التاريخ :٧/ ١/ ١٩٩٦م

قرار وزاري رقم (٤) لسنة ١٩٩٦م

وزير الصحة :

* بعد الاطلاع على أحكام القانون رقم ٢٥ لسنة ١٩٦٠ بمزاولة مهنة الصيدلة في الكويت وتنظيم الصيدليات ومخازن الأدوية والوسطاء ووكلاء مصانع وشركات الأدوية .
* وعلى القانون رقم ٧٤ لسنة ١٩٨٣ في شأن مكافحة المخدرات وتنظيم استعمالها والاتجار فيها .
* وعلى القانون رقم ٤٨ لسنة ١٩٨٧ في شأن مكافحة المؤثرات العقلية وتنظيم استعمالها والاتجار فيها .
* وبعد الاطلاع على القرارات الوزارية المنظمة لعمليات تسجيل الأدوية في البلاد .
* ورغبة في وضع نظام رقابي على تصنيع الأدوية بالبلاد للتأكد من مدى مطابقتها للشروط والمواصفات القياسية العالمية .
* وبناء على مقتضيات المصلحة العامة وما عرضه علينا السيد وكيل الوزارة .

- قـــرر -

مادة أولى : تعتمد المعايير الصادرة من الرقابة الدوائية بشأن الصناعات الدوائية والمستمدة من المواصفات العالمية المرافقة بهذا القرار والتي يجب على جميع الشركات المصنعة للأدوية استيفائها قبل البدء في الإنتاج .

مادة ثانية : تشكل لجنة من الرقابة الدوائية للقيام بالتفتيش على كيفية تطبيق معايير الصناعة الجيدة بعملية تصنيع الأدوية بدولة الكويت .

مادة ثالثة : يبلغ هذا القرار من يلزم لتنفيذه ويعمل به من تاريخ نشره في الجريدة الرسمية .

وزير الصحة

Kuwait
GUIDELINES FOR COOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PREPARATIONS
1995

DRUG CONTROL ADMINISTRATION

MINSTRY OF HEALTH, KUWAIT

INTRODUCTION

Pharmaceutical products should be manufactured by licenced manufacturers, shose procedures are regularly inspected by competent National Authorities.

Therefore, a need is felt for standardising the procedures in the manufacture of drugs, by laying down a set of guidelines for "Good Manufacturing Practices (GMP)" for compliance by all the Manufacturers in Kuwait.

Ministry of Health, State of Kuwait, through its Drug Control Administration, hence, sets out these guidelines which may be called **"Kuwait Guidelines for Good Manufacturing Practices (GMP) for Pharmaceutical Preparations, Ministry of Health, Kuwait - 1995".**

The sole purpose of these guidelines is to recommend the minimum steps and procedures to be followed by the Pharmaceutical Manufacturers to ensure that products meet the basic requirements for Safety, Identity, Strenght, Quality and Purity, which they purport or intend to possess.

These guidelines for "Good Manufacturing Practices" are mandatory for all the Manufacturers, Hospital Pharmacies, CSSD units and Clinics in Kuwait and failure to comply with them for Manufacturing, Processing, Packing and Holding of Drugs by them, may lead to regulatory action.

To ensure that these guidelines are followed by the concerned agencies, Ministry of Health, through its Drug Control Administration may send "Technical Audit teams" periodically for onsite inspection of the Manufacturers facilities for compliance of the GMP procedures.

GOOD MANUFACTURING PRACTICE (GMP):

Good Manufacturing Practice (GMP) includes the sum total of the organised arrangements made with the object of ensuring that the products are consistantly manufactured to a quality appropriate to their intended use. GMP is thus concerned with both manufacturing and Quality Control procedures and is delineated under the following heads:

1. Adequate Premises and Space.
2. Properly Trained Personnel.
3. Equipment and Servises.
4. Manufacturing.
5. Documentation.
6. Complaints and Returned Goods Handling.
7. File Sample Retention.
8. Special Handling of Sterile products.
9. Good Laboratory Practice.

1.00. ADEQUATE PREMISES AND SPACE:

Proper layout of the buliding and adequate space form a basic part of the manuracturing facility for compliance with GMP. Hence while designing a plant layout following points need consideration.

1.1.0 The layout and the design of the building should be such as to permit efficient cleaning of the rooms and equipment, allow easy and fast flow of materials and personnel and enable routine operations and maintenance.

