BPS3051

Pharmaceutical Product Development

Comprehensive Study Notes

HD 95 • Monash University

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BPS3051 Pharmaceutical Product Development

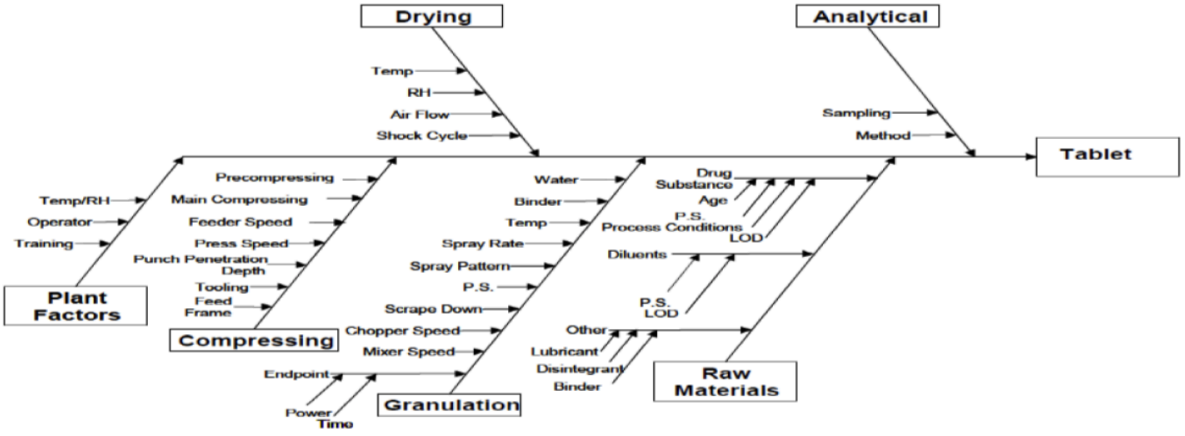
Introduction: What is a DoE?

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 2^3 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

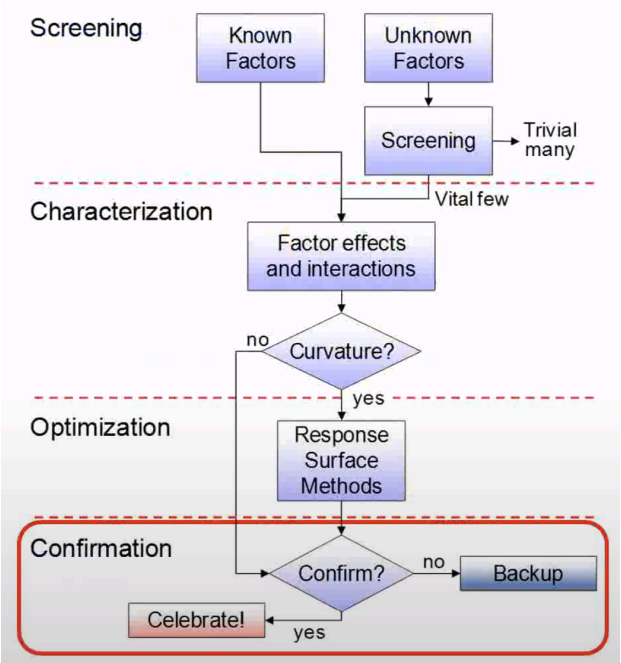
Batch No.	Factors: Formulation Variables			Responses			
	A: Drug substance PSD	B: Disintegrant level	C: % MCC in MCC/Lactose combination	Y_1: Dissolution at 30 min	Y_3: CU	Y_5: ffc value	Y_7: Tablet hardness @ 10 kN
	(d_{90}, µm)	(%)	(%)	(%)	(% RSD)	--	(kP)
1	30	1	66.7	76.0	3.8	7.56	12.5
2	30	5	66.7	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

