SITE MASTER FILE

Manufacturing Site Address:	Sanayi Mah. Ensar Cd. Hidayet Sk. No:4 K:2 Pendik-Istanbul, Turkey
Tel & Fax:	0090 216 3068812 - 0090 216 3531035
Facility:	Aseptically prepared liquids and non sterile liquids for internal use

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1. GENERAL INFORMATION ON THE MANUFACTURER

1.1 Contact information on the manufacturer

- Name and official address of the manufacturer:
  Galenka Veteriner Ilac Sanayi Limited Sirketi
  Sanayi Mahallesi Hidayet Sokak No: 4 Kurtkoy-Pendik Istanbul/Turkey

- Names and street addresses of the site, buildings and production units located on the site;
  Sanayi Mahallesi Hidayet Sokak No: 4 Kurtkoy-Pendik Istanbul/Turkey

- Contact information of the manufacturer including 24 hrs telephone number of the contact personnel in the case of product defects or recalls;
  Contact Personnel: Zeki Öztürk
  Telephone Number: +902163068812

- Identification number of the site as e.g. GPS details:
  N 40 degrees 54 minutes 16 seconds
  D 29 degrees 17 minutes 52 seconds

- D-U-N-S (DataUniversal Numbering System) Number: 36-590-6788

1.2 Authorised pharmaceutical manufacturing activities of the site

Only the pharmaceutical activities mentioned in the manufacturing authorisation are carried out.
Copy of the valid manufacturing authorisation (refer to annexe 1)
Type of the products currently manufactured in the plant (refer to annexe 1 or 4)
List of the official GMP inspections of the plant (refer to annexe 10)

2. QUALITY MANAGEMENT SYSTEM OF THE MANUFACTURER

2.1 The quality management system of the manufacturer

Galenka Pharmaceuticals operates a quality assurance system on the basis of the EU GMP Guideline on Good Manufacturing Practices for pharmaceuticals.

The quality assurance system helps to ensure the quality of the pharmaceutical products expected by the customers as well as to implement the quality objectives of the company comprehensively in all the company departments.

The principle of the quality policy is that every work step is a contribution to the quality of the end product and must hence possess the required quality itself. This objective is ensured through corresponding framework conditions such as suitable technical and organisational equipment, qualified personnel, etc.

The quality assurance system comprises all the company departments. It has been defined in SOPs, operating instructions and other documents and consists of the following elements among others:

- Current documentation system
- Personnel training, job descriptions
- Hygiene
- Self-inspections
- Supplier qualification including subcontractor
- Qualification of systems, equipment and areas
- Calibration of measuring equipment
- Maintenance of areas, systems and equipment
- Monitoring of environmental conditions
- Validation of manufacturing, cleaning and test processes
- Change control, deviation, OOS and CAPA management
- PQR
- Inspection and manufacturing in accordance with approved instructions
- Release procedures
- Processing of complaints

The Quality Assurance department is responsible. The Head of Quality Assurance leads the department.The Quality Assurance department directly reports to the Management Board.
The Management Board is involved in the quality management in different ways and is constantly informed of the integration into QA committees, a structured reporting system as well as through the inspections of the Quality Assurance department generally conducted once a year. Other options to obtain information are the protocols of the regular quality assurance meetings conducted every 14 days as well as the reports of audits and self-inspections as well as monthly reports to the Management Board.

The other departments of the company are also responsible for maintaining the QM system. They are stated in the respective job descriptions as well as in the valid SOPs and instructions.

2.2. Release procedure of finished products

The Qualified Person has the expertise necessary in accordance with the cGMP regulationas is responsible for releasing the pharmaceuticals and investigational medicinal product, for placing them on the market. She reports directly to the Management Board and has all the necessary powers for carrying out this work.

The tasks and responsibilities are specified in writing in a corresponding job description of the Qualified Person.

The QM system is adapted to the needs of the batch release.

