EAST AFRICAN (INDIA) OVERSEAS Plot No.: 1, Pharmacity, Selaqui, Dehradun-248011(U.K.), India.				
SITE MASTER FILE				
DOCUMENT NO. **SMF-01-01**	**EFFECTIVE DATE :**	**DATE OF REVIEW:**	**SUPERSEDE NO.:** **NIL**	**PAGE NO:** **1 OF 25**

SITE MASTER FILE

SITE MASTER FILE APPROVAL PAGE

PREPARED BY				
Name	**Designation**	**Department**	**Signature**	**Date**
		Quality Assurance		

CHECKED BY				
Name	**Designation**	**Department**	**Signature**	**Date**
		Production		

CHECKED BY				
Name	**Designation**	**Department**	**Signature**	**Date**
		Quality control		

CHECKED BY				
Name	**Designation**	**Department**	**Signature**	**Date**
		Engineering and Utilities		

APPROVED BY				
Name	**Designation**	**Department**	**Signature**	**Date**
		Quality Assurance		

AUTHORIZED BY				
Name	**Designation**	**Department**	**Signature**	**Date**

REVIEW PERIOD: THREE YEARS OR IF THERE IS ANY CHANGE WHICHEVER IS EARLIER.

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1. GENERAL INFORMATION:

1.1 Contact Information:

1.1.1 M/s **East African (I) overseas** is situated at **Plot No. 1, Pharmacity, Selaqui, and Dehradun- 248011 (U.K.)** which is especially allocated for pharmaceutical industries in IIE SIDCUL Dehradun. Plant is situated in a hygienic environment; free from dust, smoke, chemical & biological emission.

The Plant has been designed & constructed covering Plot No. 1 in 3600 Square meters area.

This Plant has 2 separate blocks in multi-storeyed building for different type's formulation.

The place is about 25 km away from Dehradun the location is ideal for a pharmaceutical unit. There is a wide road, on the front side, other units are locates on back, right & left side of premises.

Total area of plot = 3600 sq. meter.

Block-wise

Block-A

The covered area is = 867 sq. meter.
Covered Length = 30 meter
Covered Width = 28.96 meter

Block-B

The covered area is = 438.90 sq. meter.
Covered Length = 30 meter
Covered Width = 14.63 meter.

1.1.2 Contact information of the site (Name and Address):

	Works	**Corporate**
Address	EAST AFRICAN (INDIA) OVERSEAS. Plot No:-1, Pharmacity, Selaqui, Dehradun (U.K.)	AST AFRICAN (INDIA) OVERSEAS. 120, Suncity Business Tower Gurgaon
Phone (24 hrs)	0135-2699211-12-13-14-15-16	0135-2699211-12-13-14-15-16
Emergency No.	0135-2699211	+919927900931
FAX	0135-2699217	0135-2699217
E-mail	sales@earindia.com	ear@earindia.com
Contact Person	Mr. R. K. Jain / Saurabh Jain	Mr. R. K. Jain / Saurabh Jain

1.2 Authorized Pharmaceutical Manufacturing Activities of The Site

1.2.1 Facilities Licensed By Uttarakhand State FDA, INDIA, State GMP Certificates and WHO GMP Certificates): -Tablets, Capsules, Oral Liquid, Ointment/Gel/Cream, dry powder injection and liquid injection products are manufactured under license no. 14/UA/2007 and 16/UA/SC/P-2007. [Valid Manufacturing Authorization [Annexure : I].

1.2.2 In Addition to above, facility is approved by Poisons Board - Kenya, Kingdom of Cambodia – Cambodia, Zanzibar Food and Drugs Board - Zanzibar, Ivory Coast Certificate – Ivory Coast, Ministry of Health (MOH) – Vietnam and Tanzania Food, NDA, Uganda and Drugs Authority (TFDA) - Tanzania [Annexure : III].

1.2.3 List of product manufactured at the site - [Annexure-II].
Only products for human use are manufactured on the site.

1.2.4 List of GMP:
1. WHO GMP – 20/04/2012- FDA [Annexure-III].
2. GMP – 13/09/2011- FDA Uttarakhand [Annexure-I]

1.3 Any Other Manufacturing Activity Carried Out on the Site:
Only pharmaceutical dosage forms are manufactured at this site.

