GOOD MANUFACTURING PRACTICES: AN OVERVIEW

Basic Principles of GMP

1. Introduction to the training programme
2. Quality Management
3. Sanitation and hygiene
4. Validation
5. Complaints and recalls
6. Contract production and analysis
7. Self Inspection
8. Personnel
9. Premises
10. Equipment
11. Materials
12. Documentation
13. Sterile production
14. Active pharmaceutical ingredients

GMP Inspection Process

1. Introduction
2. The role of the inspector

Quality Management

Objectives

- To understand key issues in quality assurance/quality control.
- To understand specific requirements on organization, procedures, processes and resources.
- To develop actions to resolve your current problems.
- Determines and implements the “quality policy”

Quality Management

- Determines and implements the “quality policy”
- The basic elements are:
  - an appropriate infrastructure or “quality system” encompassing the Procedures, Processes, and Resources
  - the systematic actions necessary to ensure adequate confidence that a product (or service) will satisfy given requirements for “Quality”

  The totality of these actions is termed “Quality Assurance”

Sanitation and Hygiene

Objectives

Review measures to ensure good sanitation in:

- premises
- equipment
- processes

- To review measures to ensure good personnel hygiene
- Group session - to discuss the situation in your country and to look at some bad sanitation and hygiene practices in some photographs.

Scope

All aspects of manufacturing

- Personnel
- Premises
- Equipment
- Apparatus
- Production materials and container
- Products for cleaning and disinfection
- All potential sources of cross-contamination

Design of Premises

- Design
  - Walls, floors, ceilings, ledges, drains, air supply, dust extraction
- Prevention of build-up of dirt and dust to avoid unnecessary risks of contamination
  - Cleaning programme, appropriate cleaning, cleaning records
- Effective cleaning and disinfection
  - choice of materials and chemicals, validation
- Drains
- Protection from insects, vermin and weather
  - from receipt of raw materials to despatch of released product

Avoidance of Cross-Contamination I

- Segregated areas
- Ventilation systems and airlocks
- Clothing
- Closed processing systems
- Cleaning and decontamination

Validation

Objectives

- To review the definition and types of validation
- To understand the requirements for documentation and key stages in the process of validation
- To consider models for process validation

Definition

- Validation is the documented act of proving that any procedure, process, equipment, material, activity or system actually leads to the expected result

Essential Part of GMP

- Predetermined protocols
- Written reports
- Processes and procedures
- Periodic revalidation
- Specific attention:
  - processing
  - testing
  - cleaning

Complaints and Recalls

Product Complaint Principle

"All complaints and other information concerning potentially defective products must be carefully reviewed according to written procedures."

Objectives

- To identify the key issues in product complaint and recall handling
- To understand the specific requirements for organization, procedures and resources
- To understand and develop actions to resolve current issues applicable to you

Complaints Handling Principle

- All complaints and other information concerning potentially defective products must be carefully reviewed according to written procedures
  - Handled positively and carefully reviewed
  - Must be seen as important work
  - Managed by a senior staff member
  - Thorough investigation of the cause is essential
  - A major source of information and learning
  - Enable possible production defects to be remedied before they lead
    to a recall.
  - Necessary actions taken -- even a recall decision

Self-Inspection

Objectives

- To identify the role of self-inspection in the quality management system.
- To review the way in which a self-inspection programme should be carried out.
- To discuss what to check in a company's self-inspection.

Principle - I

- Ensures that a company's operations remain compliant with GMP
- Assists in ensuring continuous quality improvement
- Should
  - cover all aspects of production and quality control
  - be designed to detect shortcomings in the implementation of GMP
- Must
  - recommend corrective action if shortcomings are observed
  - set a timetable for corrective action to be completed

Principle - II

Special occasions may demand additional self-inspections. For example

- Recalls
- Repeated rejections
- GMP inspections announced by the National Drug Regulatory Authority

Principles - III

- Team consist of personnel who can evaluate the situation objectively
- No conflict of interest
- No revenge in mind
- Should have experience as observers of a self-inspection team before becoming team member
- Lead self-inspector with experience as team member

Personnel

Objectives

- To review general issues related to personnel
- To review requirements for key personnel
- To review the training of personnel
- To consider some specific issues

Principle

- Establishment and maintenance of satisfactory system of QA and manufacturing of products and actives rely on people.
- Must be sufficient qualified personnel to carry out tasks
- Individual responsibilities must be clearly understood by individuals concerned
- All personnel should be aware of the principles of GMP that affect them

General - I

- Adequate number of qualified people with practical experience
- An individual's responsibilities should not be so extensive as to present a risk to quality