All the finished products are in the quarantine status until the dispatch release, release for placing on the market or another decision. This status is secured by the identifications and configurations in the ERP system as well as by a physical identification with the help of supply notes with the pallets.

Manufacturing and testing must be carried out and logged in accordance with the manufacturing instructions or testing instructions. All deviations in the process and from the regulations in the specification must be documented and investigated thoroughly. After inspecting the manufacturing documents, the Head of Manufacturing must confirm proper manufacturing and labelling of the batch corresponding to the manufacturing instructions. The Head of Quality Control must confirm that the testing was conducted corresponding to the testing instructions and the batch possesses the proper quality.

The Qualified Person is responsible for ensuring that every batch of the pharmaceutical was manufactured and tested in accordance with the trade of pharmaceuticals. He has to confirm the compliance with the regulations for every pharmaceutical batch in a serial list before placing them on the market. For assuming his responsibility as a Qualified Person, the job holder has to rest on the expertise of and information from the function holders - Head of Manufacturing as well as Head of Quality Control. He can moreover rest on certificates, which have been issued by other Qualified Persons if the batch has passed through different steps of manufacturing and testing or parts of these at different locations or with different manufacturers.

The Qualified Person actively has to examine the batch documentation and the batch record review and take it into consideration. Furthermore he has to take into account essential information, especially that which is notincluded in the manufacturing and testing documents, and he has to evaluate it. If necessary, he has to use the certificates issued by other Qualified Persons for deciding on the release of the finished product batches.The Qualified Person certifies that the pharmaceutical has been manufactured in accordance with GMP and the registration documents. This is followed by the release and entry in the release register or, in some cases, another decision. The release or another decision is indicated on the product and in the ERP System. Rejected products will be stored separately and under lock and key, in an isolated manner and with the corresponding physical identification. The blocking will also be saved in the ERP system.

The release procedure is defined in the SOP for batch release of finished products.

Furthermore, SOPs are available, which describe how to deal with deviations and out-of-specification results. The system for activities that have been ordered is also stipulated in SOPs.

Another SOP describes the procedure for dealing with rejected products.

2.3 Management of suppliers and contractors

A documented procedure is available for the assessment, evaluation and approval of vendors. All materials used at the site are obtained from "APPROVED VENDORS" only. Below is a summary of the activities necessary for the approval of a vendor:

- Identification of vendor
- Calling for quotation
- Vendor evaluation through questionnaire
- Vendor selection and audit
- Vendor approval

2.4 Quality Risk Management (QRM)

The risk management system, which is installed within the scope of the quality management system, includes all the areas of manufacturing and testing pharmaceuticals and other product classes and helps to ensure the quality of the pharmaceuticals manufactured and other product classes as well as the ability to deliver on schedule.

Risk analyses are predominantly conducted in the form of informal risk inspections, 5 Why and based on FMEA. The execution of FMEA-based risk analyses is defined in a SOP.

In addition to QA, QP, Head of Manufacturing and Head of Quality Control, the heads or employees of the relevant departments are included. The Management Board will either be directly included or informed during discussions or by means of minutes of the consultation depending on the requirement.

When defining the processes in SOPs, the elements of the risk management system to be used including responsibility and employee group to be included/ informed will also be defined and described:

- Risks at the time of manufacturing and testing will be considered and minimised with the following activities: qualification of the equipment during manufacturing and quality control including supply systems, qualification of the manufacturing and storage areas taking into account the required climatic conditions, validation of the processes for manufacturing, testing and cleaning, qualification of suppliers and service providers, employment of qualified and trained personnel. The type and scope of the tests to be

conducted will be defined based on the risks. Risk analyses will be conducted in accordance with the specifications.