1.2.0 The premises shoule have adequate space for orderly placement of equipment, raw material in-process and packaging material, finished goods etc. In such a way as to avoid any possible mix up during any stage of storage, handling, processing etc. and to allow the production to take place in areas connected in a logical order corresponding to the sequence of operations.

1.3.0 The In-process area should be designed in such a way as to avoid right of way for generla personal or materials only.

1.4.0 Manufacturing area should be seperated from Animal rooms, Cafe, Toilets, Engineering workshop, cleaning equipment, Storage materials ect.

1.5.0 The building should be designed to provide adequate lighting and ventillation.

1.6.0 Proper equipment for control of air pressure, temperature, humidity ect. Must be installed to provide optimum environmental conditions for efficient operations during manufacture and storage of materials and finished products.

1.7.0 The production areas should be provided with Air filtration system dust and particulate renention.

1.8.0 Water supply to the bilding must meet the minimum standards of primary drinking water (40 CFR, Part 141).

1.9.0 Sufficent washing facilities. With cold and hot water outlets, detergents, air driers, and single use towels must be provided.

1.10 Refuses and rejects and all other disposables should be disposed

off in a safe, sanitary and environmentally friendly manner.

1.11 Building must be provided with all the facilities for the control of flies, insects, rodents, birds etc.

2.0.0 PROPERLY TRAINED PERSONNEL

The manufacturing plant must be run by sufficient personnel tith technical qualifications, training, ability, and managerial skills. Their duties and responsibilities must beclearly defined and spelt out through written job descriptions.

2.1.0 The key presonnel in the organisation are the persons responsible for production and quality control. Neither of them are responsible to each other but both of them should have the common goal of producing quality goods at minimum cost.

2.2.0 All personnel involved in production and quality control should undergo predesigned training program on recruitement and periodically to update their knowledge in the latest developments.

2.3.0 Personnel engaged in manufacture should wear clean clothing and appropriate heah, face and hand covers to avoid contamination of the products and for their own safety.

2.4.0 Any person with apparent illness or open lesion that may directly or indirectly affect the safety or quality of the drug must be excluded form any manufacturing operation till they are cleared medically.

3.0.0 EQUIPMENT AND SERVICES

Equipment used for the manufacture, processing, packing, labelling, testing, air filteration and circulation etc. Shall be maintainde in a clean and orderly manner. Their design, size and location should be such as to facilitate easy coeaning, maintenance and operation.

3.1.0 **Maintenance plan:** Plant engineering department should have a master maintenance plan for all the equipment used. A seperate log book and written maintenance procedure for each item of equipment should be maintained.

3.2.0 **Equipment cleaning:** A seperate written cleaning procedure for all the equipment should be laid down. Cleaning operation has to be carried out after processing of each batch. The in-process control inspector has to ensure that proper cleaning procedure has been followed.

3.3.0 **Calibration any Validation of Equipment :** Calibration and validation of equipment connected with production must be done periodically. Equipment has to be standardised and calibrated. For weights, volume, temperature, efficiency in processing, sealing, printing, testing etc.

3.3.1 **Standardisation of weight:** All the balances and weights used in issue of raw materials and quality control have to be calibrated and standardised through zero adjustment and against standard weights.

3.3.2 **Pocessing efficiency:** Equipment for processing include those used for mixing, blending, granulating etc. Need validatio for lot size, RPM for stirrers, temperature and total time for processing. Validation tests have to be clarfied out by separate analytical tests on samples form top middle and bottom layres of the tands. Optimum lot size, RPM, temperature and time of mixing have to be determined from several (at least three) lots of the same product.

3.3.3 **Validation of sterilizers :** All autoclaves/sterilizers have to be standardised/validated for the internal temperatures achieved during sterilization. Actual temperatures inside are determined by a) Registering thermometers: b) Microbe (Spore) susceptible to a particular temperature: c) Using a chemical of a particular melting point.

3.3.4 **Calibration for volume and weight :** Volume and witgh variation checks must be made priodically and records maintained. Weight rocord have to be analysed statistically for variation of tablets, capsules, ointments, sachets and other dry formulations. Similar tests have fo be made for volume variation for liquid formulations like syrups, suspensions, drops, SVP and LVP etc.

3.3.5 Sealing and printing: Equipment used for sealing and printing should be periodically checked for efficiency and perfection. Records for any problems and corrective actions taked must be maintained.