General - II

- Individual written job description
- Organization Chart
- No gaps or unexplained overlaps
- Adequate authority to carry out responsibilities

Premises

Objectives

1. To review general requirements
2. To list key requirements for site choice
3. To consider specific requirements for main areas
4. To list major facilities required in a multifunction site

Principle

Premises must be located, designed, constructed, adapted and maintained for the operations:

- Minimize risks of errors and cross-contamination
- Permit effective cleaning
- Permit effective maintenance
- Minimize build-up of dirt and dust
- Eliminate any adverse effects on quality

Principle

Premises must be located to minimize risks of cross-contamination; e.g. **not** located next to a malting factory with high airborne levels of yeast

Equipment

Objectives

- To review the requirements for equipment selection, design, use and maintenance
- To discuss problems related to issues around selected items of equipment

Principle

- Equipment must be
  - located
  - designed
  - constructed
  - adapted
  - maintained

  to suit their intended use

Principle

- Equipment layout and design must aim:
  - to minimize risks of error
  - to permit effective cleaning
  - to permit effective maintenance
- And to avoid:
  - cross-contamination
  - dust and dirt build-up
  - any adverse effect on the quality of products
- Equipment must be installed to:
  - minimize risks of error
  - minimize risks of contamination

Materials

Objectives

- To review specific requirements for each type of material:
  - Starting materials
  - Packaging materials
  - Intermediate and bulk products
  - Finished products
  - Rejected and recovered materials
  - Recalled products
  - Returned goods
  - Reagents and culture media
  - Reference standards
  - Waste materials
  - Miscellaneous materials.
- To examine (in groups) the problems associated with materials, and how to overcome them.

Principle

- Objective of the pharmaceutical manufacturer:
  - produce finished products
  - combination of materials
- Materials combined:
  - active pharmaceutical ingredients
  - auxiliary materials(excipients)
  - packaging materials
  - Special attention

General requirements for materials

- All incoming materials and finished products:
  - quarantined after receipt,
    - until released for use
    - distribution
  - stored
    - under appropriate conditions
    - orderly fashion (batch segregation)
    - materials management
    - stock rotation (FIFO or EEFO))

