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ESSENTIALS OF QUALITY ASSURANCE

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ABSTRACT

Quality assurance (QA) refers to the planned and systematic activities implemented in a quality system so that quality requirements for a product or service will be fulfilled. It is the systematic measurement, comparison with a standard, monitoring of processes and an associated feedback loop that confers error prevention. This can be contrasted with Quality "Control". which is focused on process outputs. The quality assurance field is rapidly evolving. The components of the quality assurance field, which include philosophy, assessment tools and methods, analysis and application of data, and research, are each growing in their conceptual validity and are also developing well defined relationships to each other. The philosophy underlying quality assurance has moved from a static concept of quality to conceptualising the quality of care as a dynamic state of health care The competitiveness of food production will soon be more dependent on the reliability of the safety and the quality of the food and acceptability of the production procedures than on quantity and price.

INTRODUCTION

The word "Quality" is often used, but not often defined. You will find a variety of usages in any dictionary but, for our purposes, a "degree of excellence" is the closest. Quality can be good or bad, or somewhere in between. Where a product or service is being provided, the end result is largely based on workmanship. A craftsperson takes great pride in producing something with flawless features. The accuracy of an effort, whether it is for data collection or training material presentation, results in a perceived level of quality for the effort – good or bad. There is little value in poor quality. Literally, it is the assurance of quality, and in the case of nuclear quality, it means assurance of high quality. In nuclear work, it is the actions planned and taken to achieve an expected result. Where a craftsperson previously built a reputation on flawless workmanship, that workmanship alone can't be depended upon in higher-risk nuclear work. Quality assurance controls work. When you control your activities, you build in safety and efficiencies, and when the work is completed, you can show evidence of satisfactory completion. All of this provides confidence in your ability to manage your work.[1]

The DOE QA Program

DOE's QA Program is made up of "the Rule" and "the Order." The Rule is 10CFR830 and its Subpart A (830.120). It provides the DOE with the ability to levy civil and criminal penalties for noncompliance of nuclear safety and quality requirements. The Order is DOE Order 414.1C. This Order and its predecessor, DOE Order 5700.6C, established the QA program format of 10 quality criteria that we use today. There are several DOE Guides that provide methods of meeting the quality criteria.

The Rule addresses Nuclear Safety and Quality. It lays out a set of requirements for contractors working on DOE nuclear facilities. It requires them to work to this Rule, and to describe how they will assure that their subcontractors will also meet these requirements. DOE reviews contractors' quality programs for adequacy in controlling work through a requirement that contractor quality programs be submitted to DOE for approval. The Rule is enforceable under the provisions of the Price-Anderson Amendments Act, a process that will be explained in more detail in a later module. The Order (currently DOE Order 414.1C) established the DOE QA Program. The QA program established the 10 criteria that are now also reflected in the Rule. The Order contains direction to DOE and includes, as an attachment, a Contractor Requirements Document. DOE must include the attachment in contracts, and contractors must work to the DOE QA Program – and require its subcontractors to do the same. Both the Rule and the Order are based on the same 10 quality criteria. They both require the development of a QA program

addressing the 10 criteria. These 10 criteria very closely reflect the 18 criteria used by commercial nuclear organizations, but DOE has reorganized them and combined a few.[2-3]

Difference between quality control and quality assurance

Quality Assurance is a set of activities designed to ensure that the development and/or maintenance process is adequate to ensure a system will meet its objectives. Quality Control is a set of activities designed to evaluate a developed work product. The process of executing a system with the intent of finding defects. QA activities ensure that the process is defined and appropriate. Methodology and standards development are examples of QA activities. A QA review would focus on the process elements of a project - e.g., are requirements being defined at the proper level of detail. In contrast, QC activities focus on finding defects in specific deliverables - e.g., are the defined requirements the right requirements. Testing is one example of a QC activity, but there are others such as inspections. Both QA and QC activities are generally required for successful software development. QA activities ensure that the process is defined and appropriate. Methodology and standards development are examples of QA activities. A QA review would focus on the process elements of a project - e.g., are requirements being defined at the proper level of detail. In contrast, QC activities focus on finding defects in specific deliverables - e.g., are the defined requirements the right requirements. Testing is one example of a QC activity, but there are others such as inspections. Both QA and QC activities are generally required for successful software development.[4]

Facility & Equipment System

Any building or buildings used in the manufacturing, processing, packing, or holding of a drug product should be of suitable size, construction and location to facilitate Cleaning, maintenance, and proper Operation. Equipment used in manufacturing, processing, packing, or holding of a drug product should be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.

