IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

"Review on QBD (Quality by Design)"

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Content

Abstract

A systemic approach to 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 a concept first outline by Dr Josep M. Juran EP

Dr. Josep M. Juran explained that most of quality crises and issues in product is only due to lack of importance of product during product planning.

QBD is describe in ICH guideline.

Quality by Design is the modern approach for quality of pharmaceuticals. This paper gives idea about the Pharmaceutical Quality by Design (QBD) and describes use of Quality by Design to ensure quality of Pharmaceuticals. The Quality by Design is described and some of its elements identified. Process parameters and quality attributes are identified for each unit operation. Benefits, opportunities and steps involved in Quality by Design of Pharmaceutical products are described. The aim of the pharmaceutical development is to design a quality product and its manufacturing process to consistently deliver the intended performance of the Product.

ICH documents on which QBD is Based

ICH document	Subject	Details
ICH Q8(R_2)	Pharmaceutical Development	Drug product development using science Principles.
ICH Q9	Quality Risk Management	How to assess control, review and manage quality risks.
ICHQ10	Pharmaceutical Quality System	Quality Systems, how to improve process performance and product quality.
ICHQ12	Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management.	Regulatory Factors in Pharmaceutical products and life Cycle Change Management.

Keywords:

- **QTPP-** Quality Target Product Profile
- **CQA-** Critical Quality Attributes
- **CMAs-** Critical Material Attributes
- **Design Space**
- **Process Parameters (PP)**
- **Screening**
- **Optimization**

Introduction:

The pharmaceutical Quality by Design (QBD) is a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management

The aim of pharmaceutical development is to design a quality product and its manufacturing process to consistently deliver the intended performance of the product.

Quality by Design (QBD) is emerging to enhance the assurance of safe, effective drug supply to the consumer, and also offers promise to significantly improve manufacturing quality performance.

Objective:

- The main Objective of QBD is to the quality Products.
- To achieve positive performance testing.
- Ensures combination of product and process knowledge gained during development.
- From knowledge of data process desired attributes may be constructed.

Importance:

- QBD will increase transparency of the sponsor's understanding of the control strategy for the drug product that it seeks to obtain approval and ultimately commercialize.
- When the sponsor can demonstrate process and product understanding then it will assist FDA in facilitating the CMC review and ultimately decrease the number of deficiencies and review time.
- In addition, with this added knowledge base, the Scale-up validation and commercialization will be transparent, rationale and predictable.

Element:

- **QTPP-** Quality Target Product Profile
- **CQA-** Critical Quality Attributes
- **CMAs-** Critical Material Attributes
- **Design Space**
- **Process Parameters (PP)**

1.QTPP (Quality Target Product Profile):

Summary of the drug development program described in terms of labelling concepts and it mainly focus on the safety and efficacy.

Description

- Clinical Pharmacology
- Contraindications
- Warnings
- Precautions
- Adverse Reactions
- Drug Abuse and Dependence
- Over dosage
- Dosage and Administration
- How Supplied
- Animal Pharmacology and/or Animal Toxicology
- Clinical Studies

It facilitates identification of what's needed/critical for the patient/consumer in the Quality Target Product Profile (such as Critical Quality Attributes, CQAs)

- Identifies risks and best approaches to manage
- Uses tools/enablers in an optimized fashion (such as integration of QBD and biopharmaceutics)
- Generates and enables knowledge sharing.
- An iterative, learning, life-cycle process for optimizing decision-making and the therapeutic outcomes for the patient benefit.

2.CQA (Critical Quality Attributes):

A CQA is a physical, chemical, biological, or microbiological property or characteristics that should be with in an appropriate limit, range or distribution to ensure the desired product quality.
CQAs are difficult to measure directly in production. Along the upstream and downstream portions of the manufacturing process it is most common to monitor the CPPs and KPIs related to the quality attributes.

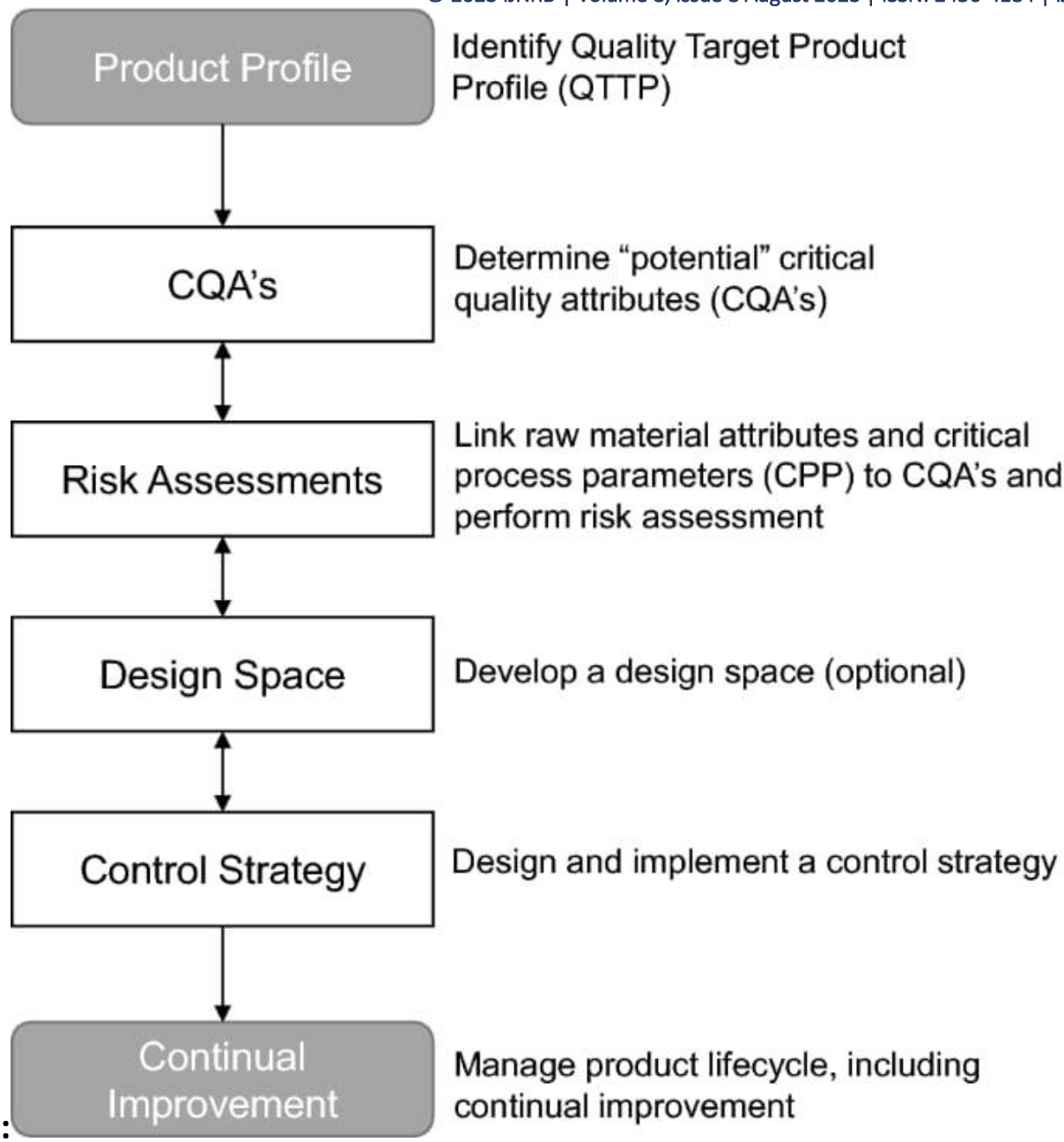
3.CAMs (Critical material attributes):

CMAs is defined as physical, chemical, biological and microbiological properly of raw material that need to be monitored to ensure the quality of product.
CMAs can significantly impact pharmaceutical unit operations, process consistency, and product quality attributes. Hence, material properties need to be tested and CMAs need to be defined and controlled.