2. QUALITY MANAGEMENT SYSTEM:

2.1 The Quality Management System

The Company has undertaken to work under the aegis of Total Quality Management (TQM) "To create customer and to retain customer within organization and outside organization" by fulfilling customer's needs, expectation and satisfaction by acting on it. Organization leadership having vision, direction, shared values by setting challenging targets and goals and implementation of same through involvement of people at all levels by using knowledge, experience and through training .A process and system approach based system results into organization's effectiveness and efficiency by continuous improvements and up gradation. Decisions and actions are based on the analysis of data and information by using suitable management's tools and technology.
Quality policy of EAST AFRICAN (INDIA) OVERSEAS is as follows:

WE ARE IN THE BUSINESS OF HEALTHCARE; ALLEVIATING HUMAN SUFFERING IS OUR PRIME OBJECTIVE. THEREFORE, EVERY PRODUCT WE PRODUCE MUST BE SAFE, EFFECTIVE AND OF HIGH QUALITY AND SHOULD BE TIMELY DELIVERED TO OUR CUSTOMERS.

WE BELIEVE THAT QUALITY HAS TO BE IN-BUILT IN THE PRODUCT AND IT IS ACHIEVED THROUGH THE FOLLOWING.

- **A GOOD PRODUCT DESIGN**
- **WELL ESTABLISHED MANUFACTURING SITE**
- **WELL-TRAINED PERSONNEL**
- **GOOD MANUFACTURING PRACTICES**

TO ACHIEVE THE QUALITY OBJECTIVE WE HAVE A WELL-DOCUMENTED QUALITY MANAGEMENT SYSTEM IN FORCE, WHICH ENSURES COMPLIANCE WITH THE CURRENT GUIDELINES OF THE GOOD MANUFACTURING PRACTICES.

WE BELIEVE THAT QUALITY IS THE KEY TO SUCCESS. HENCE, WE, AT ALL LEVELS, IN EAST AFRICAN (INDIA) OVERSEAS ARE COMMITTED TO QUALITY

This quality policy is communicated and understood at appropriate levels through training and display at proper places in English and other languages. Also reviewed for continuing suitability**.**

Elements of Quality Assurance System:

The Quality Assurance Department has responsibility and authority to define norms and regulations for various activities including Personnel Training, Sanitization and cleaning of general areas. Quality Assurance Department reviews the production records to ensure that all the manufacturing operations are carried out as per the laid down instructions.

Quality Assurance Department ensures that all production facilities are provided to meet cGMP requirements and have adequately trained and qualified persons, for carried out the operations.

All manufactured operations are clearly defined and checked routinely to confirm the quality of products**.**

Responsibility of Quality Assurance Functions:

- Has authority and responsibility of assessing and ensuring that all the products manufactured at site as per regulatory requirement.
- To monitor the entire manufacturing and quality control activities and to notify the management of any significant variation from the company standards which potentially affect the product quality.
- To ensure for each product there is an annual product quality review covering manufacturing activities, in order to provide assurance that product confirms to customers and regulatory requirements.
- To establish that manufacturing activities including any proposed changes are in accordance will regulatory requirement.
- Any changes which affect compliance with product standard should be approved by Head Quality Assurance before they are implemented.
- To review, suggest and ensure that plant is in validated state and confirms to regulatory requirements.
- Responsible for ensure the compliance of cGMP practices at all stages of production and control.
- Review of master documents and its control.
- Review of production records and in process controls.
- Review of product specifications and test procedures.
- Responsible for Release/Reject of Finished Goods.
- Quality audits and quality manual.
- Review of Stability studies.
- Vendor qualification.
- Training program.
- Deviation and failure investigation.

- Change control management.
- Product complaints and recall.
- Validations and Qualifications.
- Calibration program.
- Returned goods and their disposal.
- Monitoring of Plant preventive maintenance.

2.2 Procedure for release of finished product:

As soon as the batch is packed, Quality Assurance personnel draw samples as per the SOP for testing of Finished Products. These samples are tested by Quality Control Department against the approved specification and testing procedure. If the samples conform to the specifications, then the batch is approved through Certificate of Analysis (COA). Quality Assurance Department checks the COA and reviews the Batch Records for completeness of documents. Quality Head or his designee from QA reviews the batch records for completeness of documents. Quality Head or his designee from QA then releases the Batch for sale and distribution.

2.3 Management of Supplier and Contractors

The cGMP guidelines and Customer audits are used by the company to assess the quality system within the company and for the assessment of suppliers; the company maintains its own vendor audit and appraisal system for evaluation of Vendors.

2.3.1 Vendor Approval

A complete vendor approval plan takes care of Suppliers of critical starting materials and packing materials which are assessed by routine Audits / by questionnaires.

2.3.2 Use of Outside Technical Assistance

The site uses outside analytical service for verification of results where there may be disagreement with suppliers or other third parties or for a specialized analysis.
Name and address of the Laboratory: [Annexure-IV]

2.4 Quality Risk Management:

Quality risk management included systematic processes designed to coordinate, facilitate and improve science-based decision making with respect to risk. Possible steps used to initiate and plan a quality risk management process might include the following:

1. Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk;
2. Assemble background information and/ or data on the potential hazard, harm or human health impact relevant to the risk assessment;
3. Identify a leader and necessary resources;
4. Specify a timeline, deliverables and appropriate level of decision making for the risk management process.