Material System

Each container or group of containers for components or drug product containers, or closures is identified with a distinctive code for each lot in each shipment received. This code is used to record the disposition of each lot. Each lot is appropriately identified as to its status i.e. Quarantined Approved Rejected.[4]

Production System

There are written procedures for production, process control designed to assure that drug products have the identity, strength, quality, purity they purport or are represented to possess.[4]

Packaging & labeling System

Labeling materials issued for a batch are carefully examined for identity & conformity of "Labeling Specified" in the Master or Batch Production Record.[5]

Laboratory Control System

All equipment must have calibration / Maintenance plan. Proper documents are available and maintained. Provision for remedial action should be in place in the event of instrument breakdown.[5]

Quality System

Quality system is 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 or product specification.

Function of the Quality Assurance:

- To ensure that all personnel have undergone training as per the requirements.
- Ensure the preparation, approval and implementation of SOP, Validation Protocol, Report, Stability Protocol, Report, BMR , BPR etc.
- Issuance, control, review and retrieval of all controlled Logbooks / Formats, Records, SOP, Specification, Worksheet, Protocol.
- To Ensure Compliance to Validation and Qualification Schedule.
- To Ensure effective implementation of Change Control Proposal System.
- Preparation and review of document like Validation Master Plan (VMP) and Site Master File (SMF).
- Ensuring effective implementation of Calibration and Preventive Maintenance Schedule.
- Environment monitoring and carrying out in-process checks during Manufacturing and Packaging process.
- Handling online rejection during Manufacturing and Packaging activity.
- Receiving and maintaining details related to Vendors.
- Approval or Rejection of all Drug Product Components, Drug Product container, closure, In-process material, Packaging material etc.
- Handling of Reserve Sample.
- Handling of Incidents / Planned Deviation / OOS (Out of Specification) with proper investigation & effective implementation of CAPA.
- Monitoring of Stability Studies.
- Review Batch Manufacturing Record(BMR)/Batch Packaging Record(BPR)/Record Analysis

- Carryout periodic Self Inspection (Internal Quality Audit).
- Auditing the External Contract Laboratory.
- Preparation, review and approval of Annual Product Review (APR)
- Preparation of Management Review Report.

Role of GMP in quality assurance:

The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture of medicinal products relies upon people. For this reason there must be sufficient qualified personnel to carry out all the tasks which are the responsibility of the manufacturer. Individual responsibilities should be clearly understood by the individuals and recorded. All personnel should be aware of the principles of Good Manufacturing Practices that affect them and receive initial and continuing training, including hygiene instructions, relevant to their needs. Good Manufacturing Practices (GMPs) is that 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 or product specification. GMP is concerned with both production and quality control.[6]

Worldwide, there are different official regulatory statements and guidelines, national and international, on Good Manufacturing Practices for pharmaceutical (or "drug" or "medicinal") products. They may be regulations (as in the US, Japan or Korea), directives (as in the EU), guides (as in the UK), codes (as in Australia), or WHO code (as in many Southeast Asia Countries). Out of them, following stands out as being the most influential and most frequently referenced:

- The US Good Manufacturing Practices for Finished Pharmaceuticals regulations (the "US GMP")
- The Guide to Good Manufacturing Practice for Medicinal Products of the European Union (the "EC GMP Guide")
- ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients.
- WHO good manufacturing practices.
- The other guidelines and regulation referred by the pharmaceutical manufacturers are,
- Schedule M "Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for
- Pharmaceutical Products" The Drugs and Cosmetics Act And Rules, India.
- Centre for Drug Evaluation and Research (CDER); Manufacturing, Processing, or Holding Active Pharmaceutical Ingredients.

