



## Comprehensive Review On Gmp Of Pharmaceutical Products

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**Abstract:** The concepts of GMP are not new, it is from ancient times. The concept required for GMP are explained in this report. The main purpose of GMP is preventing mistakes and errors involved in any manufacturing activities. To achieve agreement of guidelines and laws of the manufacturing of medical products for human use there are some public and also private organizations institutes and regulatory authorities who work and cooperate with pharmaceutical industry.

GMP guidelines provide minimum requirements for pharmaceutical or a food product manufacturer must meet to assure that the products are of high quality and do not pose any risk to the consumer or public. Good manufacturing practices (GMP) is a part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

**Index Terms - GMP, Manufacturing activities, Guidelines, Quality assurance, Quality Standards.**

### I. INTRODUCTION

The concept of Good Manufacturing Processes was introduced to regulate packaging and manufacturing processes in the pharmaceutical industrial areas.[1]

Manufactures follows various procedures and principles for the therapeutic good which helps in ensures the required quality of products. Good manufacturing practices is the component of quality assurance which helps in ensure the ensure the products are consistently manufactured and controlled to the Quality Standards appropriate to their intended use.

Good manufacturing practices is mainly used to reduce risk involved in production of pharmaceuticals products that cannot be removed through testing of the final products. Good Manufacturing practices covers all views of production from initiating materials, equipment's, premises to personal hygiene and training of employees.

A basic principle of Good Manufacturing Practices is that quality cannot be tested into a batch of product but must be built into each batch of product during all stages of the manufacturing process. It is designed to minimize risk involved in any pharmaceutical production that cannot be eliminated through testing the final product.

### Good Manufacturing Practices:

The quality of formulation and bulk drug depends on the quality of those producing it.

Good manufacturing practices is the magic key that opens the door quality

In matter of GMP swim with the current and in matter of quality stand like a rock

Most countries will only accept import and sale of medicine that have been manufactured to internationally recognized GMP

Government Seeking to promote their countries export of pharmaceuticals can do so by making GMP mandatory for all pharmaceutical production and by training their inspectors in GMP requirements. [2,3]

### Why GMP is important:

- A poor-quality medicine may contain toxic substance that has been unintentionally added.
- A medicine that contains little or none of the claimed ingredients will not have the intended therapeutic effect. Provides a high-level assurance that medicines are manufactured in a way that ensures their safety efficiency and quality.
- It maintains the consistency in the manufacturing of the medical products.
- To eliminate contamination and to minimise the error GMP is important.

- Good Manufacturing Practices ensures companies execute consistent procedures in safe environments.
- Good Manufacturing Practices helps in ensure the proper design, monitoring and control of manufacturing process and facilities, while securing the identity, strength, quality of their products.
- Good Manufacturing Practices assist cutdown on facility losses and waste and also to protect consumers the manufacturer from harm. [3,4]

### How to Comply with Guidelines:

GMP guidelines and regulations address different issues that can influence the safety and quality of a product. Meeting GMP or cGMP standards helps the organization comply with legislative orders, increase the quality of their products, improve customer satisfaction, increase sales, and earn a profitable return of investment. [5,6]

Conducting GMP audits play a big part in assessing the compliance of the organization to manufacturing protocols and guidelines. Performing regular checks can minimize the risk of adulteration and misbrand. A GMP audit helps improve the overall performance of different systems including the following:

- Building and facilities
- Materials management
- Quality control systems
- Manufacturing
- Packaging and identification labelling
- Quality management systems
- Personnel and GMP training
- Purchasing
- Customer service

### Good manufacturing practice - the general/current state:

#### ➤ Pharmaceutical quality system:

This guideline describes a comprehensive model for an effectiveness quality system of medicinal products, based on the concepts of ISO quality and its implementation throughout all stages of the lifecycle of the product.

The guideline applies to supporting the development and manufacture of substances of Pharmaceutical Industry, Active Pharmaceutical Ingredient and medicinal products, including biotechnology and biological products throughout the life cycle of the product.

Quality assurance is a broad concept that includes all matters that individually or collectively influence the quality of a product, that is, management of the quality of raw materials, products and other components, services related to production, and management, production and inspection processes. It is applied in pre-production to verify what will be made meets specifications and requirements and also while manufacturing production. [7,8]

#### Personnel:

According to GMP, the management of an enterprise should determine and provide appropriate resources such as human resources, financial, materials, facilities and equipment to implement and maintain the Quality Management System and improve effectiveness. Effective coordination and management of human resources are key factors in the proper functioning of any enterprise system and improve effectiveness.

