that the parts are free from traces of previous product. Prior to start up of any equipment, the In-process Quality Officer/Chemist certify that the equipment is clean and is ready for use.

E.3.12.4 **Monitoring of Cleaning Procedure:**

Monitoring of cleaning procedure shall be done as per respective SOP on cleaning.

E.3.12.5 **Cleaning Method Used for Water Supply, Air Handling Unit and Dust Extraction System:**

Written procedure exists for cleaning methods with its frequency for water system, air handling system and dust extraction system. Records are maintained.

E.4 Documentation:

E.4.1 Preparation, Revision and Distribution of Documents:

E.4.1.1 **Description of Documentation System:**

The entire documentation system of manufacturing & quality control is very comprehensive & well

controlled to avoid any ambiguity and uncertainty in the plant and is described in "SOP on SOP".

Standard operating procedure (SOP) on preparation, review, approval, authorization & control of SOP is available. Separate SOP on documentation & data control is also available which describes the entire documentation system.

A separate area, under lock and key arrangement, is provided for storage of documents. This area is under control of QA Department.

Master Copy of SOPs is maintained by QA Department. At the time of revision, obsolete copies are withdrawn according to Distribution List. Obsolete Master Copy is maintained in archive by QA.

Master Batch Manufacturing Record (BMR) & Batch Packing Record (BPR) are prepared and controlled by Quality assurance department.

Batch Records, Equipment Logbooks and other Records, maintained on Shop Floor, and are also preserved in Archive.

Specification are maintained and updated by QA department

E.4.1.2 **Responsibility of Preparation, revision and Distribution of Documents:**

Each department has its own specific activities along with, role/responsibilities of personnel, different relevant SOPs, different formats, etc. Each department develops their respective SOPs, checked by seniors, approved by Head of Departments / QA and approved by and Q.A. after review for compliance.

E.4.1.3 **Storage of Master Documents:**

All master documents are stored by Quality Assurance department under lock and key.

E.4.1.4 **Standard Formatting for Documentation:**

The formatting of all documents are done as per written procedures related to specification, analytical methods, batch numbering records, batch packing records etc.

E.4.1.5 **Control of Documentation:**

The master documents and all instructions are reviewed and approved by the QA department before use. Any changes to be made in the master documents and master procedures have to be justified and approved by QA Department. A Change Control Procedure is followed for any change in manufacturing procedures/practices, change in vendors, equipment etc. and is implemented after approval by the Quality Assurance Department. All the approved Master Documents are kept with Quality Assurance Dept. Issuance and withdrawal of SOPs is controlled by the Quality Assurance Department. SOPs are reviewed after 3 years. In case of change, SOP with next revision number is issued and old SOP is withdrawn and is stamped as "Obsolete".

Production department sends a written request for issuing the Batch Production Record to Quality Assurance department. QA department issues a photocopy / printout or scanned copy of approved Batch Production Record to the production department.

After the completion of manufacturing and packing process the Batch Production Record is submitted to the QA department for review. The finished product samples are analysed by QC department as per specifications before the final release of the batch for distribution.

The batch documents along with QC reports are kept for at least one year after the expiry of the

product.

E.4.2 Other Documentation related to Product Quality:

A routine monitoring of water (potable and purified water) is carried out, as per the sampling plan attached with the SOP.

E.4.2.1 **Equipment Specifications:**

The equipment specification is prepared by concern department and master maintained by Q.A.

E.4.2.2 **Specification for Cleaning Materials:**

The specifications of cleaning materials are given in SOP on disinfectant policy.

E.4.2.3 **Standard Operating Procedures:**

The standard operating procedures are prepared by concerned department and master and maintained by Q.A.

E.4.2.4 **Quality Control Procedures:**

All quality control procedures are well documented in the form of SOP and the master is maintained by Q.A.

E.4.2.5 **Training Procedures:**

The training faculty is drawn from the respective area of work from the line of managers and the senior members from QA/Production along with out side experts (if required) the training program also includes practical training on working site. Following training aids are used for effective training.

