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QUALITY BY DESIGN

MASTER OF PHARMACY IN CHEMISTRY

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ABSTRACT: -

The contemporary method for pharmaceutical product quality is called "Quality by Design." This essay provides information on Pharmaceutical Quality by Design (QBD) and discusses how it is used to guarantee the high calibre of pharmaceuticals. Some of the components of the Quality by Design are discussed and mentioned. Each unit operation's process parameters and quality attributes are identified. Benefits,

The prospects and procedures for pharmaceutical product quality through design are explained. Pharmaceutical development aims to create a high-quality product and its production method to deliver the product's desired performance consistently. Products cannot be checked for quality, but quality should be incorporated during design. It comprises the Quality target product profile, important Quality characteristics, and Quality-related elements.

Keywords:-

Quality by Design (QBD), Process Analytical Technology (PAT), Quality target product profile, Critical quality attributes.

INTRODUCTION:-

Pharmaceutical development aims to create a high-quality product and its production method to deliver the anticipated performance of the drug consistently.

Scientific understanding is provided to support the establishment of the design space, specifications, and manufacturing controls by the information and knowledge obtained from pharmaceutical development research and manufacturing experience. Pharmaceutical development study data can serve as a foundation for effective risk management. It is crucial to understand that products cannot be assessed for quality; rather, quality should be incorporated into the design from the beginning. Changes in formulation and manufacturing procedures made during development and life cycle management should be viewed as chances to learn more and assist the design space's formation in new ways. Similar to

how incorporating pertinent info The applicant proposes the design space, which is subject to regulatory evaluation and approval. implementing the design

There is no such thing as a change in space. Exiting the design space is seen as a change, which ordinarily starts a regulatory post-approval change process.

The product should always be created with the patient's needs and intended use in mind.

Product development methods differ from firm to company and from one product to another. The strategy can also change, and it needs to be described in the submission. A candidate may opt for a blend of both an empirical and more methodical approach to product development. nation learned from tests yielding unexpected results might

The incorporation of prior knowledge, for instance, can be part of a more methodical approach to development (also known as quality by design).

findings from research that used experiment design, quality risk management, and knowledge management (ICH Q10) throughout the product's lifespan. Such a methodical technique can improve obtaining the intended product quality and aid regulators in comprehending a company's plan.

The understanding of products and processes can be updated with the information

Figure 1:- quality by design

1:-The product is made to satisfy both patient needs and performance standards.

Process is created to consistently meet product requirements.

2:-superior qualities.

3:_The influence of the initial raw materials and process variables on product quality is recognized.

Critical process variability sources are located and managed.

DEFINITION [ICH Q 8(R1)]

a methodical method of growth that starts with predetermined goals and stresses product and a thorough understanding of processes and their control, supported by excellent risk management

DEFINITION[FDA PAT Recommendations, September 2004]

a method for planning, evaluating, and managing production using timely measurements of vital performance and quality indicators during processing To ensure constant quality throughout time, the procedure is continuously reviewed and revised.The term "Quality by Design" (QBD) refers to a method that includes a deeper understanding of important process and product attributes from a scientific perspective.

During the development phase, designing controls and testing based on the scientific limitations of understanding and utilizing the knowledge acquired during the product's life cycle to work in a continuous improvement environment. An method to pharmaceutical development known as QBD focuses on formulation design and development as well as manufacturing procedures to uphold the required product quality. To ensure that the information on the topic is established and used in an independent and integrated manner, rules and mathematical models are used.

BENEFITS OF OBD

1:-QBD benefits business and Get rid of batch errors

2:-Reduce deviations and expensive investigations; prevent issues with regulatory compliance.

3:-Better development choices Organizational learning is an investment in the future Quality by Design is good science

4:-Giving technical employees more power

OPPORTUNITIES:-

1:-Flexible, efficient, and agile system Improve manufacturing efficiency, lower costs, and Waste and project rejections

2:-Building a scientific knowledge foundation for all goods and improving communication with business on science-related issues

3:-Consistent information must be provided, and risk management must be used.

STEPS INVOLVED IN DESIGN QUALITY PRODUCTS:-

1. Development of new molecular entity

 Pre-clinical study

 Nonclinical study

 Clinical Study

 Scale up

 Submission for market Approval

2. Manufacturing

 Design Space

 Process Analytical Technology

 Real time Quality Control

3. Control Strategy

 Risk based decision

 Continuous Improvement

 Product performance

Seven steps of quality by design start up plan:-

1. Hire an independent Quality by design expert.

2. Audit your organization and process with the expert

conducting a gape analysis.