For the maintenance of satisfactory system of quality assurance and the correct manufacture and control pharmaceutical products there must be sufficient qualified personnel to carry out all the tasks for which manufacturer is responsible.

Personnel should be aware of principles of GPM that affects them and receive initial and continuing training, including hygiene instructions, relevant to their need. [9,10]

#### Premises and equipment:

Premises and equipment must meet and comply with all rules, according to the operations to be performed in order to minimize the risk of errors and should allow effective cleaning and maintenance. [11,12]

#### Some examples are:

**a. Walls:** Walls in manufacturing areas, packaging areas and corridors should be of plaster finish on high-quality concrete blocks or gypsum board. The finish should be smooth, usually with enamel or epoxy paint. They should be washable and able to resist repeated applications of cleaning and disinfecting agents.

**b. Floors:** Floor covering should be selected for durability as well as for clean ability and resistance to the chemicals with which it is likely to come into contact. Epoxy flooring provides a durable and readily cleanable surface.

**c. Ceilings:** Manufacturing areas require a smooth finish, often of seamless plaster or gypsum board. All ceiling fixtures such as light fittings, air outlets and returns should be designed to assure ease of cleaning and to minimize the potential for accumulation of dust.

#### Raw Material:

All materials used for production should be stored properly according to the appropriate conditions which are set by the manufacturers.

There should be a proper stock management system implemented to ensure that all incoming materials are correct and of high quality. [13]

**Documentation:**

Good documentation constitutes an essential part of the quality assurance system and it is the key to operate in compliance with GMP requirements.

All types of documents and media used should be fully defined in the manufacturer's Quality Management System.

Given below is a list of the most common types of documents along with a brief description of each [14,15]

**Site Master File:** A document describing the GMP related activities of the manufacturer.

**Quality Manual:** A global company document that describes, in paragraph form, the regulations and/or parts of the regulations that the company is required to follow.

**Policies:** Documents that describe in general terms, and not with step-by-step instructions, how specific GMP aspects (such as security, documentation, health, and responsibilities) will be implemented.

**Logbooks:** Logbooks are used for documenting the operation, maintenance, and calibration of a piece of equipment.

Logbooks are also used to record critical activities, e.g., monitoring of clean rooms, solution preparation, recording of deviation, change controls and its corrective action assignment.

**Test Methods:** These documents are typically used and completed by the quality control (QC) department. Test methods provide step-by-step instructions for testing supplies, materials, products, and other production-related tasks and activities, e.g., environmental monitoring of the GMP facility.[16]

**Production:**

Production operations must clearly follow the procedures. They must comply with the principles of GM Pin order to obtain quality products and be in accordance with the relevant manufacturing.

All handling of materials and products, such as reception and quarantine, sampling, storage, labelling, dispensing, processing, packaging and distribution should be done in accordance with written procedures or instructions and where necessary, recorded.[17]

**Quality control:**

Quality control is concerned with sampling, specifications and testing as well as the organization, documentation and release procedures which ensure that the required and relevant tests are carried out, and that materials are not released for use, nor products released for sale or supply, until their quality has been judged satisfactory.

QC is not confined to laboratory operations, but may be involved in many decisions concerning the quality of the product.[18]

**Quality risk management**

Quality risk management is a systematic process of assessing risks that can affect the quality of the product. According to its principles, quality risk management should ensure that:

The evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient and users;

The level of effort, formality, and documentation of the quality risk management process is commensurate with the level of risk.

c) The general quality risk management process and integration into the product quality can be referred to in ICHQ9. [19,20]

**Validation and qualification**

Qualify systems, premises, and equipment if they are fit/ready for their intended use and validate if processes and procedures can repeatedly produce high-quality products. Critical steps in the manufacturing process should be verified to ensure that product quality is consistent and maintained at a high level. According to the WHO (World Health Organization), qualification and validation should establish and provide documentation stating that:

the premises, supporting utilities, equipment, and processes have been designed in accordance with the requirements for GMP (design qualification or DQ)

the premises, supporting utilities, and equipment have been built and installed in compliance with their design specifications (installation qualification or IQ);

the premises, supporting utilities, and equipment operate in accordance with their design specifications (operational qualification or OQ); and a specific process will consistently produce a product meeting its predetermined specifications and quality attributes (process validation or PV, also called performance qualification or PQ) [21,22,23]

**Self-inspection:**

The objectives of self-inspections are the evaluation and supervision of compliance of the manufacturer with GMP in all aspects of production and quality control. It must be designed to detect any deficiency in the implementation of GMP and to recommend corrective procedures.[24]