2.5 Product Quality Reviews:

The efficacy, safety and quality of the product are assured through a series of validations carried out upon manufacture and analysis. Each production batch is reviewed by QA for completeness of starting material, manufacturing, analysis, Packing, IPQA, Yields, deviations, environments, out of Specification (OOS), controlled changes etc. prior to the release of the batch.

3. PERSONNEL:

3.1 Organizational charts: Attached [Annexure-V]

Qualification, Experience and Responsibility of Key Personnel Related to Production and Quality.

Name of Person	Department	Designation	Experience
Mr. R. K. Jain	NA	Chief Managing Director	NA
Mr. Saurabh Jain	NA	Director/ CEO	NA
Mr. Jitendra Kumar	NA	VP Operation	27 years
Mr. Rajesh Kr. Thakur	Quality Assurance	Manager	10 Years
Mr. Sunil Singh	Quality Control & Regulatory	General Manager	25 years
Mr. Sushant Pore	Production	Chief General Manager	26 years
Mr. Alok Pathak	Production	Manager	24 years
Mr. Abhishek Chaudhari	Engineering	Manager - Engieering	14 years

3.2 Number of Employees Engaged In Production, Quality Assurance, Quality Control, Engineering, Storage and Distribution on the Site.

Department	Managers	Staff	Workmen	Total
Production	03	23	59	**85**
Quality Assurance	01	23	06	**30**
Quality Control	04	30	02	**36**
Store	01	14	07	**22**
Engineering and utilities	02	09	10	**21**
Human Resources and Admin.	01	06	11	**18**
Others	02	30	00	**32**
Total	**14**	**144**	**86**	**244**

4. PREMISES AND EQUIPMENTS:

4.1 Premises

Plan of manufacturing areas is enclosed.

- Key site Plan
- General Block
- Beta Block

Nature of Construction and Finishes

- Building is constructed of hard and non-shading materials.
- Walls are made smooth, free from pinholes, painted with synthetic enamel/ polyurethane colour to enable washing and cleaning.
- Floors are kota stone with epoxy coated
- The sanitary fitting are concealed and drainage system is under ground and provided with trapped gullies to prevent back flow.
- Insect Killers and Air curtains are provided at various entry points.
- Doors and windows are made of puf aluminium sheets with glass windows and double glass windows flushed with wall.

4.1.1 Brief description of Heating, Ventilation and Air Conditioning (HVAC) systems. Design Criteria schematic drawings for HVAC system are attached as.

A. Processing Area – TABLET

Air supply	Air Handling Unit (10 % fresh air)
Classification	ISO Class 8
Temperature	NMT 25°C.
Humidity	NMT 50% RH with respect to product specific requirements
Differential Pressure	All the process corridors are under positive pressure to reduce contamination
Air change rate	Minimum 20 air changes per hour in process area
Filter Design	Prefilter/Fine Filter /0.3µHEPA filters Efficiency – 99.997%

B. Processing Area – LIQUID INJECTION

Air supply	Air Handling Unit (10 % fresh air)
Classification	Under LAF: ISO Class 5 for Manufacturing area and Filling area Surrounding Area: ISO Class 6
Temperature	NMT 25°C.
Humidity	NMT 50% RH
Differential Pressure	All the process area under positive pressure to reduce contamination
Air change rate	Minimum 60 air changes per hour in process area
Filter Design	0.3µHEPA Filter Efficiency – 99.997%

C. Processing Area – DRY INJECTION

Air supply	Air Handling Unit (10 % fresh air)
Classification	Under LAF: ISO Class 5 for Manufacturing area and Filling area Surrounding Area: ISO Class 6
Temperature	NMT 25°C.
Humidity	NMT 30% RH
Differential Pressure	All the process area under positive pressure to reduce contamination
Air change rate	Minimum 60 air changes per hour in process area
Filter Design	0.3µHEPA Filter Efficiency – 99.997%

D. Processing Area – CAPSULES

Air supply	Air Handling Unit (10 % fresh air)
Classification	Class D
Temperature	NMT 25°C.
Humidity	NMT 40% RH
Differential Pressure	All the process corridors are under positive pressure to reduce contamination
Air change rate	Minimum 20 per air changes per hour in process area
Filter Design	Pre Filter/Fine Filter/Super Fine /0.3µHEPA Efficiency –99.997%

