Presentation on

INTRODUCTION TO VALIDATION

Presented By: Mr. Agale Krushna B.

Subject: Quality Assurance Techniques

Class: Final Year B.Pharm

MES's College of pharmacy,

Validation

Objectives

To review:

- Validation, risk analysis, and critical steps of processing
- Points to consider in process validation of:
  - *solid dose mixing*
  - *tablet compression*
  - *sterilization*
- Finalization of validation

Validation

Introduction

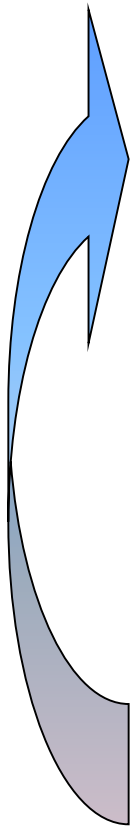
Validation

Reliable, repeatable, under control

- At least first 3 consecutive batches - repeatable
- Must investigate failures
- The rationale should be documented if experimental method is changed
  - ↗ *document deviations, decisions and reasoning*
- Does not improve processes
- Should not validate bad processes

Validation

DQ, IQ, OQ and PQ



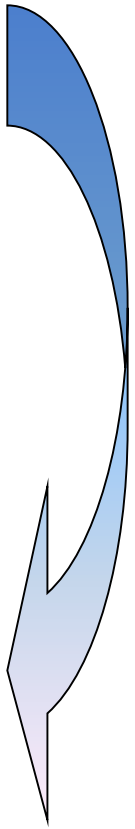
Design user or process requirements

Install installation qualification

Operate operational qualification

Validate performance qualification and process validation

Review periodically (+ change control)



Validation

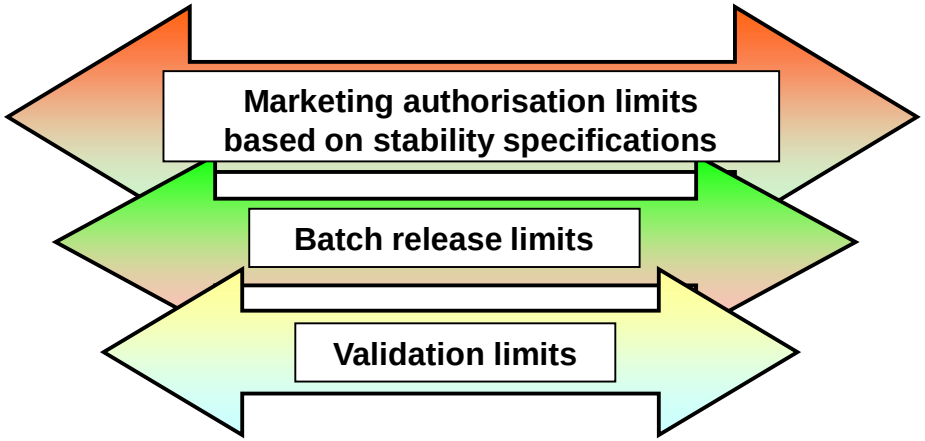
Critical factors or parameters

- Need to be determined
- Need to be monitored during validation
- May affect the quality of the product

Validation

Setting Limits

- Marketing authorization limits
  - ↗ *stability specifications*
- Release specification
- Validation limits