Documentation

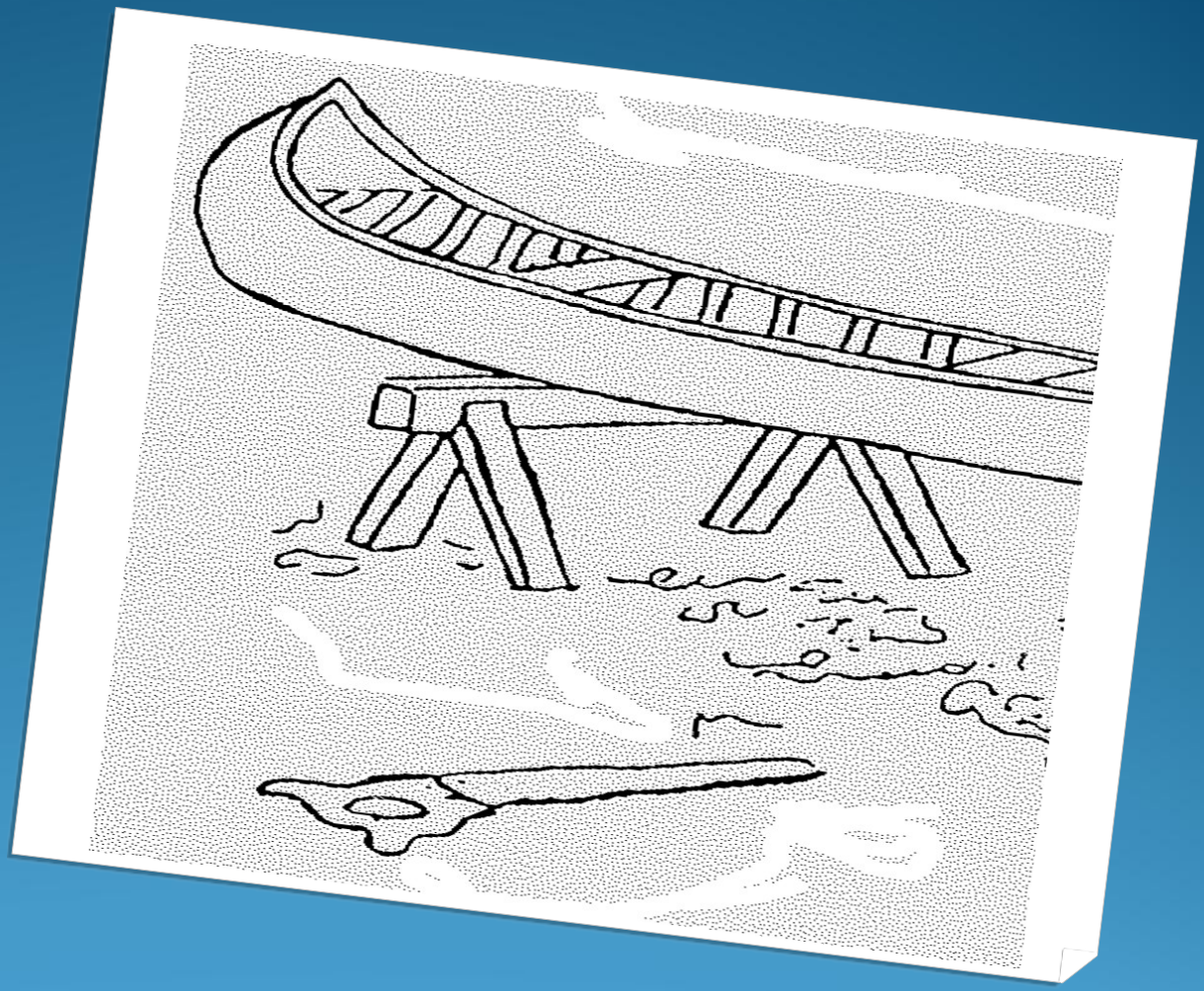
Objectives

1. To review general requirements for documents
2. To review specific requirements for each document
3. To consider current issues applicable to different countries

General Principles – I

- Documentation is an essential part of QA and relates to all aspects of GMP
- Purpose of documentation
  - to ensure that there are specifications for all materials and methods of manufacture and control
  - ensure all personnel know what to do and when to do it
  - ensure that authorized persons have all information necessary for release
  - provide audit trail

What is being made?



Most of us when attempting a task need some sort of documentation

And if the drawing is wrong!

The end product will look like this!

Sterile Production

Objectives

- To review basic GMP requirements in the manufacture of sterile products
- To review air classifications for activities related to the manufacture of sterile products
- To review the different types of sterilisation methods
- To review quality assurance aspects in the manufacture and control of sterile products
- To consider current issues applicable in your country.

Types of sterile products

- Terminally sterilised
  - prepared, filled and sterilised
- Sterilised by filtration
- Aseptic preparation

GMP Requirements for Sterile Products

- Additional rather than replacement
- Specific points relating to minimizing risks of contamination
  - microbiological
  - particulate matter
  - pyrogen

Active Pharmaceutical Ingredients

Objectives

- To discuss the GMP guidelines for the manufacture of Active Pharmaceutical Ingredients (APIs)
- To examine key problems experienced during inspections of the manufacturers of APIs and to seek possible solutions

Areas to be Covered

- General considerations
- Personnel
- Premises
- Equipment
- Sanitation
- Documentation
- Retention of records and samples
- Production

General Considerations

- Overall control
- Consistent uniform batches
- Compliance with GMP
  - production
  - quality control
- General guidelines
- Co-operation in production
- Human and veterinary preparations

GMP Inspection Process

Programme Objectives

1. Training in the WHO GMP text on inspection
2. Training in using your experience
3. Developing your own action plan

Programme Overview

- Introduction
- The fundamentals of inspection
  - the role of the inspector
  - preparing for inspections
  - the inspection process
- Types of inspection

The Role of the Inspector

Objectives

1. To discuss the ideal qualities of an inspector
2. To review the various roles of an inspector
3. To discuss the basic rules of communication

Qualifications

- Training
- Practical experience
  - manufacture and/or quality control
- Academic qualifications
  - pharmacists, chemists, scientists
  - pharmaceutical industry background

Training

- In-post training
- Accompany experienced inspectors
- Regular update of knowledge
- Courses and seminars
  - pharmaceutical technology
  - microbiology
  - statistical aspects of quality control

Responsibilities

- Detailed factual report
  - manufacture and control
  - specific products
- Assess GMP compliance
  - faults, irregularities, discrepancies
- Advice on improving manufacture and control
  - depending on national policy
  - must be consistent and available to all
  - motivate manufacturer to comply with GMP
  - correct specific deficiencies

How many basic GMP deficiencies can you detect in the photographs below:

How many basic GMP deficiencies can you detect in the photographs below?

Thank you for your Patience & Time.

Have a Nice Day