4.0.0 MANUFACTURING

Manufacturing of pharmaceutical products must be carried out according to defined, written and recorded procedures. These procendures are designed to assure that the drugs produced conform t identity, strength, quality, purity and stability under different storage conditions.

4.1.0 **Standard Operating Procedures (SOP):** Manufacture of a product must proceed according to the Standard Operating procedure, i.e,. according to the master formula, processing method and packaging instructions already recorded. Any deviation from the SOP must have the consent and agreement of responsible persons from production and quality control and all changes have to be recorded in batch history.

4.2.0 **Yield accountability:** Final yield of a batch of a product should be checked and recorded. Any deviation in the expected yield has to be recorded and the cause indetified and corrected.

4.3.0 **Cross contamination:** Cross contamination may result from release of dust, gases, vapours, sprays, organisms, materials in process, recidued in equipment and operator,s clothing. This can be controlled by one or all of the following measures:

4.3.1 Processing and filling in segregated areas.

4.3.2 Transfer of materials from one area to another area by air locks.

4.3.3 Filtration of incoming air.

4.3.4 Use of closed system in manufacturing.

4.4.0 Laboratory Controls. Laboratory controls should be based on scientifically sound and appropriate specifications, standards, and test procedures to assure that the finished products confirm to their specified standards.

4.5.0 Starting material: All starting materials used must comply with following requirements.

4.5.1 Received and held in quarantine.

4.5.2 Containers are checked for any physical damage.

4.5.3 Samples of starting materials are analysed for identity and purity.

4.5.4 Approved and rejected materials are to be indentitied by proper stikers with Q.C. reference number.

4.5.5 Approved materials are issued on first come first serve basis and the regected materal has to be disposed proberly.

4.5.6 Raw materials that requrie special storage conditions like temperature, humidity, darkness etc. have to be stored accordingly,

4.5.7 Sampling, labelling, weighing and issue have to be carried out by authorised personnel

4.5.8 Correct issue of the material must be confirmed by Pilot-Co-Pilot systim.

4.5.9 All materials have to stored off the floor.

4.6.0 **Packaging Materials:** In addition to complianec with the standard specirications for packaging materials, they have to meet follwing requirements.

4.6.1 They have to be quarantined as soon as they are received.

4.6.2 Each batch of packaging material has to be sampled and tested and indentified as "Approvd: or :Rijected".

4.6.3 Stikers for all packaging materials must bear the reference number for access to records.

4.6.4 Printed packaging material and those which may come into contact or infuence the quality of the product and its stability should be handled, stored and issued tith special care.

4.6.5 Printed packaging material should have identifying code numbers as part of the printed text.

4.6.6 Inventory of the stock and issue of the packaging material should be maintained.

4.6.7 All unusable and rejected packaging material should be destroyed.

4.7. **In-process Material:** All products must be processed strictly according to the steps detailed in Standard Operating Procedure (SOP) for the product. In addition the following points need attention:

4.7.1 All in process materials should be labelled with product name, batch number, status of the material and date.

4.7.2 Left overs at the end of the day should be stored securely and cleared off in the following morning.

4.7.3 All containers, equipoment and area must befree from previous days material.

4.7.4 There should be no transfer of material from one batch to another batch for any yield adjustment.

4.7.5 In process rejected material should be disposed off and a record made in batch history.

4.8 Labelling and Packaging

All labelling and packaging operations should proceed according to the master packaging instructions. Since mislabelling of the product is the most frequent cause of product hazard and product recall, following steps should be taken to minimise such hazards.

4.8.1 Designing and labelling of the cartons and other packaging should be done in such a way as to differenciate one from the other through different sizes, shapes, colours, bar codes etc.

4.8.2 Storage and issue of packing material should be the responsibility of authorised personnel only.

4.8.3 Stored and issued material should be segregated.

4.8.4 Packaging area must be clean and free from any product, labels, cartons etc. left over from previous operations.

4.8.5 There should be a 100% visual checking of the packaging material before they are subjected to any electronic sorting system.

4.9 **Finished Product Release:**

A finished product is passed for sale and distribution only after it has been released by the authorised quality control personne. Evaluation of the finished includes all manufacturing,Conditions such as in-process test results, Manufact uring documentation, complianec with finished product specifications and final examination of the finished pack.

Failures to comply with any specifications and any yield discrepancies should be throughly investigated.