**Sanitation And Hygiene: -**

A high level of sanitation and hygiene should be practiced in every aspect of the manufacture of medicine products. The scope of sanitation and hygiene covers personnel, premises, equipment and apparatus, production materials and containers, products for cleaning and disinfection, and anything that could become a source of contamination to the product. Potential sources of contamination should be eliminated through an integrated comprehensive programmed of sanitation and hygiene

The areas, surfaces, and equipment in and on which products are made must be kept clean. Dirt, and the microbes that it can harbor, must not get into or on products. Disinfectants can be inactivated by dirt. Dirt (particularly oily or greasy films and protein like matter) can also protect microorganisms against the action of disinfectants. So, before disinfection, it is important to first clean surfaces. Where gross amounts of dirt are present, it may be necessary to first remove most of it by scrubbing. Then surfaces may be cleaned by the application of a cleaning agent, followed by rinsing. [24,25,26]

**Basic requirements for active substances used as starting materials:**

This guideline is intended to provide guidance regarding GMP for the manufacture of active substances under an appropriate system for managing quality. It is also intended to ensure that active substances meet the requirements for quality and purity that they purport or are represented to possess.

These guidelines apply to the manufacture of active substances for medicinal products for human use and to the manufacture of sterile active substances only up to the point immediately prior to the active substance being rendered sterile.[27]

**Manufacture of medicinal products-**

Manufacture of solid and semi-solid medicinal product:

Since this type of medicinal products is particularly susceptible to microbial contaminants and other contaminants during manufacturing, it is necessary to follow preventive procedures and it should be a priority for the manufacturer MA holder.[28]

**Manufacture of herbal medicinal product:**

The procedures and techniques used in the manufacture and quality control of herbal medicines are often substantially different from those used for conventional medicinal products. The herbal substance should be of suitable quality. The supporting data should be provided to the manufacturer of the herbal medicinal products. These guidelines apply to all herbal starting materials: Medicinal plants, herbal substances or herbal preparations. These guidelines apply to all herbal starting materials: Medicinal plants, herbal substances or herbal preparations.[29]

**Manufacture of biological active substances and medicinal products for human use:**

The methods employed in the manufacture of biological active substances and biological medicinal products for human use are critical factors in shaping the appropriate regulatory control, because the manufacture of these involves certain specific considerations arising from the nature of products and manufacturing processes, being necessary take some special precautions. Unlike conventional medicinal products, which are normally produced and controlled using reproducible chemical and physical techniques, biological products are manufactured through methods that involve biological processes and materials, such as cultivation cells or extraction of material from living organisms.[30]

**Manufacture of sterile medicinal product:**

The manufacture of sterile products requires special requirements in order to minimize risks of microbiological contamination, and of particulate and pyrogen contamination, being highly dependent on knowledge, training and attitudes of the personnel involved. This type of manufacture must strictly follow methods and preparation processes, carefully established and validated, since the quality assurance, is of particular importance.[31]

**sampling of starting and packaging material:**

Sampling is an operation where a small fraction of the batch is removed integrating operations to select a portion of a pharmaceutical product for a specific purpose, in accordance with an appropriate procedure. This process should be carried out in accordance with written and approved procedures that are appropriate to the sample and the type of control intended to be applied to the sample and the sample material.[32]

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**REFERENCES**

1. Sharp, J.: Quality in the manufacture of medicines and other healthcare products, pharmaceutical press, ISBN London, 2000, 0-85369-431-1.
2. Signoret, A. A. and Jacobs, T.: Good design practices for GMP pharmaceutical facilities, Taylor & Francis group, ISBN Boca Raton, 2005, 10: 0-8247-5463-8 & ISBN 13: 978-0-247- 5463-1.
3. 21CFR 211: 2011, PART 211; current good manufacturing practice for finished pharmaceuticals, title 21-food and drugs, chapter I-food and drug administration, Department of health and human services subchapter C-Drugs: General, [Code of federal regulations, title 21, Volume 4, Revised as of April 1, 2011],
- 4 Part 1, Ch. 2. Vol. 4. Brussels: European Commission; 2013. European Commission, Health and Consumers Directorate-General. Eudralex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Personnel.
5. Geneva, Switzerland: 2008. ICH Expert Working Group. ICH Harmonized Tripartite Guideline,

