Introduction

Historical Perspective: At a glance

"A management system is defined as a system to establish the policy and objectives and to achieve those objectives."

The quality management is handled by the two important departments i.e.

1) Quality control

2) Quality assurance

According to regulatory Authority, if the product meet the following traits is well thought-out as "Quality Product"

-Identity -Strength -Purity –Safety -Efficacy

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Facets of 'Quality':

Quality is defined by customer needs and expectations and it is also referred in several ways such as "fitness for use", "fitness for purpose", "customer satisfaction" or "conformance to requirements" etc.

Quality is "The totality of features and characteristics of product or service that bear on its ability, to satisfy stated or implied needs"

Quality is not created spontaneously. It is designed and manufactured and it has its own sources. A somewhat elusive concept, quality is difficult to define and easy to perceive. This combination of qualities difficult to understand the study of factors that helps to discover, produce, and distribute quality products and services. Quality presents several aspects and during the last two decades these aspects, called dimensions, have started to be recognized. Quality is not just the result of will. It requires systems and processes to make it consistently viable. Quality sources and, in particular, the precise contribution of quality policies in a process industry, deserves study.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Three Quality Gurus

- **Deming:**
  - ✓ The best known of the "early" pioneers, is credited with popularizing quality control in Japan in early 1950s.Today, he is regarded as a national hero in that country and is the father of the world famous Deming prize for quality.
- **Juran:**
  - ✓ Juran, like Deming was invited to Japan in 1954 by the union of Japanese Scientists and engineers.
- **Philip Crosby:**

Author of popular book Quality is Free. His absolutes of quality are:

- ✓ Quality is **defined** as conformance to requirements, not "goodness"
- ✓ The **system** for achieving quality is prevention, not appraisal.
- ✓ The performance **standard** is zero defects, not "that's close enough"

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

QUALITY MANAGEMENT SYSTEM:

"QMS is defined as a system to direct and control an organization with regard the quality." So the quality is achieved by the QMS.

Quality System includes several elements:

1. Appropriate management support.
2. Development, implementation and management of QA/QC system.
3. Clear documentation of quality methods, procedures and test results.
4. Quality awareness and training of personnel.
5. Proof or certification of QA from equipment suppliers.
6. Acceptance and testing of new materials.
7. Appropriate maintenance and testing of equipment, materials and processes.
8. Calibration and verification of the calibration facilities.
9. Reliable testing of the system performance.
10. Periodic performance testing of the system.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

2 How to accomplish Quality?

A QMS management system organizes overall activities of the company in a such way that the technical, administrative and human factors affecting the quality of its products or services are under control. The QMS has to meet with the interrelated needs of the company as well as of the customer. The QMS starts with identification of the customer needs and quality requirements and ends only when the products has been placed in the hands of the customer who remains satisfied and ultimately should recommended to other customer.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Why a QA Department?

In addition to the need to obviate incidents similar to the thalidomide crisis, the need to protect public health from the works of unprofessional and unscrupulous elements gave rise to enunciation of control measures and quality assurance mechanisms. On a regular basis, the regulators are tightening the tenor of regulation to overcome the wave of compromise in the industry which is on the upward trend due to untamed profiteering and economic aggrandizement. So, it is all about the protection of public health.

Structure and personnel in the QA department

The QA department must be able to function as an unbiased umpire in the facility in order to be able to effectively account for quality deficits and cause the utmost input from all concerned units in the process of building quality into the products. So how can this be possible? – By getting the departments remain independent of production and management, free from their over-bearing influences.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Quality Concepts:

i. **QMS- Quality management system:** the overall picture of how an organization carries on its business by standard operating procedures.

ii. **TQM-Total quality management:** the commitment of packaging the company's service system and products in the best quality possible.

iii. **QbD- Quality by design -** the concept of creating quality in the product from design and development through production to packaging. This speaks to the role of formulation and production in building quality into the product from the beginning.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Some **tools of Quality Assurance Department** in a Quality Management System:

1. Investigations- of deviations, out-of-specifications and out-of-trends results.
2. Root cause analysis- tracing out-of specs to their roots.
3. Change management- nurturing change in the system.
4. Quality risk management- a risk-based approach to quality assurance.
5. Quality reviews/annual product reviews.
6. Post-marketing surveillance of the products
7. Recalls management.
8. Training of staff
9. Environmental management and hygiene.
10. Continuous improvement.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Calibration & Qulification

Definition of Calibration: ICH

The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements.