5.0.0 **DOCUMENTATION**

5.1.0 Master Formula:

5.1.1 Written instructions covering each stage of production, storage and quality control is the master formulae and they should be updated whenever necessary.

5.1.2 Master formula should be perpared for standard batch sizes with the names of starting materials and packaging material involved with their quality and quantity.

5.1.3 There should be detailed production and quality control procedures for each of the active ingredients.

5.1.4 Competent persons experienced in production and quality control shld ongy be responsible for perparing checking and signing the documents with dates. There should not be any transcription error in it.

5.1.5 Superseded master formulae must be removed and rdplaced by the new one.

5.2.0 **Batch Documentation:**

5.2.1 Batch manufacturing record (Batch History) must be completed when the production of a batch proceeds step by step. It should

have relevant parts of the master formula and should also contain the following:

5.2.2 Product name, stage, batch size and batch number.

5.2.3 Different stages of production with dates.

5.2.4 Production detalis with reference to main equipments and persons involved including yields.

5.2.5 In process control records.

5.2.6 Authorisation note in case of deviation from master formula.

5.2.7 Note on recovered materials used, if iny and its procedure.

5.2.8 Initials with dates of all production prerations and in process inspectors.

5.2.9 Review of all informations and records.

5.2.10 Final release or reject form should be signed by the Quality control chief.

5.2.11 This Batch Documentation should be retained in such a way for easy access to them and can be destoryed one year ofter the expiry of the product.

6.0 PRODUCT COMPLAINTS AND RETURNED GOODS HANDLING:

Repeated complaint of particular nature of a product or a critical complaint needs attention by the manufacturers for its correction, development or even product recall form the market. An effective product complaint and returned goods handling should proceed as per the following steps:

6.1.0 Reference samples for each batch of product must be retained systematically for easy access and comparison with the com-

plained sample. These reference samples can only be destoryed one year after the expiry of the product.

6.2.0 Standard complaing/Returned goods form should be there to have the following information:

6.2.1 Product name, batch number, quality involved.

6.2.2 Cause of complaint/Return.

6.2.3 Exact location of complaint with date.

6.2.4 Whether the product is tampered.

6.2.5 Motive of the complaint/return.

6.2.6 This blank form should be available to customers through the agents/field force.

6.3 This filled-out complaint/returned goosd from with samples should be channeled to the person responsible only.

6.4 All complaints concerning quality must be investigated very carefully. If the complaint is genuine corrective actions must be taken.

6.5 Records of complaint and actions taken must be maintained for future references.

6.6 If the action needs recall of the product from the market, all agents must be contacted immediately for closing of the sale of the product and its withdrawal from the market.

7.6 If the problem is of such nature that it is life threatening or hazardous to life, mass media like news paper, radio, TV etc. should be used to stop using the product.

6.8 Government regulatory authority of medicine should also be informed of the problem and proper and prompt action taken.

6.9 Recalled returned goods if rejected must be destroyed and record of destruction should be maintained.

7.0 FILE SAMPLE RETENTION.

Enough samples from each batch of every product must be retained in a separate room having adverse atmospheric condtion of temperature, humidity etc. as the products are supposed to be in chemists shops or their stores. The samples should be retainde in an order fashion to facilitate

7. 1 Easy access for comparison with product complaint and returnde goods.

7.2 Stability of the product.

7.3 Analytical tests regulary on routine basis on products nearing expriy to detrmine whether a products needs shange of expiry period.

7.4 Any change/development of a process of a product.

7.5 Suggesting Chemist shop to upgrade the storage condition.

8.0 SPECIAL HANDLING FOR STERILE PRODUCTS:

Special care has to be taken while manufacturing sterile products. This is needed to minimise the risk of contamination from microbial, particulate and pyrogenic bodies in the product during manufacturing. Manufacture of sterile products need special care and handling in the following areas:

1. General consideration of the clean areas.
2. Personnel.
3. Premises.
4. Equipment.
5. Sanitation.
6. Processing.

7. Sterilisation.
8. Finishing of sterile product.
9. Quality Control and Batch Release.

8.1.0 General Condition of the Clean area

8.1.1 Clean areas to be maintained with appropriate filtered air.

8.1.2 Various operations like product preparation, filling and sterilisation should be done in separate areas.

8..1.3 Clean areas for sterile production are classified as follows:

Grade	Max. # of Particles permitted/m3 0.5-5 um	> 5um	Max. # of viable Micro- organism Permitted/m3
A	3.500	0	1
B	3.500	0	5
C	350.000	2.000	100
D	3.500.00	20.000	500

8.1.4 Product category wise recommended clean area:

Product Category	Recommended clean area Perparation	Filling
a. Terminally Sterilised Product	C or D	A
b. Sterile Filtered Product	C or D	A or B
c. Product from sterile starting Material	A or B	A or B

8.1.5 The manufacturers must identity the areas as A,B,C and D and categorise their product where to be processed and filled. Mareover, they must monitor, control and keep record of the area and the product involved to be attached with batch document.

