SHREE H. N. SHUKLA INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH

B.PHARM

(SEMESTER –VII)

SUBJECT NAME: QUALITY ASSURANCE

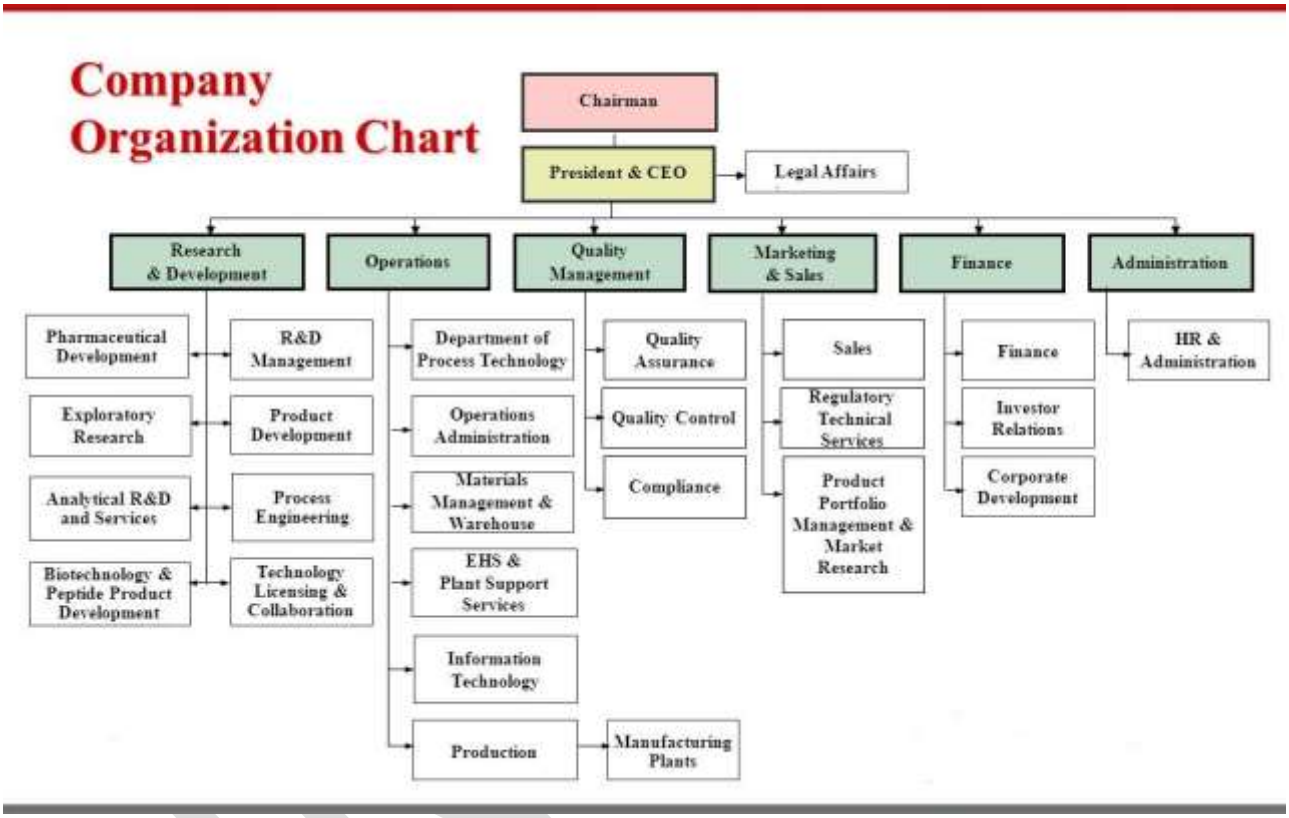
SUBJECT CODE: BP706TT

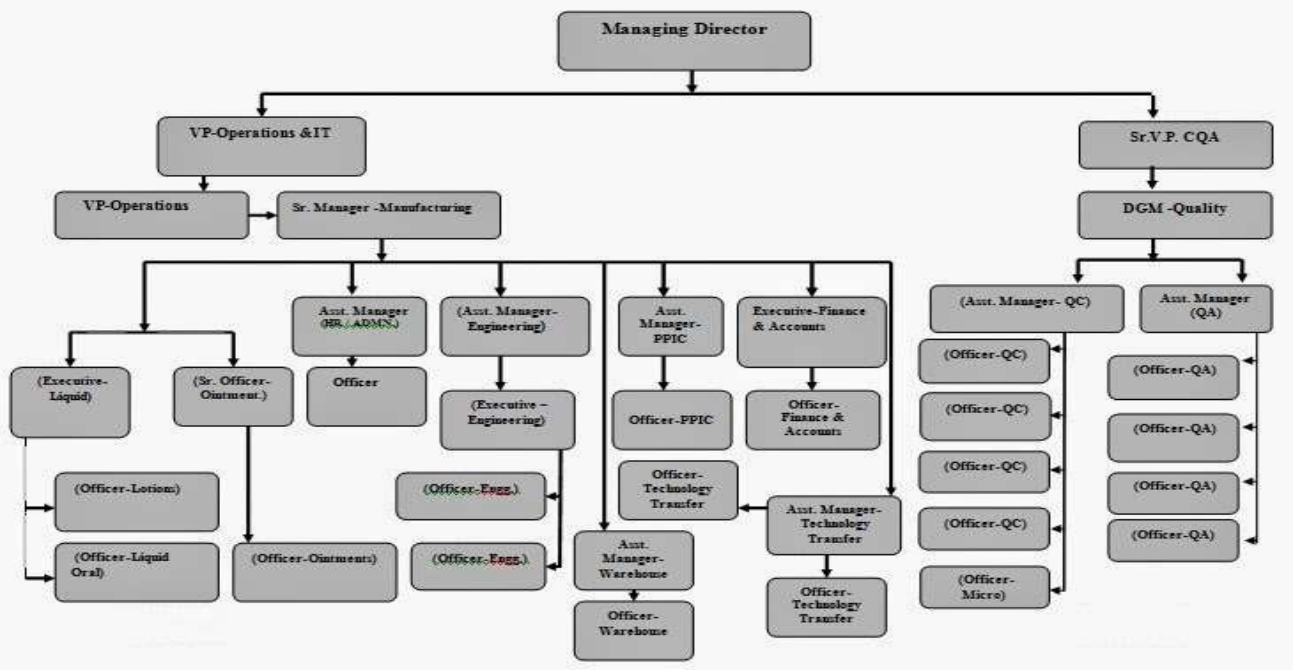
UNIT 02 (a): ORGANIZATION AND PERSONNEL

Content

Organization and personnel: Personnel responsibilities, training, hygiene and personal records.

Organization





Personnel Responsibility

Key personnel include the heads of production, the head(s) of quality unit(s) and the authorized person. The quality unit(s) typically comprise the quality assurance and quality control functions. In some cases, these could be combined in one department.

There should be an adequate number of staff with appropriate education, technical knowledge, and practical experience related to the job they perform.

Key personnel responsible for supervising the production and quality unit(s) for pharmaceutical products should possess the qualifications of a scientific education and practical experience required by national legislation. Their education should include the study of an appropriate combination of

1) chemistry (analytical or organic) or biochemistry;
2) chemical engineering;
3) microbiology;
4) pharmaceutical sciences and technology;
5) pharmacology and toxicology;
6) physiology;
7) other related sciences.

They should also have adequate practical experience in the manufacture and QA of pharmaceutical products.

Individual responsibilities should be laid down in written instructions, to ensure that there are no gaps or overlaps. The responsibilities placed on any one individual should not be so extensive as to incur any risk to quality.

Measures should be taken to ensure that no person affected by a disease in a communicable form or having open lesions on the exposed surface of the body is engaged in any production step involving direct contact with the active pharmaceutical ingredients.