Some other guidelines and requirements are also to be discussed.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Principle:

UV spectroscopy obeys the Beer-Lambert law, which states that: when a beam of monochromatic light is passed through a solution of an absorbing substance, the rate of decrease of intensity of radiation with thickness of the absorbing solution is proportional to the incident radiation as well as the concentration of the solution.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Equipment validation and Justification of URS:

They must be comprehensive. Each and every **requirement** relating to product safety, identity, strength, purity, and quality must be identified. Hence, Quality Assurance (QA) must have a significant role in reviewing and approving the final list of **requirements**, and must be an approver of changes to any requirement that can affect the above product or process attributes (e.g., **cGMP's**).

Given a comprehensive **User Requirements Specification** that has been approved by QA and is under project change management, the Design Qualification **(DQ)** process then can be reduced to two key objectives:

- Documented verification that the overall design appears to address, by some means, each and every **requirement**; in the URS, affecting the product and performance of the manufacturing process (or, in the case of unknown product or multi-product manufacturing facility, the required equipment/ system performance capabilities).
- Identification (and documentation) of the critical individual physical components, attributes, and operational features that directly support meeting each **requirement**.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Equipment Qualification:

Prior to commencing risk analysis studies must be carry out to check the critical mode of instrument. Hence, it is necessary that the equipment is to be checked and certified as properly installed, equipped and functioning as per its design.

a. Design Qualification (DQ):

- ✓ Equipment identification and code
- ✓ Utility requirements and specifications.
- ✓ Manufacturer and model
- ✓ Capacity and serial number
- ✓ Location

References

3. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
4. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Installation Qualification (IQ):

Installation qualification of **new equipment** should be based on written requirements and documented. The requirements should ensure that the pre-determined construction and installation requirements are assessed as soon as installation permits, and that these requirements are met (control of wavelength, control of absorbance, resolution power, limit of stray light, wavelength accuracy, and baseline flatness etc). All installation parameters should be documented and certified prior to operational qualification of the equipment. **b.** For **existing equipment**, **(Same as that of TD)**

An ideal protocol shall document the following:

- ✓ Verifications equipment installation
- ✓ Utility requirements-electrical, other utilities.
- ✓ Comments

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Operational Qualification: (Same as that of TD)

Procedure for OQ:

- ✓ Initiate the actual operation of the UV-Visible Spectrophotometer to ensure that machine is operating within specification.
- ✓ Check the OQ parameters against their specifications.
- ✓ Observe the functioning of all controls available on control panel
- ✓ Record the observation

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Performance Qualification (PQ):

The PQ shall be carried for establishing the performance (qualification shall be) and efficiency of the UV-Visible Spectrophotometer.

A. SPECTRAL CALIBRATION (Visible Spectral Region):

1. Switch ON the instrument. Allow for warm up at least about 15 minute.
2. By adjusting coarse and fine control set a reading of around 80.0 on read out
3. Now set the value of wavelengths in increments of 0.1 nm up to λ of 487 nm and read the value of %T at each increment of λ and draw a curve %T Vs λ.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Introduction and Concept of Good Manufacturing Practices

The legal authority for the Food and Drug Administration (FDA) to impose minimum manufacturing standards is set forth in the federal Food and Drug and Cosmetic Act (FDCA), 21 U.S.C. sec. 301 et seq. Section 351(a)(2)(B) of 21 U.S.C. requires manufacturers of drugs to operate in conformance with manufacturing regulations established by the FDA. The regulations are primarily contained in Title 21 of the U.S. Code of Federal Regulations (CFR), Parts 210 and 211, and are called the **current good manufacturing practice (cGMP)** regulations.

The actual GMP regulations are issued as a part of the Code of Federal Regulations and as such they are a federal law. The current set of GMP regulations is based on the 1978 revision of the original GMP regulations, which were first promulgated in 1963. The GMP regulations are updated every year in April; however, no major changes have been implemented since 1978

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

PURPOSE OF THE cGMP REQUIREMENT:

1. The core GMP guidelines define the authorized person as the person responsible for the release of batches of finished products for sale. The explanatory text is intended to assist manufacturers wishing to strengthen their quality assurance systems. These concepts were integrated in its revised text in 2003. The guidance on validation has been extensively revised

and expanded. The new text has been adopted in 2005.

2. To prevent injury and death "by building quality into the design and production of pharmaceuticals," so that substandard prescription drugs do not jeopardize the health and safety of the patients.