8.2.0 Personnel of Sterile Area:

The personnel working in the sterile area should ahve the following characteristics:

8.2.1 To be selected carefully to possess high standard of personal hygiene and cleanliness and they should be as minimum as possible in number.

8.2.2 To be trained with basic elements of microbiology.

8.2.3 They must wear specified clean, dry and sterilized clothes to be used for the sterile area purpose only.

8.2.4 Out door clothes must not be brought inside the change room of the sterile area.

8.2.5 Watches, jewelleries, coins, currency notes.. etc. must not be taken inside the sterile area.

8.2.6 Bacteriological swab tests on personnel to be done periodically to control their GMP practices in the area.

8.3.0 Sterile area Premises:

Proper Designing of the lay-out of the sterile area is a vital factor for effective control of microbial contamination. It should have segregated room and facilities for component preparation, solution preparaton, filling and sterilisation..etc. In addition, it should have the following facilities:

8.3.1 All the room should be continuously flushed with positive sterile air pressure.

8.2.3 In coming air should be frequently controlled for microorganism contamination.

8.3.3 Alarm system to indicate stoppage of air supply.

8.3.4 Provision for easy and regular change of air filters.

8.3.5 False sealing should be sealed to prevent contamination.

8.3.6 Pipes and ducts to be installed in a way for easy cleaning.

8.3.7 All sufraces should be exposed, smooth, impervious for better cleaning of area.

8.3.8 There should be minimum of ledges, shelves, cupboards and equipments in the area.

8.3.9 There should be no sink, drain etc.

8.3.10 The area is separated from outside through air-lock and change room, Hedges etc.

8.3.11 Room termperature and humidity should be comfortable.

8.3.12 Area must have one telephone for outside communication.

8.4.0 Equipments for Sterile Area.

Equipments designed and installed in a way for easy cleaning, disinfection and sterilisation. Moreover, they should comply with the following GMP requirements:

8.4.1 Conveyer belt should not pass through a partition between a room of lower to higher grade of cleanliness eg. from area B to area A.

8.4.2 Equipments for processing should be easy for sterilisation.

8.4.3 Equipments design should be such that routine and planned maintenance can be done by machine operators working inside the sterile area.

8.4.4 Recording apparatus should be accurately calibrated and checked at regular intervals.

8.5.0 Sanitation:

Planned and regular sanitation of the clean area is essential for effectve control of microorganism. Effective management of sanitation can be done by :

8.5.1 Monitoring the area by microbiological plate count method.

8.5.2 Monitoring the plate counts by rotating the components of spray and fumigation solutions on different days of the week.

8.5.3 All records for spray, counts, actions must be maintained.

8.6.0 Processing:

Precautions to minimise contamination during all stages of precessing should be taken, including stages before sterilisation. Some of these are:

8.6.1 Starting materials should be of the grade of sterile products. This includes water also.

8.6.2 Persons and activities should be as minimum as possible.

8.6.3 The time intervals between (a) washing and drying (b) sterilisations and cooling (c) cooling and use of components parts of processing should be as minimum as possible. Here the maximum allowable time must be validated and standardised for each operation.

8.6.4 The time interval between the preparation time of a solution and its sterilisation should be as minimum as possible. The maximum permissible time for this operation must be set by validation test.

8.6.5 All solutions, particulary LVP, should pass through a organism-retaining filter, if possible immediately befor filling operation.

8.6.6 Any purging gas must pass through sterilising filter.

8.6.7 Any new process should be validated and standardised.

8.7.0 **Sterilisation:**

There are various methods for sterilization viz.

8.7.1 Sterilisation by heat (moist)

8.7.2 Sterilisation by heat (dry)

8.7.3 Sterilisation by filtration

8.7.4 Sterilisation by irradiation

8.7.5 Sterilisation by ethylene oxide.

Each method mention above has particular application and limitations. Whenever possible and practicable heat sterilisation is the method of choice.