The head of the Quality Control Laboratory shall be independent of the manufacturing unit. The testing shall be conducted under the direct supervision of competent technical staff who shall be whole time employees of the licensee.

Number of personnel employed shall be adequate and in direct proportion to the workload.

RESPONSIBILITIES OF PRODUCTION UNIT

The head of Production Department usually has the following responsibilities:

- Approval of Instructions relating to production operations including in-process controls and their implementation.

- Checking the maintenance of the department, premises and equipment.
- Ensuring process validations, calibration of control equipment and maintenance of their records.
- Ensuring the initial and continuing training of production personnel relevant to their needs.
- Ensuring production and storage of products according to appropriate documentation.
- Ensuring evaluation of production records by an authorized person before they are made available to quality control department.

RESPONSIBILITIES OF QUALITY CONTROL UNIT

1) There shall be a quality control unit (QCU) that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, inprocess materials, packaging materials, labeling, and drug products and the authority to review production records to assure that no errors have occurred, or, if errors have occurred, that they have been fully investigated.

   The QCU shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.

2) Adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products shall be available to the QCU.

3) The QCU shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.

4) The responsibilities and procedures applicable to the QCU shall be in writing; such written procedures shall be followed.

QCU Organization

The more typical organizational structure used in the industry involves three quality groups:

Group	Quality System Responsibility or Involvement
QC	Laboratory Systems (QC and Stability): ▪ Sample Management ▪ Reference Standards ▪ SOPs and Test Methods ▪ Method Validation and Transfer ▪ Instrument Qualification/Calibration and Maintenance ▪ Data Analysis, Records, and Document Control ▪ Change Control ▪ Contract Laboratory Management
QA	Site Quality Systems:

	▪ SOPs and Document Control ▪ Master and Production Batch Records (MBR, PBR) ▪ Batch Record Review and Product Release ▪ Failure Investigations and CAPA ▪ Training ▪ Site Change Control ▪ Validation (Facilities, Equipment, and Computer) ▪ Supplier Management and Control ▪ Complaints ▪ Annual Product Review ▪ Management Notification
Compliance	▪ Policies and Standards Audit (Internal and External) ▪ Regulatory Commitments and ▪ Documents recall

The head of the Quality Control Unit usually has the following responsibilities:

- Approval or rejection of starting materials packaging materials, intermediate, bulk and finished products.
- Evaluation of batch records.
- Ensuring that all necessary testing is carried out.
- Approval of sampling instructions, specifications, test methods and other quality control procedures.
- Approval and monitoring of analysis carried out under contract, if any.
- Checking the maintenance of the department, premises and equipment.
- Ensuring initial and continuing training of quality control personnel relevant to their needs.
- Ensuring validation of quality control procedures and calibration of control equipments and their records.
- Ensuring initial and continuing training to quality control personnel.
- Establishment, implementation and maintenance of the quality system.
- Supervision of the regular internal audits or self-inspections;
- Participation in external audit (vendor audit)
- Participation in validation programmes.

There are certain joint responsibilities of the Head of Production and the Head of Quality Control. Usually the shared responsibilities are:

- Authorization of written procedures and other documents and their review.
- Plant hygiene
- Monitoring and control of environment of production areas.
- Process validation and calibration of control equipments.
- Training of personnel in GMPs.
- Monitoring of compliance with GMPs
- Approval and monitoring of suppliers of materials.
- Lying down and monitoring of storage conditions for material and product.
- Retention of records for periods specified by national legislation.
- Approval and monitoring of contract manufacturers, if any.
- Performance and evaluation of in-process control.
- Inspection, investigation and sampling to monitor factors that may affect product quality.

