Document No.:	TRAINING MANUAL	Effective Date:
		Revision Date:
Revision No.:		Page No.: 1 of 65

TRAINING MANUAL

PHARMA DEVILS
(Oral Solid Dosage & Injectable Facility)

APPROVAL:

Signing of this document indicates agreement with the training manual of …… If any changes in this document required, document shall be revised and duly approved.

Prepared By

Functional Areas	Name	Sign. and Date
Quality Assurance		

Reviewed By

Functional Areas	Name	Sign. and Date
Engineering		
Production		
Quality Control		
Quality Assurance		

Approved By

Functional Areas	Name	Sign. and Date
DGM Quality Assurance		

Authorized By

Functional Areas	Name	Sign. and Date
General Manager – QA/QC/DRA		
Vice President- Operations		

TABLE OF CONTENTS

1.0 INTRODUCTION

1.1 BRIEF INFORMATION ABOUT SITE:

……is a professionally engaged Pharmaceutical company, manufacturing various dosage forms and has emerged as a reputed pharmaceutical formulation manufacturer .The company enjoys a rich manufacturing experience of over …….years. The site manufactures oral solid dosage forms in Tablets, Capsules, liquid Injectable, dry Syrup & Dry Injectable general. The formulations manufactured are generic and patent and proprietary medicine and for HUMAN USE ONLY.

1.2 Pharmaceutical Manufacturing Activities as Permitted by the Licensing Authority.

The facility is licensed by the state FDA, The manufacturing of Tablets, Capsules, Liquid Injectable, Dry syrup & Dry Injectable are manufactured under licenses No……. with validity to …….. validity up to 15-05-2019 [Valid Manufacturing Authorization (Annexure: 1).The facility is as per GMP norms- copy of valid GMP certificate ,GLP Certificate & WHO Certificate [Copy of valid GMP certificate (Annexure: 3)]

1.3 Any other manufacturing activities carried out on the site

Only pharmaceutical finished formulations are manufactured at this site and no other hazardous activities like manufacturing of Pesticides, Bulk drugs etc. are manufactured at this site which may contaminate the environment.

1.4 Name and exact address of the site, including telephone, fax, and 24- hours telephone numbers.

Contact Persons during & outside working hours:
Contact information of the site (Name & Address):

Name of the Industry	:
Factory Address	:
Regd. Office	:
Name of contact person	:
Tel. No. of contact person	:
Mobile No	:
E-Mail ID	:
24 hour contact Tel. No	:

1.5 Type of products licensed for manufacture

List of product manufactured at the site

A. Sterile products.
   (In General Block) A.1: Liquid Injectable, A.2: Dry Injectable
   (In Cephalosporin Block) A.3: Dry Injectable
B. Non sterile products (General category)
   - B.1 Tablets (General category)
   - B.2 Capsules
   - B.3 Dry syrup
C. Biological Products - Not manufactured at site.
E. Packaging only -Not applicable.
F. Contract manufacturing- Company reported upon is - Acceptor.
G. Contract analysis - NA

H. Drugs for clinical trials- Not applicable.
I. Others- Not applicable.
Only products for human use are manufactured on the site. Each dosage form is manufactured in its dedicated facility only.

1.6 Short Description of the Site (location, surrounding environment and size)

Site is situated at Plot No. …….. The plant is only ……..km. away from Railway Station …… and well connected by road on …….. National Highway No-……. The plant is situated on a peaceful area surrounded by low height mountains on the southern side with two sides open to wide roads. No major polluting industry is located in the vicinity of the company, there by offering a perfectly neat and clean dust free area suitable for manufacturing of pharmaceuticals. …….. is well connected to all major cities of the country by air, road and railway. Shipment facilities are available from ……Delhi a air port about ……. km from the manufacturing site and regular rack movement is also available to Kandla and Mumbai ports.
Surrounding area of the site is a green belt and pollution free. The site is surrounded by on the:
East side by:
West side by:
North side by:
South side by:
There are no units nearby which generate smoke or hazardous waste.
Site Plan Drawing - Attached for General [Annexure-6A to 6R]

LOCATION OF SITE:

DETAILED INFORMATION OF ……..

PLOT AREA FOR GENERAL BLOCK

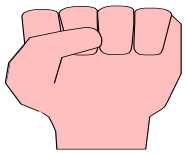
PLOT AREA ……sq. meter

Covered area Basement ……sq. meter
Covered area of general Injection Ground floor ……sq. meter
Covered area of General Injection First floor ……sq. meter
Covered area of general second floor ……sq. meter
General Tablet Section Ground Floor ……sq. meter
Covered area of Tablet & capsule Section First Floor ……sq. meter
Covered area Second floor Utility section ……sq. meter

1.7 Number of employees and workers engaged in

Department	Managers	Staff	Workmen	Total
Production				
Quality Assurance				
Quality Control				
Store (R.M., P.M., & F.G.)				
Engineering				
Personal and Admin				
Total				

OUR MISSION, VISION AND CORE VALUES



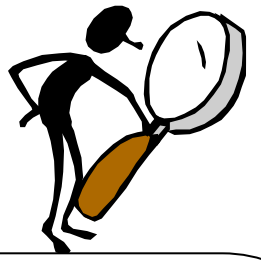
OUR MISSION

"Innovate. Improve. Inflate."

Our mission is our obligation. We have a responsibility to stand in to make every life and make it "feel good" every new rise, means that we need to resolve and pledge ourselves to forever persevere to achieve the **three -I's** that give our mission it's name **Mission i3 -**

- **Innovate -** to emerge as a key research-based organization
- **Improve -** the quality of well-being in general of the society
- **Inflate -** as a major transnational player.

OUR VISION



- **Brand of choice for flagship products at least 20% of product portfolio**
- **Employer of choice listing in Fortune 500 companies.**
- **Principal of choice for stake holders - Shareholders / Investors / Vendors**
- **And by being 'the choice' we hope to be 'the leader' and achieve - position in top 100 global generic life sciences company by profitable new business ventures from both qualitative and quantitative.**
- **Significant business (60% of business revenues) in prescription products with a strong presence in emerging markets.**

OUR CORE VALUES

……..finds itself committed and completely in adherence to the following 12 principles that ensure we serve the society in the most righteous ways and thereby be the bearers of "feel good" in true sense.

- Caring
- Transparent
- Integrity
- Teamwork
- Excellence
- Respect for individuality
- Empowerment
- Knowledge
- Win-win relationships
- Speed and efficiency
- Innovation
- Customer delight

QUALITY POLICY

"Quality is a Relentless Commitment at

……

and Management is always desirous to

provide the customer's desired

quality Medicines at competitive cost

and maintain leadership in Health Care

through continual improvement

and innovative Technology".

HEALTH SAFETY AND ENVIRONMENT POLICY

…….aims for excellence and leadership in Health, Safety and Environment protection. We are committed to protect the environment in which we operate and ensure the health and safety of our employees, community and interested parties."

OBJECTIVES

- **Aiming to achieve beyond statutory requirements.**
- **Process improvement to minimize the adverse effect on health safety and environment.**
- **Using and maintaining equipment, systems and facilities to provide a safe and hygienic working atmosphere.**
- **Conservation of natural resources and preventing pollution.**
- **Conducting management program, audits and reviews towards improving HSE aspects.**
- **Housekeeping in our plant premises.**
- **Seeking participation of employees to achieve HSE policy.**

2.0 ORGANIZATIONAL OVERVIEW

2.1 ……..is a newly developed state of art facility, aiming for marketing lifesaving drugs in regulated, non- regulated markets and in national markets. Company has its first plant ……which has a WHO from national authority.

3.0 TRAINING POLICY

"When planning for a year, Plant Corn
When planning for a decade, Plant Trees
When Planning for Life, Train and Educate People"

3.1 Training and Development

"Tomorrow illiterate will not be the man who can't read:
He will be the man who has not learn how to learn"

The pressure of rapidly changing technologies, the need to squeeze additional value from corporate resources, and, not least, strong competition, means that most organizations are under pressure to ensure that their customer recognize and appreciate high levels of quality from their product services.

"The more i train the more i realize i have more speed in time" ~ Leroy Burrell

Meeting to the new increasing national & international demands, it is only training that builds skills for individuals who must be trained for any job they perform. Training is a specialized form of education that focuses on skilled development and while it also embraces educational theories, principles and practices, it is essentially performance oriented. Training is a process, from which trainees will gain new understanding, acquire new skills or change their attitudes or behavior, which means the educational process may be complex for learning to occur at many levels.

"It's all to do with the training: you can do lot if you are properly trained"~ Queen Elizabeth

Hence, Training and Development as a part of QA activity to train upgrade and improve the skills of all colleagues of …….. To comply with stringent international standards, maintaining the product quality is possible only with the skilled and trained personnel.

"If you Train hard, you will not only be hard, you will be hard to beat"

3.2 Aims and Objectives

3.2.1 Aims

- Identification of Training Needs
- Training and Development of all colleagues time to time
- Evaluation of Training needs.

3.2.2 Objectives

The objective is to develop a **SMART** Trainee i.e.: **S**pecific, **M**easurable, **A**ction-oriented, **R**ealistic and **T**ime-related to minimise of risk of errors.

- Doing Right Things First
- Not Doing The Things Right

…….wants to have:

People	: Trained, aware and committed
Operations	: Validated and controlled
Procedures	: Written, authorized and followed

3.2.3 Requirements

We need Commitment to the Principle and Not Just Acceptance.

- Its success based on personnel, "WILL" to be trained and necessary supported by departments.
- Following DO's and Don'ts are totally dependent on the controllers of the operations.
- Participation in training is a must. Non-attendance in training will be marked "ABSENT" from duty and its responsibility lies with department heads.

3.2.4 Scope

3.2.4.1 Awareness

Training builds awareness. The employee, who has more information and better understanding about a product, process or an operation, shall perform better than other because of awareness, acquired through training, inquisitiveness to learn more and shall work with skills and knowledge. Thus awareness of individual about job, activity, system, procedures, methods etc., shall help in effective functioning, recognizing the problems quickly and provide solutions instantly.

3.2.5 Education

Ignorance is curse. Lack of education about the job, its content, do's and don'ts, know how's etc. leads to loss of quality, productivity etc. Education of employees in all the above aspects leads to success.

3.2.6 Updating

Science and technology is ever developing phenomenon. Today whatever is thought to be the best may not be the same for tomorrow. We need to meet the challenges and needs of today ourselves and getting activities, facilities, performances etc. i.e. updating our knowledge, skills and so on so forth…

3.2.7 Motivation

When an employer spends time and money on education and training, it sends a message that the company cares about the growth and development of its employees.

3.2.8 Participation

When an employee feels that he / she is a part of a team, he/ she is more likely to share the experiences and take more active part in day to day activities and suggests solutions to various problems.

3.2.9 Building Quality

Building quality into product is a part of everybody's function. It will be achieved, when employees perform their assigned tasks according to established methods designed to produce a product according to pre-determined specifications. Training enables the employees to understand the importance of each aspect of an organization facility, systems, methods, procedures etc. and in turn it helps in identifying the problems and instant solutions for smooth and efficient functioning, thus minimizing the loss with respect to safety, quality and productivity.

3.3 Training Committee/Team

3.3.1 The Training Team shall be constituted by QA Head along with the other department heads like: production, quality control, store, engineering and HR.

3.3.2 Training team shall have the overall responsibility for the execution of the various training programs. The committee shall also be responsible for the annual review of the training program and to recommend the required changes/modifications for the next years training program.

3.3.3 Topics for different training programs shall be decided by this committee and members of the faculty shall be selected by this commission.

3.4 Levels of Trainees

The personnel falls under these categories are:

Level I

Trainee

Officers

Executives

Assistant Managers

Managers

Assistant General Managers

General Managers and above

Level II

Technicians

Machine Operators

Level III

Contract Workmen

Housekeeping Staff

3.5 Identification of Trainer

The most important element in a training situation is the trainer. The trainer who shall be enthusiastic, energetic and genuinely interested in both the subject and getting his or her message across will evoke the greatest response from the trainees. The trainer who lacks interest in training, who has little or no enthusiasm for the subject of the training and who merely goes through the motions of training is a failure. The inept trainer is quickly identified by the trainees, who react with un-attention, lassitude, undisciplined behavior and absence from training sessions.

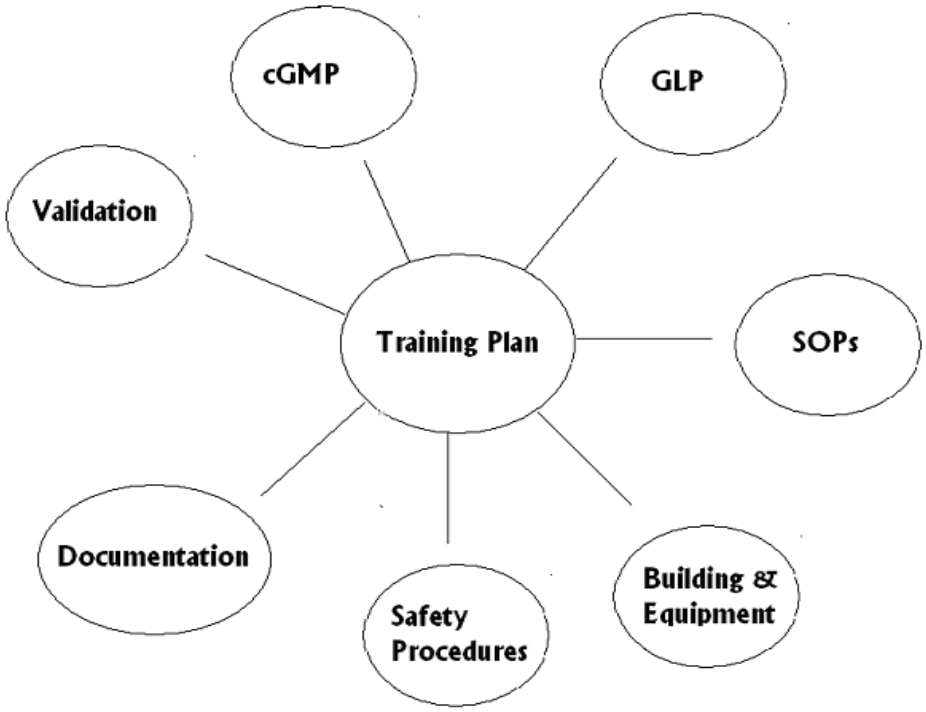
Successful training - that which produces the desired result - lies almost entirely in the hands of the trainer. In the trainer's hands lies the heavy responsibility for ensuring that the trainees achieve the maximum possible from the training.

3.6 Training Module

The technical or cGMP related topics shall be conducted in the form of classroom training. Trainer shall prepare the Training module on relevant topics in presentation styles and the same shall be reviewed by training commission. Trainer shall deliver the content as per training module but not limited to Particular topics.

3.7 Training Plan

Training plan shall be prepared in such a way that all the regulatory and in-house aspects shall be covered and documented properly for the successful completion of the training



An annual training program shall be prepared in the beginning of each year. This program acts as a tool for providing various training programs which are required for the improvement of the technical skill of the personnel since trained employees are more efficient and motivated and more valuable to the company. The training committee shall be constituted for the execution of these training programs. Members of this committee shall be drawn from Production, QC.

engineering and QA. The members can be heads or anybody nominated by them However in the light of recent advancements in the scientific literature or amendments in the regulatory requirements, this training program is subjected to revision.

3.8 Types of training

Following types of training shall be imparted

- Internal training
- External Training

3.8.1 The training which is imparted by the experienced employees to the other employees is known as **Internal Training** like:

3.8.1.1 Induction Training

This training shall be imparted by human resource department to a new joinee. through induction manual. The objective of this training is to get introduced with the other departmental activities and employees of the organization and organizational overview.

3.8.1.2 On the Job Training

On the Job Training shall be conducted by all department heads or the employee designated by them. On job training shall be executed by respective department before handling the assigned jobs. After completion of on the job training, the trainee shall be evaluated through questionnaires or by other acceptable means. Only on successful evaluation, trainee shall be qualified to perform the assigned job otherwise the trainee shall undergo retraining and reevaluation.

3.8.1.3 cGMP Training

cGMP training shall be conducted by QA department. The basic principles of GMP like quality management, sanitation and hygiene, complaints and recalls, validation, self inspection, personnel, premises, equipment, documentation etc. shall be covered during this course. After completion of cGMP training, the trainee shall be evaluated through questionnaires and by other acceptable means after each training session. Only on successful evaluation, trainee shall be qualified to perform the assigned job otherwise the trainee shall undergo retraining and reevaluation. On job training and cGMP training shall also be imparted periodically as a refresher course.