Role of GLP in quality assurance

In the experimental (non-clinical) research arena, the phrase good laboratory practice or GLP specifically refers to a quality system of management controls for research laboratories and organizations to try to ensure the uniformity, consistency, reliability, reproducibility, quality, and integrity of chemical (including pharmaceuticals) non-clinical safety tests; from physio-chemical properties through acute to chronic toxicity tests. GLP was instituted following cases of animal test fraud by pharmaceutical and industrial chemical (mainly pesticide) manufacturers. The original GLP regulatory mandate was promulgated in 1978 by US-FDA (though they may have got it from the New Zealand medicines agency) and published in the Federal Register 43 FR 59985-60020. It was followed a few years later by US-EPA, and (as outlined in the Organisation for Economic Co-operation and Development (OECD) Principles of GLP in 1992) the OECD has since help promulgate it to many countries, helping them place it into their national regulations. GLP applies to non-clinical studies conducted for the assessment of the safety or efficacy of chemicals (including pharmaceuticals) to man, animals and the environment. GLP, a data quality system, should not be confused with standards for laboratory safety - appropriate gloves, glasses & clothing to handle lab materials safely.[7]

Role of cGMP in quality assurance

A good manufacturing practice (GMP) is a production and testing practice that helps to ensure a quality product. Many countries have legislated that pharmaceutical and medical device companies must follow GMP procedures, and have created their own GMP guidelines that correspond with their legislation. Basic concepts of all of these guidelines remain more or less similar to the ultimate goals of safeguarding the health of the patient as well as producing good quality medicine, medical devices or active pharmaceutical products. In the U.S. a drug may be deemed adulterated if it passes all of the specifications tests but is found to be manufactured in a condition which violates current good manufacturing guidelines. Therefore, complying with GMP is a mandatory aspect in pharmaceutical manufacturing. Although there are a number of them, all guidelines follow a few basic principles:[8]

- Manufacturing processes are clearly defined and controlled. All critical processes are validated to ensure consistency and compliance with specifications.
- Manufacturing processes are controlled, and any changes to the process are evaluated. Changes that have an impact on the quality of the drug are validated as necessary.
- Instructions and procedures are written in clear and unambiguous language. (Good Documentation Practices)

- Operators are trained to carry out and document procedures.
- Records are made, manually or by instruments, during manufacture that demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the drug was as expected. Deviations are investigated and documented.
- Records of manufacture (including distribution) that enable the complete history of a batch to be traced are retained in a comprehensible and accessible form.
- The distribution of the drugs minimizes any risk to their quality.
- A system is available for recalling any batch of drug from sale or supply.
- Complaints about marketed drugs are examined, the causes of quality defects are investigated, and appropriate measures are taken with respect to the defective drugs and to prevent recurrence.
- GMP guidelines are not prescriptive instructions on how to manufacture products. They are a series of general principles that must be observed during manufacturing. When a company is setting up its quality program and manufacturing process, there may be many ways it can fulfill GMP requirements. It is the company's responsibility to determine the most effective and efficient quality process.

Role of pharmaceutical validation in quality assurance

In the pharmaceutical, medical device, food, blood establishments, tissue establishments, and clinical trials industries, validation is the documented act of demonstrating that a procedure, process, and activity will consistently lead to the expected results. It often includes the qualification of systems and equipment. It is a requirement for good manufacturing practices and other regulatory requirements. Since a wide variety of procedures, processes, and activities need to be validated, the field of validation is divided into a number of subsections including the following:[8]

- Cleaning validation
- Process validation
- Analytical method validation
- Computer system validation
- Equipment validation

The concept of validation was first proposed by two Food and Drug Administration (FDA) officials, Ted Byers and Bud Loftus, in the mid 1970’s in order to improve the quality of

pharmaceuticals (Agalloco 1995). It was proposed in direct response to several problems in the sterility of large volume parenteral market. The first validation activities were focused on the processes involved in making these products, but quickly spread to associated processes including environmental control, media fill, equipment sanitization and purified water production. The concept of validation was first developed for equipment and processes and derived from the engineering practices used in delivery of large pieces of equipment that would be manufactured, tested, delivered and accepted according to a contract (Hoffmann et al. 1998). The use of validation spread to other areas of industry after several large-scale problems highlighted the potential risks in the design of products. The FDA has also been very focused on this final area of distribution and the potential for a drug substances quality to be impacted by extreme temperature exposure. The validation process consists of identifying and testing all aspects of a process that could affect the final test or product. Prior to the testing of a process, the system must be properly qualified. Qualification includes the following steps: (These steps are common practice for equipment IQ, OQ and PQ).