E. Processing Area – OINTMENTS

Air supply	Air Handling Unit (10 % fresh air)
Classification	Manufacturing , Filling Area : Class D
Temperature	NMT 25°C.
Humidity	NMT 60% RH
Differential Pressure	All the process corridors are under positive pressure to reduce contamination
Air change rate	Minimum 20 in process area
Filter Design	0.3µHEPA Filter, Efficiency –99.997%

F. Processing Area – LIQUID ORAL

Air supply	Air Handling Unit (10 % fresh air)
Classification	Manufacturing , Filling Area : Class D
Temperature	NMT 25°C.
Humidity	NMT 60% RH
Differential Pressure	All the process corridors are under positive pressure to reduce contamination
Air change rate	Minimum 20 in process area
Filter Design	0.3µHEPA Filter, Efficiency –99.997%

G. Processing Area – DRY SYRUP

Air supply	Air Handling Unit (10 % fresh air)
Classification	Manufacturing , Filling Area : Class D
Temperature	NMT 25°C.
Humidity	NMT 50% RH
Differential Pressure	All the process corridors are under positive pressure to reduce contamination
Air change rate	Minimum 20 in process area
Filter Design	0.3µHEPA Filter, Efficiency –99.997%

Filter design and efficiency
The air filtration system consists of –

- 10 micron filter
- 5 micron filter and
- 0.3 micron HEPA filters of 99.997% efficiency.

The Production buildings are sealed in such a way that air enters and leaves through openings provided. All such openings are protected by devises like Filters / Air curtains / Air locks.

This Plant is designed with process dedicated air handling units using direct expansion type compressors for chilling and dedicated units for in process quarantine area.
All the process areas are designed to meet class D excluding sterile section.
All other areas meet the requirement of comfort air conditioning. Raw Material warehouse and Packing Material [PM] warehouse are under Forced Ventilation System.
Finished Goods Stores is constantly under controlled temperature of NMT 25°C.
All the process corridors are under positive pressure to reduce contamination.

INJECTION SECTION

- The injection section has been designed with process dedicated air handling unit.
- Over all process area are designed to meet Following specified class as per the cGMP Guide :

ISO Class 5: Operational areas under LAF in Manufacturing, Vial / Bottle filling and Filtration room.
ISO Class 6: Surrounding area of manufacturing, filling, cooling zone.
ISO Class 8: Vial washing room, Labelling machine, Autoclave Area, Corridor, De Cartoning room.

- Finished Goods Stores is constantly under controlled temperature of NMT 25° C.
- All the process area under positive pressure to reduce contamination

Special Areas for Handling Highly Toxic, Hazardous and Sensitizing Materials
No toxic or hazardous materials are used at the plant.

4.1.2 Brief Description of Water System

Water is drawn from the bore well through a submersible pump and stored in underground SS tank. This raw water is chlorinated and stored, then passes through the multi grade filters to remove any suspended solids. The water thus formed is dechlorinated and transferred to the softener units. The hardness of the potable water is reduced below 10 ppm after passing through these softener units. The soft water is transferred through the reverse osmosis (RO) system by prior dosing o De- chlorination. This is controlled through PLC-HMI Logic.

The RO water is then fed to the EDI (Electro-deionization) for further polishing. The water emanating from the EDI flows to the purified water double jacketed storage tank of 3000 Litre. From this tank, purified water is circulated at ambient temperature in a closed loop to all user points through UV light to eliminate the microbial load, if any. The conductivity, bio burden of the water sample collected from the return loop through UV light which meets the USP standards. The return flow rate is measured by the flow meter installed in the return loop and is maintained at minimum 1.28 m/s.

Materials of construction of the purified water storage tank, distribution pump, loop & sanitary fittings like diaphragm valves, triclamp connections are SS 316L. Membranes of the reverse osmosis system are hot water sanitizable, spiral wound polyamide membrane. Hydrophobic air filter of 0.2 µ is fitted at the vent of the storage tank with dual oring for better protection.

The system also consists of 2 dumping valves, one at the outlet of the EDI system and second in the return loop before the entry of the return water to the storage tank. These dumping valves opens if the conductivity of the water exceeds the limit and the water is dumped out.

A CIP tank is provided for hot water sanitisation of the membrane and EDI. This CIP tank is PLC controlled to check and control temperature during entire sanitisation process.

The closed distribution loop and storage tank is sanitized with hot water. Separate Purified water storage and distribution system is installed for both general block and beta block.