- The temperature and, if necessary, humidity monitoring in the storage and manufacturing areas is based on temperature mapping for ascertaining the critical measuring points. Monitoring will be implemented by a central climate monitoring system with integrated recording and alarm system.
- Environmental monitoring will also be carried out in a risk-based manner; the measuring points will be defined within the scope of the qualification.
- In order to identify the risks at an early stage, intervention limits were defined in the form of warning and alarm limits as well as specification limits and trend and other data analyses will be generated.
- The audit programme for suppliers and subcontractors will be prepared in a risk-based manner.
- The changes, deviations, OOS and complaints will be processed taking into account the risk inspections.
- The goods receipts will be tested based on the risks. The testing scope will be defined depending on the qualification status of the supplier.
- The stability tests will be defined taking into account the valid regulations and in a risk-based manner (matrixing, bracketing).
- The training programme will be defined risk-based.
- The decisions of the QP are based on the information about the manufacturing and testing as well as the information associated with it and are also risk-based.

The measures defined in the risk analysis will either be processed in the process to which the risk analysis belongs or transferred to the CAPA (corrective and preventive action) system of Galenka Ilac.

Risks will also be considered when defining processes, which must not contain any risk inspections.

2.5 Product Quality Reviews

Regular product quality reviews (PQR) will be carried out for all the pharmaceuticals manufactured/ tested/ released in the company after order by the respective customer and in a manner and scope agreed by both parties. These reviews will be prepared by the Quality Assurance department in accordance with the specifications of the valid SOP. Furthermore, the requirements of the customer will be taken into account.

The PQR will be carried out product-related for a defined period – generally a year –, but should include a minimum of five bulk product batches. If less than five bulk product batches are manufactured within a year, the period under review can be extended correspondingly in order to have the required minimum number of batches at disposal.

If a period of 3 years has passed since the last period under review, a PQR should be prepared irrespective of whether 5 bulk product batches have been reached. In case of less number of batches (< 3 batches in the period under review of 3 years), the scope and contents of the PQR must be adapted in a risk-oriented and purposeful manner. Inappropriate sections or parts can be omitted fully or in part with justification.

The report also includes all the manufactured batches, i.e. even those which were rejected and destroyed.

The information, changes and dependencies, which cropped up during the period under review when manufacturing and testing the product, will be recorded, evaluated and documented within the scope of the PQR.

The aim of the PQR is to check the consistency of the process and the suitability of the specifications for the raw materials and packaging materials as well as for the finished product. With the PQR, the Qualified Person is provided with another tool to ensure the pharmaceutical quality of the product within the scope of the release.

3. PERSONNEL

Organization chart (refer to Annex 5a)

Number of employees in the departments

Department	Number of Employees
Production	7
Quality Assurance	2
Quality Control	4
Storage and Distribution	2

4. PREMISES AND EQUIPMENT

4.1 Premises

The premises comprise of Sterile solution block, non-Steril block, warehouse block, utilities block, record room, quality control & microbiology block.

General layout of the premises and equipment are enclosed - Annex

4.1.1 Brief description of heating, ventilation and air conditioning (HVAC) systems

The components of the heating, ventilation and air conditioning system are listed below:

1- Air Conditioning External Units:

2 external air conditioning units with individual capacity of 273.000 BTU provide the air supply and work in tandem with each other.

2- Internal Air Conditioning Units:

There are 10 internal air conditioning units which are connected to the internal filter cabinets.

3- Filter Cabinets:

There are 7 Filter Cabinets with DC Fans and G4 filters, and 1 Filter Cabinet with a DC fan. These filter cabinets supply air to the following sections:

1st Filter Cabinet: Packaging Area (AMB ALN.08)

2nd Filter Cabinet: Optic Control and Labeling Section (OKE ALN. 22)

3rd Filter Cabinet: Corridors (KOR.ALN.21) and (KOR.ALN.29)

4th Filter Cabinet: Raw materials weighing room (HMD.TAR.33, HMD.MAL.34, HMD.PAL.35)

5th Filter Cabinet: Antechamber for Materials (MLZ. MAL.15), Antechamber for Visitors (ZG.PAL.14), Antechamber for Materials and Personnel of Solution Preparation Section (İML.PAL.16, İML.MAL.18)