3.8.1.4 Unscheduled training

In addition to the training imparted based on the Annual Plan training shall be given in the event of

Following:

- Introduction of new Standard Operating Procedure (SOP)
- Changes in SOP
- Observations of Audit
- Training on nonconformance
- Training on any changes or modifications

3.8.1.5 Training Needs Identification (TNI)

Specific training shall be imparted to the employee as per training needs identified in case of non compliance. TNI is categorized in two:

a) Behavioral training

b) Specific training

a) Behavioral Training

Behavioral training shall be imparted by each head of department to the employee as per training needs identified during performance appraisal or as recommended by superiors. Other reasons for performing the behavioral training but not limited to:

- Quality Aspects
- On the Job training /SOP's
- GMP/GLP Training
- Training of QA systems
- Other than GMP subjects like soft skills (Communication, Leadership, Motivation, Team building, safety, First aid, Environmental management system, fire fighting)

b) Specific training

Specific training shall be imparted by respective departmental HOD in case of non compliance by an employee during performing the assigned job or as a result of audit observations and investigation of product complaints.

Only three times an employee shall be retrained in case of any non compliance, after that the reasons of non compliance by an employee shall be carried out by the committee and perform according to the decisions.

3.8.2 External Training

When an external faculty imparts training to employees on any in house topic or any other relevant topic or the employees of the organization visits to an institution for receiving knowledge on relevant topics on the approval of their HOD, this type of training is falls under External Training.

3.9 Evaluation of trainees

The training shall be imparted by the qualified, experienced, regular employees of the company. Trainees shall be evaluated on the basis of questionnaire or other acceptable means after the training session. The test papers take the form of multiple choice questions that can be marked by the trainer in a short period of time and can be used to identify areas that require further explanation and discussion.

For good learning, it is important to review the questions and answers with all participants. For the successful completion of the training, trainee shall score minimum 80% of marks, if marks are less than that the trainee shall undergo retraining. Complete documentation shall be done in case of training and retraining and finally submitted to QA Department.

Assessment and evaluation of the employees shall be carried out on the basis of questionnaire prepared or by other acceptable means like: viva voice, brainstorming etc. by HOD and final report shall be submitted to QA department. For the successful completion of the training, trainee shall score minimum 80% of marks, if marks are less than that, the trainee shall undergo retraining and reevaluation.

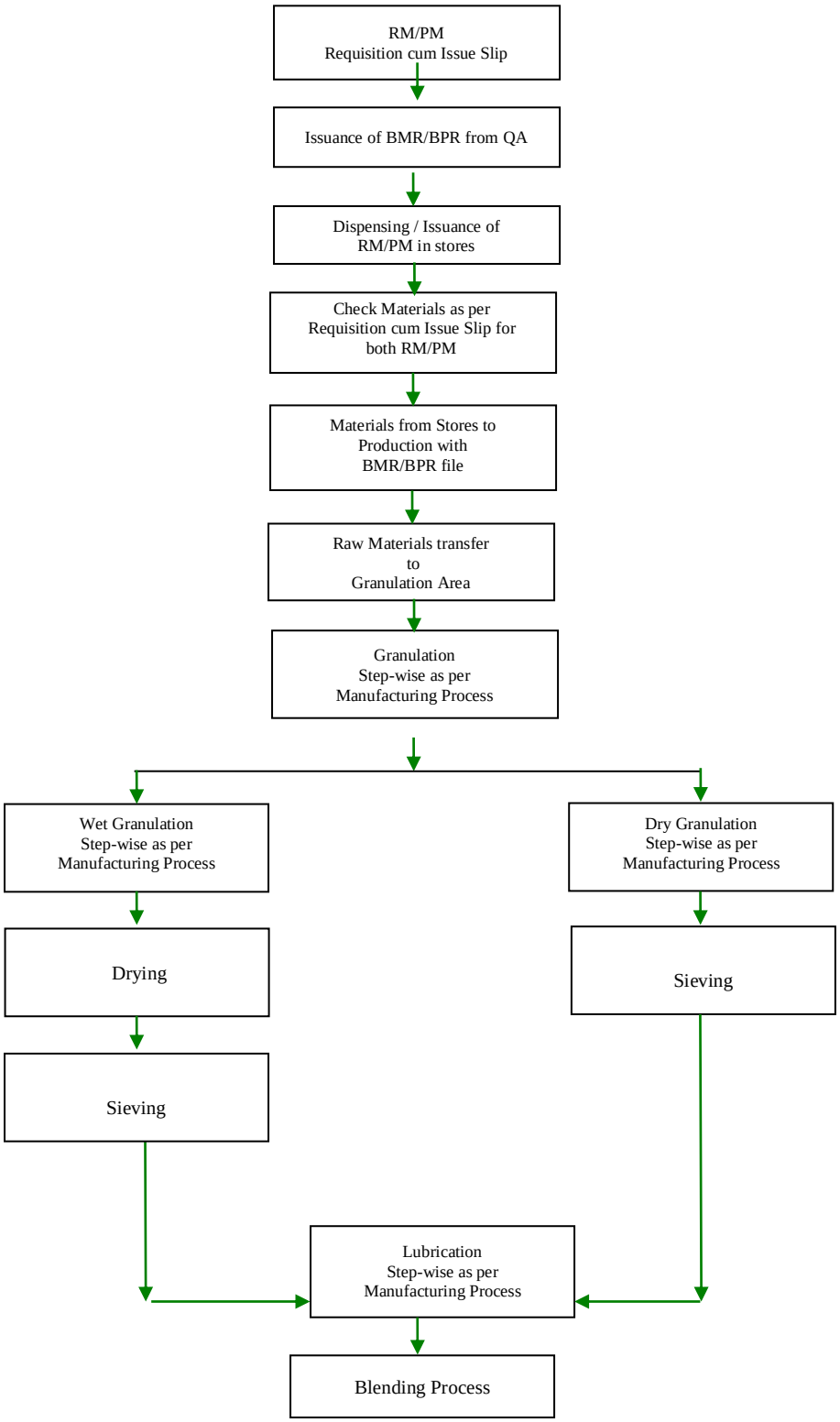
4.0 PROCESS FLOW DIAGRAMS

……meets the requirements of schedule M of the drugs and cosmetics act, 1940 of India, WHO and PIC/s guidelines with respect to current Good manufacturing practices. According to these regulatory guidelines the flow of material shall be so specific and accurate so that the risk of cross contamination and mix ups shall be zero.

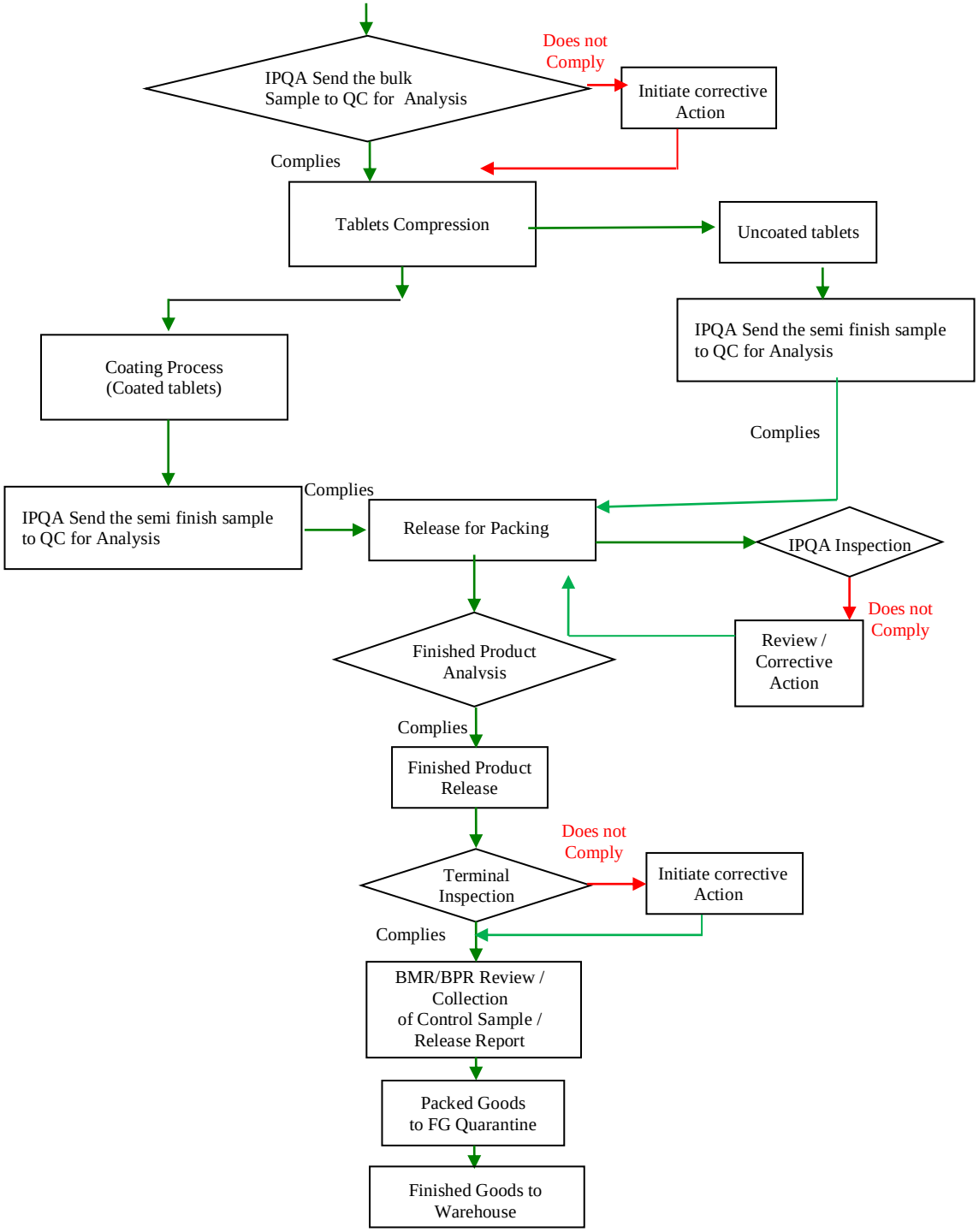
There shall be separate flow of materials for all the dosage forms which are to going to be manufactured with in the premises. The different dosage forms are:

- Manufacturing Process Flow Chart For General Tablets
- Manufacturing Process Flow Chart For General Capsules
- Manufacturing Process Flow Chart For General of Liquid Vials (Injections)
- Manufacturing Process Flow Chart General Ampoules (Injection)
- Manufacturing Process Flow Chart For General Vials (Dry Powder Injection)

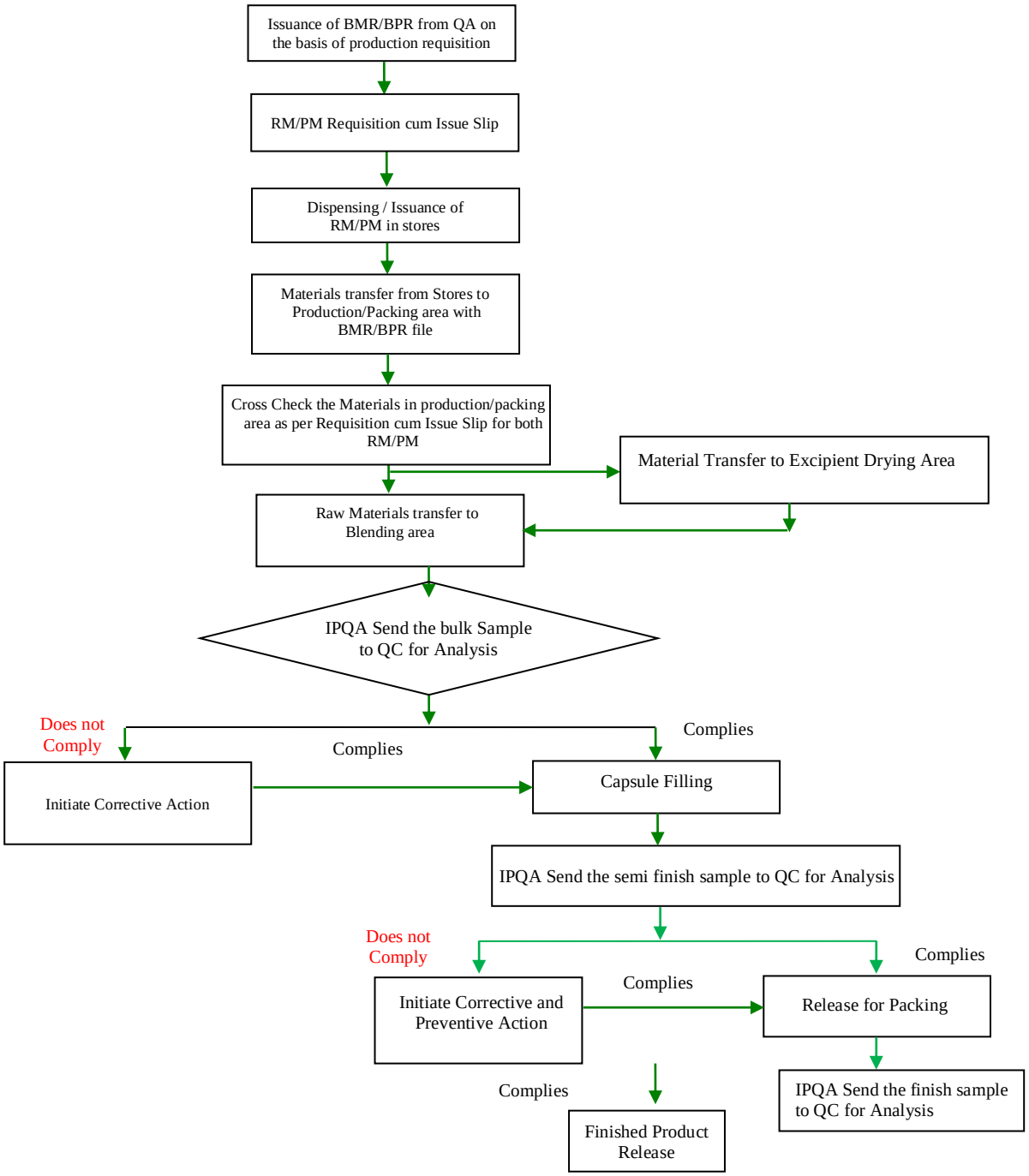
4.1 MANUFACTURING PROCESS FLOW CHART FOR GENERAL TABLETS.