Water for Injection (WFI) Generation and Distribution System:

WFI System for injection section: (Capacity 80 lit/hr)

Purified water is fed into the WFI multicolumn water still which produces the pyrogen free water for injection (WFI). In the multicolumn, boiler steam and feed purified water remain on the shell and tube side, respectively. As the purified feed water passes downwards through the tubes (by forming a thin film), due to surface film evaporation, a part of it converted into steam. The steam so formed under pressure will move with a high velocity and as it comes out of the tube, is subjected to 1800 turn in the upward direction. Steam will move up through the annular space between the condenser & separator and pass through the spiral (on the out side of the condenser) which forces the steam to move in a circular path. The resulting pure steam will be the source steam in the next column, wherein it will condense to form WFI. (This process is repeated in all the remaining columns. WFI from all the columns is collected in the top cooler where it is cooled to 950C by the cooling water and then taken to the WFI into 300 litters storage tank at the rate of 80L per hour, and stored at 80 0C. The WFI is then re-circulated in a loop to all user points and returns back to the same WFI storage tank through a heat exchanger, to maintain the temperature of the returned WFI to > 75 0C. At each step of the generation of the WFI in the multi-column, storage tank and the loop user points, the WFI quality have been validated to demonstrate that system is meeting the required quality parameters and the WFI meets the Pharmacopoeias requirements.

Materials of construction of the WFI storage tank, distribution pump, loop & sanitary fittings like diaphragm valves, triclamp connections are SS 316L. Hydrophobic air filter of 0.2 µ is fitted at the vent of the storage tank.

The system also consists of one dumping valve in the return loop before the entry of the return WFI water to the storage tank. This dumping valves opens if the conductivity of the WFI exceeds 1.3 microsiemens / cm at 25 0C (compensated), and the WFI is dumped out.

Separate WFI generation and distribution system is installed for General Block and Beta Block.

MAINTENANCE

Equipment is categorized on the basis of its use. Planned preventive maintenance is carried out as per a schedule and records are maintained on machine history cards.

Detailed services have been laid down for recording maintenance and servicing. Equipment history cards/files are maintained for each equipment that records servicing, calibration and preventive maintenance done on the particular equipment.

The machine features that could have a bearing on Quality are considered as change and will route through the change control procedure.

Schematic drawing of purified water system [Annexure-VII].

1. Purified Water system
2. Purified Water sampling Point

1.1.1 Brief Description of Other Relevant Utilities

Other Utilities consisting Steam boiler having capacity of 2000 kg/hr, Compressed air plant having capacity of 450 cfm, Nitrogen Generation plant having capacity 15 N cu.m and effluent treatment plant.

4.2 EQUIPMENTS:

4.2.1 Major Production and Control Laboratory Equipments

All the equipments used in the processing have the contact parts made of SS 316. The certificate of material of construction is available.

Only standard suitable food grade Teflon, silicon and other non-reactive plastic material are used.

Equipments are provided with sufficient space and arrangements are made to facilitate easy cleaning. All equipments are suitable for the intended use, cleaning can be easily carried out and adequate measures have been taken to prevent contamination of drugs and their containers. The equipment cleaning methods are as per standard procedure and log books for all machines and all relevant records are maintained.

List of equipment: Production and Quality Control [Annexure-VIII]

Maintenance Description of Planned Preventive Maintenance Programme and Recording Systems

The Engineering Department is responsible for the commissioning and planning of preventive maintenance of all equipments as per the standard procedure. Maintenance is in-house and for the purpose supplier gives training to employee of engineering and user department.

Preventive maintenance plan indicate the details of servicing and preventive maintenance to be done on each equipment and the details procedure to carry out the same. The equipments which are maintained by our engineering dept. and whenever required then outside agencies are identified and records of maintenance and servicing are kept.

The preventive maintenance schedule is prepared considering the equipment functions, which have a direct bearing on the quality of the product. The records are maintained of all the equipment maintenance and use in their respective history cards.

All the observations and activities are recorded through log books; machine history cards etc. The records are kept to indicate the nature and details of servicing.

The calibration of instruments, preventive maintenance of the instruments and equipment, calibration of measuring devices are carried out as per defined frequency in accordance with the standard procedures and are recorded.

4.2.2 Cleaning and Sanitation

Cleaning Procedures for Manufacturing Areas and Equipment

Areas are categorized as Process, Packing, RM store, PM store, Utility, Gardens, and Roads etc. Cleaning equipment and solutions are purchased and prepared as per standard procedure. House Keeping equipments are stored in defined area. Cleaning of critical area and equipment is supervised by production and counter checked by QA. A complete cleaning and disinfection schedule for each area defines the cleaning agent, its concentration and frequency of use.

The cleaning schedule is prepared in such a manner that the disinfectants and cleaning agents are rotated from time to time in order to prevent immunity in the microbial load.