6th Filter Cabinet: Changing Rooms (ERK.DLP.38, KDN.DLP.37)

7th Filter Cabinet: Microbiology Laboratory (MBL.ST.01, MBL.PAL.04, MBL.PAL.03, MBL.PAL.02)

4- Fan Filter Units (FFU,H14):

There are 19 Fan Filter Units (FFU) with DC fans and G4+H14 HEPA filters. The air flow of these FFUs can be adjusted individually. All of these FFUs are monitored by a PC software and they self-adjust their fan speed to reach the required air flow levels. The positioning of the FFUs are as follows:

Vial washing and preparation section	(YKM.ALN.28)	2 units
Sterile Section Antechamber for Personnel	(STR.PAL.31)	1 unit
Sterile Section Antechamber for Personnel	(STR.PAL.32)	1 unit
Sterile Filling and Capping Section	(STR.DLM.25)	7 units
Corridors	(KOR.ALN.29, KOR.ALN.21)	2 unit
Solution Preparation Section	(İML.ALN.23)	3 unit
NonSterile Filling and Capping Section	(NST.DLM.20)	2 units
Microbiology Laboratory	(MBL.ST.01)	1 unit

5- Exhaust Fans:

There are 5 exhaust fans at the following section of the facility:

1. Solution Preparation Section (İML.ALN.23)
2. Vial washing and preparation section (YKM.ALN.28)
3. Sterile Filling and Capping Section (STR.DLM.25)
4. Microbiology Laboratory (MBL.ST.01)
5. Toilets (KDN.WC.41, ERK.WC.42)

4.1.2 Brief description of water systems

Three qualities of water are used at the facility:

a) Potable Water:
Potable water is used for general purposes and the production of pure water. The potable water is stored in a 3 ton tank and it is regularly chlorinated to avoid microbial growth. The water stored in the tank is later pumped to general usage loop and the pure water production system.

b) Pure Water(PW):
The Pure Water production system is comprised of the following components: sand filter, Active Carbon filter, Fe-Mn filter, Antisucculant tank and pumps, HCl tank and pump, 5µm filter, 1500 L stainless steel storage tank, circulation pump, UV lams and stainless steel loop line.

The capacity of the pure water system is 220L/hour and the generated pure water is stored in a 1500 L tank. The water stored in this tank is pumped in the loop line and is delivered to the usage points. The unused water is continously looped in the system.

Pure Water is used for cleaning purposes, non-sterile productions and in the production of Water for Injection.

c) Water for Injection (WFI):
The Water for Injection system uses PW to generate pure steam and WFI.

The Water for Injection system is comprised of the following components: Pure Steam generation colon, 4 distilliation colons, 2 water pumps, 1 condenser colon and an automation panel.

After generation, WFI is transferred to the stainless steel storage tank. This tank has a heating system so that the water is kept at temperatures between 65-80^0 C. WFI is continously looped in the system to avoid microbial growth.

WFI is used in the sterile productions and the final cleaning of the machine parts and equipments.

Refer to Annex 7 for the schematic drawings of the system.

4.1.3. Brief description of other relevant utilities, such as steam, compressed air, nitrogen, etc.

a) Pure Steam:
The autoclave located in the production section uses its internal pure steam generator to generate stem using the pure water supply.

There is a pure steam generator located in the solution preparation section (IMO OD.07). This machine uses the pure water supply to generate the pure steam, which is later used in the heating of the production tank.

b) Compressed Air:
Compressed Air is generated by a rotary-screw compressor. The compressor has the capacity to supply 6,500 m^3/minute air at 7 bar pressure. The compressed air generation system is comprised of the following components: 500 L pressure tank, air drying filter, particle/oil filtration system and an automation panel.

