Documentation and Record Maintenance: A Need for Good Manufacturing Practices (GMP) Compliance in Pharma & Healthcare Industry

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Abstract

Proper documentation and record maintenance is a principal step in good manufacturing practice regulations that a pharmaceutical manufacturer must follow. Documentation provides a thorough knowledge of the history and the present status of the manufacturing batches. Thus it provides a basis of what should be done in future or for the improvement in the process. Effective documentation provides the required information to the authorized personnel for the release of the batch. It also provides the specifications or the procedures for manufacturing and control of the drug products. A brief overview for the importance of documentation and record maintenance in pharmaceutical sector is outlined here.

Keywords Good manufacturing practices, documentation, records, pharmaceuticals, protocols, validation.

Introduction

Good Manufacturing Practice (GMP) is that part of quality assurance which ensures that products (drug or medicinal) are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization (MA) or product specification. GMP guidelines are not normative instructions for manufacturing a drug product. These are the series of principles that a company must follow during the manufacturing process. It is concerned with both quality control and production.

GMP guidelines are laid down with an aim of providing minimum standards that must be fulfilled during the production or manufacturing of the active pharmaceutical ingredient or drug products. GMP compliance is mandatory for market authorization or in other words, a company should be in compliance with GMP of the particular country to regulate its import and export of drug products to other country. Most of the countries allow import or sale of the medicines or drug products that have been manufactured as per internationally recognized GMP only. The first GMP guideline was introduced by US FDA in 1963 for manufacturing, processing, packing or holding finished pharmaceutical. Thereafter, many countries developed their own GMP
guidelines which are based on WHO GMP guidelines. The most frequently and effectively referenced GMP guidelines by pharmaceutical manufacturers are:

- 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 EC GMP Guide)
- The ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.
- The World Health Organization (WHO) good manufacturing practices.
- Schedule M 'Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products,' The Drugs and Cosmetics Act and Rules, India.
- PIC/S (Pharmaceutical Inspection Cooperation Scheme) Guide to Good Manufacturing Practice for Medicinal Products.

**Documentation: An Authenticated Proof for GMP Compliance**

Good documentation is a crucial part of the quality assurance system and is needed in almost every aspect of pharmaceutical manufacturing. It aims to provide high degree of assurance that the manufacturing process or quality related activities are carried out in the similar manner as they are planned and approved. It provides procedures or the detailed information regarding the process of manufacturing to the personals concerned with the manufacturing and ensures that the personals know what to do and when to do. It also ensures the accessibility of the records or data required for validation, review and statistical analysis. Proper record permits to keep track over the manufacturing of particular batch, starting from the receipt of raw materials, to the final product release.

"If it's not written down then it didn't happen!"

During an audit, these records communicate that the procedures are being followed. It also provides evidence that the process is under control and known.

**10. Golden Rules of GMP**

Pharmaceutical Inspection Cooperation Scheme has laid down 10 golden rules for good manufacturing practices which are as follows:

- **Rule 1**: Get the facility design right from the start.
- **Rule 2**: Validate Processes
- **Rule 3**: Write good procedures and follow them
- **Rule 4**: Identify who does what
- **Rule 5**: Keep good records
- **Rule 6**: Train and develop staff
- **Rule 7**: Practice good hygiene
- **Rule 8**: Maintain facilities and equipment
- **Rule 9**: Build quality into the whole product lifecycle
- **Rule 10**: Perform regular audits

Among these 10 golden rules rule number 3 and 5 relate to documentation and record keeping.

**Write Good Procedures and Follow Them**

The procedures should be clear, concise and logical. Clearly written procedures or records prevent the errors that may arise from verbal communication. These procedures should include the formula or detailed description for various operations like manufacturing, processing and packaging of the drug product. Written procedures provide the data for evaluation of the process to find out the need of change in drug specification or manufacturing process.

A good procedure is that which helps the personnel to understand each and every point written in it. Procedures must not be written in technical language that may unable the reader to understand the process and ultimately leads to cheap quality products. The documents must be reviewed to ensure that these are up-to-date. Majority of the industries conduct the review after 3 years but the period of the review can be varied depending upon the changes in the process written in the document. In pharma industries, maintaining the good procedure is essential to ensure the quality and consistency of the product as per the approved specifications and moreover it is a key to GMP compliance. But the most important part is to follow these procedures. In the procedure, every step is included with a purpose so the reader should not follow any shortcuts. The shortcuts may save the time but can also create pitfalls which may cost higher at the end. The various types of documents followed in pharma industry are as follows:
Specifications: The document which lists out the active and inactive starting materials, packaging materials, intermediate, bulk and finished pharmaceutical products in terms of their physical, chemical and biological characteristics. The QC personnel will compare their test results to these specifications for the evaluation of the quality of the product.