Personnel Training

- The manufacturer should provide training in accordance with a written programme for all personnel whose duties take them into manufacturing areas or into control laboratories (including the technical, maintenance and leaning personnel) and for other personnel as required.
- Besides basic training on the theory and practice of GMP, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuing training should also be given, and its practical effectiveness periodically assessed. Approved training programmes should be available. Training records should be kept.
- Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitizing materials are handled, should be given specific training.
- The concept of QA and all the measures which aid its understanding and implementation should be fully discussed during the training sessions.
- Visitors or untrained personnel should preferably not be taken into the production and QC areas. If this is unavoidable, they should be given relevant information in advance (particularly

about personal hygiene) and the prescribed protective clothing. They should be closely supervised.

- Consultant and contract staff should be qualified for the services they provide. Evidence of this should be included in the training records.

TRAINING SYSTEM

Because the quality of the product is directly affected by actions that personnel take in their jobs, there must be assurance that they are properly trained. This assurance is built by having a training system that is robust, compliant, and sustainable and is able to produce individuals who are qualified.

Elements that are needed in a strong training system include the following:

- an accurate description of the job or role;
- specific training requirements for each job or role;
- training plan to accomplish the training;
- training materials that are applicable to each type of training;
- qualified trainers to perform the training;
- evaluations to measure the effectiveness of the training;
- a documentation and record keeping system for storage and retrieval of training records and materials.

TRAINING PLAN

To ensure that the individual receives the "right" training at the "right" time, an individual training plan should be created and executed for each individual. The training plan should include the following:

- an individual's curriculum or training topics or courses
- how the training will be performed
- the sequence of the training
- approximate training time
- a clear indication of when the individual will be fully qualified.

LEVELS OF TRAINING

The first level is an overview or general training conducted by the site HR or corporate training group as part of a new hire or induction training.

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The third level, most specific to the employee, is one-on-one training.

The sequence of training should be clearly defined. An example would be learning about equipment. Training can be monitored to see whether it is going according to plan