- ✓ Reading materials-books and notes.
- ✓ Video shows.
- ✓ Transparencies/slides with aid of projectors.

E.4.2.6 **Document Control of Process Deviation:**

Any change in process are review and approved by the QA department. Any changes to be made in the Master Procedures have to be justified and approved by QA Department. A Change Control Procedure is followed for any change in manufacturing procedures/practices, change in vendors, equipment etc. and is implemented after approval by the Quality Assurance Department.

E.4.2.7 **Calibration and Test Documents:**

All measuring instruments and gauges like pressure, temperature, vacuum gauges, temperature indicators, temperature controllers, recorders etc. are calibrated against reference standard periodically and engineering department maintains record regularly.

QA department maintains all calibration and test documents.

E.4.2.8 **Validation Documents:**

All major equipment's are qualified as per the written installation, operational and performance (wherever applicable) qualification protocols before taking them in actual operation, test data sheets are filled. Equipment's are re-qualified after major repair, change in functions or shifted to other location. All validation documents are maintained by Q.A.

E.4.2.9 **Reconciliation of Materials:**

After completion of the batch reconciliation shall be done and record shall be maintained.

E.5 Production:

E.5.1 Description of Production Operation:

(Using flow sheets and charts, specifying important parameters)

The head of production is professionally qualified and has experience of techniques and operations of production. He takes every measure to prevent and avoid errors by means of continuous check of the process. As the batch manufacturing progresses the related batch manufacturing records are filled online and completed at every stage as and when the process is completed. The batch manufacturing is carried out in strictly according to master formula card.

The packing activity of new batch starts after the clearance of the packaging line. Reconciliation is done at critical steps of manufacturing and completion of packaging operations. Process flow sheets of Raw Materials/Packing Materials, Tablets, Capsules, Dry Syrup indicate the function of the department.

E.5.2 Material Handling During the Manufacturing Process:

E.5.2.1 **Control of Raw Material:**

Each consignment of material received is examined visually. Damaged goods are labeled as "ON HOLD" and kept aside for Quality Assurance's instructions either for disposal or return to party.

After verification of quantity received and batch wise segregation, the details of receipts are entered in a register called inward register and the Goods Receipt Note (GRN) is generated with unique serial number.

All the containers are placed in designated area labeled as "UNDER TEST", with details of GRN.

Samples are drawn as per sampling plan and sampled containers are identified with "SAMPLED" sticker and tested as per the respective material specifications by Quality Control Department. 100% containers are sampled for identification and composite samples are taken for complete analysis for active raw material and random for inactive materials.

Analyst compiles the data after analysis & decides whether the material meets the specifications or not. Accordingly, QC Approves or Rejects the material.

"APPROVED or REJECTED" labels are affixed on the material containers & the same is transferred to designated storage area APPROVED or REJECTED material accordingly

E.5.2.2 **Control of printed Packing Material:**

All packaging materials are handled as per above procedure and approved / rejected status labels are affixed accordingly. Printed packaging materials are stored securely under lock and key and re-issued in requisite number only.

Dispensing of material is done as per SOP on FIFO/FEFO principle. Appropriate material handling devices are used such as trolleys, cages and other suitable containers.

The quality assurance personnel along with production personnel assures the calibration of equipment's and instruments such as balances, hygrometers etc.

All packaging materials are labeled in such a manner that the material is easily identified that the material is the one, which is currently in use.

E.5.2.3 **Quarantine and Release of Finished Product:**

After the completion of labelling and packing operation, finished goods are transferred to in-house quarantine area. On completion of testing, the batch records are sent to QA for review. On satisfactory compliance, the QA department shall release the batch for further distribution.