Procedures and Test Methods: These are written and approved documents which provide detailed instructions for performing testing, operating the instrument, other production related tasks etc.

Records and Reports: Records are the documents completed by the manufacturing departments and includes protocols, log books etc. Report provides the data regarding conduct of manufacturing procedures along with results, conclusions and recommendations.

Master Documents: These include master formula records, site master file, calibration master plans, batch processing and packaging records etc. This ensures the uniformity from batch to batch.

Lists: It contains the full catalog for example List of equipments etc.

The documents or records should not be handwritten, wherever necessary, the entry of the data can be made in clear and legible handwriting. And sufficient space should be provided for the entry of the data.

Keep Good Records

Records must provide the history of each batch of drug product manufactured in the industry. A good record maintenance enables personnel to keep the record of information that actually happened during the manufacturing operation in any pharmaceutical company. These records help to maintain the audit trial for subsequent investigations and tracking of the drug product batch.

“The Palest Ink is Better than the Best Memory”

Records must be maintained at the time of conduct of clinical trial, preclinical studies, manufacturing process and quality control checks to maintain the traceability. All essential information must be recorded after the completion of the task. After the completion of the defined procedure, the record must be duly signed by the personnel performing the task. The personnel should consult the quality department if any change is desired in the procedure. And any deviation from the written procedure must be recorded properly and reviewed by the quality control department so that it can't affect the quality of the product. The records should be maintained for each and every step of the manufacturing process. This includes:

- Product master records
- Batch manufacturing records (BMR)

- Materials/component control records
- Personnel records
- Training records
- Equipment log books
- Cleaning log books

The distribution of each batch of the product must be documented in the record book which may alleviate during the recall of any batch from the market, if needed. This distribution record must include the batch number, quantity produced, quantity supplied, date of supply, all the necessary details of the customer etc. The proper records should be maintained for returns, product recalls and customer complaints. The validation records including protocols, plan, design qualification, installation qualification, operational qualification, performance qualification etc. should be recorded in a specified manner. There must be a provision for maintenance of electronic records to have the traceability of the different operations conducted in the company. The checklist or checkpoint should be prepared to have an idea of maintenance of the records by different departments of the industry.

Case Studies

Lately, FDA has issued series of warning letters to pharmaceutical companies for GMP violations particularly for data integrity. The different companies who fail to ensure the data integrity are listed below:

- **Ranbaxy Laboratories**, a multinational pharmaceutical company has received a warning letter by US FDA for its two facilities that are Dewas and Poanta sahib facility. In Dewas facility, the company failed to maintain batch production and control records. And in Poanta sahib facility, incomplete batch and production records were there and inadequate procedures were followed for the review and approval of production and control records for drug products.

- **Wockhardt Limited**, a Mumbai based pharmaceutical company received a warning letter by US FDA for Aurangabad plants for data integrity issues. The company failed to assure that the laboratory records included complete data derived from all tests necessary to assure compliance with established specifications and standards. FDA also said the firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records or other records.

- **USV Limited**, a pharmaceutical manufacturer has recently received a warning letter by US FDA for its Mumbai plant for data integrity at control laboratories. The company failed to follow and document the required laboratory control mechanisms and also failed to have appropriate control over computer or related systems to assure that only authorized
personnel institute changes in master production and control records.

- Canton Laboratories, a manufacturer of chemical and bulk drugs has received a warning letter by US FDA for its Vadodara plant for reporting results for the tests that were never performed. Significant cGMP violations related to record maintenance were observed in the industry. The company was accused for serious documentation practices and reported missing data.

- Smurthi Organics Limited has received a warning letter by US FDA for its Solapur, Maharashtra plant for data integrity. The company failed to maintain the production and control records for currently marketed APIs. The company also failed to maintain complete and accurate laboratory test data generated in the course of establishing compliance of APIs to established specifications and standards.

**Conclusion**

As an increase in problem of data integrity in giant pharmaceutical companies, there is a need of proper and effective documentation and record maintenance in pharmaceutical companies. During the inspection of manufacturing sites, the regulators spend more time in analyzing the documents and records of the company. A good documentation helps in raising the visibility of the quality department of the company. Proper record maintenance and documentation will facilitate GMP compliance. The main purpose of documentation is to define procedures in written to the pharmaceutical manufacturer so as to minimize the errors, misinterpretations due to oral or casually written communication and to allow the tracing of historical batches which eventually leads to the quality of the product. And this quality of the product is ultimately beneficial to the company.