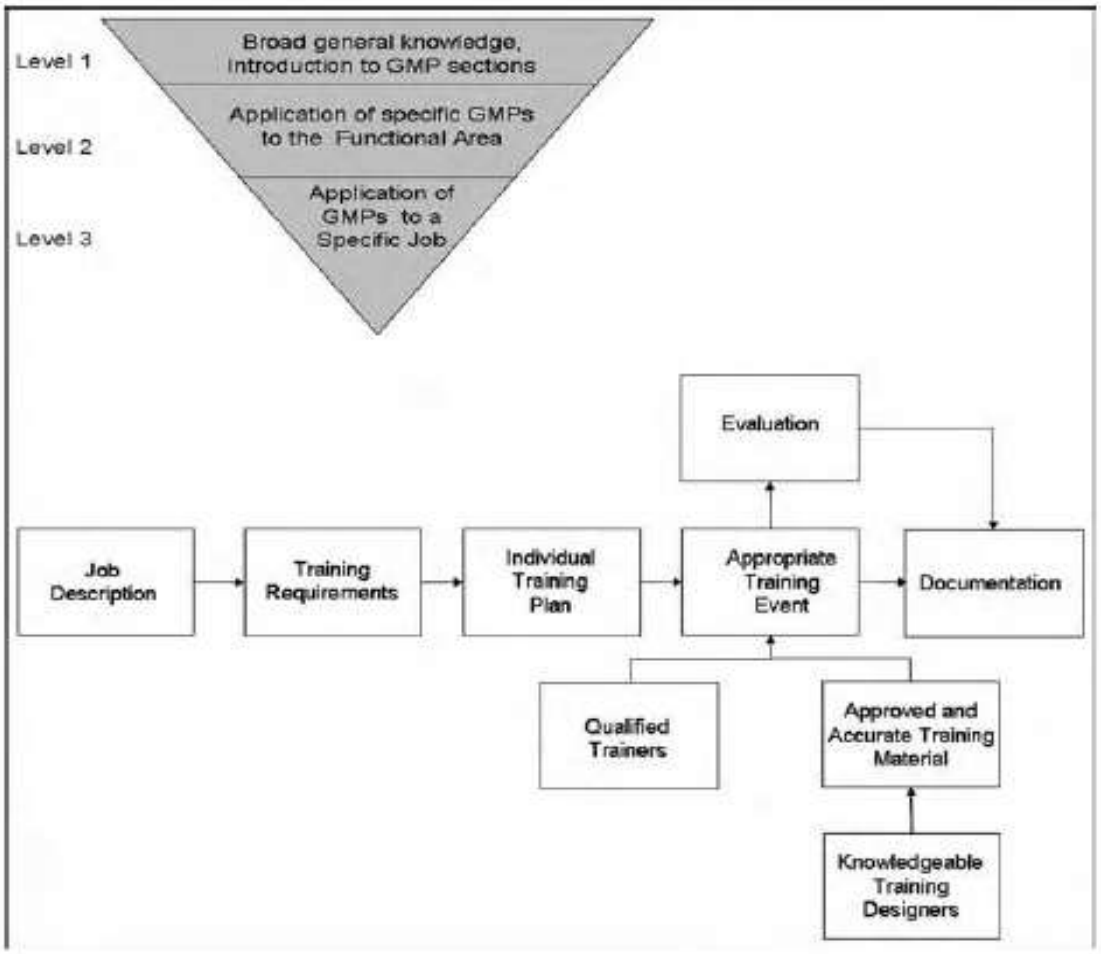

FIGURE 2 Training system.

TYPES OF TRAINING

Phase I – a general orientation

This should be started during employee's first day in the company.

Phase II – a more specific orientation based on where the new employee works:

This should be started during first week of the employee's employment.

- **PHASE I TRAINING**

This should be given to all new employees. This includes:

- ❖ History of the company.
- ❖ Organization chart.
- ❖ Facilities.
- ❖ Company policies and company standard practices.
- ❖ Basic GMP concepts.
- ❖ General safety training.

- **PHASE II TRAINING**

  This training is aimed at new employees in each area, department or section whose activities into perticular areas. This include:

  - ❖ Introduction to the department or a tour of the department.
    E.g. location of working area, job description.
  - ❖ GMP training
  - ❖ On-the job training
  - ❖ Training on SOPs
  - ❖ Safety training
  - ❖ Supervisor training
  - ❖ Manager training
  - ❖ Trainer's training
  - ❖ On-going training
  - ❖ Remedial training
  - ❖ Job change training

A. GMP TRAINING:

Once the basic concepts of GMP have been initially presented during the new employee-orientation training, other GMP topics should be incorporated, explaining GMP in more practical detail. It is advisable to complete this training during the first two months following entrance in the company or in a specific working area.

The filling-line operator needs to understand the GMPs for sterile products, the quality control technician needs to be aware of good control laboratory practices, while the new warehouse employee needs to know how to store, move and distribute materials and products according to GMPs.

GMP training should be provided to ensure that employees understand and follow the GMP requirements applicable to their jobs.

The specific GMP training should be developed according to GMP requirements for each area, for example: **Manufacturing of biological/biotechnological products** (from cell banks preparation to purification)

- Aseptic processing (vaccine formulation and filling)
- Quality control
- Quality assurance
- Product development
- Animal facilities
- Visual inspection and packaging
- Warehousing and distribution
- Maintenance
- Purchasing

B. ON-THE-JOB TRAINING (OJT):

This type of training is frequently underestimated and, in most companies, is not performed in a very professional way.

In these situations, a new employee is simply assigned to the most experienced one to watch or "shadow" what the more experienced person does. In many cases, this ensures that the new person learns the same practices – some bad, some good – of the experienced person.

The supervisor is responsible for this training, and it is based on the SOPs and the acquisition of technical skills needed for the job. It is particularly important at this stage to teach the trainee not only what he/she should do and how, but why it must be done in such a way and in no other.

"The two components of teaching are instruction and education: Instruction involves the teaching of how-to or what, and education involves the why of the training effort".

C. TRAINING ON SOPs:

Training either new or experienced personnel on new SOPs, can be conducted as follows.