3. To enforce general GMP compliance or to provide authorization for the manufacture of specific pharmaceutical products, usually in relation to an application for registration.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

COMPONENTS OF GMP:

a. Quality Management

b. QA

c. GMP for medicinal Products

d. QC

e. Sanitation & Hygiene

f. Qualification & Validation

g. Complaints & product recall

h. Contract production and analysis

i. Self-Inspection, Quality audits& supplier's audits & approval

j. Personnel, training & personal hygiene

k. Premises

l. Materials

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Following background materials are used by agency investigators to prepare for a GLP inspection:

a. the GLP regulations;

b. the Management Briefings Post-Conference Report;

c. assorted memoranda and policy issuances;

d. the GLP Compliance Program;

e. the protocol of an ongoing study, if available;

f. the final report of a completed study, if available;

g. the inspection report of the most recent inspection.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

The GLP requirements that are applicable to computerized data-acquisition systems include the following criteria:

a. Only authorized individuals can make data entries,
b. Data entries may not be deleted, but changes may be made in the form of dated amendments which provide the reason for data change,
c. The data base must be made as tamperproof as possible,
d. The SOPs should describe the procedures used for ensuring the validity of the data,
e. Either the magnetic media or hardcopy printouts are considered to be raw data.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

World Health Organization:

The WHO was established in 1948 as a specialized agency of the United Nations (UN). Its purpose is to serve as the directing and coordinating authority for international health matters and public health. One of the main functions of the WHO is to provide objective and reliable information and advice in the field of human health, a task that it partly fulfills through WHO publications [35] . The first WHO draft text on GMP was prepared in 1967 and a revised version was published in 1968 as an annex of the twenty - second report of the WHO expert committee on specifications for pharmaceutical preparations. Over the years the WHO has issued several versions of its GMP guidelines as well as other guidelines related to the GMP and quality issues of the production of therapeutic products.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

GOOD LABORATORY PRACTICES (GLP)

1 BACKGROUND

2 ORGANIZATION AND PERSONNEL

3 FACILITIES

4 EQUIPMENTs

5 TESTING FACILITIES OPERATION

6 TEST AND CONTROL ARTICLES

7 PROTOCOL FOR AND CONDUCT OF A NONCLINICAL LABORATORY STUDY

8 RECORDS AND REPORTS

9 AUDIT OF FACILITIES FOR GLP COMPLIANCE

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

INTRODUCTION AND HISTORICAL BACKGROUND:

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

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

PHARMACEUTICAL PROCESS VALIDATION (PPV):

"Process validation is defined as the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products".

Stage 1 – Process Design: The commercial manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities.

Stage 2 – Process Qualification: During this stage, the process design is evaluated to determine if the process is capable of reproducible commercial manufacturing.

Stage 3 – Continued Process Verification: Ongoing assurance is gained during routine production that the process remains in a state of control. A successful validation program depends upon information and knowledge from product and process development.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

VALIDATION TEAM:

A multidisciplinary team is primarily responsible for conducting and supervising validation studies. Personnel qualified by training and experience in a relevant discipline may conduct such studies. The working party would usually include the following staff members such as;

- ✓ Head of quality assurance.
- ✓ Head of engineering.
- ✓ Validation manager.
- ✓ Production manager.
- ✓ Specialist validation discipline: all areas.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

NEED OF PHARMACEUTICAL VALIDATION:

Validation is an integral part of quality assurance; it involves the systematic study of systems, facilities and processes aimed at determining whether they perform their intended functions adequately and consistently as specified. A validated process is one which has been demonstrated to provide a high degree of assurance that uniform batches will be produced that meet the required specifications and has therefore been formally approved. Validation in itself does not improve processes but confirms that the processes have been properly developed and are under control.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

SCOPE OF PHARMACEUTICAL VALIDATION

1. There should be an appropriate and sufficient system including organizational structure and documentation infrastructure, sufficient personnel and financial resources to perform validation tasks in a timely manner. Management and persons responsible for quality assurance should be involved.
2. Personnel with appropriate qualifications and experience should be responsible for performing validation. They should represent different departments depending on the validation work to be performed. There should be proper preparation and planning before validation is performed.
3. There should be a specific programme for validation activities.
4. Validation should be performed in a structured way according to the documented procedures and protocols.
5. Validation should be performed: for new premises, equipment, utilities and systems, and processes and procedures;
   - ✓ at periodic intervals; and
   - ✓ When major changes have been made.