Continued

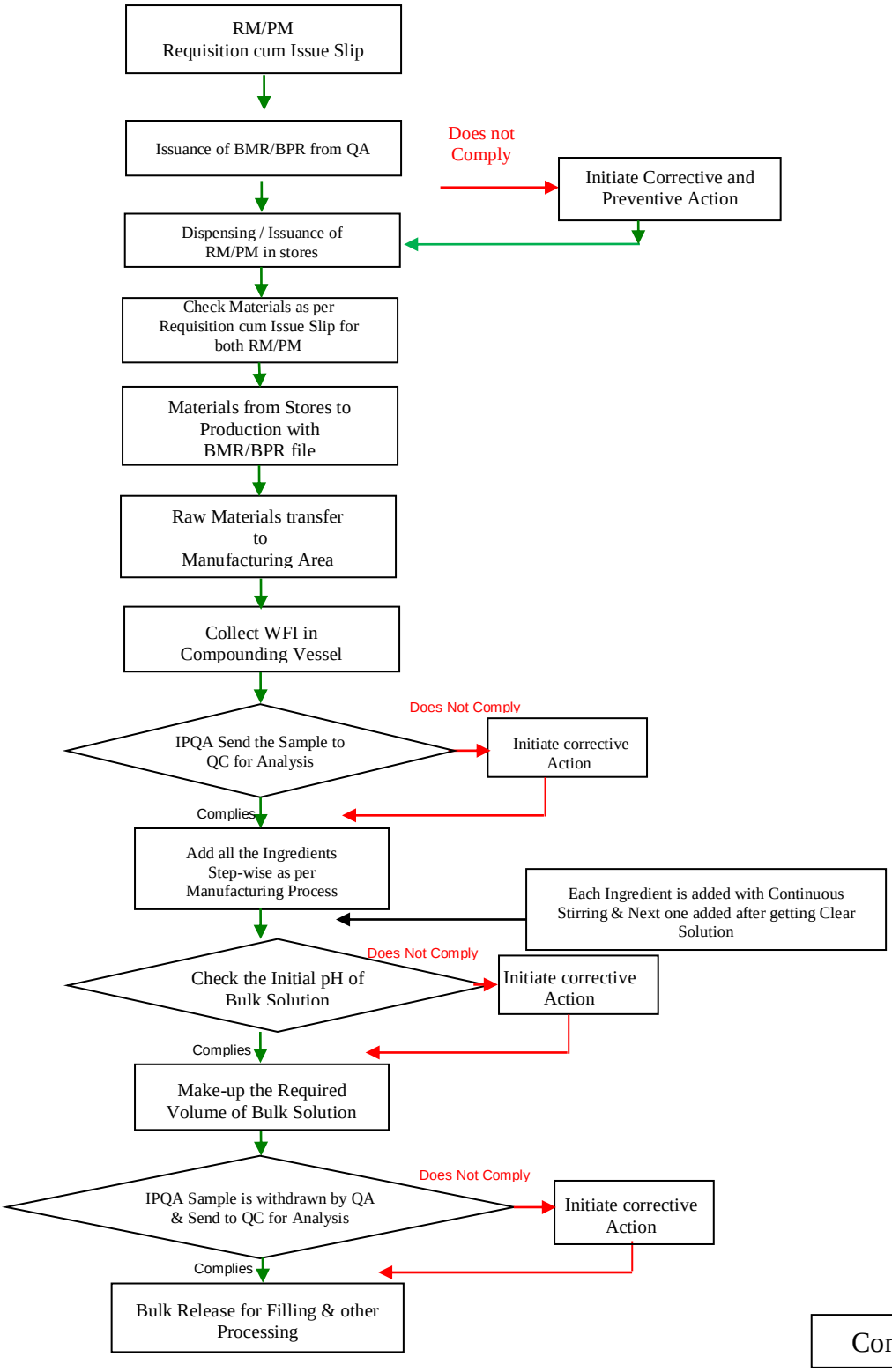

IPQA Send the bulk Sample to QC for Analysis
Does not Comply
Initiate corrective Action
Complies
Tablets Compression
Uncoated tablets
IPQA Send the semi finish sample to QC for Analysis
Coating Process (Coated tablets)
Complies
IPQA Send the semi finish sample to QC for Analysis
Complies
Release for Packing
IPQA Inspection
Does not Comply
Review / Corrective Action
Finished Product Analysis
Complies
Finished Product Release
Does not Comply
Terminal Inspection
Initiate corrective Action
Complies
BMR/BPR Review / Collection of Control Sample / Release Report
Packed Goods to FG Quarantine
Finished Goods to Warehouse

4.2 MANUFACTURING PROCESS FLOW CHART FOR GENERAL CAPSULES

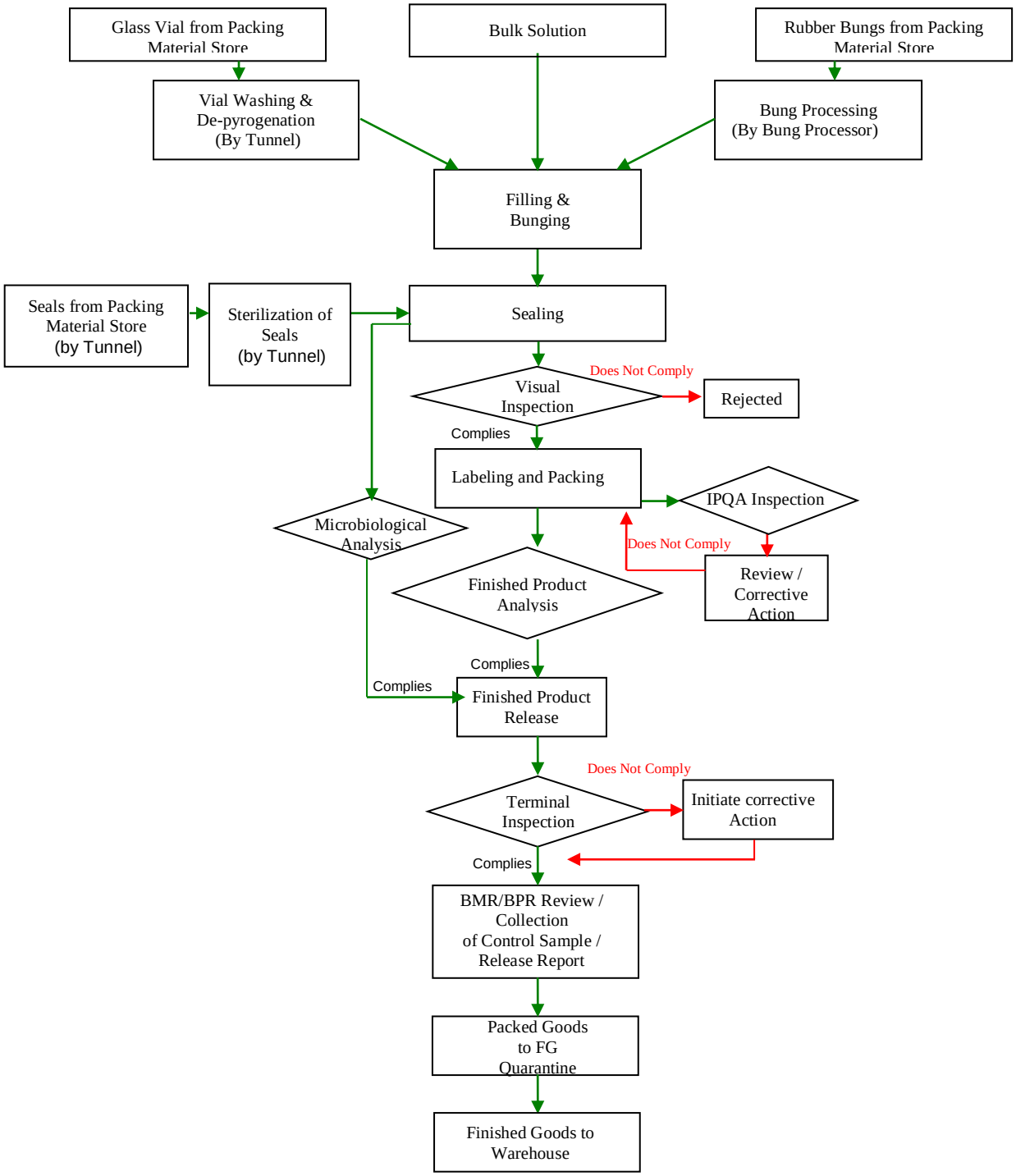


Continued.....

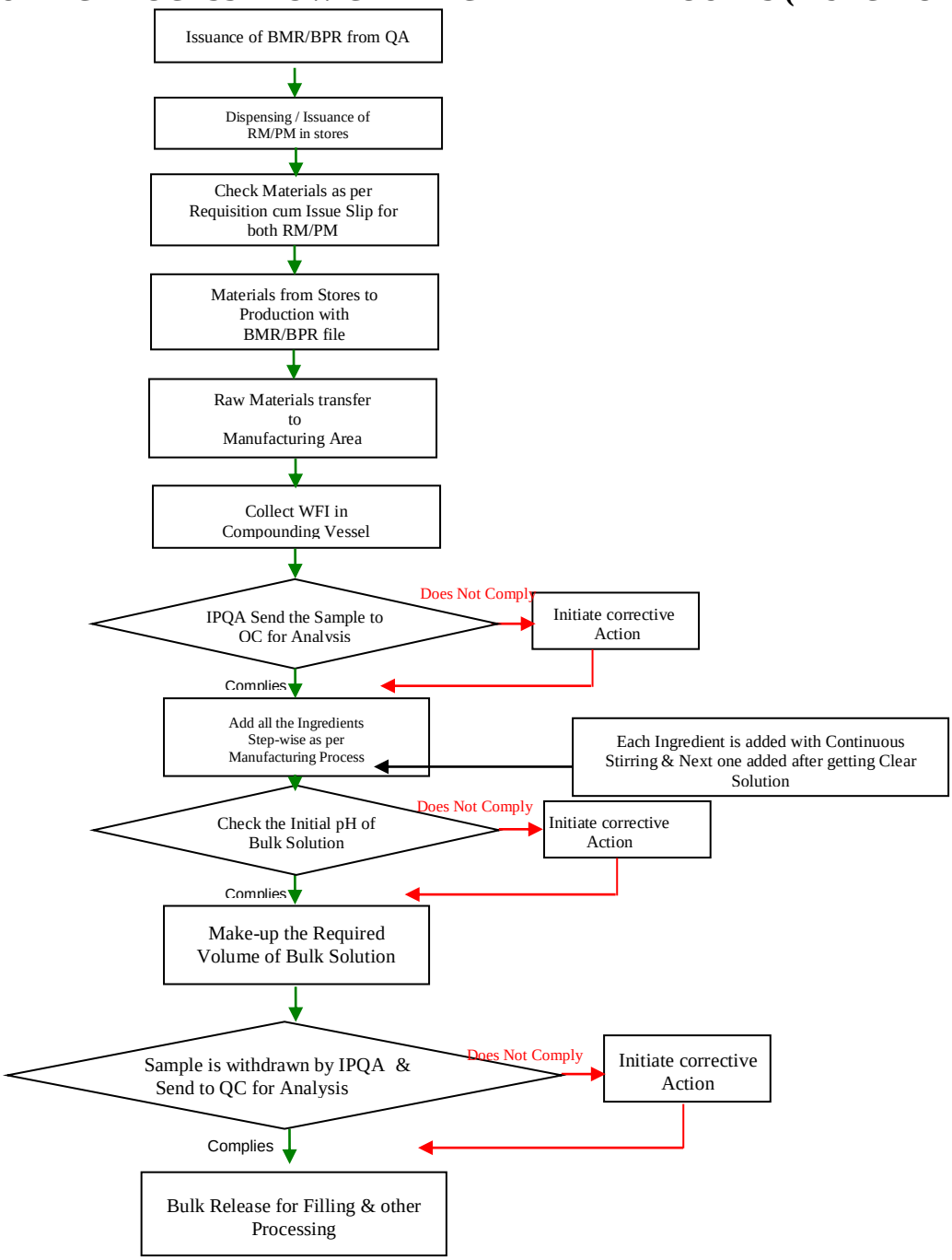
4.3 MANUFACTURING PROCESS FLOW CHART FOR GENERAL LIQUID VIALS (INJECTIONS)



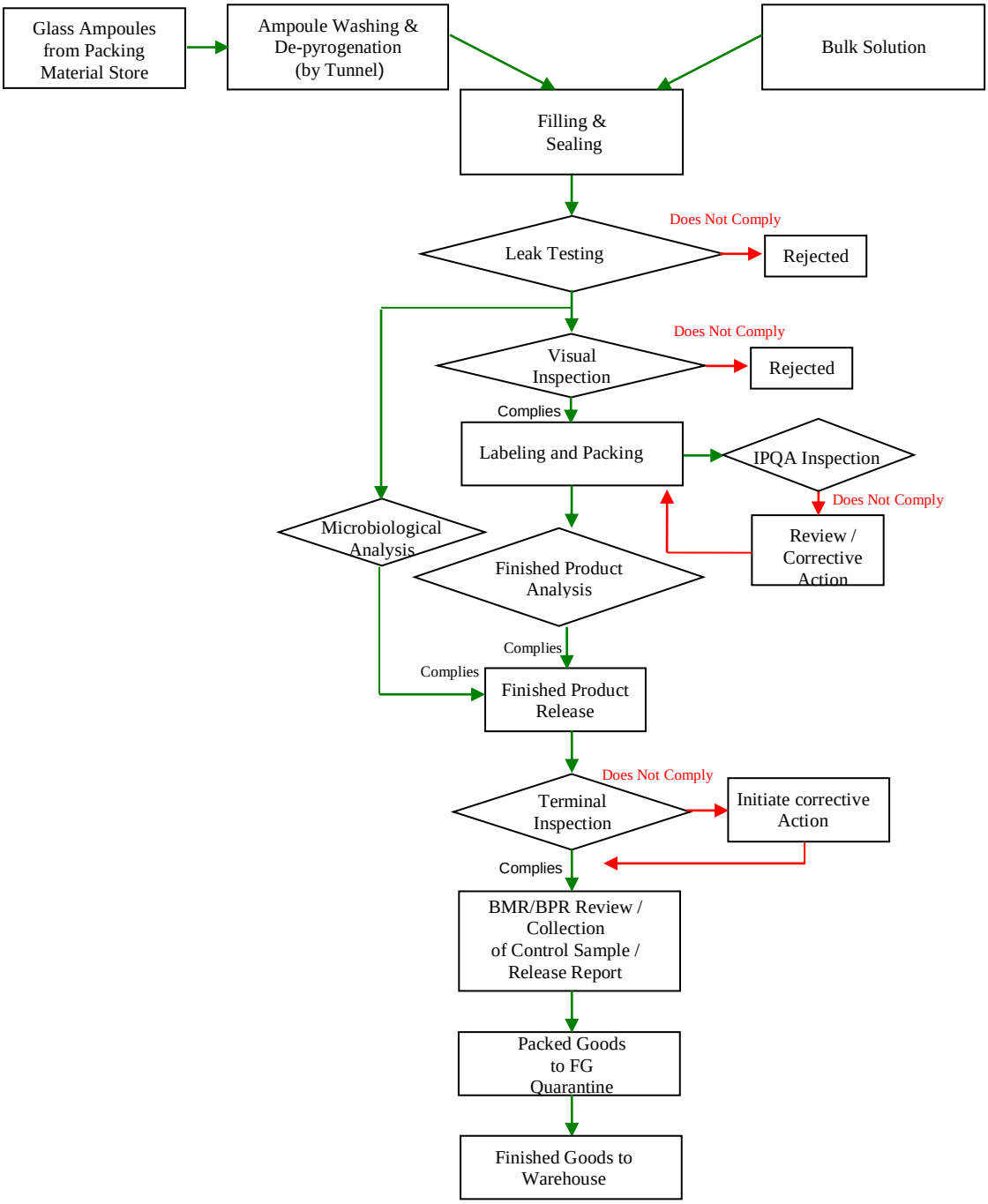
Continued


Glass Vial from Packing Material Store
Bulk Solution
Rubber Bungs from Packing Material Store
Vial Washing & De-pyrogenation (By Tunnel)
Bung Processing (By Bung Processor)
Filling & Bunging
Seals from Packing Material Store (by Tunnel)
Sterilization of Seals (by Tunnel)
Sealing
Visual Inspection
Does Not Comply
Rejected
Complies
Labeling and Packing
IPQA Inspection
Microbiological Analysis
Does Not Comply
Review / Corrective Action
Finished Product Analysis
Complies
Complies
Finished Product Release
Does Not Comply
Terminal Inspection
Initiate corrective Action
Complies
BMR/BPR Review / Collection of Control Sample / Release Report
Packed Goods to FG Quarantine
Finished Goods to Warehouse

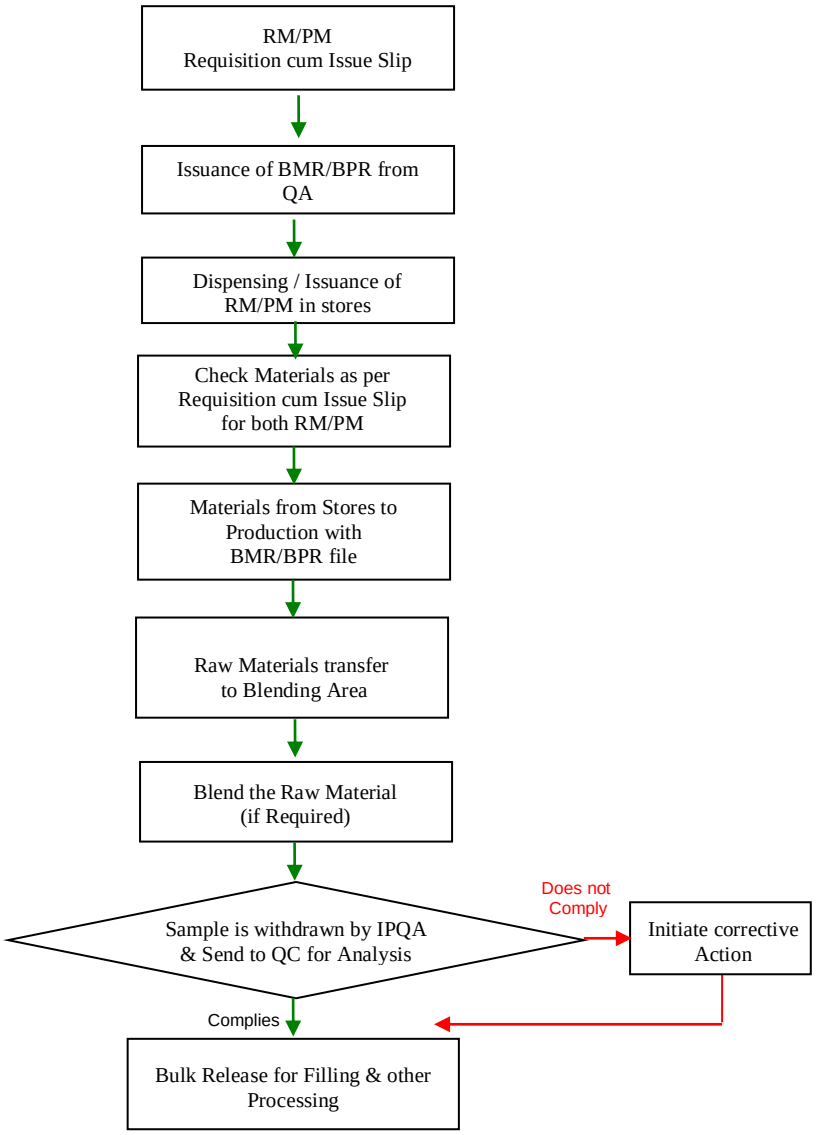
4.4 MANUFACTURING PROCESS FLOW CHART GENERAL AMPOULES (INJECTION)