- The supervisor will provide the current copy of the SOP related to the task and allocate time for reading.
- The trainee will read the pertinent document.
- The supervisor will review the SOP with the trainee and will answer any questions regarding the documents.
- The supervisor will show the trainee how to do the task.
- The trainee will perform the procedure by himself/herself under supervision.
- The supervisor will review the work in such a way that positive performance will be reinforced. A checklist to evaluate the performance of the trainee can be very helpful.
- The trainee will perform the procedure without supervision.
- When the supervisor is satisfied with the trainee's performance, the supervisor and the trainee will sign the training record.

D. SAFETY TRAINING:

Safety training will be developed from the specific safety requirements for the area. It will be given to all those employees in at-risk occupations.

The safety department identifies those who need to have safety training, which may be given individually or to a group of employees in the same or related occupations.

The topics approached will be defined according to the existing risks and complexities. These should cover:

- The knowledge of mechanisms of exposure to the specific risk agent, including toxic chemicals and biohazards;

- The appropriate use of personal protection items;
- How to proceed in an emergency.

E. SUPERVISOR TRAINING:

It is the responsibility of the supervisor to provide clear direction, to lead by example, to set high standards of performance, to provide feedback (mostly positive), and to ensure adequate resources (especially time).

The supervisor training should be conducted to guarantee that supervisors be adequately trained in:

- The areas they are going to supervise;
- The SOPs used in their department;
- Their responsibilities under GMP, especially their responsibility for training, for reviewing documents, and for reviewing safety procedures to avoid danger to their staff.

It is advisable that new supervisors should be trained in the following topics:

- Deviation handling
- Change control
- GMP trends

They should also be trained in aspects such as:

- Communication
- Motivation
- Decision-making
- Problem solving

Existing supervisors should be trained to update and reinforce the knowledge and skills they have. Because the supervisor is often considered a role model to those working in the area, many supervisors participate in area GMP training efforts as well.

F. MANAGER TRAINING:

Understanding the importance of training in meeting regulatory requirements and improving the efficiency of vaccine manufacturing by managers is essential for implementing a successful training programme. Quality, motivation and education are very closely related and managers play an important role in motivating their staff.

"It is more important to train management than anyone else in the plant".

"Training should be carried out from the top to the bottom of the staff and with managers involved as much as possible".

Managers and supervisors need to be trained in their responsibilities under GMPs and good laboratory practice (GLPs) for non-clinical studies.

This includes knowing what their signature means from a legal perspective. High-level managers must understand the consequences of negligence, for example. If a serious quality

problem occurs or if a serious problem exists in clinical trials, and it is later discovered that a manager was negligent in following the law or in directing others to follow the law, then he or she can be sent to prison, or the facility or the study can be shut down.

They should also be updated in GMP trends.

Managers should learn to communicate effectively with supervisors and subordinates and also to learn diverse ways to motivate and encourage their staff. The following aspects may be included in the manager training.

- Communication
- Motivation
- Decision-making
- Leadership
- Empowerment
- Business skills
- Team building
- Managing change
- Time management and delegation
- How to orient and train employees
- Conducting productive department meetings
- Performance appraisal and coaching.

G. TRAINER'S TRAINING:

Not everyone who is knowledgeable in a given topic can be an effective trainer. The desires to train, help others, and continually learn are traits trainers have in common. In addition, trainers need to have and continually develop their skills as communicators and coaches.

Typically, trainers (both those who teach to groups in classrooms, as well as those who work individually with people during structured on-the-job training) should have an understanding of how adults learn and in providing effective feedback to trainees.

On-the-job and SOP trainers should be recognized experts in the area or in the tasks that they perform. They should also understand the best ways to teach tasks and procedures.

Group trainers should have "presentation skills" to use various training media (e.g. slides, overheads, flipcharts), methods (e.g. discussions, games, case studies, lectures), and know how to respond to questions and difficult situations.