3. Hold a basic quality by design workshop with all your

personal.

4. Review the expert's report and recommendation.

5. Draft an implementation plan, timelines and estimated

costs.

6. Assign the resources (or contract out).

7. Retain the independent expert as your "Project

Assurance" advisor

QBD (quality by design) and clear products and procedures

-All significant sources of variation are recognized.The process regulates variability, as previously stated.

-The design space defined for the materials utilized, process parameters, climatic conditions, and other factors allows for the accurate and reliable prediction of product quality features.

-To obtain better understanding of how products operate across a variety of material characteristics, manufacturing process alternatives, and process parameters while taking into account the proper application of quality risk management principle

QBD BY CHEMICALS

The pharmaceutical industry places a strong emphasis on quality, but it has lagged behind other sectors in terms of productivity and production efficiency.

Current scenario in the Pharmaceutical Industry:

- Cost of re-validation
- Off-line analysis for in-process - need based
- Product specifications as primary means of control
- Unpredictable Scale-up issues
- Inability to understand failures

Systematic approach to development:

- That begins with predefined objectives
- Emphasizes products and process understanding

Quality target product profile [QTPP]

-An overview of the medication development programme with a primary focus on safety and efficacy is provided in terms of labelling concepts.

Indications and Usage

Contraindications

Warnings

Precautions

Adverse Reactions

Drug Abuse and Dependence

Over dosage

Dosage and Administration

and How Supplied

Clinical Studies

Animal Pharmacology

Animal Toxicology

A logical extension of the target product profile is the quality characteristics (attributes) that the drug product should have in order to consistently deliver the therapeutic benefit stated in the label guide, in order to establish formulation strategy and maintain efficient and effective formulation efforts.

It makes it easier to determine what the patient's or consumer's quality target product profile needs or is crucial (such identifies dangers and the appropriate management strategies.

-identifies dangers and the appropriate management strategies.

-Makes optimal use of tools and enablers, such as combining quality through design with bio pharmaceutics)

-Promotes and facilitates the sharing of knowledge.

-A life-cycle process that interactively learns and optimisms

-decision-making and the results of the therapeutic patience advantage.

a made, developed, and designed pharmaceutical product with respect to Quality Target Product Profile (Specifications like release/dissolution acceptance criteria) that correspond to the intended in-vivo performance of the item.

CRITICAL QUALITY ATTRIBUTES

-The crucial quality characteristics, such as those defining purity, potency, and a substitute for bio availability criticality, must be identified

-. It is founded on the effect of a quality trait or parameter on the product's safety, effectiveness, and quality (maneuverability).

-Create a connection between CPP and Qantas: Finding a characteristic or set of parameters that can serve as a stand-in for clinical safety and efficacy (patient-important)

-Manufacturing is another trait that is essential to quality and is crucial to business.

-A manufacturing process for an API may be more crucial than a manufacturing process for a medicinal

Figure 2:-Decision Tree to Decide CQAs

Certain Key Aspects of QBD

TARGET PRODUCT QUALITY PROFIE

The Target Product Quality Profile (TPQP) is a method for "planning with the goal in mind," or creating the strategic framework for drug development. In recent years, an The TPP is now being used more widely in risk management, clinical and business decision-making, engagement with regulatory agencies, and development planning

.Drug Substance and its Properties

To constantly meet the required drug-product quality The drug substance needs to be completely described on the label. Described in terms of its physical, chemical,mechanical and biological characteristics like solubility,Stability, particle size, and flow characteristics of polymorphic.

Formulation Design and Development

Since not all prototype formulations may be tested on people, developing sensitivity in vitro

Manufacturing Process Design and Development

dissolution techniques is essential to a successful development programme.It is impossible to separate process development from formulation design since a formulation cannot become a finished product without following a specified process. Process design is the first phase of process development, during which an overview of the desired manufacturing scales and commercial manufacturing procedures are documented. All necessary considerations for the design of the process, such as facility, machinery, material transfer, and manufacturing variables, should be included in the blueprint. The QTPP and are additional aspects to take into account while developing processes.