The compressed air is used in the pneumatic systems as process air. It is not used in the production processes.

c) Nitrogen:
Nitrogen is supplied through industrial size nitrogen tanks purchased through approved vendors. The pressured Nitrogen is transferred to the points of usage through PVC pipes. In the production sections, stainless steel pipes are used to transfer Nitrogen. The gas is filtered through 0,2 µm filters prior to usage.

4.2 Equipment

4.2.1 Listing of major production and control laboratory equipment

List of the important equipment for the production and quality control (Annex 8)

4.2.2 Cleaning and sanitation

Well defined, approved procedures for cleaning of the manufacturing areas are available. The procedure covers the following:

- Persons responsible for cleaning activity
- Frequency of cleaning
- Cleaning devices to be used
- Cleaning agents to be used, their concentration and mode of preparation
- Rotation of cleaning agents

- Cleaning methods
- Recording of cleaning activity
- Cleaning and storage of cleaning devices

The cleaning activity is carried out at specific intervals. The record of cleaning is maintained along with the cleaning agents used and their concentration. Cleaning activity is checked by responsible person.

For individual equipment, a detailed cleaning procedure has been established. The procedure covers cleaning procedure to be followed during batch changeover as well as product changeover.

The cleaning was done as per the defined procedure. The samples were collected by both swab method and rinse method.

The samples were tested for the presence of traces of previous product by the validated method. Carry over of traces of previous product in the single dose of next product has been proved to meet the norms of cleaning validation.

Filter cleaning procedures, cleaning frequency for AHU's and dust extraction systems are defined and the activities are recorded. Regenaration of water system and sanitation of water systems is done as per defined procedures and frequency.

4.2.3 GMP critical computerised systems

The complete materials management and the order processing are generally implemented with the help of an ERP system. The access is regulated by means of passwords and user profiles. Computers and microprocessors are used during manufacturing as well as packaging for process control and monitoring.

When weighing, the weighed components are recorded by a log printer according to the quantities.

A paperless recorder is used during manufacturing for recording the process data. The measured data is saved and evaluated using special software.

During the packaging, scales are used with printers and statistics programmes, which allow the fill quantity to be checked in accordance with the pre-packaging ordinance and its proper documentation.

In the Quality Control laboratory, the computers are used as stand-alone solutions, mostly for controlling measuring devices and for evaluating the analysis results. The archiving of raw data

is defined in a SOP. The management of reference substances, chemicals, reagents and standard solutions is implemented using the ERP system.

5. DOCUMENTATION

A well-defined system of document control is followed by the site. There is an approved procedure which explains the system of document preparation, revision, distribution, storage and destruction of the obsolete documents.

All documents are identified by their title and a unique document number with revision level and date of next review. Master copies of all the documents are maintained by the site Quality Assurance Department. Photocopies of the MASTER COPIES are issued to the user departments as a CONTROLLED COPY, which are identified with blue color stamps. The procedures are reviewed every two years or when any change occurs. When document is revised, the master copy is retained as Obsolete copy and other copies are destroyed.

QA Manager or her authorized QA personnel is responsible for distribution through document control system.

There is an approved standard procedure for preparation of Standard Operating Procedures. Personnel from the respective departments prepare standard operating procedures. They are checked by department managers and finally authorised by Quality Assurance Head.

There are approved documents for:

- Product/Process Specifications
- Raw Material Specifications
- Packaging Component Specifications
- Master, product Specific Batch manufacturing and packaging records
- Product Master Formula
- Analytical Methods
- Recall Procedures
- Utility Procedures
- Validation Protocols
- Maintenance Procedures
- Pest and Rodent Control Procedures
- Health and Hygiene
- Batch Release Procedures
- Training Procedures
- Quality Policies
- Cleaning Procedures

Master formula / Product Manual exists for each product. Batch manufacturing record is prepared as an extract from the master formula / product manual. The master formula / product manual and batch record for each product is available at the Quality Assurance Department. Whenever there is a requirement from production for a batch record, master batch record is photocopied and each page is authorized by the Quality Assurance personnel before being issued to production.

