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Quality by Design (QbD)

In Pharmaceutical Packaging Development

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Overview

- Quality by Design (QbD) in pharmaceutical development
- Elements of QbD
- QbD in packaging development (container closure system)

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QbD in pharmaceutical development

- QbD is systematic approach to pharmaceutical development that begins with predefined objectives and emphasizes product and process understanding and process control based on **sound science** and **quality risk management**
- QbD is to enhance assurance of safe, effective drug supply to patient needs and also offers promise to significantly improve manufacturing quality performance throughout its **life cycle**
- QbD is based on
  - Scientific, risk-based, holistic and proactive approach to pharmaceutical development
  - Deliberate design effort from product conception through commercialization
  - Full understanding of how product attributes and process relate to product performance

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QbD in pharmaceutical development

Quality by Design approach

QTPP	Target - product profile
CQAs	Determine - critical quality attributes (CQAs)
Risk Assessment	Link - material attributes and process parameters to CQAs and perform - risk assessment
Design Space	Develop - a design space
Control Strategy	Design and implement - a control strategy
Continual Improvement	Manage - product lifecycle, including continual improvement

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Elements of Quality by Design

Quality Target Product Profile (QTPP)

- **Summary of quality characteristics to ensure desired quality, considering safety and efficacy of drug product considering**
  - **Intended use in clinical setting, route of administration, dosage form, delivery systems**
  - **Dosage strength(s)**
  - **Container closure system**
  - **Drug product quality criteria such as sterility, purity, stability, and drug release appropriate for drug product**
- **Critical quality attributes (CQA) are physical, chemical, biological, or microbiological properties or characteristics that should be within an appropriate limit, range, or distribution to ensure desired product quality**

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Elements of Quality by Design

- **Critical process parameter** (CPP) - whose variability has an impact on a critical quality attribute, monitored or controlled to ensure process that produces desired quality
- **Risk assessment** is a valuable science-based process that can aid in identifying which material attributes and process parameters potentially have an effect on product CQAs and is performed early in pharmaceutical development process and is repeated as more information becomes available and greater knowledge is obtained
- **Design space** is multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality

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Elements of Quality by Design

- **Process analytical technology** (PAT) is system for designing, analyzing and controlling manufacturing through timely measurements of critical quality and performance attributes of packaging with goal of ensuring final product quality
- **Product lifecycle management** and **continual improvement** is to evaluate innovative approaches to improve product quality. Process performance can be monitored to ensure that it is working as anticipated to deliver product quality attributes as predicted by design space such as trend analysis of packaging as additional experience is gained during routine manufacturing
- Expansion, reduction, or redefinition of design space could be desired upon gaining additional process knowledge. Change of design space is subject to regional requirements

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QbD in Packaging Development

- QbD can be implemented irrespective of size of organization as it to meet final objective of pharmaceutical business
- USFDA reviewers expects container closure information in NDA/ANDA based on QbD
- QbD shall be critical for **inhalation aerosols/solutions/nasal sprays**, **inhalation powders** which require accurate dosing devices, **injections/injectable suspensions**, **sterile powders/ powders for injections**, **ophthalmic solutions/suspensions**
- Integrity of container closure is pivotal for product stability
- Interaction between product and container closure and or label to be evaluated
- Protection from moisture and light and seal integrity as appropriate to be ensured

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QbD in Packaging Development

- Compatibility (leachable and extractable materials) to be checked
- Dosing devises - accuracy, reproducibility and compatibility with container closure and drug product shall be evaluated
- Packaging component vendors are to be taken into confidence while designing package and explain QbD
- Vendors can take some cue from QbD application in their processes
- User industry can train on GMP and QbD to vendors in understanding principles and requirements

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QbD in Packaging Development

Applying Quality by Design to packaging development

QTPP

- Define quality target profile for PPM and dosing devices based on route of administration for safety and efficacy of drug product
- Focus on chemical and functional aspects
- List out quality characteristics required considering
  - Reliable and accurate
  - Stable and dimensionally consistent
  - Mechanically robust
  - Protection of formulation
  - Patient friendly (variable and rugged use)

CQA

- Define physical, chemical and functional properties within acceptable range each in relation to packing operations, machinability and drug product characteristics
- Share requirements with PPM vendors, consult and make agreement to specifications
- Study impact of PM attributes, packaging process parameters on CQAs of the drug product

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QbD in Packaging Development

Applying Quality by Design to packaging development

Risk Assess-ment

- Conduct risk assessment by linking variability in chemical, physical and functional properties of each packaging component , packaging process parameters and impact on product quality and performance
- Consider handling and storage at plant, transportation and storage at warehouses till retailers
- Evaluate qualitative and quantitative profiles of plastic and elastomeric packaging components from vendors and assess effect on product quality
- Develop risk mitigation strategies

Design Space

- Define physical, chemical and functional properties within acceptable range each in relation to packing parameters, machinability and drug product characteristics
- List and perform design of experiments (DoE) on functional aspects of packaging component
- Change in vendor site, and vendor to be critically assessed
- Change in materials of construction by vendor to be studies specific to formulation

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QbD in Packaging Development

Applying Quality by Design to packaging development

Control Strategy

- Define set of controls of that ensure package performance
  - Attributes of packaging components
  - Packaging process parameters
  - Challenge tests and in-process controls on packaging lines
- Establish control strategy with combined efforts of packaging development, engineering, production and in-process quality assurance
- Make agreement with vendors on specification

Continual Improve-ment

- Develop program of interaction with logistics, marketing personnel, physicians and nurses, users for the feedback on CCS
- Review of inputs and incorporating changes within design space
- Proactive approach on possible effects and preventive measures
- Trend analysis of packaging components and packaging process parameters

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QbD in Packaging Development

- QbD is refined, comprehensive systemic approach to pharmaceutical development moving to 21st century
- Should move from copying from innovator pack to design with rationale for generic product with a decade of experience to Indian generic industry
- Evolve various options available and select container closure system optimum for intended protection, safety and efficacy for the dosage form
- Coordinated efforts between vendor, engineering, packaging development, production, validation and technology transfer in selection and optimization of container closure system yield best results
- Knowledge of previous experience to be taken when CCS of new products of similar dosage forms are added

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Thanks for your attention

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