Cleaning agents are evaluated for their efficacy against known microbial load and the cleaning procedures are validated through samples drawn and evaluated after the complete cleaning is done. A protocol to establish the cleaning procedure is in place.

Cleaning methods are routinely monitored by QA by analyzing the samples through chemical and microbiological methods. The test method is also evaluated / validated as per the standard analytical method validation protocol.

Scrubbing and washing of the tanks perform the cleaning of water storage tanks. There exists a SOP for cleaning of the storage tanks, which defined the procedure and frequency. The sanitation of Purified water system is done through hot water circulation for 1 hour. The design contains in-built arrangement to generate hot water and circulate the same. Existing frequency of sanitation of purified water storage and recirculation loop line is once in every month.

4.2.3 GMP Critical Computerized System:

Computer is utilized for Material Management and Inventory system. Microprocessor (PLC) is utilized in the Automation of many productions Machine**.**

5. DOCUMENTATION

Arrangements for the preparation, revision and distribution of all necessary documentation. SOPs are available for the preparation, revision and distribution of necessary documentations for manufacturing, analysis, storage, maintenance and validations. Documents are prepared by the user dept. in conjunction with QA, who finally approves it. QA is responsible for revision, control, and distribution of documents.

Documents are prepared under a standard format and procedure. Documents are available for product and process specifications, Raw material specifications, Packaging component specifications, standard process instructions for manufacturing and packaging, Batch records for manufacturing and packaging, standard analytical procedures, QA release procedures. Documentation is controlled system is followed as described in the SOP. (List of SOP is attached as [Annexure-X].

The shelf life for each category of document has been laid down.

Documents in the form of electronic records are preserved in QA's computer and are protected by its password. The backup of these documents is kept with Quality assurance.

Other Documents Related to Product Quality

Besides the general cleaning procedures and procedures for maintaining and improving quality of medicinal products, we have following procedures to control microbiological content of water and environment:

- Plate Exposure
- Contact Plates
- Air Sampling
- Swab Test
- Water Analysis for Microbiological Control and presence of pathogens.

Documents are available for equipment specifications, cleaning material specifications, SOPs, QC procedures, Training procedures, computer program specifications, documentation and data control, deviation control, calibration of manufacturing and test equipments, validation master plan and protocols, Reconciliation raw material, Packaging material and in process material.

Additional Documents Maintained Routinely Include-

1. Equipment log books
2. Equipment history cards.
3. Preventive maintenance records.
4. Analytical reports for Raw material, packing material
5. Analytical report for in process and finished product.
6. Cleaning and disinfections records.
7. Temperature and humidity records.
8. Dispensing and Issue records.
9. Self-inspection records
10. Training records
11. Validation records.
12. Deviation control records.
13. Change control records, etc
14. Handling of Market complaint
15. Out of specification records etc.

6. PRODUCTION:

6.1 Types of Products

Tablets	Uncoated tablet, Coated tablets, Sustained released tablets,
Capsules	General Hard Gelatin Capsules,
Ointment	Gels, Creams and Ointments
Injection	Dry Powder Injection, Liquid Injection
Liquid	Clear liquid, Liquid Suspensions, Dry Syrup

Flow Charts for -
Manufacturing process of Tablets (Uncoated, Coated), Capsules Products, Oral Liquid Products, Oral Suspension products, Ointment Products and injection solution is attached as Annexure-IX.
(List of Products manufactured at site is attached as Annexure-II.

Arrangement for the handling of starting materials, packing materials, bulk and finished products including sampling quarantine release and storage.

GRN (Goods Receiving Note) number is assigned to the incoming raw packaging and other miscellaneous materials; the number is generated by the software and is traceable.

Detailed sampling plans have been laid down for RM, PM, in process and finished goods that include stability and control samples.

Status is indicated by means of labels and the employees have been trained on usage and discard of status labels. Authority is given at various levels for issue of labels.

Materials (RM and PM) are issued to production and packing in dedicated areas as per the standard bill of material authorized by QA.

Weighing during the issue is counter checked by competent person from production and QA and the balances as well the weights used for weighing are calibrated.

Various parameters like weighing of materials, storage conditions, receipt from approved vendors, quality and quantity of consignment, temperature and humidity, status labelling, etc. are monitored.

Material identity is confirmed at the time of manufacturing by means of labels that are preserved with the batch manufacturing records.

Control of Bulk manufacture-

Key parameters like cleaning of equipments, blending time, sifting, granulation and bulk manufacturing and filling are checked by the production supervisor during each batch production and the records are kept with the batch manufacturing record.

Various In process checks as shown in the flow charts like Line clearance, wt variation, DT, Friability, hardness, thickness volume checking, visual inspection are carried out at various stages as per the detailed in process Quality plan and the records are kept with the batch manufacturing record. The bulk products comply with the specifications laid down specifically considering the finished goods specifications.