E.5.3 Arrangement for Handling Rejected Materials and Products:

All rejected materials are separated from 'APPROVED' or 'QUARANTINE' area and the quality control persons will affix 'REJECTED' labels. The rejected material is transferred to a secured "Rejection" area. Quality assurance decides the fate of such rejected material as to destroy or to return. No printed packaging materials are returned but are destroyed on the premises under supervision of quality assurance. The rejected materials are kept under lock and key and only authorized persons are allowed to handle such materials.

E.5.4 Brief Description of the General Policy for Process Validation:

The Validation Master Plan is written to serve as a guide, in achieving the overall objective of providing products, which consistently meet their predetermined quality attributes and help us to achieve the reliability of customers. The Validation Master Plan also provides direction and control during the execution of the Validation Project.

The Validation Master Plan is a written document that describes the company's intentions and Validation need through the proper description of the facility, equipment, services, materials, analytical methods and processes, at the Sanand plant. The Validation Master Plan describes the approach of validation, responsibilities, general guidelines for validation, stepwise validation activities and frequency of revalidation.

The document states the elements of the Validation Program. It encompasses aspects of the project, including installation, operation and performance qualification of equipment as well as Process Validation.

It defines the responsibilities of the various functional groups in performance of validation and presents a validation schedule.

Though detail validation methodology is described in the individual validation protocol, master validation plan gives general guideline to the designer of the validation protocol about the methods.

As a policy of the company all major equipment has to be qualified for installation, operation and Performance Qualification before commercial production starts. Any changes in a validated process have to be re-validated prior to switch over.

Process revalidation is applicable on account of following:

Change in process parameters & key raw materials/quantities & equipment/facility.

A process is considered to be validated when three consecutive batches give results within the specified limits. Validation is carried out by a team consisting of Quality Assurance Manager, Production Manager and Engineering Manager.

Equipment, processes & procedures undergo periodic critical revalidation to ensure that they are capable of achieving intended results. A detailed SOP prepared describing the detailed process validation procedure.

E.6 Quality Control / Quality Assurance:

E.6.1 Description of Quality Control / Quality Assurance system:

SOTAC Healthcare Pvt. Ltd is committed to the manufacture and distribution of Quality Products meeting prescribed specifications. Quality Assurance Management is carried out by team of scientifically qualified personnel headed by experienced Manager. This Manager is independent and responsible for all activities pertaining to Quality appraisal and directly reports to Managing Director. SOTAC Healthcare Pvt. Ltd. employees fully understand that Quality has to build into product. For this purpose, operating procedures are strictly adhered to:

Activities of Quality Control Department consists of but not limited to the following:

- Prepares and finalizes the Specifications for Raw and Packing Materials, in–process controls, Finished Goods.
- Inspect, sample and test (Raw and Packing) Materials. Assign QC reference no. and retest dates.
- Sample and test in–process samples.
- Sample and test Finished Goods.
- Procedure for release of finished Goods is as follows:

A) For Tablets: Uncoated Tablets after compression are tested as semi-finished product and physical parameters are checked, on release of Uncoated Tablets, it is taken for Coating. After Coating stage tablets are tested for description & again for physical parameters and are taken for packing. In process controls are exerted during primary and secondary packing. After completion of packing, Finished Goods are transferred to Finished Goods Store Room. During Tablets are packed, samples for analysis and the Control (Reference) Samples are drawn. Analytical samples are tested to confirm the compliance. Batch release is given only after the batch is found passing in testing as per the specifications and auditing of the completed Batch record (BMR). A test report is prepared and written authorization issued to stores to dispatch the product distribution.

B) For Capsules: Capsule blend is tested as semi-finished product and on release of blend, it is taken for Filling. In process controls are exerted during primary and secondary packing. After completion of packing, Finished Goods are transferred to Finished Goods Store Room. During Capsules are packed, samples for analysis and the Control (Reference) Samples are drawn. Analytical samples are tested to confirm the compliance. Batch release is given only after the batch is found passing in testing as per the specifications and auditing of the completed Batch record (BMR). A test report is prepared and written authorization issued to stores to dispatch the product distribution.