References

M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

GENERAL CONSIDERATIONS FOR PROCESS VALIDATION:

In all stages of the product lifecycle, good project management and good archiving that capture scientific knowledge will make the process validation program more effective and efficient. The following practices should ensure uniform collection and assessment of information about the process and enhance the accessibility of such information later in the product lifecycle.

1. An integrated team approach to process validation that includes expertise from a variety of disciplines (e.g., process engineering, industrial pharmacy, analytical chemistry, manufacturing, and quality assurance). Project plans, along with the full support of senior management, are essential elements for success.
2. Throughout the product lifecycle, various studies can be initiated to discover, observe, correlate, or confirm information about the product and process
3. The terms attribute(s) (e.g., quality, product, component) and parameter(s) (e.g., process, operating, and equipment) are not categorized with respect to criticality in this guidance.

References

6. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
4. A text book Pharmaceutical Quality Assurance by O. M.

TYPES OF PROCESS VALIDATION:

Prospective Validation or Premarket Validation:

In prospective process validation, an experimental plan called the validation protocols executed (following completion of the qualification trials) before the process is put into commercial use. Most validation efforts require some degree of prospective experimentation to generate validation support data. This particular type of process validation is normally carried out in connection with the introduction of new drug products and their manufacturing processes.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

DOCUMENTATION:

Documentation at each stage of the process validation lifecycle is essential for effective communication in complex, lengthy, and multidisciplinary projects. Documentation is important so that knowledge gained about a product and process is accessible and comprehensible to others involved in each stage of the lifecycle. Information transparency and accessibility are fundamental tenets of the scientific method. They are also essential to enabling organizational units responsible and accountable for the process to make informed, science-based decisions that ultimately support the release of a product to commerce.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Introduction to Regulatory Agencies

The World Health Organization (WHO) is a specialized agency of the United Nations (UN), which is concerned with international public health. It is the directing and coordinating authority for health within the UN system. The WHO is a member of theUNDevelopment Group; its predecessor, the Health Organization, was an agency of the League of Nations. The constitution of the WHO had been signed by 61 countries on 22 July 1946, with the first meeting of the assembly (World Health Assembly (WHA)) finishing on 24 July 1948.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

ICH NEED TO HARMONISE:

1. To have an independent evaluation of medicinal products before they are allowed on the market was reached at different times in different regions.
2. A rapid increase in laws, regulations and guidelines for reporting and evaluating the data on safety, quality and efficacy of new medicinal products.
3. The industry, at the time, was becoming more international and seeking new global markets; however the divergence in technical requirements from country to country was such that industry found it necessary to duplicate many time-consuming and expensive test procedures, in order to market new products, internationally.
4. The urgent need to rationalize and harmonise regulation was impelled by concerns over rising costs of health care, escalation of the cost of R&D and the need to meet the public expectation that there should be a minimum of delay in making safe and efficacious new treatments available to patients in need.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

The **Food and Drug Administration** (**FDA** or **USFDA**)

A federal agencyof the United States Department of Health and Human Services, one of the United States federal executive departments. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical
drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed[4] and veterinary products.

The FDA was empowered by the United States Congress to enforce the Federal Food, Drug, and Cosmetic Act, which serves as the primary focus for the Agency; the FDA also enforces other laws, notably Section 361 of the Public Health Service Act and associated regulations, many of which are not directly related to food or drugs. These include regulating lasers, cellular phones, condoms and control of disease on products ranging from certain household pets to sperm donation for assisted reproduction.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

FDA-Approved" vs. "FDA-Accepted in Food Processing

The FDA does not approve applied coatings used in the food processing industry.[28] There is no review process to approve the composition of nonstick coatings, nor does the FDA inspect or test these materials. Through their governing of processes, however, the FDA does have a set of regulations that cover the formulation, manufacturing, and use of nonstick coatings. Hence, materials like Polytetrafluoroethylene (Teflon) are not, and cannot be, considered as FDA Approved, rather, they are "FDA Compliant" or "FDA Acceptable".

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

TGA – how we operate

We are part of the **Australian Government Department of Health**

Every decision the TGA makes is based on the ***Therapeutic Goods Act 1989***

Main offices in Canberra – satellite offices in Sydney, Melbourne, Adelaide and Brisbane

Operations are primarily cost recovered (98%) industry pays fees for making applications and annual charges for products they are responsible for Certain Procedures.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Other education modules include TGA:

Medicines

Biologicals

Medical devices

Postmarket monitoring

Good Manufacturing Practice

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

How does the MHRA work?