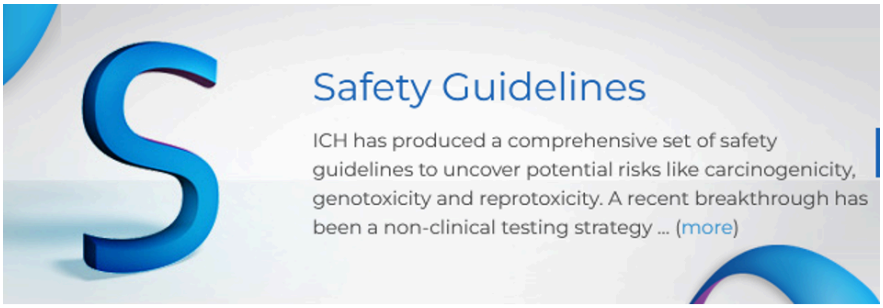
- What:
  - Approach to product development
  - Design effort from product conception through commercialization
  - Understanding of how product attributes and process relate to product performance
- Key elements:
  - Target the product profile
  - Determine critical quality attributes (CQAs)

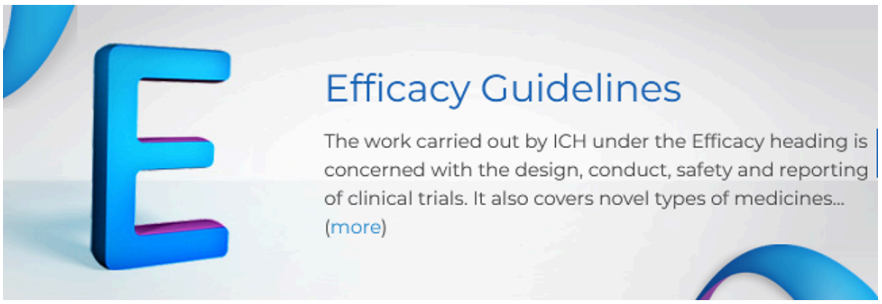
- Link raw material attributes, formulation and process parameters to CQAs and perform risk assessment
- Develop a design space
- Deiosng and implement a control strategy
- Manage product life cycle, including continual improvement

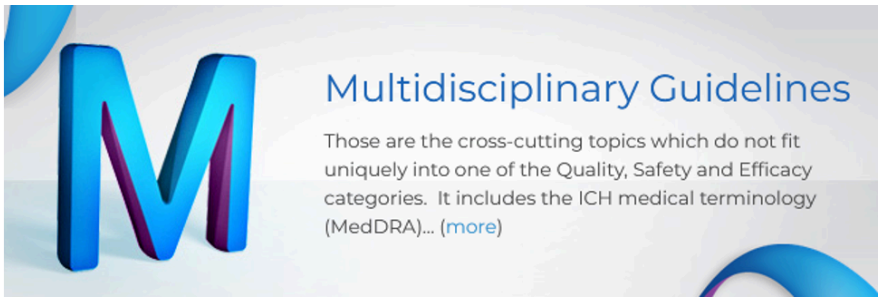
Process



- 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

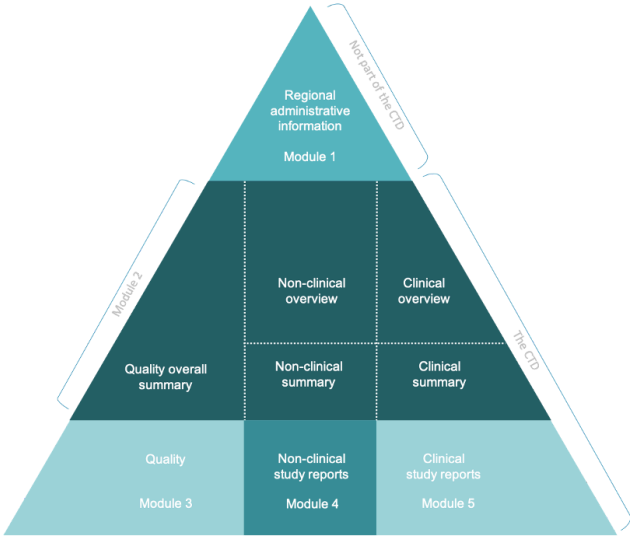






- Regulation by the ICH (International Conference of Harmonisation)

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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