C) For Dry Syrup: Dry Syrup blend is tested as semi-finished product and on release of premix, it is taken for Filling. In process controls are exerted during primary (Filling, Sealing) and secondary packing. After completion of packing, Finished Goods are transferred to Finished Goods Store Room. During packing, samples for analysis and the Control (Reference) Samples are drawn.

D) Analytical samples are tested to confirm the compliance. Batch release is given only after the batch is found passing in testing as per the specifications and auditing of the completed Batch record (BMR). A test report is prepared and written authorization issued to stores to dispatch the product distribution.

Quality Assurance Activities in Departments:

QA monitors the production as well as the supporting activities of departments. This includes

monitoring for the adherence to the specific SOP & GMP. Any activity which affects the quality of the product is stopped & corrective action is taken immediately.

Quality Assurance personnel draw samples of each batch of each product at specified intervals during entire batch production as per the sampling program. Complete analysis is done as per the release specifications (Pharmacopoeia or In-house). Results are recorded in test protocols and reports. The Head of Quality Assurance after checking the in-process reports releases the finish product for packaging.

E.6.2 Procedure for Release of Finished Products:

As soon as any batch has been finally packed, the In-process Quality Assurance personnel draw random samples of the finished product. These samples are tested against approved specifications by the Quality Control Department. If the samples meet the specifications, the Quality Control Department certifies the batch as approved.

The Batch Production Record is reviewed by the Quality Assurance Department for the completeness of the document and for the compliance with cGMP's at various steps / deviation (if any). On the satisfaction that the Batch Record is complete and the batch was manufactured complying with all GMPs and SOPs, the QA Department releases the batch through for further distribution.

Adequate number of control samples of key raw materials and finished products are retained for future evaluation. Stability study samples are collected separately as per Stability programme.

E.6.3 Procedure for Release of Packing Material:

All packaging material on receipt from vendor is stored in Warehouse with 'Quarantine' status. A Goods Receipt Note (GRN) for the material is made and sent to Quality Control Department. A Quality Control Reference Number is assigned to the material; sampling of the same is done as per SOP and affix the 'Under test' status label in Under Test area.

Samples are tested as per the approved specifications and compared with approved standards and shade cards. If the samples conform to the specifications, then the consignment is released and 'Approved' label is pasted over the 'Under Test' label. The consignment is then moved to the 'Approved' storage area or 'Rejected' label in case of rejection of material in rejected area.

NOTE: Quality Assurance releases intermediate batch for packing only after the release of quality control.

E.7 Contract Manufacturing and Analysis:

SOTAC Healthcare Pvt. Ltd. is in business of contract manufacturing i.e. Formulations of only Beta-lactam products are manufactured on job work/contract basis.

Analytical assistance is taken from approved analytical testing labs for few specific tests that cannot be carried out at the site.

E.8 Distribution, Complaints and Product Recall:

E.8.1 Distribution:

Finished goods are stored on pallets in finished goods store. It is ensured that the finished packs are kept separately, product wise and batch number wise up to specified height.

- There is an effective labeling system to identify the status of products.

The records-maintained permits full batch traceability from the factory to the customer, in terms of

date of dispatch, customer details and quantity dispatched. The importing party maintains the distribution records.

The distribution records of domestic products are maintained in such a way that traceability of the product marketed can be ensured fast, in case of withdrawal or recall.

E.8.2 Environment Control of Warehouse:

The environmental condition of the warehouse is controlled.

The temperature in warehouse is NMT 25 and humidity is NMT 60%.

E.8.3 Storage of Materials:

The Finished Goods are stored in the controlled environment in the finished goods store. The finished goods are kept on the pallets and stacked on the racks provided in the finished goods store. After getting clearance (release note) from Quality Assurance Department, the finished products are dispatched to various depots.