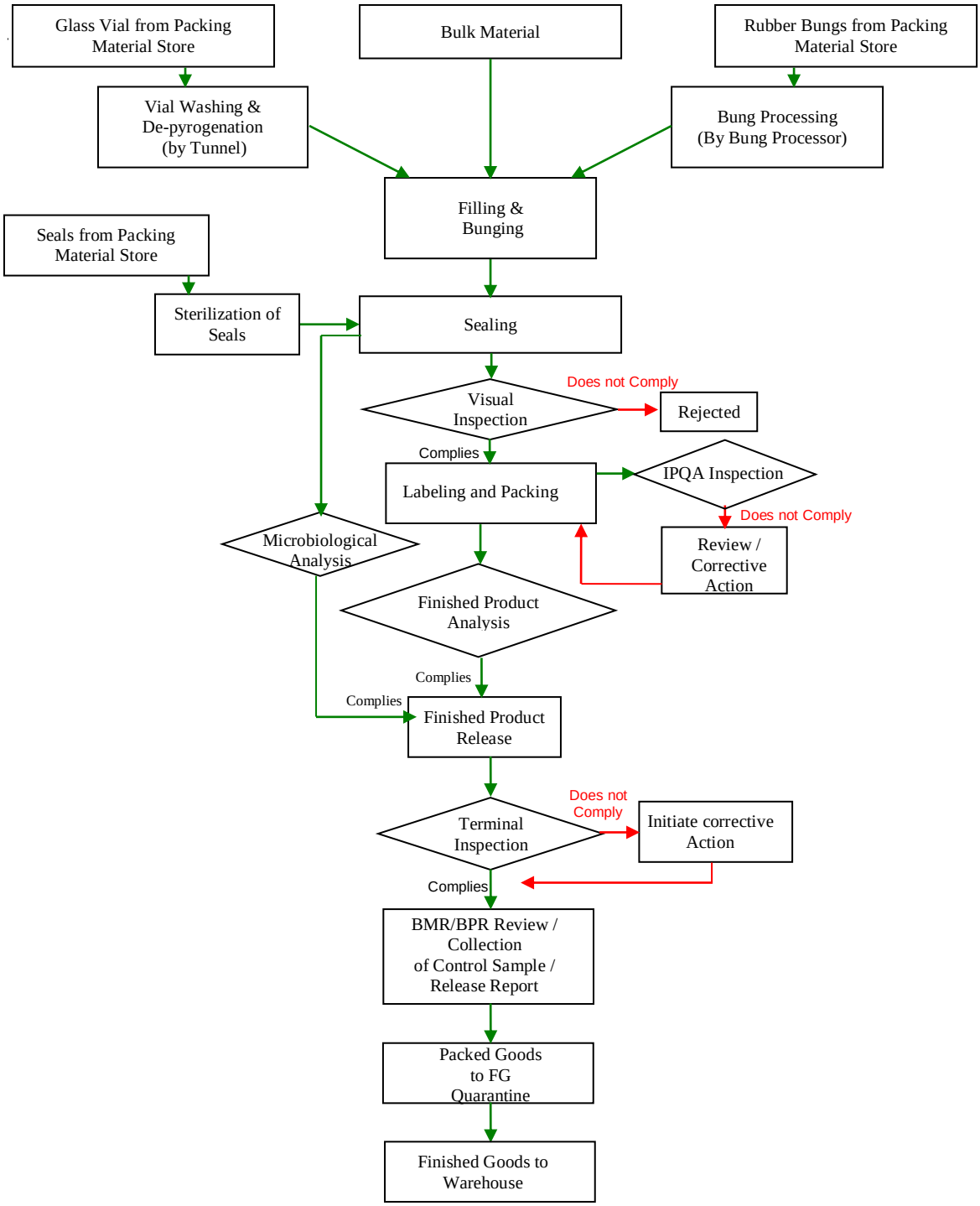
Continued


Glass Ampoules from Packing Material Store
Ampoule Washing & De-pyrogenation (by Tunnel)
Bulk Solution
Filling & Sealing
Leak Testing
Does Not Comply
Rejected
Visual Inspection
Does Not Comply
Rejected
Complies
Labeling and Packing
IPQA Inspection
Does Not Comply
Review / Corrective Action
Microbiological Analysis
Finished Product Analysis
Complies
Complies
Finished Product Release
Terminal Inspection
Does Not Comply
Initiate corrective Action
Complies
BMR/BPR Review / Collection of Control Sample / Release Report
Packed Goods to FG Quarantine
Finished Goods to Warehouse

4.5 MANUFACTURING PROCESS FLOW CHART FOR GENERAL VIALS (DRY POWDER INJECTION)



Continued


Glass Vial from Packing Material Store
Bulk Material
Rubber Bungs from Packing Material Store
Vial Washing & De-pyrogenation (by Tunnel)
Bung Processing (By Bung Processor)
Filling & Bunging
Seals from Packing Material Store
Sterilization of Seals
Sealing
Visual Inspection
Does not Comply
Rejected
Complies
Labeling and Packing
IPQA Inspection
Does not Comply
Review / Corrective Action
Microbiological Analysis
Finished Product Analysis
Complies
Complies
Finished Product Release
Terminal Inspection
Does not Comply
Initiate corrective Action
Complies
BMR/BPR Review / Collection of Control Sample / Release Report
Packed Goods to FG Quarantine
Finished Goods to Warehouse

5.0 BASICS OF cGMP AND INTRODUCTION TO SCHEDULE M

5.1 Fundamentals of GMP

GMP is defined as "A part of quality assurance which is aimed at ensuring that products are consistently manufactured to a quality appropriate to their intended use".

cGMP is termed as "Quality and standards of a product is ever changing phenomenon and accordingly one has to modify, add and upgrade the practices to meet the challenges".

5.2 Why GMP

5.2.1 By following GMP, It can be assured that all our medicines meet the customer's requirements of safety and have the identity, strength, quality and purity characteristics that they are represented to possess.

5.2.2 It is impossible to test every unit that is manufactured and by merely testing, even repeatedly, the finished product samples the manufacturer is unable to guarantee the identity, strength, quality, purity and safety of the same. Hence by following GMP at every stage, the product quality shall be assured.

5.2.3 Quality is the most effective way of reducing costs and wasted time. The cost of rework, reappraisal, lacks of to detail and errors can, account for 20% or more of turn over in manufacturing operations.

5.2.4 GMPs are government regulations and controls, which are mandatory.

5.2.5 Follow the GMP strictly and bring quality or harmless product (Zero Defect Product).

5.3 Requirements of GMP

5.3.1 Manufacturing and quality control facilities.

5.3.2 Sanitation and Hygiene

5.3.3 Control of raw and packaging materials

5.3.4 Control of manufacturing process including minimization of contamination.

5.3.5 Control of finished products

5.3.6 Documentation

5.3.7 Complaints

5.4 Ten Golden Rules of GMP

5.4.1 Be sure that the written instructions are correct before starting any job.

5.4.2 Always follow the written instructions EXACTLY with no "cutting corners" and ask if not clear.

5.4.3 Ensure that the correct equipment is being used and it is cleaned.

5.4.4 Prevent contamination and mix-up.

5.4.5 Always guard against labeling errors.

5.4.6 Always work accurately and precisely

5.4.7 Keep yourself and surroundings clean and tidy.

5.4.8 Always be on the look out of mistakes, error and bad practices and report them immediately ("Covering-up could cost lives").

5.4.9 Make clear and accurate records of what has been done, and the checks carried-out.

5.4.10 Make regular audits for compliance and performance.

5.5 Description of Schedule M

Schedule M is one of the schedules of drug and cosmetic Act-1940, under notification of Government of India in the ministry of health and family welfare (Department of health)

- Schedule M is having the guidelines for "Good Manufacturing Practices and Requirements of premises, plant and equipment for pharmaceutical products".
- Schedule M is divided into two parts

  - **Part-I** contains "**Good manufacturing Guidelines for Premises and materials**".
  - **Part-II** "**Requirements of plant and Equipment**".

- **Part-I is further categorized into following parts as described below:**
  - Part-IA –Specific requirements for manufacture of sterile products, parental preparation (Small Volume Injectable and large Volume Parental) and sterile ophthalmic preparation.
  - Part-IB – Specific requirements for manufacture of oral solid dosage forms (Tablet and Capsule).
  - Part-IC – Specific requirements for manufacture of oral liquids (Syrups, Elixirs, Emulsions and Suspension).
  - Part-ID – Specific requirements for manufacture of Topical products i.e. External Preparations (Creams, Ointments, Pastes, Emulsions, Lotions, Solutions, Dusting Powders and Identical Products).
  - Part-IE – Specific requirements for manufacture of METERED- DOSE INHALERS (MDI).
  - Part-IF – Specific requirements of Premises, Plant and Materials for Manufacture of Active Pharmaceutical Ingredients (API).

- Part-II contains the recommendations for the equipment required for various plants as stated in part I.

Following modules are described in schedule M

5.6 Building Facilities and Equipment

5.6.1 Building and Facilities

5.6.1.1 Any building or buildings used in the manufacture, processing, packing or holding of a drug product shall be of suitable size, construction and location to facilitate cleaning, maintenance, and proper operations.

5.6.1.2 Building shall have adequate space for the evenly placement of equipment and materials to prevent mix-ups between different components, drug product containers, closures, labeling, in-process materials, or drug products and to prevent contamination.

5.6.1.3 Location of services like water, steam, gases etc. shall be such that their servicing or repair shall not pose any threat to the integrity of the facility. Water lines shall not pose any threat of leakage to manufacturing area.

5.6.1.4 Operation relating to the manufacture, processing, and packing of penicillin shall be performed in facilities separate from those for other drug products.

5.6.1.5 Walls, floors and ceiling should be impervious, non-shedding, non-flaking and non-cracking. Flooring shall be unbroken and provided with a cove both at the junction between the wall and the floor as well as the wall and the ceiling.

5.6.1.6 Separate and adequate washing facilities shall be provided, including hot and cold water, soap or detergent, air dryers or single-single towels, and clean toilet facility shall be easily accessible to working areas.

5.6.1.7 Doors shall be made of non-shedding material preferably aluminum or steel.

5.6.1.8 Doors shall open towards the higher pressure areas so that they close automatically due to air pressure.

5.6.1.9 Windows shall be made of similar material as the doors, preferably with double panel and shall be flush with the walls.

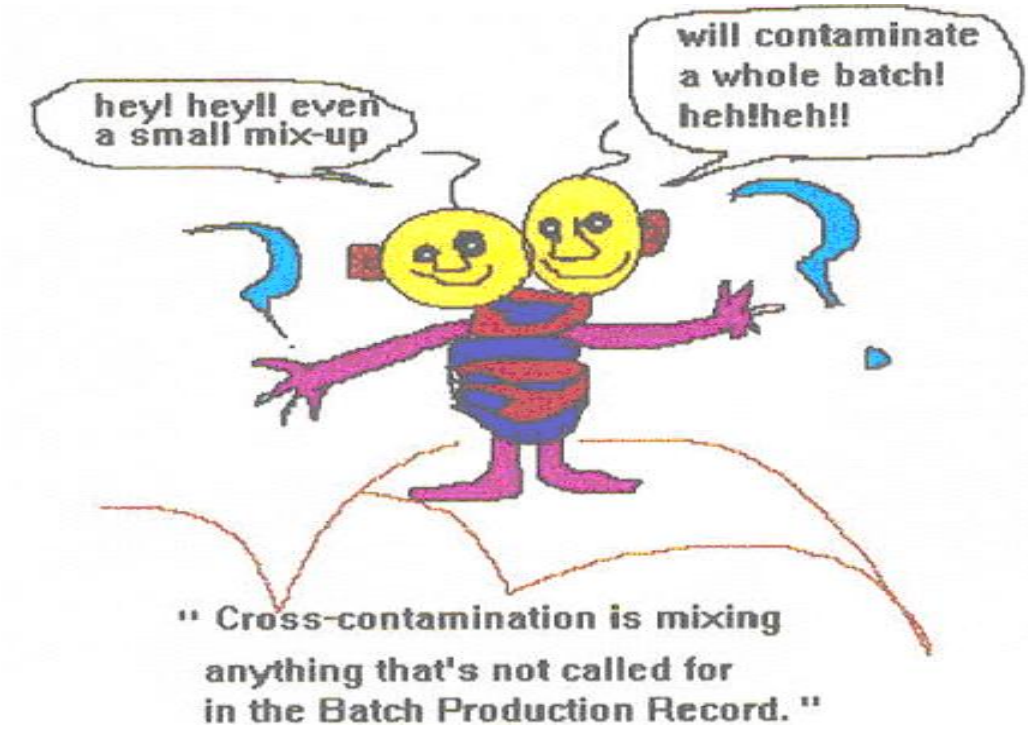
5.6.1.10 The furniture used shall be smooth, washable and shall be made of stainless steel.

5.6.1.11 A building shall be free of infestation by rodents, birds, insects and other vermin other than laboratory animals.

5.6.1.12 For communication between adjacent areas, intercom telephones, speak phones shall be used. These shall be minimum in number.

5.6.1.13 Adequate lighting and air ventilation shall be provided.

5.6.1.14 Air handling systems for the manufacture, processing and packing of penicillin shall be completely separate from other drug products.



5.6.2 **Equipment**

5.6.2.1 Equipment shall be located, designed, constructed and maintained to suit the operations to be carried out.

5.6.2.2 The layout and design of the equipment shall aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross contamination, build-up of dust or dirt and any adverse effect on the quality of products.

5.6.2.3 Each equipment shall be provided with a log book, recording all the important parameters required by the SOP or guidelines.

5.6.2.4 All measuring equipment shall be of an appropriate range, accuracy and precision as per the requirement of the respective areas.

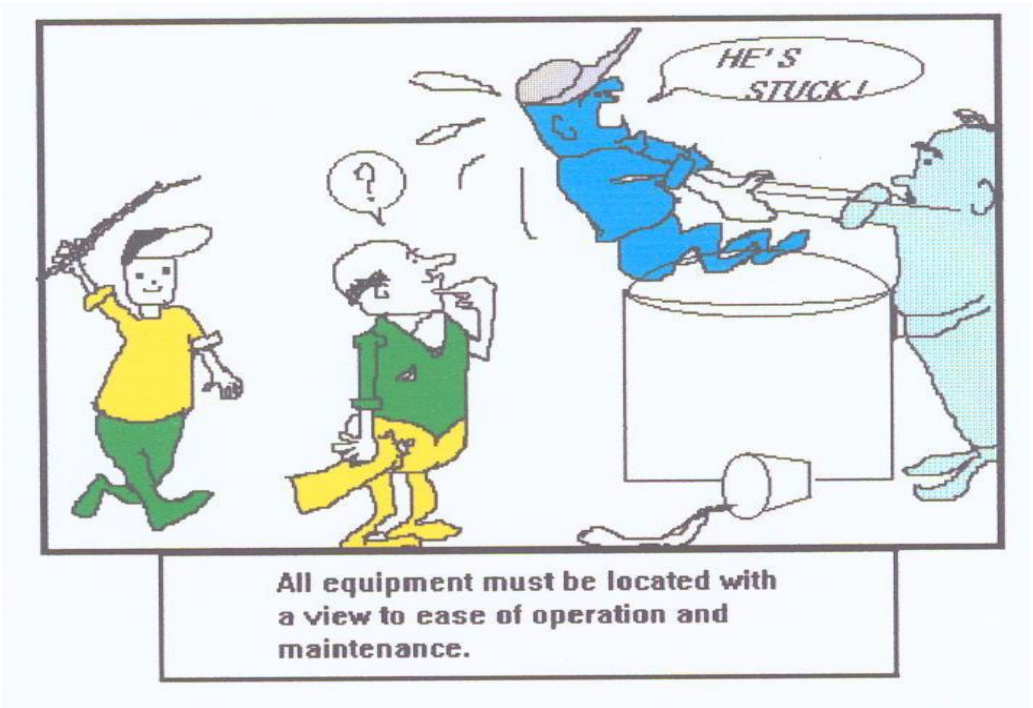
5.6.2.5 The parts of the equipment that come in contact with the product shall not be reactive, additive or absorptive to an extent that shall affect the quality of the product.