H. REMEDIAL TRAINING:

Remedial training is given when there is evidence that the original training was not adequate, resulting in a person who cannot correctly, safely, effectively or efficiently perform the task.

Remedial training is frequently used incorrectly, as corrective actions to deviations or failures. "Retrain the operator" or "retrain the lab analyst" are seen much more often in investigation reports than actually warranted.

"Retraining" is an easy, but usually invalid corrective action that is used when the real root cause of the problem is not obvious.

"Training is a powerful tool. It plays an important role. But using it inappropriately is a waste of time, money and opportunity. If training is not done properly, this can have significant regulatory and compliance consequences".

I. JOB-CHANGE TRAINING:

Companies that have a defined, well-functioning training programme consider the training needs of someone who moved from one position in the company to a new position.

"The training must cover the particular duties performed in the employee's position. Adequate training must therefore be given to every employee when she or he is assigned to a new job function.

Work-specific training (GMP, on-the-job and safety training) should be conducted for the employee's new needs, taking into account the previous knowledge, skills and attitudes that they have developed.

The supervisor and the GMP trainer or training coordinator should identify the specific training required and when and how it can be provided by creating an individual training plan.

Job change training may be organized and accomplished in the following way.

- Review the employee's training record.
- Review the training requirements for the new job position.
- Prepare a training plan for the employee based on the analysis of the employee training record vs the training requirements for the new job; consider the orientation to the department in case of movement to another department.
- Perform the trainee's assessment.

Personnel hygiene

- All personnel, prior to and during employment, as appropriate, should undergo health examinations. Personnel conducting visual inspections should also undergo periodic eye examinations.

- All personnel should be trained in the practices of personal hygiene. A high level of personal hygiene should be observed by all those concerned with manufacturing processes. In particular, personnel should be instructed to wash their hands before entering production areas. Signs to this effect should be posted and instructions complied with.

- Any person shown at any time to have an apparent illness or open lesions that may adversely affect the quality of products should not be allowed to handle starting materials, packaging materials, in-process materials or medicines until the condition is no longer judged to be a risk.

- All employees shall be instructed to report about their illness or abnormal health condition to their immediate supervisor so that appropriate action can be taken.

- All employees should be instructed and encouraged to report to their immediate supervisor any conditions (relating to plant, equipment or personnel) that they consider may adversely affect the products.

- Direct contact should be avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product.

- To ensure protection of the product from contamination, personnel should wear clean body coverings appropriate to the duties they perform, including appropriate hair covering. Used clothes, if reusable, should be stored in separate closed containers until properly laundered and, if necessary, disinfected or sterilized.

- Personal hygiene procedures, including the wearing of protective clothing, should apply to all persons entering production areas, whether they are temporary or full-time employees or non-employees, e.g. contractors' employees, visitors, senior managers and inspectors.

- Smoking, eating, drinking, chewing, and keeping plants, food, drink, smoking material and personal medicines should not be permitted in production, laboratory and storage areas, or in any other areas where they might adversely influence product quality.

- The personnel handling Beta-lactum antibiotics shall be tested for Penicillin sensitivity before employment and those handling sex hormones, cytotoxic substances and other potent drugs shall be periodically examined for adverse effects. These personnel should be moved out of these sections (except in dedicated facilities), by rotation, as a health safeguard.

Personal Records

CERTIFICATE FOR MEDICAL CHECK-UP:

XYZ PHARMACEUTICALS LTD.

Name and address of the person examined	
Sex	
Age	
Marital status	
Blood group	
He/she is examined for the following:	

Height	
Weight	
Pulse	
Eye-sight	
Respiratory diseases	
Gastrointestinal diseases	
Cardiovascular diseases	
Abnormality of CNS	
Leprosy, skin disease, aids	
Any contagious and communicable diseases	
Sensitivity test of penicillin	

He/ she needs following treatment /investigation.

1.

2.

3.

Declaration

He/she is medically fit/unfit for any type of job

Place: signature of doctor

Date: Seal

SANITATION RECORD:

XYZ PHARMACEUTICALS LTD.