- Design qualification (DQ)- Defines the functional and operational specification of the instrument, program, or equipment and details the rationale for choosing the supplier.
- Installation qualification (IQ) – Demonstrates that the process or equipment meets all specifications, is installed correctly, and all required components and documentation needed for continued operation are installed and in place.
- Operational qualification (OQ) – Demonstrates that all facets of the process or equipment are operating correctly.
- Performance qualification (PQ) – Demonstrates that the process or equipment performs as intended in a consistent manner over time.
- Component qualification (CQ) – is a relatively new term developed in 2005. This term refers to the manufacturing of auxiliary components to ensure that they are manufactured to the correct design criteria.

This could include packaging components such as folding cartons, shipping cases, labels or even phase change material. All of these components must have some type of random inspection to ensure that the third party manufacturer's process is consistently producing components that are used in the world of GMP at drug or biologic manufacturer.

There is often overlap between Installation, Operational, and Performance Qualification and sometimes these are performed simultaneously.[8]

Relevance of QA systems in pharmaceutical industry

Quality Assurance, in contrast to quality control, is the implementation of quality checks and procedures to immediately correct any failure and mistake that is able to reduce the quality of the interim products at every production step. Thus, the desired high quality of the final product is planned and obtained by conducting standard operating procedures (SOP's) that guarantee the desired quality of the interim products at every production step. If an entire production chain is following a written description (handbook) of all SOP's along the entire production chain, the demands for a Good Manufacturing Practice (GMP) are met. The management approach to long-term success through customer satisfaction, based on the participation of all members of an organization (suppliers included) in improving processes, products, services and the working culture is called:Total Quality Management (TQM).

Pharmaceutical quality assurance is a dynamic process, a state of mind or an understanding of the regulations and guidance relating to the development and manufacture of pharmaceutical products. Quality Assurance is a constituent of quality management riveted to assure, generate precise and reliable results on all lab activities that are undertaken. Drugs that are marketed must be safe and therapeutically active. Performance should be consistent and predictable. Or it can be defined as the sum of all activities and responsibilities required to ensure that the medicine that reaches the patient is safe and effective.[9]

System of Quality Assurance

This department can be divided into four major areas: Quality control, production, distribution, and inspections. QA ensures the arrangements made for the manufacture, supply and use of the correct starting and packaging materials. Any deviation from the written production and process control procedures which are followed in the execution of various production and process control functions shall be reported investigated and recorded by the quality dept. Deviations from the established time limits for the completion of each phase of production shall be justified and documented by the assurance dept. All the activities involved in the manufacturing process, in-process control and bulk testing shall be approved by the QA dept. All necessary control on intermediate products and any other in-process controls and validations are carried out by the dept. It involves;

Quality improvement plans.

- Validation and Technology Transfer.
- Review of stability date and shelf life of products.
- Quality team frequently conduct periodic GMP training to personnel at organization.[10-11]

Objectives of Quality Assurance

- Make sure that each medicine reaching a patient is safe, effective and of standard quality.
- Incurring medicaments that are safe and effective.
- Assuring superiority of a product from selection to use.
- Persistent products those are safe and effective through structured selection and procurement methods.
- Exerting products through appropriate storage, distribution, monitoring and use methods

CONCLUSION

Quality Assurance does its best to maintain the reliability at every stage of manufacturing process starting from Research, Clinical studies, Quality Control, Production, Distribution and provides information on appropriate use, and analyzes safety and information of the products. The Department will also assist in the strategic direction and development of Quality Systems, standard operating procedures and document control programs, to ensure with the company policies and regulatory requirements. It is a multi fold activity, where in all the industries want professionally qualified, competent, skilled managerial and entrepreneurial talent workforce to lead the industry. Quality assessment tools and methods are more valid and reliable, and research is emphasising outcomes of care and effectiveness studies, as well as methods of disseminating information to practitioners. This paper provides an overview of the quality assurance field, describing the changes that are taking place in each of its components and the relationships among them. The Importance of Quality Assurance and Food Safety in Modern Food Production Systems. The liberalization of the global trade, and the fact that the consumers in the industrialized countries are more and more demanding food to be not only economical, but also healthy, tasty, safe and sound in respect to animal welfare and the environment, are changing the so far quantity-oriented food production, guaranteeing the nutrient supply for a nation, into an international quality-oriented food market, where commodities, production areas, production chains and brands compete each other. Thus, apart from the steady increase of the national and international standards for food safety and public health, there is a growing influence of the consumer's demands (often completely ignorant of agriculture) on the animal production, its allied industries, advisers, consultants and food animal veterinarians.

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