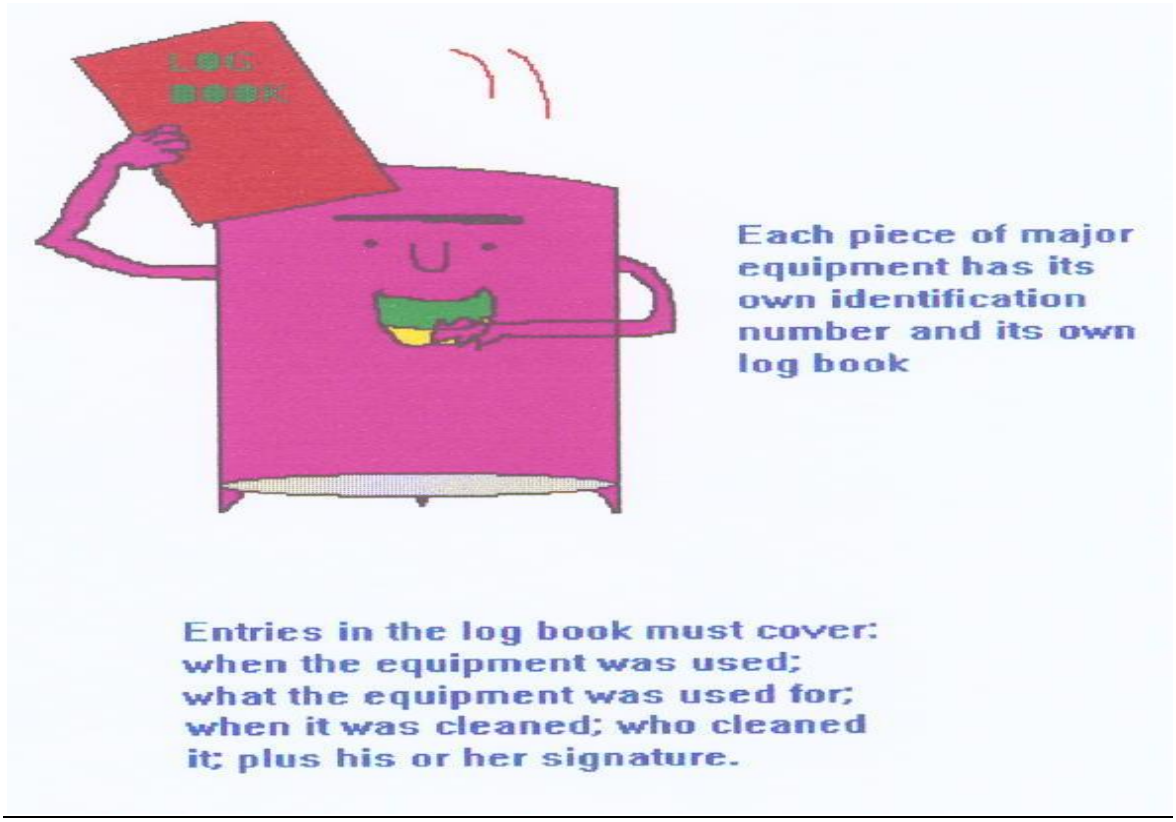
5.6.2.6 To avoid accidental contamination, non toxic/edible grade lubricants shall be used and the equipment shall be maintained in a way that lubricants do not contaminate the products.

5.6.2.7 Defective equipment shall be removed from the manufacturing area and Quality Control Department or properly labeled.

5.6.2.8 Proper Preventive maintenance program and its recording shall be maintained regularly.

Part numbers shall be given to each smallest possible part of equipment





5.7 Sanitation and personnel Hygiene

5.7.1 The personnel are the most important asset of an organization.

5.7.2 The establishment and maintenance of a satisfactory system of quality assurance and GMP relies upon people who develop the system, the people who use the system and the people who examine the system to see if it has worked.

5.7.3 People are involved, no matter how automated the process or how capital intensive the operation.

5.7.4 The behaviour of the people is fundamental to any system of GMP.

5.7.5 Sufficient number of staff must be available to carry out the work for which the manufacturer is responsible.

5.7.6 These people must have the level of training and experience that will enable them to do their work.

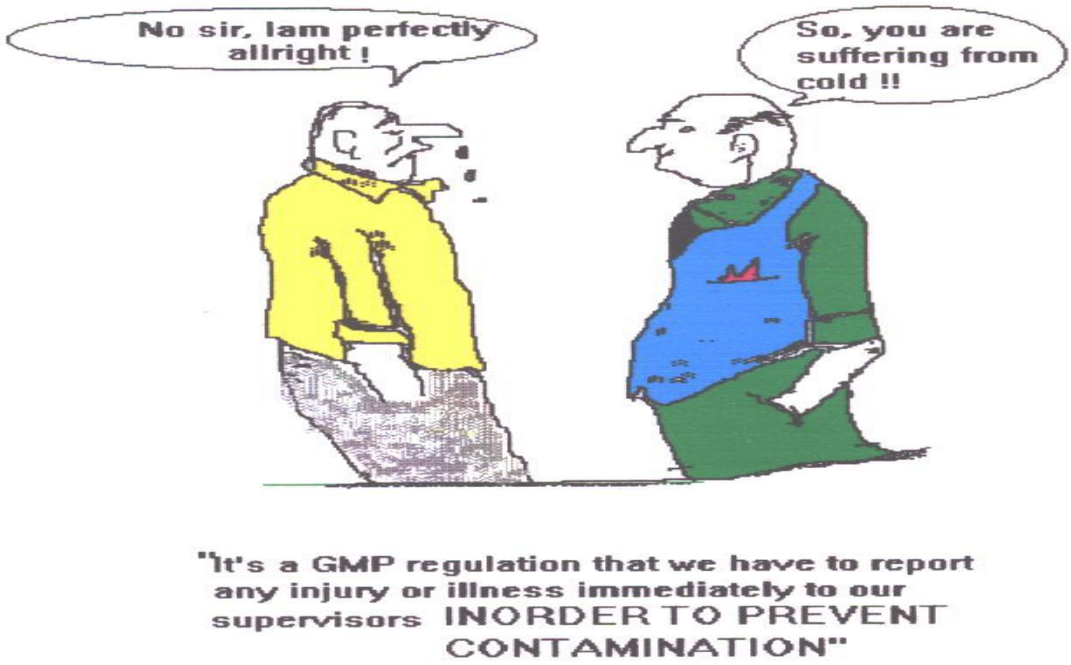
5.7.7 The staff must have written job descriptions to ensure that they understand clearly what it is that they have to do, and what they are responsible.

5.7.8 Personnel must have a knowledge and understanding of GMP to enable them to carry out their duties in accordance with GMP.

5.7.9 For successful and good quality pharmaceutical production, it is essential to have people with sufficient knowledge and experience.

5.7.10 They must have the authority and the means to do that work, and there must be enough of them available to carry out tasks effectively.

5.7.11 Operators working with cytotoxic products may need blood tests at the time of recruitment and at six monthly intervals thereafter. Operators who will work on visual inspection processes should also undertake an eye test at the time of recruitment with a regular check on a periodic basis afterwards.



5.7.12 There shall be proper division of work among the personnel depending upon there capabilities.

5.7.13 The company shall have a written organization chart.

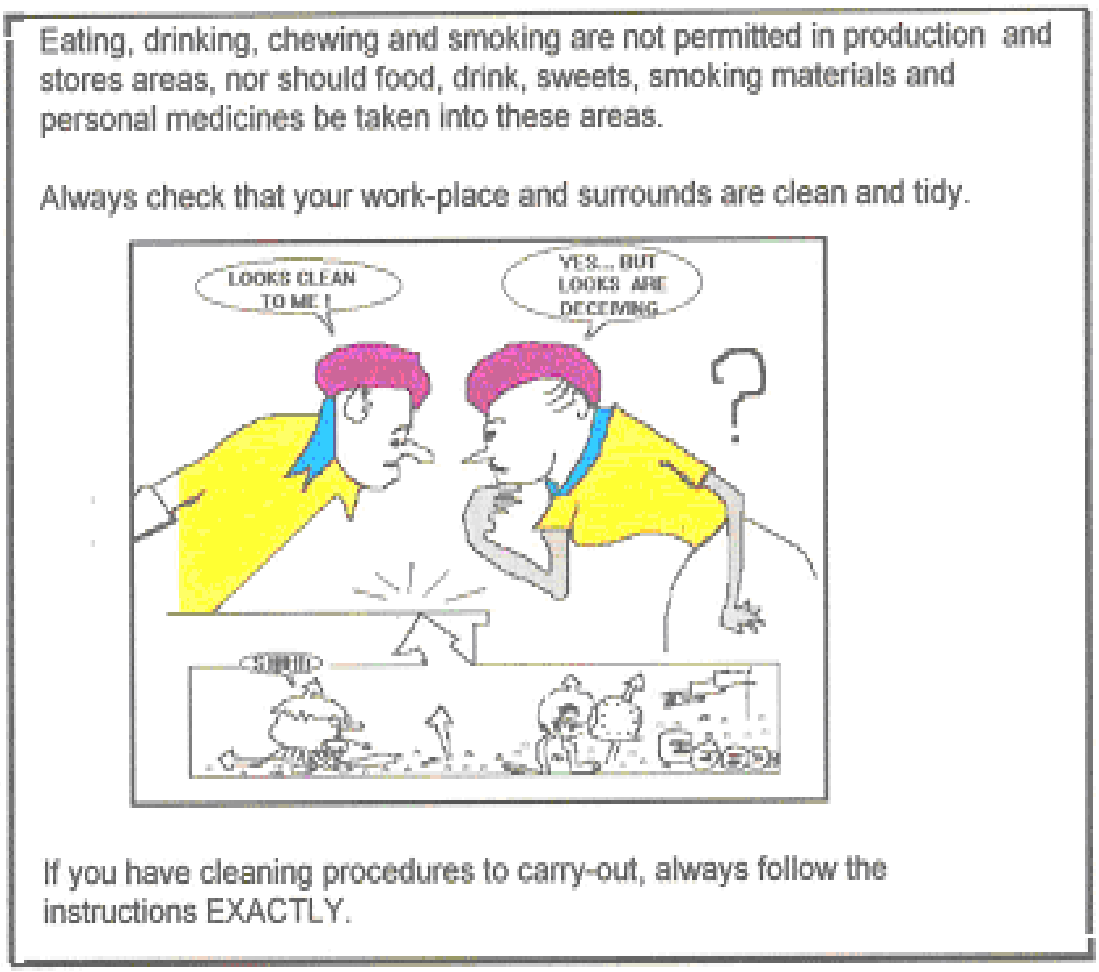
5.7.14 The combination of organization chart and written job descriptions enables the company to see quickly whether there are any gaps or whether there are any areas of overlap, owing to too many people being involved.

5.7.15 The organisation chart should make clear and ensure the independence of QA/QC from production.

5.7.16 All personnel involved with materials and products shall receive GMP training and GLP training for quality control department personnel. The training shall be appropriate to their needs and position within the company.

5.7.17 The heads of production, quality control, sales and distribution and the authorized person who releases product for sale are all **key personnel**.

5.7.18 **Key personnel** shall have the educational background specified by local legislation and with the requirements set out in company policy.



5.7.19 This shall include a combination of chemistry, biochemistry, chemical engineering, microbiology, pharmaceutical sciences and technology, pharmacology and toxicology, physiology or other related science subjects relevant to the responsibilities to be undertaken.

5.7.20 Engineers are crucial to the maintenance and operation of the facility and equipment, in particular, for the processes of planned preventative maintenance and validation.

5.7.21 Both production and quality control have a role to play in the development and maintenance of an appropriate factory **sanitation and hygiene** management system.

5.7.22 Both have a major contribution to make in the **validation** of processes and the calibration of equipment.

5.7.23 A comprehensive **training** programme is required for personnel. The production and quality control department have a role to play in the development of the training programme. The heads of these departments, therefore, have a shared responsibility for the implementation of that programme.

5.7.24 All training activities as per requirement shall ensure by Quality assurance.

5.8 Standard Operating Procedure (SOP)

A written authorised procedure which gives instructions for performing operations not necessarily specific to a given product or material, but of a more general nature the. Equipment operation; maintenance and cleaning; recall of products; purchasing; cleaning of premises and environmental control; sampling and inspection; etc.). Certain Standard Operating Procedures may be used to supplement the product-specific Master and Batch production documentation.

5.8.1 Standard Operating Procedure (SOP) is the internal document of any organization. SOP can be defined as "the detailed stepwise written procedure to a process".

5.8.2 The training of SOP is must and shall be imparted to all personnel for correct handling of machines, processes etc. and manufacturing of good quality products. The respective department head shall train the trainees as per the instructions written in SOPs and explains the need, objective, etc. of the SOP.

5.8.3 The trainer shall also explain the documentation required for verifying the SOP. There shall be written Standard Operating Procedures for all process related activity for all departments.

5.8.4 By following the instructions of SOP, the systems shall be smooth and chances of error is very less.

5.8.5 QA Department shall ensure that appropriate and technically valid standard operating procedures shall be established and followed, and approve all original and revised standard operating procedures.

5.8.6 A unique number has to be given to each and every SOP. The code and the number shall not be repeated again.

5.8.7 There shall be one principle SOP named as "SOP on SOP" shall be in place with all the details of preparing the other SOPs.

5.8.8 All SOPs shall only be approved by QA HEAD

5.8.9 In ……there are several departments like Capsules, Tablets, injection, QC, QA, Engineering, HR, and Store of each department shall have their own SOPs.

5.9 Batch Manufacturing Record (BMR) and Batch Packaging Record (BPR)

5.9.1 **Batch Manufacturing Record (BMR)**

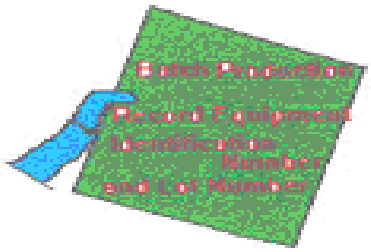
Batch Manufacturing Records shall be kept for each batch manufactured and shall carry a batch reference number and be based upon the currently approved version of the master formula and method. The method of preparation shall be designed to avoid transcription errors. Photo copying or some similar method of preparing the basic document is to be preferred.

If batch manufacturing records do not include complete details of the method, the operator must have ready access to the currently approved method.

Before any manufacture proceeds there shall be recorded checks that the equipment and work-station are clear of previous products and documents and of materials not required for the process in hand and that equipment is clean and suitable for use.

During manufacturing the following shall be entered onto the batch manufacturing records, at the time that each action was taken and, after completion, the record shall be dated and signed in agreement by the person responsible for processing operations:

- After planning of the batch to be processed, a requisition shall be generated for issuance of BMR by the authorized person of respective area to QA Department, supplying all the relevant information of the batch to be processed.
- Then QA shall issue the BMR to respective department on the basis of the requisitions.
- Every BMR has a unique number and that number shall not be repeated for any other product's BMR.
- The line clearance report of the all machine shall be attached to BMR before starting the processing of new product for the checking availability of previous product.
- During processing following information shall be recorded at the time of each action taken and record shall be dated and signed by the person responsible for the operation.



1. The batch identifying number of each of the starting materials used and the amount used.

2. The quantity of starting material, a record of the amount actually used.

3. Dates of commencement and completion of manufacture and of significant intermediate stages.

4. Where more than one batch of a given starting material is used, a record of the actual amount of each batch.

5. The batch identifying number and amount of any recovered or re-work material added and at what stage of the manufacturing process it was added to the mix.

6. The initials of the person(s) who weighed or measured each material and the initials of the person(s) who checked each of these operations, this check being not only of the quantity but also of the labelled identity and batch number of the material.

7. Critical steps such as weighing, measuring and 'adding to the mix' shall be checked and signed for

by a pharmacist (Production) and verified by QA.

8. The amount of product obtained at pertinent intermediate stages of manufacture.

9. The initials of the person responsible for each critical stage of manufacture.

10. The results of all in-process controls, with the initials of the person(s) carrying them out.

11. Reference to the precise items of major equipment used, where several of the same type are available for use (i.e. where equipment is replicated). This information may be recorded in **'Equipment Log Book'**. A cross-reference to this should be included in the batch manufacturing record [BMR].