Packing –

Semi-finished products are released for packing after testing and compliance as per the laid procedures and specifications respectively. The packing materials issued as per the standard bill of material authorized by QA, are checked on line for correct specifications and coding. The line clearance checks are clearly documented and observed. Various in process checks like leak test are done and the records are kept with the batch packing records.

Quarantine and release of finished products -

The finished products are stored in a quarantine area awaiting the release. The products are released after compliance with the release specifications and review of BMR/BPR.

The authorities of the employees have been clearly laid down. The persons engaged in supervisory operations during the manufacture and packing of batches are responsible for maintaining the documentation.

The IPQA personnel are responsible for checking cGMP compliance and its records.

QC head is responsible for testing of Bulk and Finished product.

QA head is responsible for the release of the batch.

6.2 Process Validation:

6.2.1 Brief Description of General Policy on Process Validation

Written validation protocols for each major operation are prepared. Validation is carried out to ensure that equipments and processes meet their designed parameters.

First three batches of all products are subjected to validation.

Validation policy –

Validation master plan is prepared by quality assurance head in reference of the entire facility and as per guidelines of cGMP. The VMP form the basis of protocols for design qualification, Installation qualification and performance qualification of equipment. The protocols are prepared separately as per nature and area of the machine. e.g. there exist protocol for design qualification of Rapid Mixer Granulator and protocol for Blister packing machine. Prospective process validation is followed for new product developed and retrospective validation in the form of annual product review is been done for all the products manufactured in substantial quantity in the previous year. Further the **concurrent validation** is been done on all the products at start up or after any major change in process, material or equipments as per the validation guidelines.

Prospective or concurrent process validation is followed for any new product and retrospective validation wherever applicable.

A complete validation master plan takes care of following validation categories -

- Area validation
- Utilities validation
- Equipment validation
- Process validation
- Cleaning validation
- Analytical method validation
- Software validation

All the equipments are subjected to the detailed qualification procedure, and there is a written protocol for validation and calibration of all the important equipment.

Revalidation is carried out only when the process goes through change. It can be any of equipment, method or utility concern.

All production and cleaning processes are clearly defined and validated. Process validation is carried out for following parameters in tablet manufacturing – mixing, drying, blending, Compression, coating, packing etc. The protocols have been prepared and are issued by QA at the time of validation.

The processes are clearly defined and are validated upon initiation and routinely as concurrent validations. These include processing parameters as well as cleaning procedures. The set procedures are validated from time to time through revalidation and retrospective validation is also carried out to establish quality of products.

All measuring equipment like balance, thermometer, pressure gauges, Flow meter, scales, and level indicators, Manometers etc. located in Production, QC and Utility block are calibrated through Calibration program. The volumetric glassware's are also calibrated.

Calibration is either through out side agency or In-house. A complete calibration program gives information about equipment to be and part calibrated, its part or equipment number, calibration details, calibration frequency, calibration date and due date for calibration, calibration agency.

Validation of all Non Compendial Analytical Method (s) being used at the Quality Control Laboratory is performed as per International Conference on Harmonization (ICH) / United State Pharmacopeia (USP) Guidelines.

6.3 Material Management and Warehousing

6.3.1 Arrangements for Handling Materials and Products

There is a separate area for storage of all materials of RM, FG as well as PM and there are detailed protocols for handling such materials. The entry to these areas is restricted in order to avoid chances of mix-up.

6.3.2 Arrangements for Handling Rejected Materials and Products

There is a separate area for storage of rejected materials of RM, FG as well as PM and there are detailed protocols for handling such materials. The entry to these areas is restricted in order to avoid chances of mix-up. Detailed procedures have been written for handling of rejected material in each area.

Material is disposed as per the waste and rejected material disposal and destruction policy which clearly defines the procedure for disposal or destruction, its responsibility and documentation required.

7. QUALITY CONTROL:

Activities of Quality Control Department:

- Sampling and analysis of raw materials, packing materials, Intermediates and Finished Products.
- Release of raw material and packing material for processing and packaging.
- In process quality checks.
- Microbiological testing of raw materials, finished products and water.
- Environmental control test.

Activities of Quality Assurance Department:

- Approval /authorization, distribution, control, Review, storage and destruction of production records.
- Review of product specifications and test procedures
- Quality audits
- Stability studies
- Product complaints and recall
- Self inspection
- Release procedure (Finished products)
- Products are analyzed as per laid down specifications. The products that meet the specification are released as APPROVED and released for dispatch. Any product not

meeting specifications, follow for OOS procedure and is REJECTED if it does not comply.