The Agency has the power to withdraw a product from the market, and in the case of medicines, to suspend production. The Agency can also prosecute a manufacturer or distributor if the law has been broken. The regulations need to be robust enough to protect the public's health, and this costs money. The MHRA is funded largely by public monies from government for the regulation of devices, and by fees from the pharmaceutical industry for the regulation of medicines.

The Agency's regulatory decisions are impartial and based solely on the extensive evidence of quality, safety, and efficacy required for each product. Different products are treated differently but the MHRA considers the particular characteristics, drawbacks and advantages of each one.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

INTRODUCTION TO QBD

"Don't Find Fault, Find Remedy to Get Quality"

Since the concept of quality by design (QbD) emerged nearly a decade ago, the pharmaceutical industry has been trying to understand and put into practice a more flexible and risk-based approach to manufacturing. Although the introduction of US Food and Drug Administration guidance's and International Council for Harmonization (ICH) guidelines- ICH Q8, Q9, and Q10 have provided some details on how QbD can be applied, many questions remain. The development and use of excipients in drug-product formulations has posed several challenges, including understanding excipient variability and functionality when implementing a QbD-based approach. The common theme of the various initiatives is **"Planning for Quality"** that is, building quality into the products compared to the traditional paradigm of testing the product to ensure quality.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

OBJECTIVE OF QbD:

To understand how process and formulation parameters affect the product characteristics and subsequent optimization of these parameters should be identified in order to monitor these parameters online in the production process.

Explores the processes used in developing a market formulation and requisite supportive data, particularly in light of the industry's current movement toward submissions based on quality by design (QbD).

It outlines activities that should be performed early in the drug development process before initiating manufacturing and attempting market entry.

The Food and Drug Administration (FDA) Office of Generic Drugs (OGD) has developed a question based review (QbR) for its chemistry, manufacturing and controls (CMC) evaluation of Abbreviated New Drug Applications (ANDAs). QbR is a new quality attributes. It is a concrete and practical implementation of some underlying concepts and principles outlined by the FDA's Pharmaceutical CGMPs for the twenty first century and quality by design (QbD) initiatives.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

PHARMACEUTICAL QUALITY BY DESIGN

ICH Q8 defines quality as the suitability, of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength and purity. Pharmaceutical QbD is a systematic, scientific, risk based, holistic and proactive approach to pharmaceutical development that begins with predefined objectives and emphases product and processes understanding and process control.

It means designing and developing formulations and manufacturing processes to ensure predefined product quality objectives. QbD identifies characteristic that are critical to quality from the perspective of patients, translates them into the attributes that the drug product should possess, and establishes how the critical process parameters can be varied to consistently produce a drug product with desired characteristics. Fig. 3.2 shows a simplified quality control diagram under the current Quality by Design (QbD).

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Advantages of QbD:

1. It provides a higher level of assurance of drug product quality.
2. It offers cost savings and efficiency for the pharmaceutical industry.
3. It increases the transparency of the sponsor understands the control strategy for the drug product to obtain approval and ultimately commercialize.
4. It makes the scale-up, validation and commercialization transparent, rational and predictable.
5. It facilitates innovation for unmet medical needs.
6. It increases efficiency of pharmaceutical manufacturing processes and reduces manufacturing costs and product rejects.
7. It minimizes or eliminates potential compliance actions, costly penalties, and drug recalls.
8. It offers opportunities for continual improvement.
9. It provides more efficiency for regulatory oversight:
10. It streamlines post approval manufacturing changes and regulatory processes.
11. It more focused post approval CGMP inspections
12. It enhances opportunities for first cycle approval.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Steps in QbD:

1. **Examining all of the formulation and process parameters,** typically by employing statistical design-of-experiments (DoE) approach to assess the impact of each parameter and the interaction between parameters on the final product. The outcome of this approach would be to facilitate effective formulation and process optimization.
2. **Conducting a risk-assessment analysis of the formulation and the manufacturing process** to determine which parameters have the greatest impact on product quality and characteristics.
3. This analysis involves examining all parameters that are likely to have a an effect, **determining what that effect will be, what the likelihood that an even that could have an effect will occur, how frequent that occurrence might be, and how likely is it that such an event will be observed.**
4. For each of these characteristics, a rating system is used to apply a total score to each parameter. Parameters that receive the highest score are deemed to pose the highest risk and should be investigated to reduce that risk to acceptable levels.
5. Based on the results of the DoE and risk-assessment, a design space can be created that will define the operating ranges (both formulation and process) within which a product can be manufactured and be expected to consistently meet the required quality standards and performance attributes.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

Benefits of QbD

Proper implementation of QbD can potentially provide three main benefits for development:

- More efficient use of development time and costs
- Ability to meet FDA submission guidelines and expectations
- Reduced approval times – and fewer queries – from the FDA

QbD can potentially provide significant benefit in manufacturing. Even after drug has gained FDA approval, routine QC testing may detect an out of specification (OOS) result Absent the data that QbD provides, test results may suspect questions difficult to answer, and long delays inevitable.