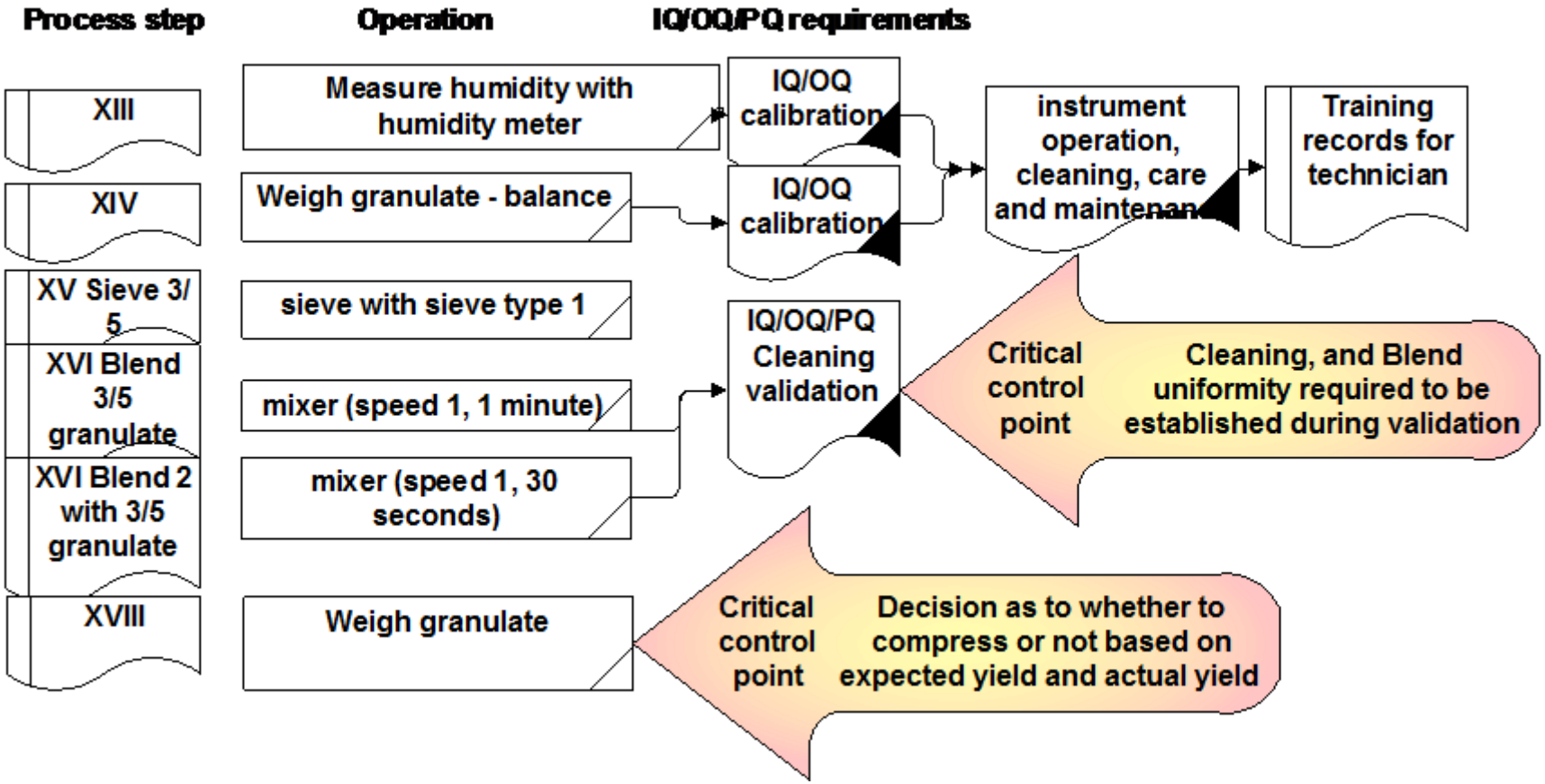
Validation

Determining critical control point example of a tablet granulation process

- Particle size distribution of the active(s)
- Blending time for the powder
- Granulating time and speed,
- Amount of granulating fluid-binder concentration
- Drying time - final moisture content, granule particle size distribution
- Granule active content and homogeneity, blending time of external phase

Validation

Determining critical control points



Validation

Solid dose mixing (1)

- Homogeneity in blending – the key to quality!
- Sampling strategy
- Sample site, label, container
- Storage
- Transport
- Sample thief