- Training related to cGMP requirement

cGMP training are conducted for both staff and workman on following subject:

b) Workmen

- Quality: QA/QC/cGMP
- Requirement of a quality system
- Documentation: SOP/BMR/BPR
- Cleanliness, Hygiene
- Personal Hygiene
- Plant and equipment cleaning and sanitization method and schedule
- Clothing
- Equipment maintenance.

c) Staff

- cGMP
- Quality system documentation.
- Pharmaceutical dosage form and packs
- Job Responsibilities
- Batch recall
- Process Control
- Documentation
- Cleanliness, Hygiene
- House keeping
- Equipment cleaning method and schedule
- Environment monitoring
- Microbial cross contamination
- Clothing
- Regulatory requirements
- Safety

Workmen are given the following training at the time of their employment.

1. The ideal working environment in the pharmaceutical industry.
2. Hygiene and sanitation.
3. On-the-job training on shop floor.
4. Safety during working.
5. General discipline and work conduct.

Management staff personnel are given an induction in different departments at plant at the time of joining. Job orientated training is given by Departmental Heads. The employees are provided with the opportunities, whenever possible to attend seminars/workshops on specialized subjects.

Examples of In-house trainings are as follows -

- cGMP Training
- Creativity training
- Safety Training
- Motivation Training
- Fire Fighting Training

Experts in various subjects conduct the above training sessions.
Skill development training is given on the job at the work site or in the classroom.
Motivational training is provided in the classroom by external or internal faculty.
Evaluation of effectiveness of training
Effectiveness of training is evaluated by feedback form and by conducting test / discussion.
Retraining needs are identified by personal discussion with the employee and on the basis of day-to-day observation by respective department head.
Brief details of training records
Various records maintained for training are-

1. Identification of training needs.
2. Training calendar
3. Training material.
4. Training attendance.
5. Evaluation form.

8. DISTRIBUTION, COMPLAINTS, PRODUCT DEFECTS AND RECALL:

8.1 Distribution

Products are stored in the warehouse only after being declared as "ready for dispatch" by QA. The warehouse is a secured area with restricted entry. The temperature requirements are maintained and recorded. The materials are stored on pallets such that there is clear segregation of two lots. Labelling identifies the status of the material. There is a separate space for rejected material storage and Recalled product storage.

RECORDS OF DISTRIBUTION:
The records of distribution are kept and are available to establish traceability in terms of date of sale, customer details and quantity dispatched. These records are maintained for 1 year beyond the expiry date of the product.

8.2 Complaints, Product Defects and Recalls

Quality Assurance (QA), maintains a Customer Complaints Register, and handles the complaints. On receipt of the complaint, complaint investigation is initiated by QA. Depending on the nature of the complaint the related departments are involved in complaint investigation .A complete investigation report is prepared which includes the control sample test results, batch record review results to understand the cause of the complaint, and action taken to avoid recurrence. An Immediate action/reply is given to the complainant. The investigation report is reviewed by manager QA. The records of complaint shall be kept for at least 7 years to check reoccurrence and for academic interest. Quality Assurance Dept. would make the decision if a recall is necessary

and define the class of recall. Quality Assurance informs Marketing/Distribution Dept. to trace the distribution of the product of the batch, which is to be recalled.

Procedure for handling of recalls have been laid down which includes

- Retrieval of distribution data
- Notification to customer by phone, fax ,e-mail or post.
- Segregation of recall material upon receipt
- Immediate information to relevant authority.
- Its inspection, investigation of cause, corrective and its documentation.

Any recall in the last 2 years: No recall.

9. SELF INSPECTION:

Short description of the self-inspection system

A detailed procedure for self-inspection has been prepared. A Self-Inspection team comprising seiner and experience member of Production section, Quality Assurance section, Quality control section, Eng. /Maintenance section and Store section conduct Internal Audits.

A self-inspection questionnaire is prepared which is referred as a checklist during the inspections. An inspection report is prepared after the inspection of facilities and systems. The report is circulated to the people concerned with an action plan and target date and responsibility for completion. QA Manager looks after follow-up action on target dates and prepares a follow-up report. The responsible person is asked to take and document the corrective action on non-conformances found during the inspection.

10. ABBREVIATIONS:

SMF: Site Master File

QC: Quality Control

QA: Quality Assurance

IPQA: Inprocess Quality Assurance

SOP: Standard Operating Procedure

OOS: Out of Specification

GRN: Goods Receiving Note

C.O.A.: Certificate to Analysis

PM: Packing material

RM: Raw material

FG: Finished Goods

11. REVISION HISTORY:

Revision History	Date of revision	CC Number	Reason for revision
SMF-01-00	--	--	Initial Version