The business benefits can be significant, including:

- Fewer lost batches, typically costing $250 - $500K per batch
- Fewer manufacturing deviations, saving hundreds of costly hours and $10 - $15K per deviation
- Faster time to market and more reliable supply, when each day on the market could mean $100K (or more)
- Fewer inspections of manufacturing sites A many-fold ROI via cost savings and increased revenue.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

i. Enablers of Quality By Design

Knowledge management and quality risk management are two of the primary enablers of QbD. They play a critical role both in development and in the implementation of QbD. They are **instrumental in achieving product realization**, establishing and maintaining a state of control, and lastly **facilitating continual improvement**.

Quality Risk Management

Quality risk management (QRM) is a key enabler for the development and application of QbD. During development, it enables resources to be focused on the perceived critical areas that affect product and process. It is one of the tools that provide a proactive approach to identifying, scientifically evaluating, and controlling potential risks to quality. It also facilitates continual improvement in the product and process performance throughout the product life cycle.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

STAGES IN QbD DEVELOPMENT PROCESS:

A. A target product profile describes the use, safety and efficacy of the product.

B. Defining a target product quality profile is used by formulators and process engineers as a quantitative surrogate for aspects of clinical safety and efficacy during product development.

C. Drawing together relevant prior knowledge about the drug substance, potential excipients and process operations into a knowledge space. Use a risk assessment to prioritize knowledge gaps for further investigation.

D. Designing a formulation and identify the critical material attributes of the final product that must be controlled to meet the target product quality profile.

E. Designing a manufacturing process to produce a final product having critical material attributes.

F. Identifying the critical process parameters and raw material attributes that must be controlled to achieve critical material attributes of the final product. Use of risk assessment to prioritize process parameters and material attributes for experimental verification. Combine prior knowledge with experiments to establish a design space or other representation of process understanding.

G. Establishing a control strategy for the entire process that may include input material controls, process controls. The control strategy should encompass expected changes in scale and can be guided by a risk assessment.

H. Continuous monitoring and updating the process to assure consistent quality.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

General Consideration for Formulation Design and Development

A. Biopharmaceutics Classification System is valuable in guiding formulation development. To establish formulation robustness, sponsors of abbreviated new drug applications (ANDAs) generally evaluate relevant quality attributes of product manufactured at the laboratory scale. The availability of drug substance may influence the number of studies and therefore, product understanding.

B. In order to design and develop a robust generic product that has the desirable TPQP, a product development scientist must give serious consideration to the **biopharmaceutical properties** of the drug substance. These biopharmaceutical properties include physical, chemical, and biological properties.

C. Chemical properties include pKa, chemical stability in solid state and in solution as well as photolytic and oxidative stability while biological properties include partition coefficient, membrane permeability, and/or oral bioavailability.

D. The BCS is a scientific framework for classifying a drug substance based on its aqueous solubility, dose, and intestinal permeability. The BCS guidance is generally considered to be conservative with respect to the class boundaries of solubility, permeability, and the dissolution criteria. Thus, the possibility of modification of these boundaries and criteria has received increasing attention.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.

TOOLS OF QUALITY BY DESIGN

Design of Experiments (DOE)

Design of experiments (DOE) is a structured and organized method to determine the relationship among factors that influence outputs of a process. A methodology for designing experiments was proposed by Ronald A. Fisher, in his innovative book The Design of Experiments (1935).

DOE Applications:

1. Application of DOE in QbD helps in gaining maximum information from a minimum number of experiments.
2. When DOE is applied to a pharmaceutical process, factors are the raw material attributes (e.g., particle size) and process parameters (e.g., speed and time),
3. Scientists have to use prior knowledge and risk management to identify the key input and output variables and process parameters to be investigated by DOE.
4. DOE results can help identify optimal conditions, the critical factors that most influence CQAs.

References

1. M. A. Potdar, Pharmaceutical Quality Assurance, Nirali Prakashan, Pune.
2. A text book Pharmaceutical Quality Assurance by O. M. Bagade, Career Publication, Pune.