12. Details of, and signed authorisation for, any deviation from the master formula and method.

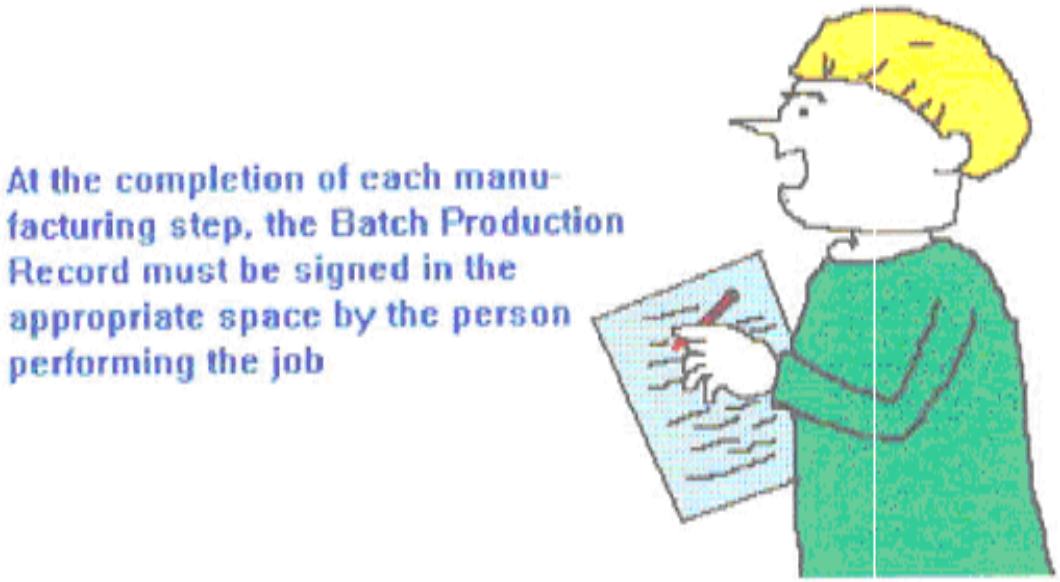
13. The final batch yield and the number of bulk containers.

14. Signed agreement by the process supervisor that apart from any deviation noted in above, manufacture has proceeded in accordance with the master formula and method, and that process or yield variations are adequately explained.

Before any manufacturing begins :-

1. A "lot" number is assigned to the product to be manufactured.

2. All of the equipment to be used must be properly cleaned and maintained. Records of maintenance and cleaning must be kept.



5.9.2 Batch Packing Record (BPR)

Batch packaging records shall be kept for each batch or part-batch processed and shall be based upon the currently approved version of the master packaging instruction and prepared from it by a method designed to avoid transcription errors (photocopying or some similar method is to be preferred). The Record shall carry the quantity of bulk product to be packed, the planned quantity of finished product and shall bear a batch reference number, which is specific to a particular packaging run. The batch number which appears on the finished product shall be this number, or one which may be easily related to it.

The bulk product and packaging reference numbering system must make it possible to relate a packaging operation to a bulk batch and the bulk batch to any packaging operation(s).

Before any packaging is undertaken checks shall be made that each packaging line or station is clear of previous product, packaging components records or materials not required for the planned packaging operations, and that equipment is clean and suitable for use. These checks shall be recorded and each packaging line opened and closed by a pharmacist, other legally authorised person or quality control.

During packaging, the following shall be entered onto the batch packaging records, at the time that each action is taken:

1. The batch number and expiry date of the bulk product to be packaged.

2. Dates and times of commencement and completion of packaging and of significant intermediate stages.

3. The initials of the person(s) who issued the bulk product and printed packaging materials and of the person(s) who confirmed their correct identity and quantity

4. The identity of the bulk product and printed packaging material shall be checked and signed for by a pharmacist (Production and QA).

5. The batch over-coding details shall be approved from QA

6. The total quantities of the packaging materials used, with a batch identifying reference to primary and printed packaging materials (specimens of printed packaging materials used including specimens of the overprinting shall be attached, or alternatively there shall be an arrangement which will permit later reference to specimens of the printed packaging materials used).

7. The results of any in-process controls, together with the initials of the person responsible for carrying them out.

8. The initials of the persons who carried out each significant stage of the packaging operation.

9. A record of the packaging machines, line or area used.

10. Records shall be kept of the amount of bulk product supplied, printed materials issued and finished packs produced and reconciliations performed where required.

11. Notes on any special problems including details of any deviations from the packaging instructions with written authorisation by an appropriate person shall be kept.

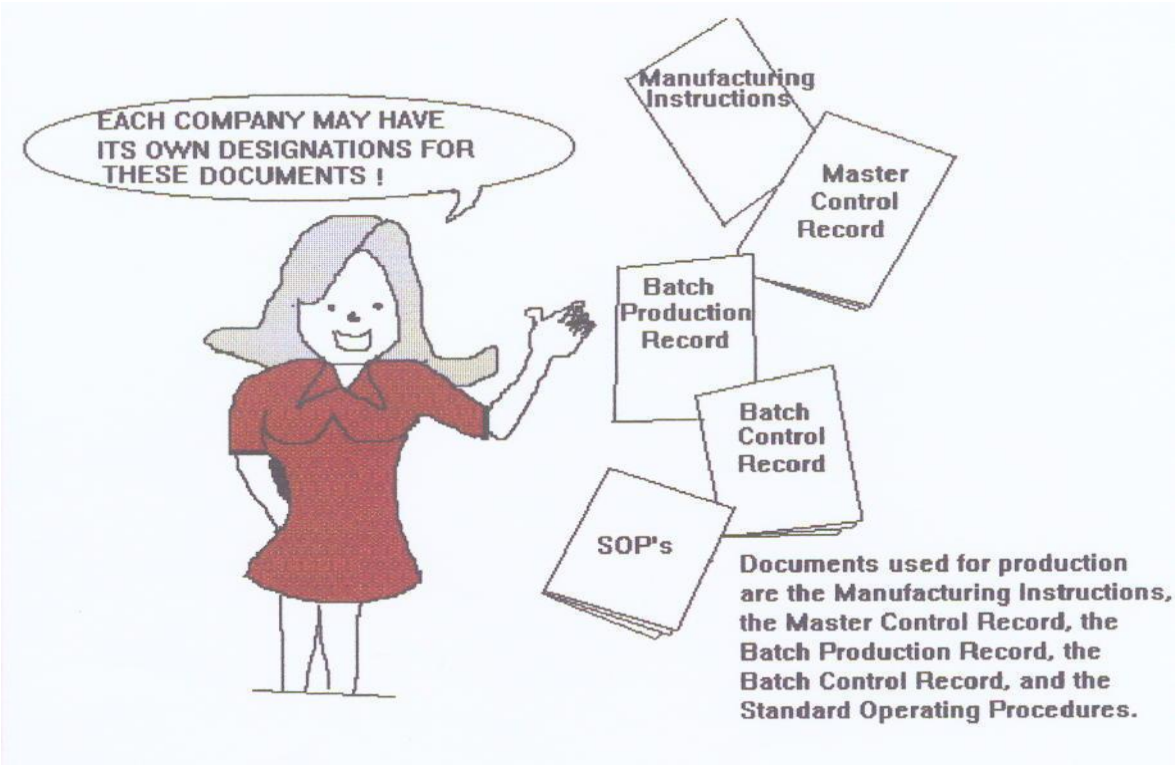
5.10 Documentation

Documentation is an essential part of the quality assurance system. Its purposes are to define the system of control, to reduce the risk of error inherent in purely oral communication, to ensure that personnel are instructed in the details of, and follow, the procedures concerned, and to permit investigation and tracing of defective products. The system of documentation shall be such that the history of each batch of product, including the utilisation and disposal of starting materials, packaging materials and intermediate, bulk and finished products, may be determined.

There shall be authorised (signed and dated) specifications for raw materials, master formula of the product, manufacturing method, printed packaging material, final product specification, in process tests, test methods and packaging material.

Master documents should be authorised, and the name of the applicant or holder of a registration certificate shall be visible. Master documents should be kept at the registered premises of the applicant or holder of the registration certificate. Master documents shall be properly controlled, and access thereto limited.

There shall be a written procedure for updating of master documentation and the system shall endure that current, approved master documentation is being used. A formal system shall be in place to control changes to master documentation. Changes to master documents shall be communicated to the appropriate departments and written approval prior to implementation of changes shall be obtained from the regulatory authority where applicable.



5.10.1 Preparation, Issue and Control of Documents

To facilitate proper and effective use, documents shall be designed and prepared with care, and with particular attention to the following points:

1. The company's name, the title (which shall be unambiguous), nature and purpose of the document shall be clearly stated. The document shall be laid out in an orderly fashion, and be easy to check. Each page shall be sequentially numbered. Where a document has been revised, systems should exist to prevent inadvertent use of superseded documents.
2. The way the document is to be used, and by whom, shall be clearly apparent from the document itself.
3. Documents bear instructions, they shall be written in the imperative as numbered steps. They shall be clear, precise, and unambiguous and in a language the user can understand. Such documents shall be readily available to all concerned with carrying out the instructions.
4. Documents which require the entry of data should:
   - Provide sufficient space for the entry.
   - Allow adequate spacing between entries.
   - Show headings clearly indicating what is to be entered.
5. Persons making entries shall do so in clear legible writing, and shall confirm the entry by adding their initials or signatures. Ticking shall be avoided.
6. All entries should be made in ball pen or other indelible medium.
7. The size and shape of documents and the quality and colour of the paper used shall be considered in relation to the typing / printing, reproduction and filing facilities available.

8. Reproduced documents shall be clear and legible. The reproduction of working documents from master documents must not allow any error to be introduced through the reproduction process. If working documents are computer generated these shall be checked against an authorised master and signed for correctness.

9. Documents shall contain all necessary, but no superfluous data. Any headings, or places for entries, which cease to be used shall be removed at the earliest opportunity.

10. Documents shall be approved, signed and dated by appropriate, competent and authorized persons.

11 Records shall be completed at the time each action is taken in such a way that all significant activities concerning the manufacture of medicinal products are traceable.

12. Data may be recorded by electromagnetic or photographic means, but detailed procedures relating to the system in use shall be available and the accuracy of the records shall be checked. If documentation is handled by electronic data processing methods, only authorised persons shall be able to enter or modify data in the computer; access shall be restricted by passwords or other means and entry of critical data shall be independently checked.
Batch records electronically stored shall be protected by back-up transfer on magnetic tape, microfilm, paper or other means. It is particularly important that, during the period of retention, the data can be rendered legible within an appropriate period of time.

13. If an error is made or detected on a document it shall be corrected in such a manner that the original entry is not lost and the correction initiated and dated. Where appropriate, the reason for the correction shall be recorded. No correction fluid shall be used.

14. Documents shall be kept up to date. Any amendments shall be formally authorised and signed. In the case of permanent amendments, the amended document shall be replaced at the earliest opportunity by a newly prepared document.

15. The documentation system shall include provision for regular review and revision as necessary.

16. An out-dated or superseded document shall be removed from active use. The marked "Superseded" copy shall be retained for reference purposes.

17. Master documents shall revise through change control procedures; systems shall exist to prevent inadvertent use of superseded documents.

18. Documents and other records, including original data such as laboratory notebooks shall be retained for at least one year after expiry date of the batch. Documents shall be easily retrievable.

5.11 Validation

Validation can be defined as "A documented evidence which provides a high degree of assurance that the process, product, equipment, batch is consistently produced and meeting the predetermined specification for their intended use".

A process is in a state of control when all the assignable causes of variation have been eliminated, only chance causes of variation are present. Such a process has thus been demonstrated to be capable of consistently delivering specified results, i.e. the process has been validated.

- Validation is an integral part of current good manufacturing practice; it is therefore, also an element of the quality assurance programme associated with a particular product or process.
- Validation involves the accumulation of documentary evidence relating to a process, item of equipment, or facility. This is achieved by means of a validation protocol which shall exist for every

product and which details the tests to be carried out, the frequency of testing, and the results anticipated (acceptance criteria).

- A validation programme shall be co-ordinated by a multidisciplinary committee comprised of the different functions that are involved in the programme. Typically, the members of this validation committee would be drawn from departments such as production, quality assurance, microbiological and analytical quality control, pharmaceutical development, engineering, and maintenance. The committee approves and issues written protocols, and reviews the data obtained in order to approve or reject the programme results.

5.11.1 Validation Master Plan (VMP)

The validation programme shall be co-ordinated by means of a formal policy document, usually referred to as a validation master plan (VMP).

Every organization shall have a validation master plan which describes its overall philosophy, intention and approach to be used for establishing performance adequacy, and which identifies which items are subject to validation and the nature and extent of such testing and the applicable validation and qualification protocols and procedures.

5.11.2 The Validation Protocol (VP)

The validation protocol shall clearly describe the procedure to be followed for performing validation.

The protocol shall include at least the objectives of validation and qualification study, site of the study, the responsible personnel, description of equipment to be used (including calibration before and after validation).

SOP's to be followed; standards and criteria for the relevant products and processes, the type of validation, and time/frequency should be stipulated.

The processes and/or parameters to be validated (e.g. mixing times, drying temperatures, particle size, drying times, physical characteristics, content uniformity etc.) shall be clearly identified.

5.11.3 The Validation Report (VR)

A written report shall be available after completion of the validation.

The results shall be evaluated, analysed and compared with acceptance criteria. All results shall meet the criteria of acceptance and satisfy the stated objective.

5.11.4 Qualification

Before a process can be validated the equipment, facilities, and services used in that process must be validated. Such an operation is referred to as qualification. Qualification is, therefore, an integral part of process validation which, in turn, is part of good manufacturing practice.

5.11.4.1 Installation qualification (IQ)

An installation qualification (IQ) protocol is used to document the specific (static) attributes of a facility or item of equipment, in order to prove that the installation of the unit has been correctly performed and that the installation specifications of the manufacturer have been met.

The IQ protocol shall be numbered, dated, and approved for issue by appropriately authorised personnel.

5.11.4.2 Operational qualification (OQ)

An operational qualification (OQ) protocol is used to document specific (dynamic) attributes of a facility or item of equipment to prove that it operates as expected throughout its operating range. As with the IQ protocol, to OQ protocol should be numbered, dated and formally approved.

The tests shall be designed to demonstrate that the unit performs properly at the limits of its operating conditions, as well and within its normal operating range. If measurements are made on a statistical basis, then this must be fully described in the protocol.

5.11.4.3 Performance qualification (PQ)

A performance qualification (PQ) protocol may be used in cases where performance data are gathered over a long period of time. Under these circumstances, it is difficult to "sign off" the operational qualification (OQ) as complete. One solution is to define and approve the OQ at a single point in time, and to create a PQ protocol which is then used as a vehicle for amassing the on-going data.

5.11.5 Process validation (PV)

When qualification is complete, process validation (PV) can begin. In some cases, PV may be conducted concurrently with IQ, for example, where an item of equipment is dedicated to one process producing one product. Process validation is organised and administered in the same way as qualification, by the writing and issuing of process validation protocols and the accumulation and review of data against agreed acceptance criteria.

Validation shall be considered in the following situations:

- Totally new processes
- New equipment
- Processes and equipment which have been altered to suit changing priorities
- Processes where the end product test if poor and an unreliable indicator of product quality

5.11.5.1 Prospective Validation (Validation during Development)

When any new manufacturing formula or method of preparation is adopted, steps shall be taken to demonstrate its suitability for routine processing by breaking the critical steps. The defined process, using the materials and equipment specified, shall be shown to yield a product consistently of the required quality.

In this phase the extent to which deviations from the chosen processing parameters can influence product quality should also be evaluated.

In general the final batch size should not be more than ten times the batch size of the representative development batches.

5.11.5.2 Concurrent validation (Validation during Production)

The validation in the production unit mainly comprises the determination and evaluation of the process parameters of the facilities applied for the scale-up to final batch size. The control of all critical process parameters, the results of the in-process controls, final controls and stability tests should prove the suitability of the important individual steps of a procedure.

At least three batches (including at least two production batches in the final batch size) shall be validated, to show consistency. Worst case situations shall also be considered.

5.11.5.3 Re-validation

Re-validation is as a rule required under the following circumstances:

- change of formulae, procedures or quality of raw materials
- change of equipment, installation of new equipment, major revisions to machinery or apparatus and breakdowns
- major changes to process parameters
- changes to facilities and installations which influence the process
- on appearance of negative quality trends
- on appearance of new findings based on current knowledge, e.g. sterilisation where the frequency of checking is dependent on sophistication of in-process methodology

5.11.5.4 Retrospective Validation

The analysis of in-process and end product testing has been widely used retrospectively in process validation. Usually statistical packages as well as manual reviews (including the monitoring of trend analysis) are used. In some cases retrospective validation is sufficient to establish a process is under validated state.

Retrospective validation may be allowed, when the formulation procedure and equipment have not been altered. A critical examination of the in-process control data and of the analytical results shall be performed. Where existing data is not adequate, additional tests shall be performed.