- Pharmaceutical Quality System Q10. International Conference of Technical Requirements for Registration of Pharmaceuticals for Human Use; 2008 June.
6. Geneva: ICH Legal Mentions; c2014. [Last cited on 2014 Feb 19]. ICH. Harmonization for Better Health. ICH Quality Guidelines; Pharmaceutical Quality System Q10.
7. Part 1, Ch. 1. Vol. 4. Brussels: European Commission; 2010. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Pharmaceutical Quality System.
8. Part I, Ch. 1. Geneva: PIC/S Secretariat; 2013. Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme. Guide to Good Manufacturing Practice for Medicinal Products, Quality Management.
9. 2nd ed. Vol. 2. Geneva: WHO Library Cataloguing in Publication Data; 2007. World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials. Good Manufacturing Practices and Inspection, Quality Management in the Drug Industry; pp. 15–18.
10. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Quality Management in the Medicines Industry: Philosophy and Essential Elements. WHO Technical Report Series, No 961, Forty-fifth Report.
11. Part 1, Ch. 2. Vol. 4. Brussels: European Commission; 2013. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Personnel.
12. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Personnel; Training; Personnel Hygiene. WHO Technical Report Series, No 961, Forty-fifth Report
13. Geneva, Switzerland: 2008. ICH Expert Working Group. ICH Harmonized Tripartite Guideline, Pharmaceutical Quality System Q10. International Conference of Technical Requirements for Registration of Pharmaceuticals for Human Use; 2008 June.
14. Geneva: ICH Legal Mentions; c2014. [Last cited on 2014 Feb 19]. ICH. Harmonization for Better Health. ICH Quality Guidelines; Pharmaceutical Quality System Q10.
15. Part 1, Ch. 1. Vol. 4. Brussels: European Commission; 2010. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Pharmaceutical Quality System.
16. Part I, Ch. 1. Geneva: PIC/S Secretariat; 2013. Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme. Guide to Good Manufacturing Practice for Medicinal Products, 3Quality Management.
17. 2nd ed. Vol. 2. Geneva: WHO Library Cataloguing in Publication Data; 2007. World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials. Good Manufacturing Practices and Inspection, Quality Management in the Drug Industry; pp.

15–18.

18. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Quality Management in the Medicines Industry: Philosophy and Essential Elements. WHO Technical Report Series, No 961, Forty-fifth Report.

19. Part 1, Ch. 2. Vol. 4. Brussels: European Commission; 2013. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Personnel.

20. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Personnel; Training; Personnel Hygiene. WHO Technical Report Series, No 961, Forty-fifth Report

21. Geneva, Switzerland: 2008. ICH Expert Working Group. ICH Harmonized Tripartite Guideline, Pharmaceutical Quality System Q10. International Conference of Technical Requirements for Registration of Pharmaceuticals for Human Use; 2008 June.

22. Geneva: ICH Legal Mentions; c2014. [Last cited on 2014 Feb 19]. ICH. Harmonization for Better Health. ICH Quality Guidelines; Pharmaceutical Quality System Q10.

23. Part 1, Ch. 1. Vol. 4. Brussels: European Commission; 2010. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Pharmaceutical Quality System.

24. Part I, Ch. 1. Geneva: PIC/S Secretariat; 2013. Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme. Guide to Good Manufacturing Practice for Medicinal Products, Quality Management.

25. 2nd ed. Vol. 2. Geneva: WHO Library Cataloguing in Publication Data; 2007. World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials. Good Manufacturing Practices and Inspection, Quality Management in the Drug Industry; pp. 15–18.

26. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Quality Management in the Medicines Industry: Philosophy and Essential Elements. WHO Technical Report Series, No 961, Forty-fifth Report.

27. Part 1, Ch. 2. Vol. 4. Brussels: European Commission; 2013. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Personnel

28. Geneva: WHO Press; 2011. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Annex 3-WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles, Personnel; Training; Personnel Hygiene. WHO Technical Report Series, No 961, Forty-fifth Report

29. Geneva, Switzerland: 2008. ICH Expert Working Group. ICH Harmonized Tripartite Guideline,

Pharmaceutical Quality System Q10. International Conference of Technical Requirements for Registration of Pharmaceuticals for Human Use; 2008 June.

30. Geneva: ICH Legal Mentions; c2014. [Last cited on 2014 Feb 19]. ICH. Harmonization for Better Health. ICH Quality Guidelines; Pharmaceutical Quality System Q10.

31. Part 1, Ch. 1. Vol. 4. Brussels: European Commission; 2010. European Commission, Health and Consumers Directorate-General. EudraLex-EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Pharmaceutical Quality System.

32. Part I, Ch. 1. Geneva: PIC/S Secretariat; 2013. Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme. Guide to Good Manufacturing Practice for Medicinal Products, Quality Management.