All the completed batch records from production department are returned to Quality Assurance for the final review and release. Quality Assurance holds the sole responsibility to release the batches. The released batch records are retained with Quality Assurance till one year after the expiry of the product.

6. PRODUCTION

6.1. Type of products

At Galenka Ilac, the manufacturing of non-sterile and sterile liquid as well as the packaging of sterile and non-sterile liquid pharmaceutical dosage forms is carried out. These products exclusively concern pharmaceuticals for veterinary use.

The preparations are non-sterile ans sterile liquid preparations for oral and paranteral use. A detailed list of the preparations can be taken from the annexes 1 or 4 (closed part).

6.2 Process validation

First three consecutive batches of each product shall be validated to ensure that the manufacturing process consistently produces the product to meet the pre-determined specifications. Any change, thereafter is through change control approval. If the change asks for revalidation of process, the same is again carried out. Validation activities shall be executed through approved protocols and SOPs shall be strictly adhered. SOP shall take precedence over protocol for all compliances.

Annual Product Reviews shall be carried out for all the commercial products manufactured during the year as per defined procedures.

Process is considered for validation, whenever there is a technology transfer of a product from Formulation development or from the product owner to the manufacturing site. Process Validation is applicable for the following batches.

- New product is manufactured.
- Existing product, undergoes a change in process, formula, source of active ingredient or equipment.
- The results of process validation must reveal consistency in product quality attributes.

Validation is initiated with writing of protocol and its approval. The Protocol describes the objective, scope, validation team with their responsibilities, procedure, product specifications with acceptance criteria, formula, batch details, equipment to be used with their standard operating procedure numbers, re-validation criteria, stability, documentation and modalities for preparation of summary report. Validation is carried out as per protocol.

The results of the various activities are recorded. Based on these results, a validation report is prepared and a conclusion arrived at after review of the results.

The process is termed validated if defined process meets all the acceptance criteria as mentioned in the protocol. The validation protocol along with the report is maintained by Quality Assurance after approval of the report. If at any stage, the process is found to be unacceptable, then a suitable corrective action is initiated.

Revalidation
Qualified equipment undergoes major modification, replacement of critical spares that shall affect equipment performance.

- Location of equipment is changed
- Facility Modification
- Modification/ Change in support services
- Change of cleaning agent/method
- Process/ Formula Change
- Change of any critical equipment in the chain of equipments used for product manufacturing
- Change in analytical method etc

Based on sufficient trend data, the process/ specification parameters are reviewed and tightened

6.3 Material management and warehousing

Upon receipt of the raw materials/packing materials, the material is unloaded on the receiving bay. The correctness of the material received is checked with the delivery note. The details are logged in the inward register. Supplier's batch number and the quantities are cross verified. A goods receiving note is prepared and affixed on each and every packs. Sampling is done by trained samplers as per the approved procedure. Sampled containers are labeled with **"QUARANTINE" label in yellow**. The label indicates name of the material, item code number, batch number of the supplier, analytical report number, date of manufacturing, date of expiry and the retest date. Anaytical report number is assigned to each lot of material received. The material is identified with this number. Samples are analysed as per the approved

specifications. If the sample complies with the approved specifications, an **"APPROVED" label in green** is affixed and if it does not meet the specifications , **a red "REJECTED" label** is affixed on the pack (s)**.**

Sampling as per the sampling procedure. Approved materials are transferred from quarantine to the approved area and the rejected materials are moved to secured rejected material area.

Materials are accepted only from the approved vendors. The list of appoved vendors is available in warehouse. Dispensing of materials is a controlled operation carried out by stores personnel in presence of production and quality assurance personnel. Dispensing and sampling of raw materials is done under classified conditions.

Materials are issued by stores on receipt of authorised requisition sheet, which is a controlled document and approved by QA Manager or his authorised deputy. Dispensing is done by using calibrated balances.