5.11.6 Cleaning Validation

There shall be written Standard Operating Procedures (SOPs), detailing cleaning processes for different sections in the manufacturing facility, with appropriately documented and completed cleaning logs.

There shall be written SOP's detailing the cleaning process for equipment and apparatus.

There shall be a written SOP detailing how cleaning processes will be validated, referring to accountabilities, acceptance criteria and revalidation requirements. Acceptance limits shall be scientifically justifiable. The complexity and design of the equipment, training or operators, size of the system, and time delay between end of processing and cleaning shall be kept in mind when designing the cleaning SOP.

Written protocols to be followed during validation shall detail sampling procedures (direct sampling, rinse samples, in-process control monitoring), and the analytical methods (specificity and sensitivity) to be used.

Evidence shall be provided to ensure that equipment is consistently cleaned to an acceptable level, of product, cleaning agent and microbial residues.

5.11.7 Analytical Method Validation

Analytical testing procedures including stability testing methods must be validated to demonstrate their reliability. This shall be done during product design.

Revalidation may be necessary in the following circumstances:

- changes in the synthesis of a drug substance;
- changes in the composition of a finished product;
- changes in the analytical procedure
- changes in the manufacturing process that will effect the method

The degree of revalidation required depends on the nature of the changes. Certain other changes may also require validation.

Analytical method validation shall not be confused with system suitability tests. System suitability testing verifies the suitability of an analytical system at the time the test is performed.

Analytical methods, (other than Pharmacopoeial methods), shall be validated. Typical validation characteristics which should be considered, include accuracy, precision, (repeatability and intermediate precision), specificity, limit of detection, limit of quantification, linearity and range. Robustness shall be considered at an appropriate stage in the development of an analytical procedure.

5.12 Packaging and Labeling

"Packaging may be defined as all the activities involved in designing and producing the container or wrapper for a product"

5.12.1 Functions of Packaging.

- Packaging gives protection to the product
- Packaging improves product dependability
- Packaging leads to ease of product handling
- Packaging aids product differentiation
- Packaging gives separate identity to a product
- Packaging makes the product attractive in appearance there by increases the company's profitability.

5.12.2 Purpose of packaging

- To hold, or contain, a defined quality of product.
- To protect the product from – damage, contamination and deterioration
- To identify the product by its batch number, manufacturer, date of mfg., date of expiry and so on.
- To indicate required storage condition, expiration date or shelf life.
- To present the product in a form that is easy to use with no side effects etc.

5.12.3 Stages of packaging

There are broadly two stages of packaging

- Primary Packaging
- Secondary Packaging

➢ Primary Packaging: is the packaging which immediately surrounds the product, and which is in direct contact with the product. This includes the container itself and its cap, closure, or other seal. Such materials are called **primary packaging materials**

➢ Secondary Packaging: Very often a primary pack is placed in carton, a box, or a tray, which in turn may be film wrapped. Sometimes these secondary packs are even further wrapped or packed together (usually in 10's or 12) using film- or shrink wrapping, or larger carton boxes ("outer"). All this is called **secondary packaging,** and the materials used are called **secondary packaging materials**

Sometimes Primary Packaging is called "Intermediate Packaging" and Secondary packaging is called "Outer Packaging"

5.12.4 Golden Rules of packaging

- The right product is packed in the correct, properly cleaned container, which is correctly labeled, and also that any other printed materials (for example cartons and leaflets) are the correct ones for the job.
- The products are packing shall be right products, but also that it is a right batch.
- The product is filled, or placed, into the right pack, all the components of which (i.e. the containers, caps, labels, cartons, leaflets and so on) are correct, clean and as specified by the packaging instructions.
- The containers are correctly labeled and are marked with the correct batch number, and as necessary such deals as the correct price, manufacturing and expiry dates.
- The pack contains the correct amount of the product in terms of number, weight or volume.
- The packed is properly caped or otherwise sealed.

5.12.5 Labeling

Labels are absolutely necessary for identification of the drugs and their use. The printing shall be done in bright colours and in legible manner. The labels shall carry the prescribed details about the product.

- Labeling is an important part of GMP and never accepts any material without proper label as it furnishes information about the material present in it.

5.12.6 Rules about Labels

- All sorts of labels shall be handled carefully and securely. They shall not be left loosely "lying around".
- Always report to supervisor on finding of stray labels, coming adrift or falling off, or which appear to be in a way on the wrong thing or in a wrong place.
- All information on the labels must be clear and easy to read.
- Damaged, dirty or faded labels shall not be longer used.
- Never place the status labels on the lids.
- "OLD" labels shall always be removed or clearly crossed out or defaced.
- Never stick a new label over an old one.
- All containers and equipment shall bear the labels of the current activity.
- Different colour coded labels shall be used to indicate the status of a product.
- To avoid the mix up of printed packing materials, product leaflets, relating to different products, shall be stored separately.
- Prior to release, all labels for containers, cartons and boxes and all circulars, inserts and leaflets shall be examined by QC Department.
- Prior to packing and labeling of a given batch of a drug, it shall be ensured by QA department that all the information required are correctly written.

Anytime labels aredestroyed, they must be accounted for and signed for on the appropriate record form.

5.13 Maintenance Program

- Maintenance workshops shall be separate and away from the production areas.
- Whenever spares, changed parts and tools are stored in the production area, these shall be kept in dedicated rooms and lockers.
- Tools and spare pasts for use in sterile areas shall be disinfected before these are carried inside the production areas.
- A preventive maintenance plan shall be prepared for each instrument and equipment and preventive maintenance of the equipment shall be done according to the plan.
- History cards shall be maintained for each equipment.
- Inventory of the spares and changed parts shall be checked by the maintenance personnel.
- There shall be separate dress code for the maintenance personnel and which is to be followed strictly.
- In-house calibration of measuring devices shall be done periodically according to Calibration Master Pan.
- Training of "Safety and Precautions against handling of Equipment's" shall be executed.

5.14 Basics of GLP and role of Quality Control Department

5.14.1 Fundamentals of GLP

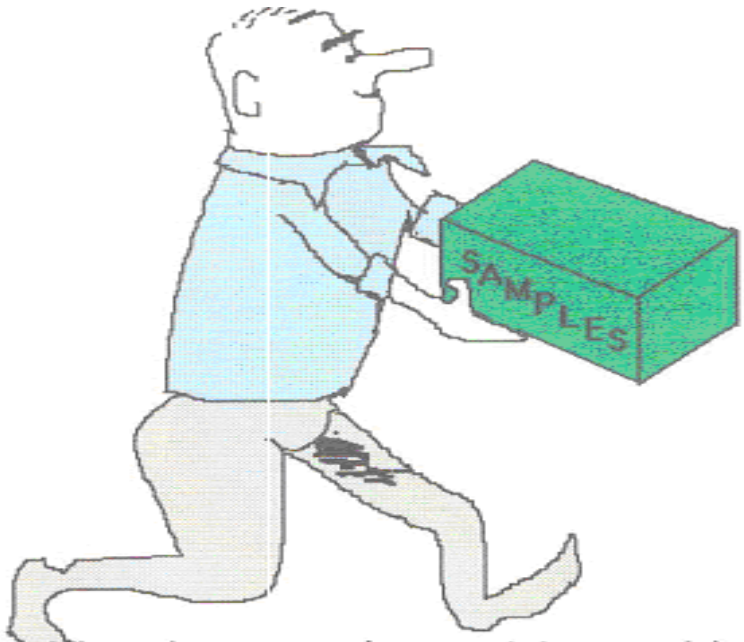
GLP is defined as "A part of quality control which is aimed at sampling, specification, documentation, analyzing and releasing the Starting material, In-process material, Finished products as per the predetermined specifications according to quality standards".

5.14.2 Responsibility of Quality Control

- QC department ensures that the recruited personnel within a test facility shall fulfill the responsibilities of management as defined by the principles of good laboratory practice.
- QC department ensures that test and reference items are appropriately characterized as per GLP guidelines.
- QC Department shall establish procedures to ensure that computerized systems are suitable for their intended purpose, and are validated, operated and maintained in accordance with the principles of good

laboratory practice.

- QC Department ensures that all raw data generated are fully documented and recorded, as required in final assessment.
- QC shall sign and date the final report to indicate acceptance of responsibility for the validity of the data and to indicate the extent to which the study complies with these principles of good laboratory practice
- The test facility should have a sufficient number of rooms or areas to assure the isolation of test systems and the isolation of individual projects, involving substances or organisms known to be or suspected of being bio hazardous.
- Handling and disposal of wastes should be carried out in such a way as not to jeopardize the integrity of studies. This includes provision for appropriate collection, storage and disposal facilities, and decontamination and transportation procedures.
- Apparatus used in routine analysis shall be periodically inspected, cleaned, maintained, and calibrated according to Standard Operating Procedures. Records of these activities shall be maintained. Calibration shall, where appropriate, be traceable to national or international standards of measurement.



These materials and components are samples and then tested by quality control.

All materials and components come into a receiving areas of plant

The GMP regulations require that these newly arrived materials and components must be immediately identified, inspected, and quarantined until approved for release.

- Chemicals, reagents, and solutions shall be labeled to indicate identity (with concentration if

appropriate), expiry date and specific storage instructions. Information concerning source, preparation date shall be available.

- Records of source date of arrival, and arrival condition of test systems shall be maintained.
- During use, housing or containers for test systems shall be cleaned and sanitized at appropriate intervals. Any material that comes into contact with the test system shall be free of contaminants at levels that would interfere with the analysis.
- Records including test item and reference item characterization, date of receipt, expiry date, quantities received and used in studies should be maintained.
- Access to electronic stored documents shall be restricted by "password" or other means and results of critical data shall be independently checked by authorized persons.
- Periodic backup of all the stored data shall be taken and kept with respective department heads.

5.15 Self Inspection

The purpose of self-inspection is to evaluate the compliance with GMP in all aspects of production and quality control. The self-inspection programme shall be designed to detect any shortcomings in the implementation of GMP and to recommend the necessary corrective actions.

Self-inspections shall be performed routinely, and may, in addition, be performed on special occasions, e.g. in the case of product recalls or repeated rejections, or when an inspection of the health authorities is announced.

The team responsible for self-inspection shall consist of personnel from cross functional department who can evaluate the implementation of GMP objectively; all recommendations for corrective action shall be implemented. The procedure for self-inspection shall be documented, and there shall be an effective follow-up programme.

It can also be a good training exercise to involve operators in the process. It is also possible to bring in people from other parts of the company, or even outside the company, if it will add value to the process.

There shall be written instructions for self-inspection detailing what is to be inspected and at what frequency.

The self-inspection team is appointed by the authorized personnel of the company and is made up of a mixture of people, including experts in GMP and persons familiar with the area to be inspected. It is useful to have people from production, QC and engineering on the team, as they will bring different perspectives to the inspection.

The team leader needs to be someone who has access to the resources to produce a report at the end of the process, and with the authority and experience to organize and manage a team activity.

It shall be used to ensure that a consistent approach is achieved. The areas to be inspected will include (but will not be limited to):

- Personnel
- Permises including personnel facilities
- Maintenance of buildings and equipment
- Storage of starting materials and finished products
- Equipments
- Production and in-process controls
- Quality control
- Documentation
- Sanitation and hygiene
- Validation and revalidation programme
- Calibration of instruments or measurement systems
- Recall procedure
- Complaints management
- Labels control
- Results of previous self-inspections and any corrective steps taken.
- Quality assurance

5.16 Complaints, Recalls and Withdrawals

5.16.1 Complaints

1. A system shall be established for dealing with complaints which shall include written procedures indicating the responsible person(s) through whom the complaints are to be channelled. The responsible person must have appropriate knowledge and experience and the necessary authority to decide the action to be taken.
2. All complaints concerning a product defect shall be recorded with all the original details and thoroughly investigated. The responsible person shall decide whether, and what, subsequent action is necessary.
3. Complaint records shall be regularly reviewed for any indication of specific recurring problems requiring attention and possibly the recall of marketed products.
4. Written records involving a medicine shall be maintained until at least one year after the expiration date of the medicine, or one year after the date that the complaint was received, whichever is longer.
5. The written record shall include the following information, where known:

   · Date of receiving complaint

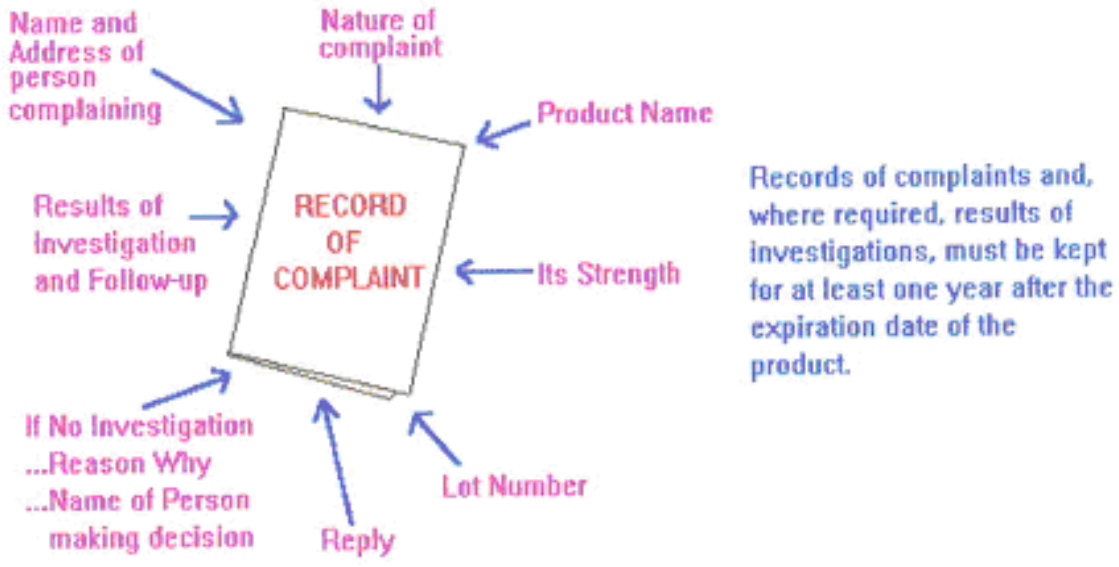
   · The name and strength of the medicine and lot number

   · Name of complainant, nature of complaint

   · Detailed record of the investigation

   · Details of the action taken to prevent recurrence of the problem that led to the negative effect on the product.

   · Reply to complainant.
6. If a product defect is discovered or suspected in a batch, consideration shall be given to whether other batches should be checked in order to determine whether they are also affected. In particular, other batches which may contain reworks (if done) of the defective batch should be investigated.



7. All the decisions and measures taken as a result of a complaint shall be recorded and referenced in the corresponding batch records.

5.16.2 Recalls

Withdrawal implies the total withdrawal of the product from the market.

Recall refers to the removal from the market of a specific batch or batches of the product.

1. The recall of a particular batch or batches of a product from the market may be occasioned by the manufacturer or distributor, either following reports of adverse reactions to a particular batch of a product, or as the result of on-going stability studies, or by the regulatory authorities as a result of adverse reaction reports or for other reasons such as formulation, labelling or other errors.
2. The authorized person shall initiate and co-ordinate all recall activities which should involve the head of Quality Management. In the event of an adverse event a crisis committee involving key personnel should be set up and involved.
3. There shall be a written recall procedure which is capable of being initiated promptly and put into operation at any time, inside or outside normal working hours. It shall include emergency and 'out of hours' contacts and telephone numbers.
4. The recall procedure shall be shown to be practicable and operable within reasonable time (e.g. by conducting internal 'dummy runs'). It shall be revised as necessary to take account of changes in procedures or responsible person(s).
5. The distribution records shall be readily available to the person(s) responsible for recalls and contain
6. sufficient information on wholesalers and customers (e.g. addresses, telephone numbers inside or outside working hours, batches and amounts delivered) including exported products and medical samples.
7. Recalled products shall be identified and stored separately in a secured area while awaiting a decision.
8. The progress of the recall process shall be recorded and a final report issued, including reconciliation between the delivered and recovered quantities of the products.

