

SAMPLE PREVIEW

BPS3051

Pharmaceutical Product Development

Comprehensive Study Notes

HD 95 • Monash University

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BPS3051 Pharmaceutical Product Development

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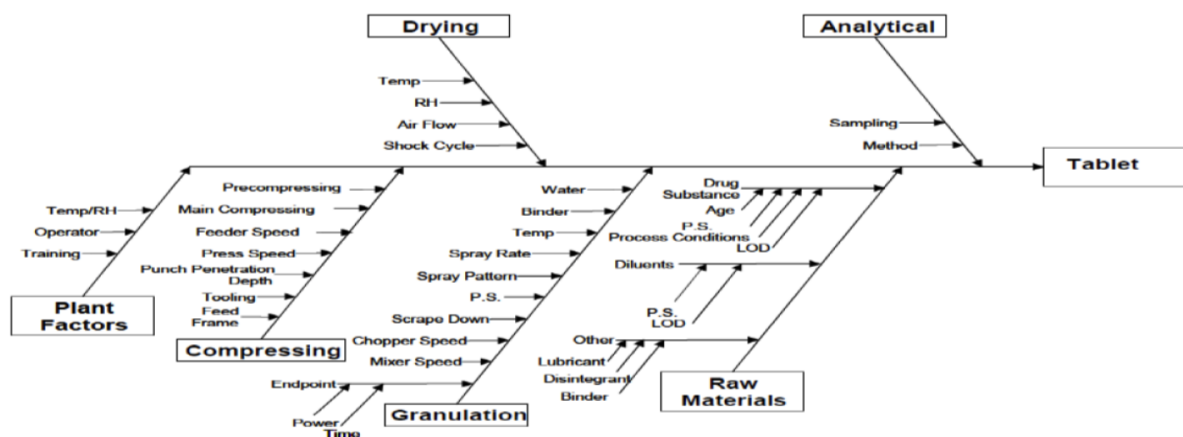
Introduction: What is a DoE?

Design of experiment

- Experimental design to achieve results with effectiveness and efficiency

Steps:

1. Identify the factors that can be controlled in your experiments
 - a. Make these factors vary in a range that is chosen and see if this change of level impacts the responses of interest e.g. hardness, dissolution...
 - b. Factors include excipient factors and process factors, and plant factors like temperature and humidity of the manufacturing room
 - c. Make a Ishikawa diagram that identifies and categorizes these factors



Other notes:

- formulators need to write the 3.2.P.2 part that is "Pharmaceutical Development"
- ICH (International Council for Harmonisation)
 - bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines

Example DOE

- Factors and responses

Table 21. Design of the 2³ full factorial DOE to study intragranular excipients and drug substance PSD

Factors: Formulation Variables			Levels		
			-1	0	+1
A	Drug substance PSD (d ₉₀ , µm)		10	20	30
B	Disintegrant (%)		1	3	5
C	% MCC in MCC/Lactose combination		33.3	50.0	66.7
Responses		Goal	Acceptable Ranges		
Y ₁	Dissolution at 30 min (%) (with hardness of 12.0 kP)	Maximize	≥ 80%		
Y ₂	Disintegration time (min) (with hardness of 12.0 kP)	Minimize	< 5 min		
Y ₃	Tablet content uniformity (% RSD)	Minimize % RSD	< 5%		
Y ₄	Assay (% w/w)	Target at 100% w/w	95.0-105.0% w/w		
Y ₅	Powder blend flow function coefficient (ffc)	Maximize	> 6		
Y ₆	Tablet hardness @ 5 kN (kP)	Maximize	> 5.0 kP		
Y ₇	Tablet hardness @ 10 kN (kP)	Maximize	> 9.0 kP		
Y ₈	Tablet hardness @ 15 kN (kP)	Maximize	> 12.0 kP		
Y ₉	Friability @ 5 kN (%)	Minimize	< 1.0%		
Y ₁₀	Friability @ 10 kN (%)	Minimize	< 1.0%		
Y ₁₁	Friability @ 15 kN (%)	Minimize	< 1.0%		
Y ₁₂	Degradation products (%) (observed at 3 months, 40 °C/75% RH)	Minimize	ACE12345: NMT 0.5% Any unknown impurity: NMT 0.2% Total impurities: NMT 1.0%		

- Results per response

Table 22. Experimental results of the DOE to study intragranular excipients and drug substance PSD

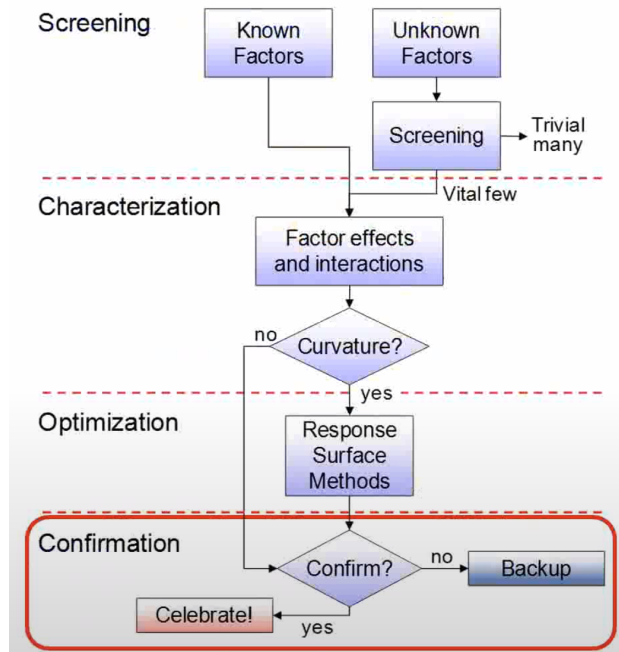
Batch No.	Factors: Formulation Variables			Responses			
	A: Drug substance PSD	B: Disintegrant level	C: % MCC in MCC/Lactose combination	Y ₁ : Dissolution at 30 min	Y ₃ : CU	Y ₅ : ffc value	Y ₇ : Tablet hardness @ 10 kN
	(d ₉₀ , µm)	(%)	(%)	(%)	(% RSD)	—	(kP)
1	30	1	66.7	76.0	3.8	7.56	12.5
2	30	5	66.7	84.0	4.0	7.25	13.2
3	20	3	50.0	91.0	4.0	6.62	10.6
4	20	3	50.0	89.4	3.9	6.66	10.9
5	30	1	33.3	77.0	2.9	8.46	8.3
6	10	5	66.7	99.0	5.1	4.77	12.9
7	10	1	66.7	99.0	5.0	4.97	13.5
8	20	3	50.0	92.0	4.1	6.46	11.3
9	30	5	33.3	86.0	3.2	8.46	8.6
10	10	1	33.3	99.5	4.1	6.16	9.1
11	10	5	33.3	98.7	4.0	6.09	9.1

Qdb (Quality by Design) and design space

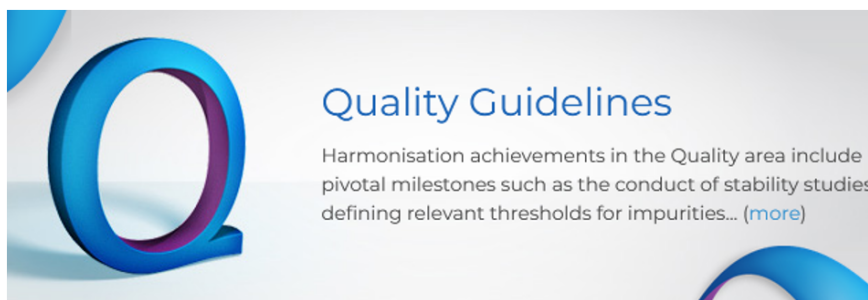
- What:
 - Approach to product development
 - Design effort from product conception through commercialization
 - Understanding of how product attributes and process relate to product performance
- Key elements:
 - Target the product profile
 - Determine critical quality attributes (CQAs)

- Link raw material attributes, formulation and process parameters to CQAs and perform risk assessment
- Develop a design space
- Designing and implement a control strategy
- Manage product life cycle, including continual improvement

Process



- Confidence interval pads our design space to give us confidence that the process mean is within boundaries
- Tolerance interval gives us confidence that a stated proportion of the population is within specifications



S

Safety Guidelines

ICH has produced a comprehensive set of safety guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy ... [\(more\)](#)

E

Efficacy Guidelines

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines... [\(more\)](#)

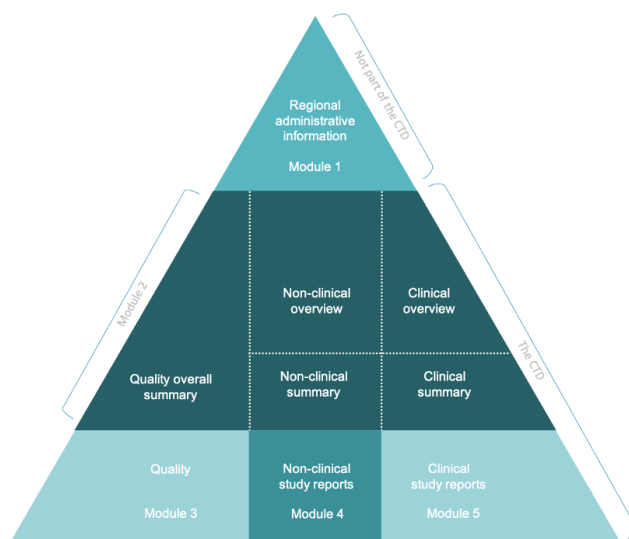
M

Multidisciplinary Guidelines

Those are the cross-cutting topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA)... [\(more\)](#)

- Regulation by the ICH (International Conference of Harmonisation)

Common Technical Document



PREVIEW

Get the full notes

A free preview of the complete BPS3051 notes.

The full set is 76 pages, covering every topic with all diagrams and a clickable table of contents.

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