Line clearance procedures are followed for all manufacturing and packing operations. Identity of materials at processing stage is confirmed by reading dispensing labels. Weights are counter checked. The dispensed raw materials are processed as per the instructions defined in the product specific batch manufacturing record.

In-process control/ tests are carried out as per the frequency and procedure defined in product specific batch records. In-process checks are conducted by Production and the
Quality assurance, independently at defined intervals. Intermediate products are analysed and approved by the Quality control prior to the packing operation. The finished product is transferred to the finished product quarantine area. The goods are released for dispatch after the completion of the finished product analysis and the review of the batch documents and the analytical reports by Quality Assurance. Products released by Quality Assurance are transferred to the finished product storage area for despatch.

Control of non-conforming products
A procedure for control of non-conforming products has been evolved, covering raw materials, packing materials, intermediates and finished products.

If raw material is not conforming to the specifications, it is labeled "rejected" and is isolated. It is sent back to the vendor.

If printed packing material is rejected, it is isolated and destroyed at the site in the presence of the vendor. A record of the destroyed material is maintained.

If any intermediate or finished product is found to be non-conforming, it is isolated and marked with the appropriate label. It is then referred to the Quality Assurance Manager, who investigates the problem. The matter is referred to technical team for action.

Reprocessing and reworking will be considered if there is a need and technically justified. Details of any non-conforming products and any corrective action taken are recorded and a record is maintained

7. QUALITY CONTROL (QC)

Quality control department has experienced, competent and technically qualified personnel to shoulder various activities of the department. The head of quality control has sufficient experience in the Quality control functions, as applicable to pharmaceutical formulations.

Quality Control personnel is responsible for sampling and analysis shall is done by Trained Quality Control personnel as per approved specifications. Release/reject authority for all raw materials, packing materials, intermediate products and finished products lies with quality control only, but final release authority for product lies with Quality assurance.

The laboratory has been designed and equipped with facilities for chemical, instrumental, microbiological and stability testing. Instrumental room is temperature controlled. Microbiological area is provided with laminar airflow and other facilities to carry out limit tests and environment monitoring.

The instruments used for the analytical purpose are operated and calibrated as per the respective operating and calibration procedures.

All working standards used are carefully selected and analysed. They are analysed by two separate experienced analysts in duplicate, Reference standards are necessary if the assay method used is a comparative method such as HPLC and In case if any of the required reference standard is not available in the lab to perform the required test, then a portion of the sample to be sent to an approved testing lab and get it analyzed in duplicate, so as to assess their suitability for use as a working standard. The storage conditions for the working standards as well as their validity for use are specified and all the relevant documents are maintained.

All volumetric solutions used in tests are prepared from material of a suitable grade in accordance with the approved procedures. Standardization of volumetric solutions is performed by experienced analysts. The results are verified and records are maintained. Containers holding volumetric solutions are labelled with details like name of the solution, strength of solution, date of preparation, date of standardization, use before date, and the initials of the person who standardized and checked the solution.

The microbiology laboratory is handled by a qualified microbiologist, who has the appropriate experience in carrying out bio-burden monitoring, microbial counts and pathogen characterizations etc.

Staff recruited to the Quality control department undergoes initial training for analyst validation to ensure the technical competence.

Quality control plays an active role in the validation activities. Quality control department provides analytical support for process and cleaning validation samples. Quality Assurance reviews the validation data prior to final approval.

RETENTION/ CONTROL/ RESERVE SAMPLES:
From each batch of a drug product defined quantity in original primary/secondary packing is randomly selected for retention. They are retained for 1 year after the shelf-life of the product and stored under the specified storage conditions. These samples subjected for visual inspection, once in a year.

Defined quantity of each drug substances and excipients also is being stored as a control samples, retained for minimum for one year after the expiry date.

STABILITY STUDIES:
Stability studies are carried out as per ICH guidelines and pharmacopoeial requirement as mentioned below:

40 C / 75 % Relative Humidity
25 C / 60 % Relative Humidity

For developed and existing products, stability is also studied under the specified storage conditions till the end of shelf life as specified, to confirm its ability to comply with the specifications set for that product.