6.0 MATRIX FOR TRAINING SYLLABUS AT DIFFERENT LEVELS OF TRAINEES

6.1 Quality Control Section

S.No	Section	Date	Level I	Level II	Level III
1	Microbiology Section	dd.mm.yyyy to dd.mm.yyyy	SOPs related to handling, calibration, maintenance and cleaning of equipment's	---	Gowning and Degowning SOPs
			SOPs related to various microbial tests.	cGLP & cGMP Training	Area Cleaning SOPs
			cGLP & cGMP Training.	Glassware cleaning SOP	Glassware Cleaning and storage SOP
			Departmental SOPs Training	Area Cleaning SOPs	Instruments cleaning SOPs.
			Identified Cross- functional SOPs	---	---
			Analytical Technique Validation	Departmental SOPs Training Specific to job assigned.	---
			Quality Control System SOPs	Procedure Sampling, handling and disposal of Starting Material	---
			Procedure Sampling, handling and disposal of Starting Material.	Procedure Storage of Samples.	---
			Procedure Storage of Samples.	Safety	---
			Procedure of recording stability samples	---	---
			Safety	---	---
2	Chemical Section	dd.mm.yyyy to dd.mm.yyyy	SOPs related to handling, calibration, maintenance and cleaning of quipment's.	---.	Gowning and Degowning SOPs
			SOPs related to various chemical tests.	cGLP & cGMP Training	Area Cleaning SOPs

Quality Control Section

S.No	Section	Date	Level I	Level II	Level III
			cGLP & cGMP Training.	Glassware cleaning SOP	Glassware Cleaning and storage SOP
			Departmental SOPs Training	Area Cleaning SOPs	Instruments cleaning SOPs.
			Identified Cross-functional SOPs	---	---
			Analytical Technique Validation	Departmental SOPs Training Specific to job assigned.	---

			Procedure Sampling, handling and disposal of Starting Material.	Procedure Sampling, handling and disposal of Starting Material.	---
			Procedure Storage of Samples.	Procedure Storage of Samples.	---
			Procedure of recording stability samples	---	---
			Safety	---	---
3	Instrument Section	dd.mm.yyyy to dd.mm.yyyy	SOPs related to handling, calibration, maintenance and cleaning of instruments like HPLC, GC, FTIR etc.	---	Gowning and Degowning SOPs
			cGLP & cGMP Training.	cGLP & cGMP Training.	Area Cleaning SOPs
			Departmental SOPs Training	Departmental SOPs Training Specific to job assigned.	Glassware Cleaning and storage SOP
			Identified Cross-functional SOPs	---	Instruments cleaning SOPs.
			Analytical Technique Validation	Glassware handling SOPs	---
			Procedure Sampling, handling and disposal of Starting Material.	Procedure Sampling, handling and disposal of Starting Material.	---
			Procedure Storage of Samples.	Procedure Storage of Samples.	
			Procedure of recording stability samples	---	---
			Safety	---	---

Department: Production Department

S.No	Section	Date	Level I	Level II	Level III
1.	Granulation	dd.mm.yyyy	Departmental SOPs.	Departmental SOPs	Gowning and De

S.No	Section	Date	Level I	Level II	Level III
	Section/ Compounding	to dd.mm.yyyy		Specific to job assigned	gowning SOPs
			cGMP Training.	cGMP Training.	Area Cleaning SOPs
			Area Cleaning SOPs	Area Cleaning SOPs	Instrument cleaning SOPs
			Identified Cross-functional SOPs	---	---
			Reprocessing of material SOP	---	---
			SOPs of Preventive maintenance of equipment	---	---
			Safety	Safety	---
2.	Compression Section/Filling	dd/mm/yy to dd/mm/yy	Departmental SOPs Training	Departmental SOPs Training Specific to job assigned.	Gowning and Degowning SOPs
			cGMP Training.	cGMP Training.	Area Cleaning SOPs
			Identified Cross-functional SOPs	---	Instrument cleaning SOPs
			Reprocessing of material SOP	---	---
			SOPs of Preventive maintenance of equipment	---	---
3.	Coating Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs Training (General, set up, operation and cleaning)	Departmental SOPs Training Specific to job assigned	Gowning and Degowning SOPs
			cGMP Training.	cGMP Training.	Area Cleaning SOPs
			Cross functional SOPs	Identified Cross functional SOPs	Instrument cleaning SOPs
			SOPs of Preventive maintenance of equipment	---	---
4.	Packing Section/Filling	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs Training	Departmental SOPs Training Specific to job assigned.	Gowning and Degowning SOPs
			GMP Training.	Basics of GMP Training.	Area Cleaning SOPs
			Cross functional SOPs	Identified Cross functional SOPs	Instrument cleaning SOPs

S.No	Section	Date	Level I	Level II	Level III
			SOPs of Preventive maintenance of equipment	---	---

Department: Quality Assurance Department

S.No	Section	Date	Level I	Level II	Level III
1	Documentation Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs, Protocols and Manuals.	SOP of handling of records.	Area Cleaning SOP
			GDP Training.	Gowning and Degowning SOP.	Gowning and Degowning SOP.
			Recording Procedure of Documents.	Area cleaning SOP	---
			Cross functional SOPs	---	---
			Electronic retrieval of Records.	---	---
2	Validation Section	dd.mm.yyyy to dd.mm.yyyy	Validation Protocols Training.	---	Area Cleaning SOP
			Departmental SOPs Training.	Gowning and Degowning SOP.	Gowning and Degowning SOP
			Description of schedule M	Area cleaning SOP	---
			General Regulatory Guidelines.	---	---
3	Batch Release Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs Training	Basics of GMP Training.	Area Cleaning SOP
			GMP Training.	---	Gowning and Degowning SOP.
4	IPQA Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs Training	Departmental SOPs Training Specific to job assigned.	Area Cleaning SOP
			GMP Training.	Basics of GMP Training	Gowning and Degowning SOP.
			Cross functional SOPs	---	---
			Safety	Safety	---

Department: Warehouse Department

S.No	Section	Date	Level I	Level II	Level III
1	Raw Material Storage Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Safety	Safety	---
2	Packing Material Storage Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
3	Rejected Material Storage Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
4	Scrap Yard Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
5	Recall material Storage Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure

Department: Engineering Department

S.No	Section	Date	Level I	Level II	Level III
1	Boiler Section	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning Degowning procedure
			Safety	Safety	---
			Calibration SOPs	---	---
2	Water Section	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Calibration SOPs	---	---
			Validation SOPs	---	---
			Safety	Safety	---
3	Chiller Section	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Calibration SOPs	---	---
			Safety	Safety	---
4	Compress	dd.mm.yyyy	Operational and	Departmental SOPs	Area cleaning and

	ed Air Section	to dd.mm.yyyy	Maintenance SOPs	Specific to job assigned	gowning, Degowning procedure
			Calibration SOPs	---	---
			Validation SOPs	---	---
			Safety	Safety	---
5	DG Section	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Calibration SOPs	---	---
			Safety	Safety	---
6	HVAC and Dust Extraction Section	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Calibration SOPs	--	---
			Validation SOPs	---	---
			Safety	Safety	---
7	Electrical Substation	dd.mm.yyyy to dd.mm.yyyy	Operational and Maintenance SOPs	Departmental SOPs Specific to job assigned	Area cleaning and gowning, Degowning procedure
			Safety	Safety	---
8	Engineering Stores	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Departmental SOPs Specific to job assigned	---

Department: Human Resource Department

S.No	Section	Date	Level I	Level II	Level III
1	Recruitment Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Area cleaning procedure	Area cleaning procedure
			Identified Cross functional SOPs	---	---
2	Performance Appraisal and Salary Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	Area cleaning procedure	Area cleaning procedure
			Identified Cross functional SOPs	---	---
3	Training and Development Section	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs and Manuals.	Area cleaning procedure	Area cleaning procedure
			Identified Cross functional SOPs	---	---

4	Time Office	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs.	Area cleaning procedure	Area cleaning procedure
			Identified Cross functional SOPs	---	---
5	Canteen Management	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	---	Department cleaning procedure
			Identified Cross functional SOPs	---	---
6	Security Management	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs	---	Department cleaning procedure
			Identified Cross functional SOPs	---	---
7	Housekeeping Management	dd.mm.yyyy to dd.mm.yyyy	Departmental SOPs.	---	Department cleaning procedure
			Identified Cross functional SOPs	---	---

7.0 CROSS FUNCTIONAL SOPS MATRIX FOR DIFFERENT DEPARTMENTS

7.1 Department: Production

S.No	Level I	Level II	Level III
1	SOP on SOP.	Gowning and De Gowning Procedure.	Gowning and De Gowning Procedure.
2	Gowning and De Gowning Procedure.	Procedure of Area Cleaning.	Procedure of Area Cleaning.
3	Procedure of Area Cleaning.	Reading and recording of Temperature and % RH.	---
4	Reading and recording of Temperature and % RH.	Recording of Differential pressure using Magnehelic Gauges.	---
5	Recording of Differential pressure using Magnehelic Gauges	Calibration and Operation of weighing Balance.	---
6	Change Control Procedure	Status Labeling System.	---
7	Calibration and Operation of weighing Balance.	---	---
8	Allocation of room numbers of production Department.	---	---
9	Allocation of equipment numbers of production Department.	---	---
10	Batch Numbering System.	---	---
11	Handling of Deviations.	---	---
12	Incident Reporting System.	---	---
13	Line Clearance.	---	---
14	Drainage System	---	---
15	Self Audits	---	---

16	Training of Employees	---	---
17	Correction Procedures for errors in documentation Entries.	---	---
18	Status Labeling System.	---	---
19	Checking of LOD	---	---

7.2 Department: Quality Control

S.No.	Level I	Level II	Level III
1	SOP on SOP.	Gowning and De Gowning Procedure.	Gowning and De Gowning Procedure.
2	Gowning and De Gowning Procedure.	Procedure of Area Cleaning.	Procedure of Area Cleaning.
3	Procedure of Area Cleaning.	Reading and recording of Temperature and % RH.	---
4	Reading and recording of Temperature and % RH.	Recording of Differential pressure using Magnehelic Gauges.	---
5	Recording of Differential pressure using Magnehelic Gauges.	Calibration and Operation of weighing Balance.	---
6	Change Control Procedure	Status Labeling System.	---
7	Calibration and Operation of weighing Balance.	---	---
8	Allocation of room numbers of Quality Control Department.	---	---
9	Allocation of equipment numbers of Quality Control Department.	---	---
10	Batch Numbering System.	---	---
11	Handing Out Of Specification.	---	---
12	Drainage System	---	---
13	Self-Audits	---	---
14	Training of Employees	---	---
15	Correction Procedures for errors in documentation Entries.	---	---
16	Status Labeling System.	---	---
17	Calibration and Operation of DT Apparatus.	---	---

18	Calibration and Operation of Hardness Tester.	---	---
19	Calibration and Operation of pH Meter.	---	---
20	Calibration and Operation of		

	Friability Apparatus.		
21	Sampling of In-process Products.	---	---
22	Sampling of Finished Products.	---	---
23	On Going Stability of Finished Products.	---	---
24	Collection, Storage and Periodic Observation of Retained Samples.	---	---
25	Destruction of Retained Samples of finished Products.	---	---
26	Destruction of Raw, Product and Packaging Material	---	---

7.2 Department: Quality Assurance

S.No.	Level I	Level II	Level III
1	Receipt of Starting Materials.	---	---
2	Handling of Damaged Containers.	---	---
3	Sampling of Materials.	---	---
4	Handling of Sampling and dispensing Tools.	---	---
5	Procedure of Dispensing of Materials.	---	---

8.0 GLOSSARY

Definitions given below apply to the words/terms as used in this guide. They may have different meanings in other contexts.

Air-lock

An enclosed space with two or more doors, and which is interposed between two or more rooms, e.g. of differing class of cleanliness, for the purpose of controlling the airflow between those rooms when they need to be entered. An air-lock is designed for and used by either people or goods.

Analytical method

A detailed description of the procedures to be followed in performing tests for conformity with a specification.

Audit

A planned and systematic examination and check of a system, procedure or operation in order to monitor compliance with and the effectiveness of established standards and to allow for improvement and corrective measures where required.

Batch (or Lot)

A defined quantity of starting material, packaging material or bulk, intermediate or finished product that is intended or purported to be homogeneous in character and quality, and which has been produced during a defined cycle of manufacture. To complete certain stages of manufacture it may be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final uniform batch.

A batch is sometimes described as a lot.

Batch number (or Lot number)

A distinctive combination of numbers and/or letters which specifically identifies a batch or lot and permits its history to be traced.

Batch Manufacturing Record

A document stating the materials used and the operations carried out during the processing of a given batch, including details of in-process controls, but normally excluding packaging information. It should be based on the Master Formula and Method and be compiled as the manufacturing operation proceeds.

Batch Packaging Record

A document stating the bulk product and packaging materials used, and the processes carried out during the packaging of a given batch, with details of in-process controls. It should be based on the Master Packaging instruction and be compiled during the packaging operation.

Biological

Biological medicines comprise those derived or extracted from living organisms or tissues and those which contain living or inactivated organisms in the end product.

Bulk product

Any product which has completed all processing stages up to, but not including, final packaging.

Calibration

Calibration is the formal, methodical and documented comparison of the measuring and reading accuracy in measuring and control circuits relative to a set of reference systems.

Contract manufacture, analysis or servicing

Manufacture (or partial manufacture), analysis or service work ordered by one person or organisation (the Contract Giver) and carried out by an independent person or organisation (the Contract Acceptor).

Dedicated facility

A room or suite of rooms with attendant equipment and services (including air-supply as necessary) used only for the manufacture of one product, or a closely related group of products. (Equipment may be similarly 'dedicated').

Documentation

All the written production procedures, instructions and records, quality control procedures, and recorded test results involved in the manufacture of a medicinal product.

Finished product

A medicinal product which has undergone all stages of production, including packaging in its final container.

Good Manufacturing Practice

Good Manufacturing Practice (GMP) is that part of Quality Assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and legal requirements. GMP is thus concerned with both production and quality control matters.

In-process control

Tests, checks and measurements made during the course of manufacture (including packaging) to ensure that the resultant product will comply with its specification and to provide feedback to production for process adjustment. The control of the environment or equipment may also be regarded as a part of in-process control. In-process control may be a responsibility of either production or quality control.

Intermediate product

A partly processed material which must undergo further processing before it becomes a bulk or finished product.

Manufacture

The cycle of processing of a medicinal product from the acquisition of all materials up to but normally not including, packaging of the finished product.

Master document

A master document is a formally authorised source document relating to specifications and/or manufacturing/analytical methods, which is protected from unauthorised access or amendment.

Monitor

To monitor a process or a situation is to carry out repeated measurements or observations of one or more characteristics of the process or situation to determine whether or not it is continuing as intended. Monitoring may be continuous or intermittent and not necessarily performed on every batch.

Packaging

All operations, including filling and labelling, which a bulk product has to undergo in order to become a finished product.

Packaging material

Any material employed in the packaging of a medicinal product, excluding any outer packaging used for transportation or shipment

NOTE · There are various categories of packaging materials e.g.

(a) Packaging materials which come in contact with the product (often called 'Primary Packaging Materials')

(b) Printed packaging materials

(c) Other packaging materials.

Although these categories are not necessarily mutually exclusive, the nature and extent of the control which needs to be applied to them may vary.

Procedures

Description of the operations to be carried out, the precautions to be taken and measures to be applied directly or indirectly to the manufacture of a medicinal product.

Processing stages

The separate operations (or groups of related operations) involved in the manufacture of a medicinal product.

Production

All operations involved in the preparation of a medicinal product, from receipt of materials. through manufacturing and packaging, to its completion as a finished product.

Qualification

Qualification is a documented program which provides the assurance that the equipment and installations operate consistently within the pre-determined mechanical, electrical or other operating parameters.

Quality assurance

Is the sum total of all organised arrangements made with the object of ensuring that medicines are of the quality required for their intended use. It is Good Manufacturing Practice plus factors outside the scope of this Guide (such as original product design and development).

Quality control

Is that part of Good Manufacturing Practice which is concerned with sampling, specifications and testing, and with the organisation, documentation and release procedures which ensure that the necessary and relevant tests are, in fact, carried out, and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory

Recall

Refers to the removal from the market of a specific batch or batches of the product.

Reconciliation

A comparison, making due allowance for normal variation, between the amount of product or materials theoretically and actually produced or used.

Records

Records provide a history of each batch of product, including its distribution, and also all other pertinent information relevant to the quality of the final product.

Reprocessing

The reworking of all or part of a batch of product of an unacceptable quality from a defined stage of production so that its quality may be rendered acceptable by one or more additional operations; or the introduction of all or part or residues of previous batches of the required quality into another batch at a defined stage of manufacture.

Specification

A document giving a description of a starting material, packaging material, intermediate, bulk or finished product in terms of its chemical, physical and (possibly) biological characteristics. A specification normally includes descriptive clauses and numerical clauses. the latter stating standards and permitted tolerances.

Status

The classification of any goods, materials, containers or machines in relation to their acceptance (or otherwise) for use, further processing or distribution (e.g. 'Quarantine', 'Under Test', 'Released', 'Rejected', 'Online Rejected', 'Cleaned', 'To be Clean').

Withdrawal

Implies the total withdrawal of the product from the market.