LVP fluids should be passed through a bacteria retaining filter just before filling and sterilisation. So microbial contamination levels of products should be monitored before sterilisation process, irrespective of method of sterilisation used.

All sterilisation processes must be validated and their suitability must be determined for a particular product. Each process of sterilisation must be validated at scheduled interval of at least a year. Record and results must be evaluated for continuous updating of process parameters.

Biological indicators or registering thermometers should be used for monitoring the sterilisation process.

8.7.1.0 Sterilisation by heat:

Each heat sterilisation operation must be monitored by Temp/Time chart. This Temp/Time chart should be periodically validated by the use of registering thermometer or biological indicator.

8.7.1.1 Sterilisation temperature is the uniform temperature at highest range and sterilisation time is the run time at that highest range of temperature.

8.7.1.2 Precaution should be taken during cooling process.

8.7.1.3 In-coming cold air should be free from contamination.

8.7.14 Sterilised products/components should be used up as soon as possible after cooling.

8.7.15 Minimum personnel should be there for handling.

8.7.16 Monitoring charts should be attached with the relevant Batch History of the product

8.7.2.0 Moist Heat Sterilisation:

8.7.2.1 Applicable to water-wettable materials and aqueous solutions.

8.7.2.2 This operation is again run with time, temperature and pressure. Steam pressure is needed to raise the temperature only.

8.7.2.3 Recommended Temperature is 121 Dregree centigrade and time varies from 15' to 30' depending on load size and materials. The steam used should be of suitable quality free from anyadditives that may cause contamination of the product under sterilisation.

8.7.2.4 Monitoring each load and periodical validation is essential.

8.7.3.0 Dry Heat Sterilisation :

Dry heat sterilisation is suibale for equipments, glass containers, non-aqueous liquids that can withstand the high temperature. Various combinatins of time and temperature can be stablished by the proper one for a particular material has been established by validation tests. Records of these tests are Preserved and monitoring charts of temperature and time is to be attached with the batch record. Sufficient time should be allowed to reach the desire temperature at the remote corner of the steriliser. This time should be determined for each material and different load size.

8.7.4.0 Sterilisation by Filteration :

The products which cannot be sterilised after filing are only to be sterilised by filtration. Solutions for sterilisation by filtration should go through:

8.7.4.1 0.22 um of pore size filters.

8.7.4.2 Some heat treatment, if possible.

8.7.4.3 Second filtration process just before filing.

8.7.4.4 Non fibrous filters.

8.7.4.5 Integrity tests like "bubble point tests" for monitoring the process of filtration.

8.7.4.6 Use of fresh filters every day.

8.7.4.7 Non-interference of quality by the filters.

8.7.4.8 Operations in clean are A/B.

8.7.4.9 Containers used for collection of filtrate must be sterile.

8.7.5.0 Sterilisation by Irradiation:

This method of sterilisation is applicable particularly tothe materials that are heat sensitive and not suitable for filtration process.

This process should be monitored and validated for each material. Dose, time and volume are the important factors of consideration for efficacy of the process.

8.7.6.0 Sterilisation by Ethylene Oxide:

Various gases and fumigant can be used for sterilisation. Ethylene oxide is such a gas for sterilisation. This method should be the last choice and should be used only when any other method of sterilisation is not available.

This method has got a lot of limitations.

8.8.0 Finishing of Sterile Products:

8.8.1 All Containers must be sealed hermatically.

8.8.2 Sealing perfection should be monitored by standard leak-test.

8.8.3 Containers sealed under vacuum, should be tested before final release of the product.

8.8.4 Finished products for parenteral use must be inspected individually (100%) under controlled illumination and proper background.

8.8.5 Eye-sights of the inspecting personnel should be checked at least once a year.

8.8.6 In case of automated electronic device for sorting out the defective product containers, the device should be monitored, validated for efficacy of sorting.

8.9.0 Quality Control and Batch Release of Sterile Products:

8.9.1 Samples for sterility testing should be representative of the whole batch, including beginning and end of operations.

8.9.2 Samples for sterility test should come from the remotest part of steriliser.

8.9.3 Sterility test result should be regarded as the last control measure in a series operations.

8.9.4 Only the satisfactory sterility results is not an indication that the product is safe.

8.9.5 Satisfacory test result in conjunction with other satisfactory environmental and batch processing records assures the product safety.