Dept.	Month
Area	Ref sop no.
Room no.	

Factory compound	Floor mates	Corridors	Stair cases	Wash basins	Celling	Toilet seats	Walls	Doors	Tube light/fans	Approach roads	Cleaned and checked

DISINFECTANT / CLEANSING RECORD:

Days	Disinfectant / cleansing agent(conc. water)	**Floor**	**Wall**	**celling**	**Area doors & corridor**	**Tables and**	**Toilet**	**Water tank**	**View panel**	**Done**	**Check by**
M	Dettol										
	Savlon										
	Washing powder										
	Colin spray										
T	Dettol										
	Savlon										
	Washing powder										
	Colin spray										
W	Dettol										
	Savlon										
	Washing powder										
	Colin spray										
T	Dettol										
	Savlon										
	Washing powder										
	Colin spray										
F	Dettol										
	Savlon										
	Washing powder										
	Colin spray										
S	Dettol										
	Savlon										
	Washing powder										
	Colin spray										

UNIFORMS LAUNDERING RECORD:

XYZ PHARMACEUTICAL LTD.

Month:	
Ref sop no:	

For laundering to sub contractor					Received after laundering			
Date	Item	No of item	Received by	Given by	Date	item	Qty	Received by

There are some common records those should be kept:

1. **Equipment cleaning and use log**

   A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed.

   As new computerized technology became available it has been possible to move to paperless control of manufacturing processes. These computerized controls had several advantages over manual systems:

   - More consistent control.
   - Only approved (trained) personnel could perform a process.
   - Processing could be prevented until any prior steps or checks were performed.
   - Precise recording of the times of operations were possible.

2. **Component, Drug product container, closure, and Labeling records**

   These records shall include the following:

   a) The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labeling; the name of the supplier; the supplier's lot number(s), if known; the receiving code and the date of receipt. The name and location of the prime manufacturer, if different from the supplier, shall be listed if known.

   b) The results of any test or examination performed and the conclusions derived there from.

c) An individual inventory record of each component, drug product container and closure and, for each component, a reconciliation of the use of each lot of such component. The inventory record shall contain sufficient information to allow determination of any batch or lot of drug product associated with the use of each component, drug product container and closure.
d) Documentation of the examination and review of labels and labeling for conformity with established specifications.
e) The disposition of rejected components, drug product containers, closure, and labeling.

3. Master production and control records

To assure uniformity from batch to batch, master production and control records for

each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person.

The master production and control records for each drug product describe all aspects of its manufacture, packaging, and control (inspection and testing).

Master production and control records shall include:

(1) The name and strength of the product and a description of the dosage form.
(2) The name and weight or measure of each active ingredient per dosage unit or per unit of weight or measure of the drug product and a statement of the total weight or measure of any dosage unit.
(3) A complete list of components designed by names or codes sufficiently specific to indicate any special quality characteristic.

4. Batch production and control records

The batch production and control record follows every production batch through the plant. It provides a detailed description of all processing operations and controls, when they are performed, by whom, and where.

The batch records that accompany material through processing provide information for operators and also serve as a means for documenting which ingredients were added, which control measures were exercised in process and final assay of the drug product, and the huge amount of information produced during the manufacturing cycle.

5. LABORATORY RECORDS

Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays as follows:

a) A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing.

b) A statement of each method used in the testing of the sample. The statement shall indicate the locations of data, which establish that the methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested.
c) A statement of the weight or measure of sample used for each test where appropriate.
d) A complete record of all data secured in the course of each test, including all graphs, charts, and spectra from laboratory instrumentation properly identified to show the specific component, drug product container, closure, in-process material, or drug product, and lot tested.
e) A record of all calculations performed in connection with the test, including units of measure, conversion factors, and equivalency factors.
f) A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, drug product container, closure, in-process material, or drug product tested.
g) The initials or signature of the person who performs each test and the date(s) the tests were performed.
h) The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.