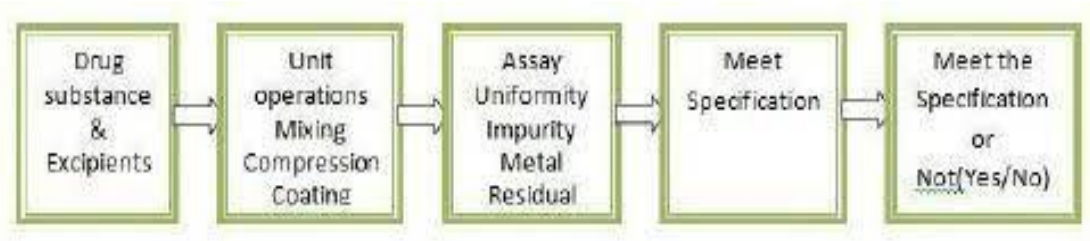


figure 3:- flow chart for product quality by end product testing

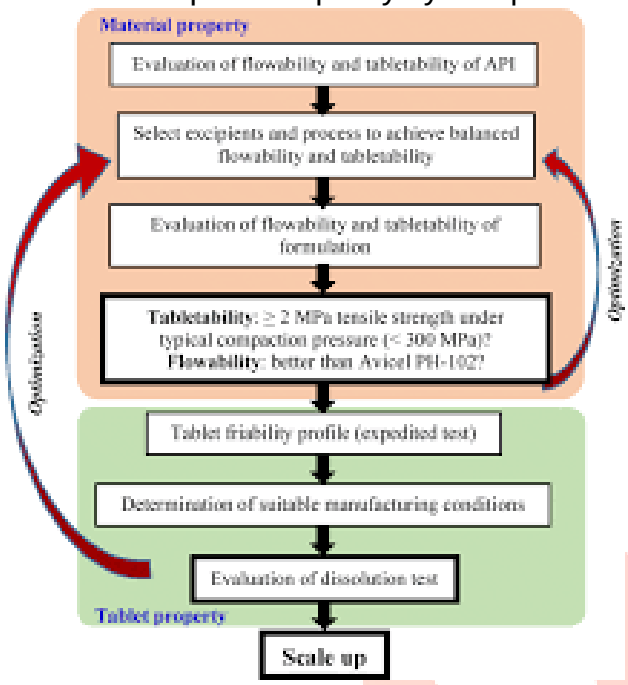


Figure 4:- simplified flow Chart for QBD process

Successful adoption

- Regulatory pliability to accept submissions for quality by design Regulatory authorities around the world recognize the common dossier

-With regulatory flexibility, post-approval alterations that are made in a per-established design space can be carried out.

-The existence of procedures and laws to safeguard intellectual property (IP)

crafted to continuously meet the desired level of product quality

-Space design concept

-A scientifically based experimentally defined process operating space.

-Critical process variables have been found.

-Critical - have an effect on product quality

-Operating range in space with acceptable product Space.

Critical process variables are reliably under control.

The quality of the process's output is constantly desired. Product.

Testing on the final product may be diminished.

created to encourage ongoing progress

-Control of the process is a process control strategy.

-Performance and ongoing process enhancement.

-Instantaneous process feedback Process refinements in the design environment Experience increases one's knowledge

-Use information and modern technologies.

ICH Q8, Q9, Q10 GUIDELINES: THE FOUNDATION OF OBD

Figure 5:-the foundation of QBD

QbD2,3,6,18ICH Guidelines Q8 for Pharmaceutical Development, Q9for Quality Risk Management, Q10 for Quality systems are

Quality by Design relative to ICH20,21

- Concepts aligned

- Design Space - Key to understanding

- Process robustness

- Design of Experiments (DOE)

- Quality management Quality management

Critical Concept: Design Space19-21

-Multidimensional combination with interactions

Multidimensional interactions put variables (e.g. raw

material attributes) and process parameters

- Demonstrated to provide assurance of quality

-Defined by applicant and reviewed by regulator

Defined regulator

- Once design space is approved, regulatory post

approval change requirements will be simplified

approval Inside vs. outside design space Inside space

- regulatory flexibility to operate within the design

space Regulatory space

Experience with Merck

Science-based Product and Process Design is Being Developed in the Design Space

-Improve process comprehension to support a science-based strategy

-Development of the interaction between drug substance and drug product processes.

-Drug compound characteristics tailored for the subsequent production stage

Using the Design Space: An efficient system for process control and quality

-Use of intensive monitoring to improve process comprehension during development.

-Utilize scientifically based controls during producing.

-However, the amount of time required for biological testing could restrict process control.

An essential component of Quality by Design is Process Analytical Technology (PAT)

-which is used during development to analyse processes.

-Used in normal manufacturing to keep an eye on the production process, manage product quality, and minimize release testing controls

-PAT testing may take the place of further laboratory testing.

