Good Manufacturing Practices - Overview and Mutual Recognition Agreements

August 2019

By: Kumar Bhat

Author Bio:

Kumar holds a Master of Science degree in Chemistry from Karnatak University. He has been working in the pharmaceutical industry for the last 10 years and has experience in data research and content development.

Good Manufacturing Practices (GMP) are a set of regulations and guidelines for the manufacture of drug substances and drug products, medical devices and foods. GMP guidelines, as a part of quality assurance, provide minimum requirements which a manufacturer of pharmaceuticals or food products must meet to assure that the products are of high quality and do not pose any risk to the consumer or public. GMP is recognised worldwide for the control and management of manufacturing and quality control testing of pharmaceutical products. GMP inspection has gained a new momentum with recent advancements such as Mutual Recognition Agreements which benefit both the regulatory authorities and the pharmaceutical manufacturers.

Overview of GMP

At the beginning of the 20th century, there were no federal regulations to protect the public from dangerous products, and technology was primitive. Over a period, due to an increasing need for consumer protection and tragic incidents involving various drug products, governments formed different laws and put requirements in place to govern the safety of food and drugs, with amendments whenever necessary. This led to the initiation of GMP in 1941, followed by the establishment of GMPs for Drugs in 1963.

Worldwide, there are different official regulatory statements and guidelines, both national and international, for GMP for pharmaceutical products. These may be regulations (as in the US, Japan, or Korea), directives and guides (as in the EU), codes (as in Australia), or a WHO code (as in many Southeast Asia Countries). Among them, the following stand out as the most influential and most frequently referenced:

- The US Current Good Manufacturing Practices for Finished Pharmaceuticals regulations (the US cGMPs).
- The Guide to Good Manufacturing Practice for Medicinal Products of the European Union (the EU GMP Guide).
- The International Conference on Harmonization (ICH Q7) Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.
- The World Health Organization (WHO) Good Manufacturing Practices.

Importance of GMP

For the pharmaceutical and food industries, products must be manufactured under conditions and practices mentioned by the GMP regulations or guidelines to ensure that every step of the manufacturing process is of high quality. Final testing on a small sample of a batch of the product cannot always ensure the quality, efficiency, safety or reproducibility. It is also vital that facilities themselves are in good condition, equipment is properly maintained and calibrated, and processes are reliable and reproducible, all of which is covered by GMP requirements.

Consequently, GMP builds customer confidence and aids in building company image and reputation, which can help boost pharmaceutical export opportunities. The majority of countries worldwide only accept the import and sale of medicines that have been manufactured to internationally recognised GMP standards. Considering this fact, IQVIA Chemical Intelligence provides customers with access to pharmaceutical companies holding various GMPs including US cGMPs, WHO GMP and EU GMP.

Basic principles of GMP guidelines

GMP guidelines are not enforceable instructions on how to manufacture products, they only provide guidance for manufacturing, testing, and quality assurance. Within this guidance, there are a series of general principles[1] that must be applied during manufacturing:

- **Written Procedures:** Development of detailed step-by-step procedures to be followed to ensure consistency in workplace performance.
- **Documentation:** Prompt and accurate documentation of work, allowing for compliance with regulations and the ability to trace any problems.
- **Validating Work:** Ensuring that all systems and processes are working as expected and according to plan.
- **Facilities and Equipment:** Outlines the importance of integrating productivity, product quality and employee safety into the design and construction of the company's facilities and equipment.

- **Maintenance:** The facilities and manufacturing equipment must be properly maintained, with documented written records of any work done or repairs.
- **Competent Employees:** GMP requires clearly defined job competencies for employees in relevant job positions.
- **Prevention of Contamination:** Appropriate cleanliness guidelines must be in place to ensure a product is protected from contamination by impurities of a chemical or microbiological nature, or of foreign matter.
- **Quality Control:** Involves building quality directly into products via the systematic control of components and processes relating to each product.
- **Audits:** Periodic audits are used to assess how well GMP is being implemented and if compliance with GMP regulations is successful.

GMP Inspection and Mutual Recognition Agreements

GMP audits and inspections are fundamental elements of managing quality in the pharmaceutical industry. Pharmaceutical companies as well as the suppliers are frequently inspected by the regulatory authorities (both national and international inspectorates like the US Food and Drug Administration (FDA)) as a central element of supervision. The objective of the inspections is either to enforce GMP compliance or to provide authorisation for the manufacture of specific pharmaceutical products, usually in relation to an application for marketing authorisation.

With the increasing globalisation of medicine manufacturing and supply chains, there is a need for regulatory authorities across the world to co-operate in the overall interest of public health. The European Medicines Agency (EMA) has started participating with partner organisations outside the European Union on GMP inspections and has signed Mutual Recognition Agreements (MRAs) with third-country authorities concerning the conformity in the assessment of regulated products. For example, in 1998 the EU and FDA signed the EU-US MRA, which included a Pharmaceutical Annex on the mutual recognition of GMP inspections. The EU-US MRA allows drug inspectors to rely upon information from drug inspections conducted within each other's borders.

The FDA is now collaborating with many European inspectorates and is reviewing their recent inspection reports and related information to determine each manufacturer's suitability for the US market, in lieu of an FDA site inspection. The FDA expects to complete its suitability assessment of all EU inspectorates by 2019[2].

GMP compliance can be a huge cost and time burden to manufacturers and authorities. MRAs benefit regulatory authorities by reducing duplication of inspections on each other's territory, allowing for greater focus on sites that could have a higher risk and broadening the inspection coverage of the global supply chain. MRAs also facilitate trade in pharmaceuticals because they can reduce costs for manufacturers by reducing the number of inspections taking place at facilities and by allowing any re-testing of imported products to be waived.

Conclusion

It is evident that Good Manufacturing Practices must be followed to produce safe and high-quality products. The food and pharmaceutical industries cannot work without consulting the relevant GMP principles and putting these into practice because those in the industry have a legal and moral responsibility to produce food and drugs which will not harm consumers. With the increasing emphasis on setting standards and regulation, knowledge of regulations in different countries is essential for understanding pipeline planning as well as for the international supply of products. Mutual Recognition Agreements benefit the regulatory authorities with greater efficiencies and benefit manufacturers with reduction in costs associated with GMP inspections.

IQVIA™ Chemical Intelligence is a leading information provider to purchasers, sellers and researchers in the Pharmaceutical and Chemical industries worldwide. To find out more, please click here.

1. Brent, Michael. "The 10 Principles of the GMP Lifestyle" *bizfluent.com*, https://bizfluent.com/info-8429579-10-principles-gmp-lifestyle.html 22 July 2019
2. https://www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra