Review Article

Quality by Design: Predefined Objected Quality and Quality Risk Management

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Received: 07-09-2020; **Revised:** 23-10-2020; **Accepted:** 30-10-2020; **Published on:** 15-11-2020.

ABSTRACT

Quality by Design (QbD) is one of the most powerful strategies which act as a part of modern approach to pharmaceutical industry. The quality in the process and product is neither assures just by inspection nor testing the products, the quality should be built in by design. 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. It includes the Quality target product profile, critical quality attributes and key aspects of Quality by Design. It also gives comparison between product quality by end product testing and product quality by Quality by Design. The foundation of Quality by Design is ICH Guidelines. It is based on the ICH Guidelines Q8 for pharmaceutical development, Q9 for quality risk management, Q10 for pharmaceutical quality systems. It also gives application of Quality by Design in pharmaceutical development and manufacturing of pharmaceuticals.

Keywords: Quality by Design (QbD), critical process parameters (CPP), Quality target product profile (QTPP), Critical quality attributes (CQA).

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DOI:
10.47583/ijpsrr.2020.v65i01.002

DOI link: http://dx.doi.org/10.47583/ijpsrr.2020.v65i01.002

INTRODUCTION

The pharmaceutical Quality by Design (QbD) is a organized approach to improvement that begins with predefined objectives and emphasizes product, process understanding and process control, based on scientific knowledge and quality risk management. Quality means suitability for intended use. Pharmaceutical quality refers to product free of microbial and other contamination, reproducibly delivers the effective therapeutic benefit promised in the label to the patients. Customer or patient satisfaction can be achieved by various ways i.e. features like performance, trust worthiness, robustness, ease of use and service ability have to build in the product and such product should be free from deficiencies. Quality by design approach assures in vitro and In vitro product performance[1].

Quality activities must try to detect quality problems early enough to allow actions without requiring pacification in cost, schedule or quality of product.

The statistics and knowledge gained from various pharmaceutical studies and manufacturing processes provide a base for scientific understanding to maintain establishment of design space, specification and manufacturing control. Informative data from pharmaceutical development studies can be an origin for quality risk management. Lifecycle management allows making changes in formulation and manufacturing processes during development and providing additional opportunities to gain added knowledge and it further supports establishment of the design space. Design space is planned by the applicant and will undergo regulatory assessment and approval. QbD requires identification of all critical formulation attributes and process parameters which can impact the quality of the finished product. Three fundamental aspects of quality planning as Juran trilogy concept [2].

Figure 1: Benefits of quality by design [3]

Figure 2 explains the various process in QbD, which will help for understanding and determination of risk factor to improve quality of product.

Figure 2: Process of QbD [4-7]

Diverse variables are monitored for their effect on product quality during manufacturing which are assessed and conclusions will be frame out as a device for QbD. The pharmaceutical product formulation can be constructed based on the data obtained from product development studies. Before conducting the development studies, the Quality Target Product Profile (QTPP) of the product must be resolute and have the final product quality and evaluation steps to be performed for desired product quality. Which includes design space, specifications and manufacturing controls [8,9].

The purpose of product design and understanding is to develop a robust product which have desired QTPP over the product shelf life. Key elements of product design and understanding include the following [10, 11]:

- Physical (particle size distribution, aqueous solubility as a function of pH, intrinsic dissolution rate, hygroscopicity, and melting point polymorphism, transformation and particle morphology), chemical (pKa, chemical stability in solid state and in solution, as well as photolytic and oxidative stability), and biological characterization (partition coefficient, membrane permeability, and bioavailability.) of the drug substance.
- Identification and selection of excipient type and grade, and knowledge of intrinsic excipient variability: because they carry out functions of
  - Aid in the processing of the dosage form during its manufacture eg: binders, disintegrants, fillers (diluents), lubricants, glidants (flow enhancers), compression aids, colors, sweeteners, preservatives, suspending/dispersing agents, pH modifiers/buffers, tonicity agents, film formers/coatings, flavors, and printing inks
  - Protect, support, enhance stability, bioavailability, patient acceptability by improving colour, odor, taste. They added in safety limits mentioned in FDA
  - Assist in product identification
  - Enhance safety, effectiveness, delivery of the drug during storage, use.
- Interactions of drug and excipients
- Optimization of formulation and identification of CMAs of both excipients and drug substance: Which provide Vital data regarding

- ❖ Robustness of the formulation including establishing functional relationships between Critical Quality Attributes and critical material attributes: physical, chemical, biological, or microbiological property or characteristic of an input material that should be within an appropriate limit, range, or distribution to ensure the desired quality of that drug substance, excipient, or in-process material.
- ❖ Identification of critical material attributes of drug substance, excipients, in-process materials: which act as input materials including drug substance and excipients.
- ❖ Development of control strategies for drug substance and excipients

As shown in below diagram.

QbD tools for Analytical development

Analytical Quality by Design (AQbD). As per ICH, QbD is defined as "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.".

- ICH Q11 : QbD approach for API synthetic process development but there is no specific discussion on AQbD.
- ICH Q3 : explained the consideration of impurities in the API synthetic route.

AQbD method validation approach is the validation of analytical method over a range of different API batches. It uses both DoE and MODR knowledge for designing method validation for all kinds of API manufacturing changes without revalidation [12,13].

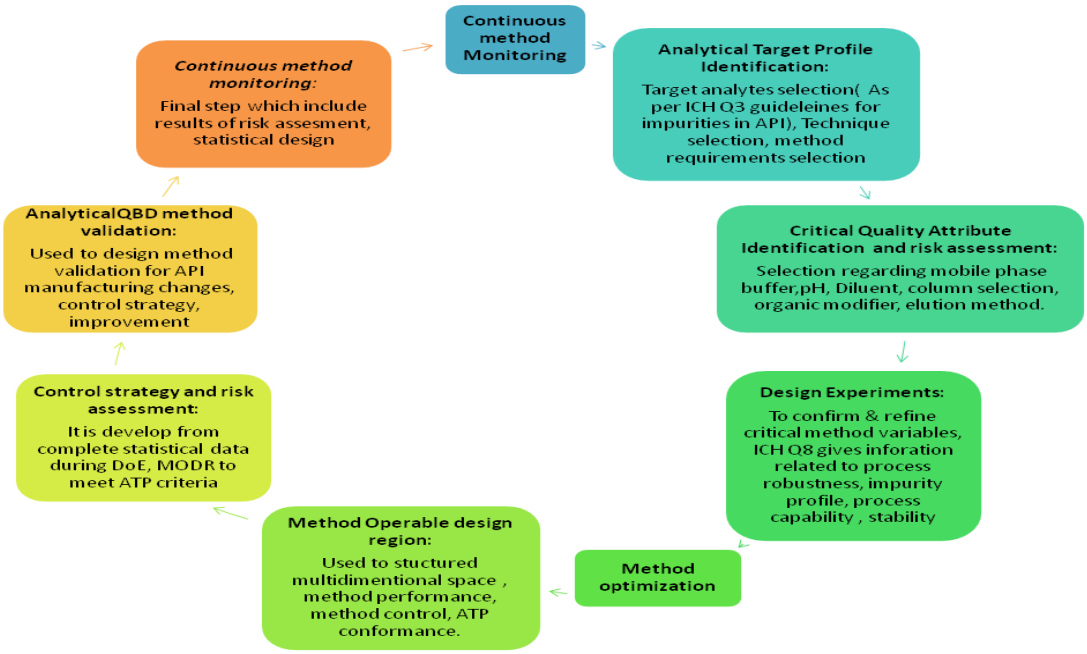

Figure 3: QbD tools for Analytical development (AQbD) [12,13].

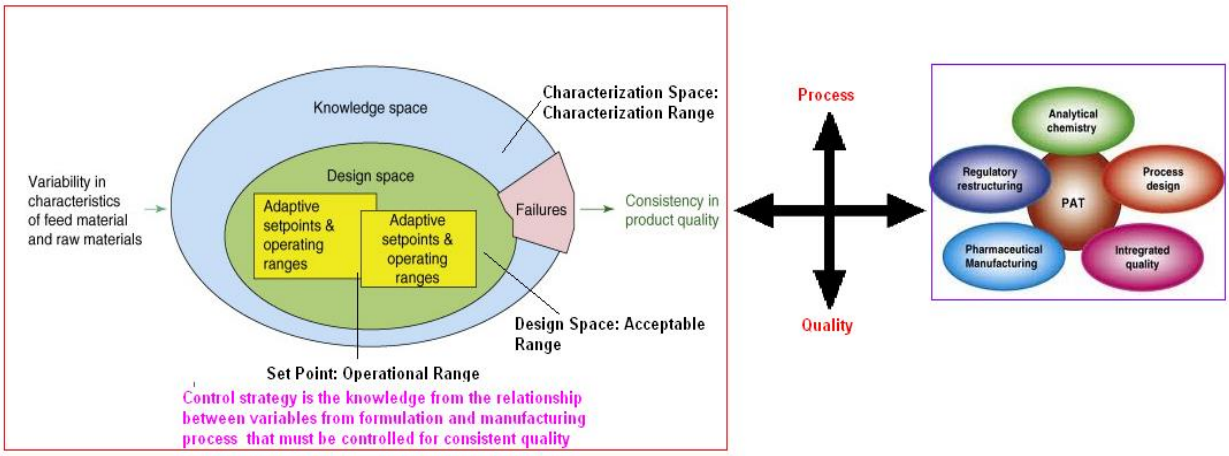

Figure 4: Design Space [14].

The design of experiment approach, in which process variables are 'screened' to determine which are vital to the outcome. After which formulation can undergo Optimization with best setting parameter.

Advantages [15].

- Utilized to evaluate variable of quality target product profile
- Risk- based approach, identification.
- Improve processes help in innovation.
- Less batch failures and more efficient technology transfer
- Robust products and regulatory flexibility
- Innovative process validation approaches.
- Greater product consistency in a product meeting the defined quality attributes.
- Approved, regulatory post approval change requirements will be simplified
- Evaluation of the changes is carried out by quality risk management.
- Design space limits constructive for establishing the acceptance criteria for process validation.

Risk-Based Approach [16].:

Process Development

• Experimental design (DoE)

• Control Strategy

Process Qualification

• Equipment qualification

• Process performance qualification (PPQ)

Continued Process Verification with Primarily ICH Q8 through Q11

• Q8- Pharmaceutical Development

• Q9- Quality Risk Management

• Q10- Pharmaceutical Quality System

• Q11- Development and Manufacture of Drug Substances

But there may be confusion due to validation and verification process.

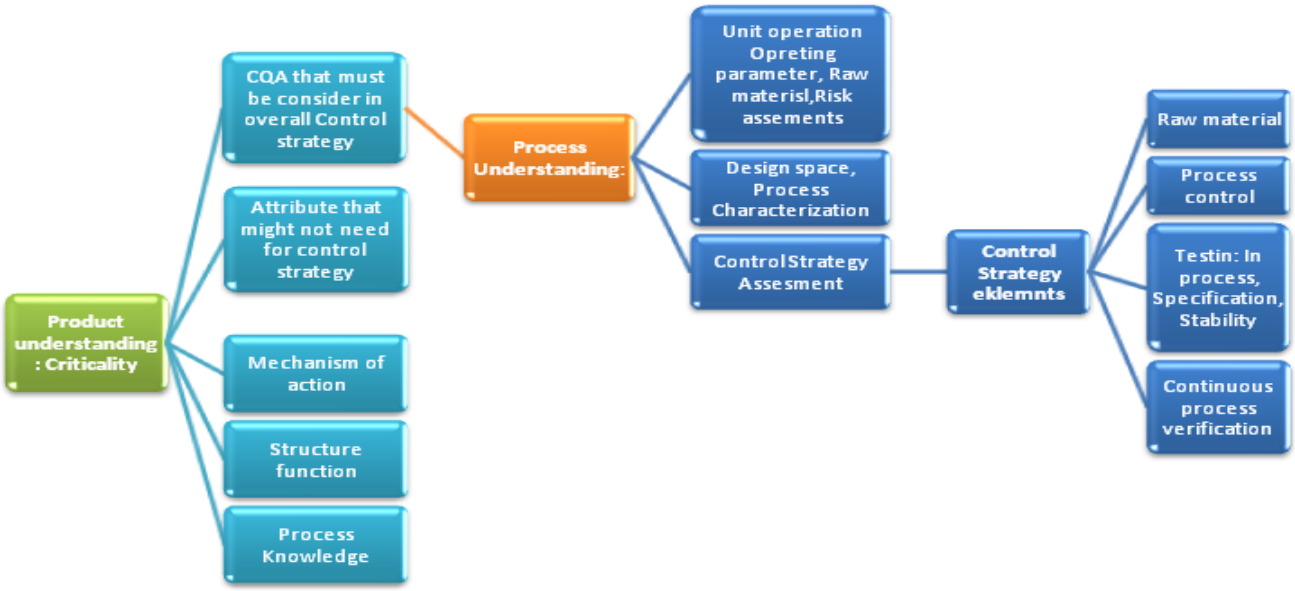

Figure 5: Risk-Based Approach [16]

Some of the most common barriers to adoption include:

- Insufficient understanding of the process and its benefits
- Organizational resistance to change
- Denial of the need ("Our process is under control")
- Competing priorities
- Lack of resources and expertise in QbD.

Process Development and Risk Assessment: The FDA has given us the green light to assess and manage risk earlier in the drug development cycle. Risk assessment is a valuable science-based process, and the Q8 Pharmaceutical Development guidance encourages the application of scientific approaches and risk management to the development of a product and manufacturing processes[17] .

Q9 Quality Risk Management guidance is an overview of the principles and its applications of risk management[18]

Details of process development risk management explained in Figure No.06.

Methods of risk assessment: As per ICH guideline Q9 as follows:

- Failure Mode Effects Analysis (FMEA)
- Failure Mode, Effects and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA);

- Hazard Analysis and Critical Control Points (HACCP)
- Hazard Operability Analysis (HAZOP)
- Preliminary Hazard Analysis (PHA)
- Risk ranking and filtering;
- Supporting statistical tool

Figure 6: Process Development Risk Assessment

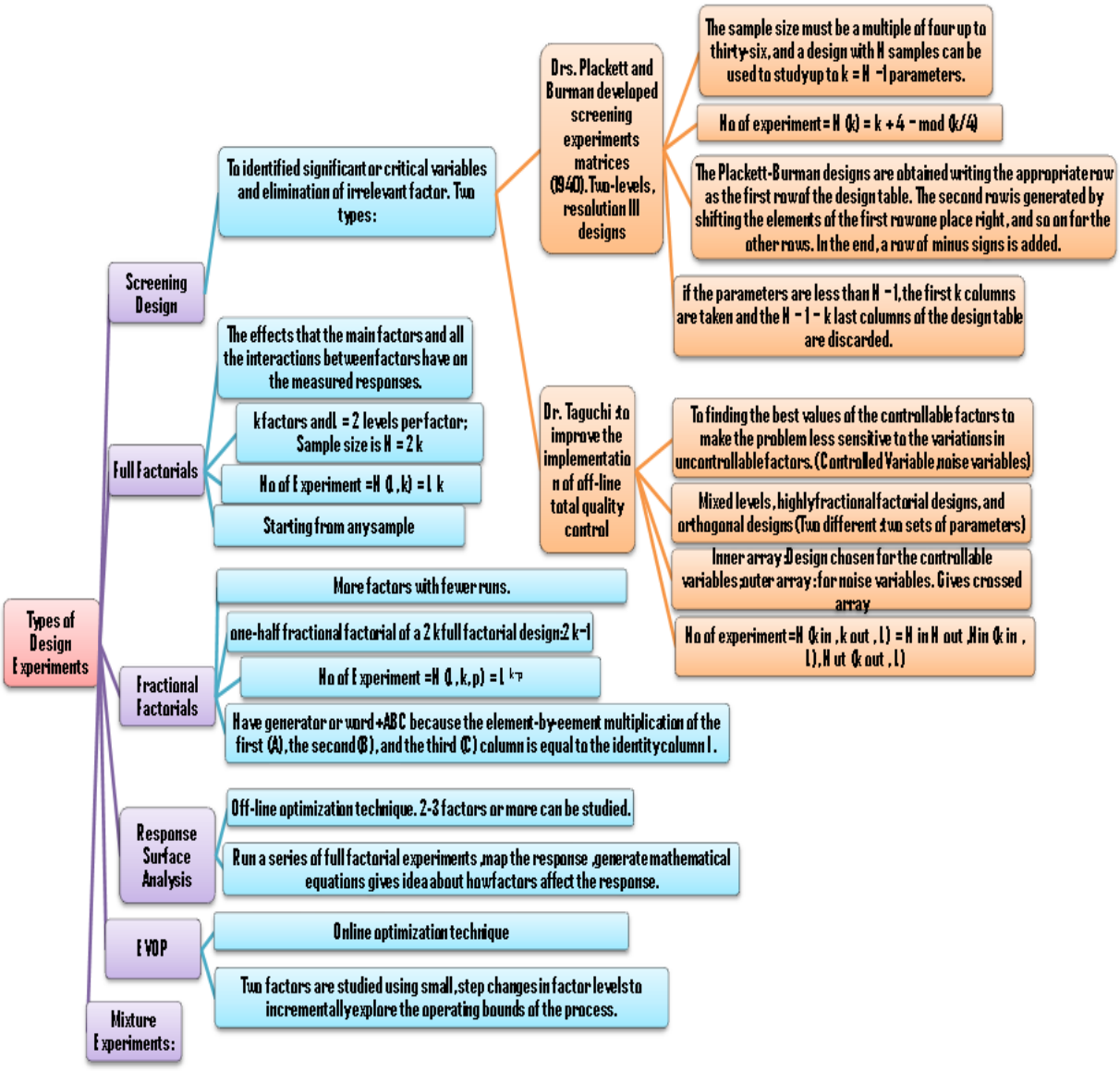

Figure 7: Design of experiment [19]

There are some common critical material attributes (CMA) mentioned in Table 1.

Table 1: Critical Material Attributes (CMA)

Parameter type:	Definition	Sensitivity
Non-critical process parameter (non- CPP)	Not critical	• No failure in target product quality profile (QTPP) observed /predicted in the potential operating space (POS), and • No interaction with other parameters in the proven acceptable range
Critical process parameter (CPP): Any measurable input or output (process state variable or output material attribute) of a process step that must be controlled to achieve the desired product quality and process consistency	Critical (control needed to ensure quality)	• Failure in target product quality profile (QTPP) observed / predicted in the potential operation space (POS), • Interactions with other parameters

Quality Target Product Profile (QTPP) [20,21,22]

QTPP is a device for setting the calculated groundwork for drug development which includes development planning, clinical, commercial decision making, regulatory agency interactions, risk management etc. The Target Product Profile provides a statement of the overall intent of the drug development program and gives information about the drug at a particular time in development. Usually, the TPP is organized according to the key sections in the drug labelling and links drug development activities to specific concepts intended for inclusion in the drug labeling and focus on labeling concepts, safety and efficacy as follows

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

Many aspects of the TPP determine the actions of formulation and process development scientists. It is the task of a pharmaceutical scientist to interpret the qualitative TPP into what we define as the target product quality profile (QTPP) for further use in a quality by design process.

Quality target product profile (QTPP) Includes, but not limited to:

- Dosage form
- Route of administration
- Strength
- Release or Delivery of the drug
- Pharmacokinetic characteristics: e.g., dissolution, aerodynamic performance
- Drug product quality characteristics for intended use: e.g., sterility, purity.

Critical Quality Attributes [21,22]

A Critical Quality Attributes defined as a physical, chemical, biological or microbiological property or characteristics that should be within specified appropriate limit, range, or distribution to ensure the preferred product quality.

Critical Quality Attributes are applicable to for product purity, stability

- ❖ Drug substance
- ❖ Excipients
- ❖ Intermediates
- ❖ Drug product

Critical Quality attributes includes the properties that impart the desired quality, safety, and efficacy.

Table 2: Necessary and Desired elements for QTPP

Necessary Elements	Desired Elements
Quality characteristics: sterility, purity etc. (including specific safety-related impurities where necessary)	Dosage form: liquid for injection, solid tablet etc.
Pharmacokinetic characteristics: dissolution etc. Therapeutic effect	Route of administration: oral, IV, IM, SC
Target patient population: neonate, adult etc., clinical diagnosis	Clinical setting: self or clinic administration
Shelf life: temperature, light conditions etc	Primary/secondary packaging: glass or plastic vial/syringe; blister packaging etc

Risk Management [25]

Table 3: Example of risk filter during initial drug development

Critical parameter factors	*Polymer*	*Roll gap/ Roll force (ribbon porosity)*	*Compression force*	*Amount of fine after RC*	*Lubricant distribution*	*Process speed*	*API*	*Precompression force*
Appearance	Low	Low	High	Low	High	Low	Low	Low
Identity	Low	Low	Low	Low	Low	Low	Low	Low
Assay	Low	Low	Low	Low	Low	High	Low	Low
Impurity	Low	Low	Low	Low	Low	Low	Low	Low
Dissolution	High	Low	Low	Low	Low	Low	Low	Low
Tablet Hardness	High	High	High	High	High	High	Low	High
Friability	High	High	High	High	Low	Low	Low	Low
Yield	Low	Low	Low	Low	Low	Low	Low	Low

It is used for comparing and ranking risks. Basic Risk Management Facilitation Methods are flow charts, check sheets, process mapping, cause and effect diagrams are the most commonly used simple methods for RA and management [26]

Process mapping [27]

Which relates critical process parameters and/or critical material attributes and critical product quality to a response surface derived from an experimental data.

Fishbone diagram

cause and effect diagrams: Represents all aspects which show influence on a critical product quality. Fish Bone diagram contains horizontal line, the end of which points toward the affected product quality. The major influencing factors are then represented as diagonal lines. The influence of the critical process parameters and critical material attributes is then representing as sublines for the diagonal lines. A fishbone diagram is divided into categories like instrumentation, materials, methods, measurements, laboratory climate, and human factors.

Once the risk is assessed it is grouped into three categories:

A. High-risk factors:

B. Potential noise factors:

C. Factors with acceptable ranges:

Steps for risk management includes:

Table 4: Risk Management steps [27]

1.	**Define the Problem**	1. Effective 2. Time consuming 3. They either try to diagram a symptom, or secondary effect
2.	**Assess Information Needs**	1. Copious amounts of data are available like video of a process, a printout from a quality database, or a process walk which act as a starting point. 2. Decide plan of action for how to collect information to spur brainstorming prior to gathering to start the fishbone diagram.
3.	**Plan Your Fishbone Diagram**	These options are available 1.On a whiteboard, 2.With sticky notes pasted to a sheet of butcher paper, 3.With the use of a computer and projector
4.	**Gather Information**	Any data gaps identified
5.	**Develop Your Cause and Effect Diagram**	Whether real time, or as a second step, the results of the brainstorming session are organized onto the spines of the fishbone. Note that the process of brainstorming separately and then adding the ideas, normally on sticky notes, is commonly referred to as CEDAC, or Cause and Effect Diagram with the Addition of Cards. Ideas are assigned to the diagram based on the major categories, and then grouped by similarity. Some of these sub-groups will turn into branches off the main spines as shown in the earlier graphic (i.e. car broke down–>never changed oil).

		Combine this step with an application of the 5 Whys. For each of the causes, ask why that happened, and add branches if further layers of the problem are uncovered. Note that during this step, the ideas should be added with little regard as to whether it is truly a cause. The goal is to start with a diagram of potential causes and winnows it down in the next step.
6.	**Review Your Cause and Effect Diagram**	Once the first pass of the diagram is complete, the facilitator should lead a discussion about key observations. Continue to add new ideas throughout this process. The discussion often spurs more brainstorming. At this point, ideas that are unlikely to be a real cause of the problem should be removed. Ideas that are undetermined should be flagged for further review. Once you get these likely ideas laid out on the diagram, you will then have to prove whether these are actually causes, or if they were incorrect guesses. Because brainstorming is an unscientific activity, many of the suspected causes do not actually have a relationship with the effect. It is also important to distinguish between causal relationships and correlation. Some of the ideas that initially make it to the fishbone diagram are related, but only through a third factor. For example, umbrellas and worms on sidewalks are linked, but only through another factor, namely rain.
7.	**Act on Your Findings**	Because fishbone diagrams are commonly done as a team effort, there is a considerable cost to them. Make sure that the effort drives an improvement plan. Frontline team members tend to be extremely discouraged when they are pulled away from their jobs for a project, and they see no benefit for their time.

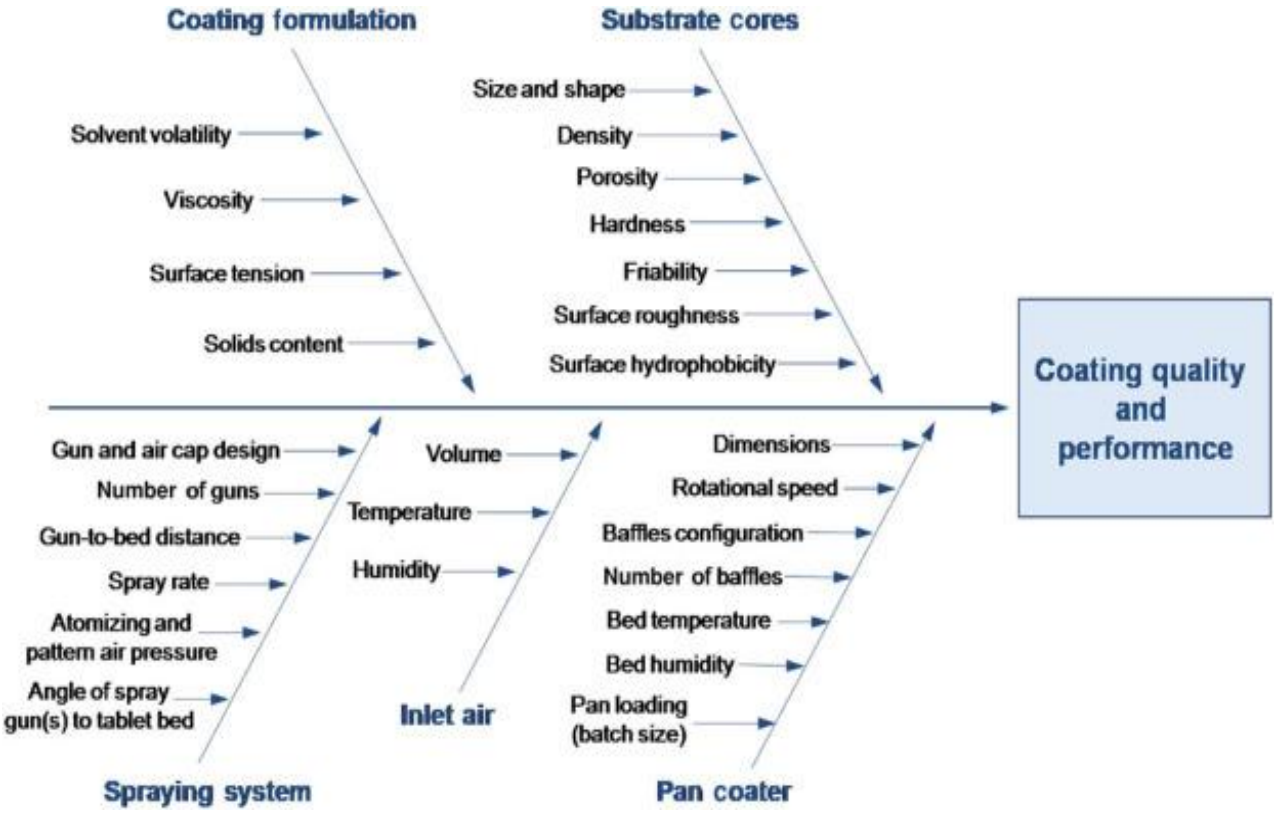

Figure 8: Fishbone diagram for scale up of pan coating process.

Which explain the breaking down the coating process variables into three main types: pan-related, spray-related, and thermodynamic-related factors as shown in above diagram [28]

Critical Process Parameter

A parameter is critical when a realistic change in that parameter can cause the product to fail to meet the TPQP.

Thus, the first step in classifying parameters is to define the range of interest which we call the potential operating space (POS) which is the region between the maximum and minimum value of interest to the sponsor for each process parameter. Criteria for identifying critical and non-critical parameters are that a parameter is non-critical when there is no trend to failure within the potential operating space and there is no evidence of interactions within the proven acceptable range, which is the range of experimental observations that lead to acceptable quality.

Table 5: Classification of process parameters

Parameter Type	Definition	Sensitivity
Non-critical process parameter (non-CPP)	Not Critical	• No failure in Target Product Quality Profile (TPQP) observed or predicted in the potential operating space (POS), and • No interaction with other parameters in the proven acceptable range
Unclassified process parameters (UPP)	Critically unknown	• Not established • The default in the absence of pharmaceutical development
Classified process parameters (CPP)	Critical (control needed to ensure quality)	• Failure in target product quality profile(TPQP) observed or predicted in potential operation space (POS) • Interactions with other parameters in the proven acceptable range (PAR)

Some examples of dosage forms with their:

QTPP For IR Tablet

QTPP	Target	Justification
Dosage Design	IR tablet without a score or coating	Immediate release of drug as mentioned on label
Route of administration	Oral	Pharmaceutical equivalence requirement: same route of administration
Dosage strength	20 mg	Pharmaceutical equivalence requirement: same strength
Pharmaco-kinetics	Immediate release enabling T max in 2.5 hr or less; Bioequivalent to RLD	Bioequivalence requirement needed to meet required rate & extent of drug absorption
Container System	Qualified container for IR tablet	Needed to achieve the target shelf life and ensure tablet integrity during shipping
Administration	Similar food effects	High fat meal increases AUC, C max by 8-12 %
Stability	At least 24 month	Equivalent to or better than RLD shelf life.
Drug product quality attributes:	• Description • Identification • Assay • Content Uniformity • Impurity • Dissolution • Microbial limit • Water content	Pharmaceutical equivalence requirement: must meet the same compendia or other applicable reference standards (i.e., identity, assay, purity & quality).

QTPP For Solution

QTPP	Target	Justification
Dosage Design	Immediate release formulation	Pharmaceutical equivalence requirement as same dosage form
Route of administration	Oral / External	Immediate release as label claimed
Dosage strength	X mg	Pharmaceutical equivalence requirement: same strength Drug Product
Pharmaco-kinetics	Not required	
Drug product quality attributes:	• Description • Identification • Assay drug, preservative • Content Uniformity • Impurity • Dissolution • Microbial limit • Purity & quality	Pharmaceutical equivalence requirement: Must meet the same compendia or other applicable reference standards

Container System	Container (Glass/Plastic/Metal) & Closure (Plastic/Metal/ Rubber) system should be qualified as suitable for drug product with desired Compatibility & Stability. Should product from heat, moisture, oxygen, carbon dioxide, light & microbial attack. Plastic should not allow permeation, leaching, sorption, or any other chemical or physical deformation.	Required to achieve the target shelf-life and to ensure product integrity during transportation, storage & during routine-use
Ease Of Storage & Distribution	Can be stored at real time storage condition as a normal practice with desired stability & can be distributed from the manufacturer to end user same as per Reference Product.	Required to handle the product easily with suitable accessibility
Stability & Shelf Life	Should be stable Hydrolysis, Oxidation, Photodegradation & Microbial Growth. At least 12-months shelf-life is required at room temperature. At least 28 Days of in-Use Shelf Life is required during routine use of multidose product	Equivalent to or better than Reference Product shelf-life
Patient Acceptance & Patient Compliance	Should possess acceptable taste, flavor, odour & attractable pleasant color most probably as similar with Reference Product. Can be easily administered (pourable & palatable)/ used/ applied similarly with Reference Product labelling	Required to achieve the desired patient acceptability & suitable compliance

QTPP For Suspension

QTPP	Target	Justification
Dosage Design	Immediate release formulation	Pharmaceutical equivalence requirement as same dosage form
Route of administration	Oral	Immediate release as label claimed
Dosage strength	X mg/ ml	Pharmaceutical equivalence requirement
Pharmaco-kinetics	Rate of absorption, Extent of absorption	Limits of 80-125 With reference standard
Drug product quality attributes:	• Description • Identification • Assay drug, preservative • Content Uniformity • Impurity • Dissolution • Antioxidant content • PSD • pH • Viscosity • Specific Gravity • Leachable/ Extractable • Microbial limit • Purity & quality	Acceptable limits of specification
Container System	Container (Glass/Plastic/Metal) & Closure (Plastic/Metal/Rubber) system should be qualified as suitable for drug product with desired Compatibility & Stability.	Required to achieve the target shelf-life and to ensure product integrity during transportation, storage & during routine-use
Ease Of Storage & Distribution	Can be stored at real time storage condition as a normal practice with desired stability against sedimentation, caking, hydrolysis, oxidation, photo degradation, microbial growth with at least 28 days of use shelf life	Required to handle the product easily with suitable accessibility
Stability & Shelf Life	Should be stable Hydrolysis, Oxidation, Photodegradation & Microbial Growth. At least 12-months shelf-life is required at room temperature. At least 28 Days of in-Use Shelf Life is required during routine use of multidose product	Equivalent to or better than Reference Product shelf-life
Patient Acceptance & Patient Compliance	Should possess acceptable taste, flavor, odour & attractable pleasant color. Can be easily redispersed, administered (pourable & palatable)/ used/ applied similarly with Reference Product labelling	Required to achieve the desired patient acceptability & suitable compliance

QTPP For nanoparticles (SLN)

Quality Attributes of the Drug Product		Target	Justification
Physical Attributes	Appearance	Color should be acceptable, odour and taste should be masked	Color, odor and appearance are not directly linked to safety and efficacy. Therefore, they are not critical.
	Size	Size of the SLN should be in Nanometer range	Small size of the SLN is responsible for its prolonged release of action. Therefore, it was considered as CQA.
% Entrapment Efficiency		70-90%	%EE is critical while adjusting the dose of the formulation