4.Design Space:
The relationship between the process inputs (material attributes and process parameters) and the critical quality attributes can be described as the design space.
Design Space is a Y(Quality Attributes) = F (Process Parameters, Material Attributes) — a function or a relationship between (critical) process parameters and (critical) quality attributes /material attributes.

Benefits:

- Better design of Product with lower Problems.
- Eliminate batch failure.
- Minimize deviation.
- Continuous improvement.
- QBD is good science.
- Better development decision.
- Empowerment of technical staff.
- Organisational learning is an investment in the future.
- Increase manufacturing efficiency, reduce costs and project rejections and waste.
- Build scientific knowledge base for all products.
- Incorporate risk management.



Process:

Limitation:

- Culture challenges
  - Move from prescriptive approach
  - More sharing of scientific and risk information
- Business Challenges
  - Business justification
  - Management Support
  - Budgeting silos across business units
- Implementation Challenges
  - Collaboration between functions
  - Experience with new concepts
  - Workload and resource limitations

Tools of QBD:

- Screening
- Optimization

Screening –

Designs are made to Screen large no. of factors by using less no. of experiments to identify the significant One.

Main Purpose of these designs is to Identify Main effect.

EG- Fractional Factorial Design.

Optimization –

These Design are Only applied at once to a Selected factor in Formulation Process.

Main Purpose of these designs is to identify main effect.

EG- Full Factorial design

QBD In CMC Review Offices:

- Science-based assessment
- Restructured organization and reorganized staff –
- premarket staff and post-market
- CMC Pilot
- A number of applications submitted
- Lessons learned
- Evaluation of information
- Implementation of PMP

Office of New Drug Quality Assessment (ONDQA)

- Science-based assessment
- Restructured organization and reorganized staff –
- premarket staff and post market
- CMC Pilot
- A number of applications submitted
- Lessons learned
- Evaluation of information
- Implementation of PMP

Office of Generic Drugs (OGD)

- QBR contains the important scientific and regulatory review questions
- Evaluate whether a product is of high quality
- 416 applications received using QBR by June 2007
- Successful in ensuring that questions address issues regarding QBD

Office of Biotechnology Products

- Have more complex products
- Already doing some aspects of QBD
- In process of preparing to accept applications using QBD
- Beginning a pilot for biotech products for QBD –using mainly comparability protocol

Conclusion

During method development, all potential factors (the inputs) and all critical analytical responses (the outputs) are studied to determine the relationships. Critical analytical factors are identified in an approach that parallels what is described for process development in ICH Q8 and Q9. The QBD process on an active partnership of analytical scientists at both the development and operational laboratories as methods are developed and as factors that lead to potential method failures are identified and controlled. A corporate knowledge repository is required throughout the process to ensure critical information is captured that can be reviewed and added to in the future such that lessons learned can be applied to the specific method under consideration and also to other similar methods being applied to other products. Such a repository (in line with concepts described in the draft ICH Q10) will enable continuous improvement and change control of the method to take place throughout its lifecycle.

References:

Callis JB, Illman DL, Kowalski BR, Process analytical chemistry. Analytical Chemistry, 59, 1987, 624A–637A

https://www.slideshare.net/NavaneethakrishnanPa4/quality-by-design-qbd-162665917

https://www.hamiltoncompany.com/process-analytics/process-analytical-technology/critical-quality-attributes#:~:text=A%20CQA%20is%20a%20physical,ensure%20the%20desired%20product%20quality

https://images.app.goo.gl/hQWNrkMsMfsuuQLK8

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7952360/

https://images.app.goo.gl/kBmHtBQtLq44DMmz6