8.9.6 A batch failing in the initial sterility test but passing in the next does not dicate that the product passes Q.C. REquirements, unless investigation shows that environmental and processing records invalidate the first sterility test.

8.9.7 Endoxin test (LAL test) on injectable, particularly on LVP products must be done. Such monitoring on intermediates like water etc. should always be done.

8.9.8 If a sample fails a test, possible causes may be identified from these intermediate test results for endotoxin.

9.0 Good Laboratory Practice (GLP)

It is very essential that control laboratories should have appropriate facilities, with properly trained, managed and motivated staff, in order that reliable results are obtained. Steps should be taken to ensure the reliability of the laboratory's own systems and test methods. Quality control is the part of Gmp concenned with sampling specifications documentation and release procedures which ensures the reccssaryand relevant tests are actually carried outand that the materials and products are not released for sale or supply until their quality has been judged to be hisfactory. The Q.C. department should be independent of other departments and under the authority of a qualified and experienced person.

9.1. Premise :

The Q.C. Laboratories should be designed equipped, maintained and of sufficient space to suit the operations to be performed in them.

9.1.2 Chemical, pharmacology and microbiological laboratories should be separated from each other and from manufacturing areas. Separate rooms may be necessary to protect sensitive instruments from vibration, humidity etc.

9.1.3 Provision should be made for the safe storage of waste materials awaiting disposal.

9.1.4 All services should be marked with an indication of identity.

9.2.0 Equipment :

9.2.1 Q.C. Laboratory equipment and instrumentation should be appropriate to testing procedures.

9.2.2 Equipment and instruments should be serviced and calibrated at proper intervals by competent persons and records maintained. These records should indicate when the next calibration or servicing is due.

9.2.3 Written operating instruction should be readily available for each instrument.

9.2.4 Defective equipments should be withdrawn from use until the fault has been rectified.

9.2.5 All analytical methods must be validated by proper calibration check.

9.3.0 Cleanliness:

9.3.1 Q.C. Laboratories and equipments should be kept clean according to written cleaning schedules.

9.3.2 Personnel should wear clean protective clothing appropriate to duties being performed.

9.3.3 The disposal of waste material should be carefully and responsibely undertaken.

9.4.0 Reagents etc.

9.4.1 Where necessary reagents should be carefully dated upon receipt or preparation.

9.4.2 Reagents made up in the laboratory should be prepared by competent persons, following laid down procedures. Labelling should indicate the concentration, standardisation factor, shelf life and storage conditions. The label should be signed and dated by the person preparing the reagent. If required, date of restandardisation should be recorded.

9.4.3 Periodic check should be made to ensure that the reagent is suitable for the purpose for which it is to be used.

9.4.4 Both positive and negative controls should be applied to verify the suitabltity of microbiological cultue media.

9.4.5 Reference standards and any secondary standards from them should be dated and be stored, handled and used so as not to prejudice their quality.

9.5.0 Sampling :

9.5.1 Samples should be taken in such a manner that thay are representative of the batches of material from which they are taken. Any sampling procedure should follow a standardised, approved neat method.

9.5.2 Each sample container should be labelled with all important informations e.g. lot no., date of sampling, bulk container from which samples have been withdrawn etc.

9.5.3 Sampling equipment should be cleaned after each use and stored separately from other laboratory equipment.

9.5.4 Care should be taken to avoid contamination during sampling.

9.6.0 Documentation:

9.6.1 Laboratory documentation method should be inline with general qquidance of the main documentation methods.

9.6.2 Retention samples should be regarded as part of the laboratory records.

9.7.0 Records of Analysis :

The records should contain: name of the product or material and code reference, dates of receipt and testing, source of product or materials, decision regarding release, rejection or other status, analyst's own basic data and calculations from which test results were derived and signature of analyst etc.

9.8.0 Specifications:

Specifications approved by Q.C. should be established for all starting materials, packaging materials, and Bulk, Intermediate and Finished products and documented in a very clear manner.

9.9.0 Testing

9.9.1 The persons responsible for laboratory management should ensure that suitable test methods, validated in the context of available facilities and equipment, and developed and adopted.

9.9.2 Samples should be tested in accordance with the test methods referred to or detailed, in the relevant specifications. The validity of the results obained should be checked before the material is released or rejectd.

9.9.3 In process control work carried out by production staff should proceed in accordance with methods approved by the persons responsible for Q.C. Department.