Application of quality by design

A thorough, systematic approach to pharmaceutical research and production is known as "quality by design" (QBD). QBd's advancements in pharmaceutical discovery and production can be described

Aspects	Traditional	QbD
Pharmaceutical Development	Empirical	Systematic; Multivariate experiments
Manufacturing Process	Fixed	Adjustable within design space; opportunities for innovation
Process Control	In process testing for go/on-go; offline analysis wide or slow response	PAT utilized for feedback and feed forward at real time
Product Specification	Primary means of quality control; based on batch data	Part of the overall control strategy, based on the desired product performance
Control Strategy	Mainly by intermediate product and end product testing	Risk based; controlled shifted up stream, real time release
Lifecycle Management	Reactive time problem and OOS; Post approval changes needed	Continual improvement enabled within design space

Table 1: Pharmaceutical aspects: Traditional versus

QBD IN CMC REVIEW Offices

-Assessment based on science

-Organizational restructuring and staff reorganization, including upmarket and postmarked personnel

-A number of applications were received; CMC Pilot; and Lessons learned

-Information evaluation; PMP

Office of New Drug Quality Assessment (ONDQA)

implementation; and science-based assessment

-Organizational restructuring and staff reorganization, including upmarket and postmarked personnel

CMC Pilot Several applications were submitted

-Lessons learn Information evaluation PMP

Office of Generic Drugs implementation (OGD)

-The key questions for regulatory and scientific reviews are included in QBR.

-Determine if a product is of a good calibre.

-Establish the degree of risk connected to the creation and planning of this product.

-By June 2007, 416 applications were received using QBD

BENITIT OF IMPLEMENTING QBD FOR FDA

-Better coordination between review

- compliance, and inspection

-better information in regulatory submissions

-better consistency; improved review quality (creating a QMS for CMC)

-more flexibility in decision-making

-assurance that decisions are based on science rather than empirical data

-involvement of multiple disciplines in decision-making; and use of resources to address higher risks.

Advantages for Industry

-Allows for the implementation of new technology to improve manufacturing without regulatory scrutiny allows for a potential reduction in overall costs of manufacturing

- allows for less waste; ensures better design of products with fewer manufacturing issues reduces the number of manufacturing supplements required for post-market changes

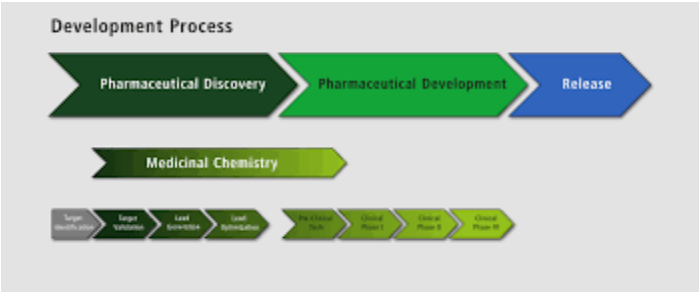
- ensures less hassle during review; reduces deficiencies

and expedites approvals.

-**Pharmaceutical Development**

Widely used in pharmaceutical development and

manufacturing (Figure: 6)



Used in PAT

A system for designing, analyzing and controlling

manufacturing through timely measurement of critical

quality performance attributes of raw and in process

materials and processes with the goal of ensuring final product quality(figure7)

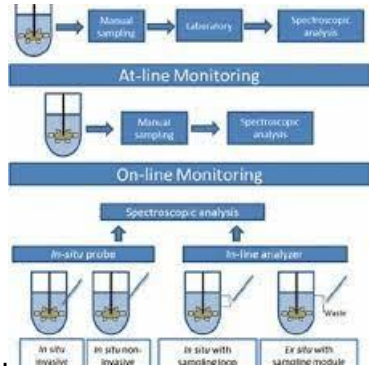


Figure 7:- off-line and online analysisFor experimental design

A structured organized method for determining the

relationship between factors affecting a process and the

output of that process (Figure: 8)

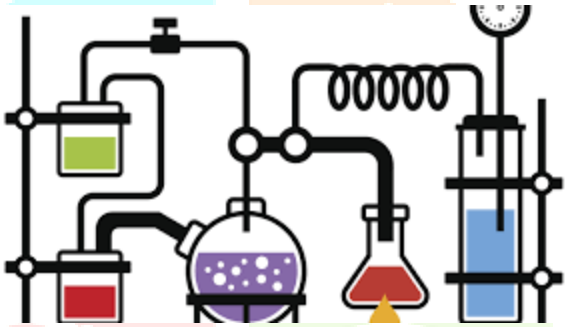


Figure 8 :- for experimental Design Space

Multidimensional combination of and interaction of input

variables and process parameters that have been demonstrated to provide Quality Assurance

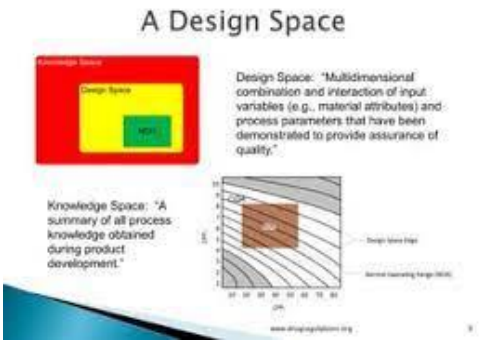


Figure9 :- design of space

-Linkage between important quality features and process inputs (input variables and process parameters).