The stability chamber are controlled for recording the temperature and humidity conditions. The laboratory has sufficient stability chambers with respect to the conditions.

8. DISTRIBUTION, COMPLAINTS, PRODUCT DEFECTS AND RECALLS

8.1 Distribution (to the part under the responsibility of the manufacturer)

Adequate area is provided at the site for the storage of finished products as per the product requirements. Products are stored to a specified height with proper segregation. Released Products are despatched in closed pre-inspected vehicles or containers.

The Products are despatched to end distribution warehouse, who shall maintain the distribution records at their end. The products are dispatched by road, sea shipment or by air

route as per logistics requirements. Product distribution is the responsibility of our customers/ product owners/ contract givers.

8.2 Complaints, product defects and recalls

The process of dealing with complaints is regulated in a SOP.

The Sales department is responsible for processing the commercial complaints.

Complaints about the pharmaceutical quality fall within the scope of responsibility of that manufacturer, where the products are produced based on contract manufacturing. In case of subcontracting of manufacturing steps to third parties, contract manufacturers and contract laboratories are involved in the processing. The Head of Quality Assurance is responsible for the processing flow. The processing is done by including all the relevant
departments. The resulting decisions and initiated measures will be documented. After the inspection is complete, a report is sent to the customer, who has complained about the product.The documentation of the complaints will be regularly checked for references with respect to special or recurring problems, which require special attention and additional measures in order to derive subsequent measures if necessary.

The records about quality-relevant complaints will be maintained in the Quality Assurance department for at least 10 years.

The customer is responsible for processing medically relevant complaints as well as notifications of unknown, undesired or serious side effects and this is mandatorily the responsibility of the respective customer (pharmacovigilance).

In case of product recalls, the Qualified Person who released the product will be informed by the relevant customer; the recall of finished medicinal products will be noted in the batch register by the Qualified Person.

9. SELF INSPECTIONS

Self inspection has been identified as one of the key tools for self improvement. Hence a procedure has been evolved for carrying out self inspections.

Departments, whose activities directly or indirectly affect the quality of the product are audited once every six months. The audit team comprises of the Quality Assurance Manager, Quality Control Manager, Production Manager and Manager Engineering or any designated auditor(s) as per the audit schedule. QA Head / management representative will lead the audit team. Out of two inspections in the year, one audit will be conducted as per the readily available checklist which is a part of the approved SOP for self inspection and the other audit is carried out without the checklist. The audit consists of verification of all documents, personal discussion

with the concerned auditee's and verification of the activities being carried out on the day of the audit and GMP Compliance.

Based on the observations of the audit team, audit leader prepares an "Audit Report", listing system non-conformances, procedural errors and deviations by classifying them as critical, major and minor. The corrective actions are suggested if possible and the report is forwarded to the Head of QA / Management representative and thereafter to the Management for Final Approval.

The audit report is then reviewed and analyzed by the Head QA / Management representative and the concerned Department Manager. A time bound corrective and preventive action plan to address non-conformance is agreed upon and initiated. Responsible person to implement the action plan is also identified. The corrective and preventive action is implemented by the respective department in-charge and the Quality Assurance manager ensures the implementation.

The effectiveness of the corrective action is verified subsequent to audit. The nonconformance report raised is closed by the auditor after implementation of the action plan. Quality Assurance Manager maintains.

Appendix 1 Copy of valid manufacturing authorisation
Appendix 2 List of dosage forms manufactured including the INN-names or common name (as available) of active pharmaceutical ingredients (API) used
Appendix 3 Copy of valid GMP Certificate
Appendix 4 Organisational charts
Appendix 5 Lay outs of production areas including material and personel flows, general flow charts of manufacturing processes of each product type (dosage form)
Appendix 6 Schematic drawings of water systems
Appendix 7 List of major production and laboratory equipment

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