E.8.4 Arrangements for Handling Complaints and Product Recall:

We have written procedure for market complaints handling which defines responsibility for logging and investing. Head-quality Assurance with the Production Head is responsible for investigating complaints as per written procedure. Details of complaint, investigation report, Action plan and reply to the complainant constitutes documents of complaint handling procedure.

E.8.5 Retention Period of Market Complaints:

The record remains with the Head-Q.A. Complaint records are stored minimum for three months after the expiry of the product.

E.8.6 Product Recall:

Written procedure (SOP) exists for the sequence of actions required to be followed in the event of any product recall. The SOP includes retrieval of distribution records, notification to customers, receiving, segregation and inspection of recalled products, investigation and reporting of cause and the corrective actions. Head Quality Assurance is responsible for product recall, whether it is on the instructions from drug authorities (FDA) or it is a voluntary withdrawal. Details in approved format are filled. FDA is informed about stock manufactured, distribution details and quality recalled.

The quantity received if any, after recalling a batch is kept in secured dedicated area until the decision about its disposal is taken. If recall of a product is at the instance of local drug authorities, the final disposal will do in their presence, but if it is a voluntary withdrawal, the decision of Head – QA and plant Head is final.

E.9 Self-Inspection:

Self-Inspection Program (Internal Audits) is conducted by cross-functional team, which is headed by QA Department. The audits are conducted as per the Audit Planner, which includes routine inspection of the facility or inspection of some part of the function or follow up inspection after external audit. The frequency of self-audit is once in year. This frequency can be increased for any department, depending upon the number / seriousness of deviations, failure, complaints etc.

After inspection, QA Head discusses the identified deficiencies / non-conformities, with the Head of concerned Department, for corrective and preventive action.

After discussion, the audit report is prepared and forwarded to the Head of Department. If required,

copy is marked to plant Head.

Follow up inspection, if required, is planned to ensure compliance.

E.10 Abbreviation:

AMC	:	Annual maintenance contract	DQ	:	Design Qualification
SMF	:	Site master file	IQ	:	Installation Qualification
HVAC	:	Heating ventilation and air conditioning	OQ	:	Operation Qualification
PAO	:	Poly Alfa Olefin	PQ	:	Performance Qualification
HEPA	:	High efficiency particulate air	IP	:	Indian Pharmacopoeia
NMT	:	Not more than	BP	:	British Pharmacopoeia
cGMP	:	Current Good manufacturing practice	USP	:	United States Pharmacopoeia
GRN	:	Goods receipt note	RCC	:	Reinforced Concrete Cement
DQ	:	Design qualification	WHO	:	World health organization
IQ	:	Installation qualification	AHU	:	Air Handling Unit
OQ	:	Operational qualification	RH	:	Relative humidity
PQ	:	Performance qualification	cfu	:	Colony forming unit
RO	:	Reverse osmosis	EDI	:	Electro Deionization Unit.

E.11 Revision History:

Sr. No.	Current document No.	Revised Document No.	Ref. CRF No.	CRF Approved date	Reason for revision
1.	SMF/SH/01-00	NA	NA	NA	New SOP
2	SMF/SH/01-01	SMF/SH/01-00	HQAC21003	22/01/21	To incorporate WHO –GMP Certificates details and Editorial changes. Pg.- 05 and 35 Revision History Added. Pg- 06 – Site master approval format revised. Pg. 07 List of Annexures updated and Note added. Pg 08 E.1.2 Details of regulatory up-dation shall be updated to incorporate WHO –GMP Certification number and Validity Pg.11 Key person list updated. Pg.34 Abbreviation updated.

3	SMF/SH/01-02	SMF/SH/01-01	HQAC21004	11/03/21	$ to incorporate E.1.4 remove manufacturing facility,E.1.8.1 remove, E.3..6 remove frequency and frequency as per SOP., E.3.8 purified water specification remove as per USP, E.3.11.5 easy to define concurrent process.
4	SMF/SH/01-03	SMF/SH/02-02	HQAC21012	21/12/21	SMF revised to update Annexure as existing and some editorial changes .

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