-Implementation before or after MA; proposed by applicant; subject to regulatory review and approval

-Created for a single unit operation, several unit operations, or the entire process

-Working inside the design environment is not regarded as a change.

-QbD-based HPV vaccine production process

Utilizing QbD, the HPV vaccine manufacturing process may be carried out

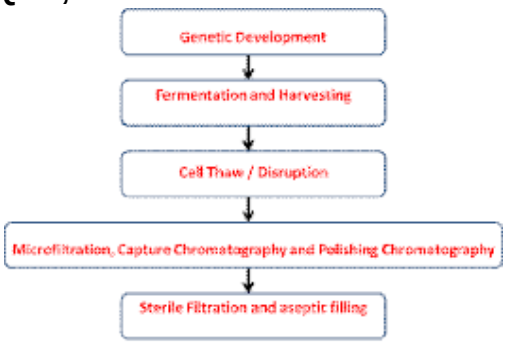


Figure 9 :-manufacturing process of hpv vaccine

quality-by-design methodology for coating processes

-Although quality cannot be evaluated into a product, it should be included.

The following are variables that have an impact on the coating process (Figure: 10).

For the coating process, the traditional and Quality by Design approaches can be presented (Figure: 11).

Figure 10:-Paramaters that affects coating process

Figure 11: Traditional and Quality by Design approach in coating process

For the ANDA product, a high-quality target product profile

The Quality Target Product Profile (QTPP) is "a prospective description of the quality features of a drug product, taking into account safety and efficacy of the drug product, that will ideally be reached to assure the intended quality."

A QBD method is not complete without the QTPP, which serves as the foundation for product development design.

Early in the development process for ANDAs, the target should be established based on the characteristics of the drug substance (DS), the RLD product's description, the RLD label, and the intended patient population.

Development produces a solid formulation and production process with a workable control plan by starting with the end in mind.

Conclusion:-

An effort to produce a reliable method that can be proved with a high degree of assurance is the aim of a well-characterized method.When carried out within predetermined limits, consistently yield data that satisfy preset requirements. Analytical method development and evaluation can be done using QBD.

All conceivable factors (the inputs) and all crucial analytical results (the outputs) are investigated to ascertain the relationships during method development. Critical analytical factors are discovered using a methodology similar to that of ICH Q8 and Q9's process development guidelines. As methods are created and risk factors for potential method failures are recognized and managed, the QBD process relies on an active partnership of analytical scientists at both the development and operational laboratories.Throughout the process, a corporate knowledge repository is necessary to ensure that crucial information is recorded and can be examined and added to in the future so that knowledge gained can be used to improve the method being considered specifically as well as other similar approaches being used to improve other items. Such a repository will make it possible for the method to be continuously improved and changed during its life cycle (in keeping with the ideas outlined in the draught ICH Q10).

A QBD technique was used instead of continuing with analytical technology transfer exercises and ICH validation in Internet

A risk analysis should be carried out each time a procedure is modified. where the modification is deemed to have the potential to change the approach To make sure the method performance criteria are still met outside of its known design space, a method evaluation and, if necessary, an equivalency exercise should be carried out. This will make it possible to improve methods through internal change control processes, and it might even make it much simpler to transition between other techniques (like HPLC versus NIR).

Compared to ICH validation criteria (Q2(R1)), a QBD strategy for analytical methods that incorporates risk assessment, robustness testing, and ruggedness testing is substantially more stringent. One of the most crucial technique assessments is an evaluation of method variability in relation to the specification limits. One of the most crucial method attributes to test is method variability, which is evaluated in relation to the specification limitations.

when assessing the method's suitability for the task at hand.The strategy outlined here shows that, while offering some value, ICH Q2(R1) has to be significantly updated to take into consideration the QBD risk-based strategies outlined in this article.

Future regulatory flexibility could be greatly increased thanks to this novel QBD procedure. Potentially, the method performance criteria rather than the actual method would be registered. The technique employed could serve as an illustration of how to meet the necessary method performance requirements. Internal change control processes would apply to any modifications to this approach.

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