For Soft gelatin capsule

QTPP Element	Target	Justification
Dosage form	Soft gelatin capsule	Pharmaceutical equivalence requirement: same dosage form
Dosage design	Immediate release / modified release formulation	Immediate release design needed to meet label claims
Route of administration	Oral	Pharmaceutical equivalence requirement: same route of administration
Dosage strength	x mg	Pharmaceutical equivalence requirement: same strength
Drug product quality attributes: **1. description** **2. assay** **3. uniformity** **4. impurity** **5. dissolution** **6. microbial limit** **7. water content** **8. residual solvents**	Pharmaceutical equivalence requirement: must meet the same compendia or other applicable reference standards (i.e., identity, assay, purity & quality).	
Primary packaging	Plastic container & closure/ metal blister system should be qualified as suitable for drug product with desired appropriate compatibility & stability. should protect product from heat, moisture, oxygen, light & microbial attack.	Required to achieve the target shelf-life and to ensure product integrity during transportation, storage & during routine-use
Pharmaco-kinetics	Fasting bio-equivalence study 90 % confidence interval of the pk parameters, auc0-t, auc0-∞ and cmax, should fall within bioequivalence limits of 80-125 with reference product	Bioequivalence requirement needed to meet required rate & extent of drug absorption
Ease of storage & distribution	Can be stored at real time storage condition as a normal practice with desired stability & can be distributed from the manufacturer to end user same as per reference product.	Required to handle the product easily with suitable accessibility
Stability & shelf life	Should be stable against hydrolysis, oxidation, photo degradation & microbial growth. at least 24-month shelf-life is required at room temperature	Equivalent to or better than reference product shelf-life
Patient acceptance &patient compliance	Should be suitably flavored & colored for possessing acceptable taste (in case of soluble/ dispersible/ effervescent tablet) similar with reference product. can be easily administered/used similar with reference product labeling	Required to achieve the desired patient acceptability &suitable compliance

Process Control Strategy[29]

Many Control Strategy elements are developed via risk assessments: CQA/CPP, Raw Material, Components, Specifications. Control Strategy is the final outcome of process development ("Process Design" if using FDA terminology). A Control Strategy is not a "point-in-time" activity, but rather should evolve as knowledge increases. A Control Strategy is constituted of many parts, many of which are developed/written at different points in time throughout

process development.

Process validation:

Which include three stages

Stage 1

Process Design, which include identification of critical process parameter, determination of control strategy.

Control strategy includes:

- Quality attribute assessment
- Material specification
- Drug specification
- Process parameter assessment
- In-process control
- Manufacturing documentation, narrative
- Component specification
- Packaging specifications
- Storage stability

Stage 2

Process qualification; which includes equipment, utility, facility qualification, process performance qualification. Process performance qualification is a dynamic part of the validation concept

• Provides proof the process is well controlled

• Establishes an initial baseline for future process evaluation

Stage 3

Process Monitoring, which include critical process parameters, and monitoring programs.

Lifecycle Management

Throughout the product lifecycle, the manufacturing process performance will be monitored to ensure that it is working as anticipated to deliver the product with desired quality attributes. Process stability and process capability will be evaluated. If any unexpected process variability is detected, appropriate actions will be taken to correct, anticipate, and prevent future problems so that the process remains in control.

Applications of Quality by design [29, 30]

Quality by design (QbD)–a comprehensive systematic approach to pharmaceutical development and manufacturing.

Advancement in the pharmaceutical development and manufacturing by Qbd can be explained against traditional approach.

In Pharmaceutical Development

To design a quality product and a manufacturing process to consistently deliver the intended performance of the Product.

Benefits of Implementing QbD for FDA:

- Enhances scientific foundation for review
- Provides for better coordination across review, compliance and inspection
- Improves information in regulatory submissions
- Provides for better consistency
- Improves quality of review (establishing a QMS for CMC)
- Provides for more flexibility in decision making
- Ensures decisions made on science and not on empirical information
- Involves various disciplines in decision making
- Uses resources to address higher risks

Benefits to Industry

- Ensures better design of products with less problems in manufacturing
- Reduces number of manufacturing supplements required for post market changes –rely on process and risk understanding and risk mitigation
- Allows for implementation of new technology to improve manufacturing without regulatory scrutiny
- Allows for possible reduction in overall costs of manufacturing –less waste
- Ensures less hassle during review –reduced deficiencies –quicker approvals
- Improves interaction with FDA –deal on a science level instead of on a process level
- Allows for continuous improvements in products and manufacturing process.

Pharmaceutical Development

- Widely used in pharmaceutical development and manufacturing

CONCLUSION

QbD has gain significance in the vicinity of pharmaceutical processes like drug development, formulations development, analytical method and biopharmaceuticals. Qbd also support to develop a reliable method as per ICH Q8 and Q9 assurance to constantly reproducible data meeting predefined criteria for high quality and safety. This new QbD process offers the opportunity for much better regulatory flexibility in the future by risk assessment and risk management through various methods.

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Source of Support: None declared.

Conflict of Interest: None declared.