Validation

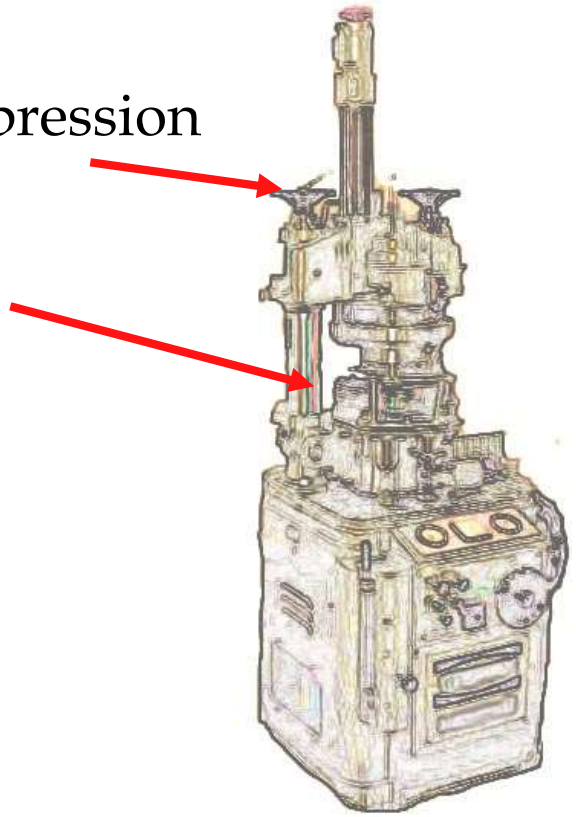
Solid dose mixing (2)

- *In situ* analysis
- Methods of analysis
- Statistical analysis
  - *inter-batch*
  - *intra-batch*
  - *within-sample-site*

Validation

Tablet compression variables

- Fill volume
- Pre-compression force, compression force
- Turntable speed
- Dwell time
- Granule size and feed
- Ejection force, lubrication



Validation

Tablet compression parameters

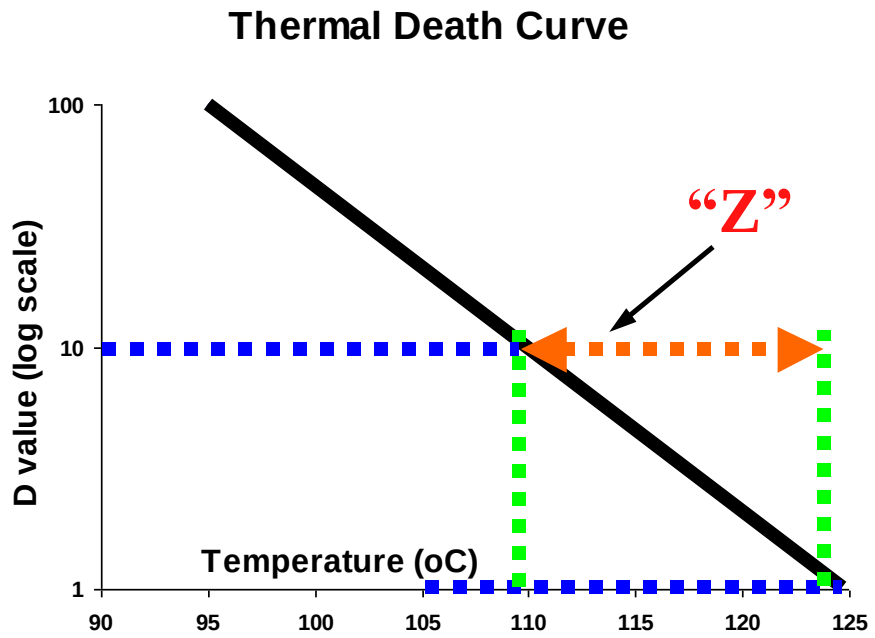
- Mass
- Hardness
- Moisture
- Friability
- Disintegration
- Dissolution
- Thickness

Tablet coating variables

- Spray rate
- Inlet and outlet air temp
- Coating weight

Validation

Moist heat sterilization



- Lethality of cycle
- D value
- Z value
- F value
- F_o value min 8

Validation

Sterilization validation (1)

- Sterility test
- Physical measurements
- Chemical and biological indicators
- Loading patterns

Validation

Sterilization validation (2)

- Cooling fluid or gas
- Automated process
- Leak tests
- Control instrumentation
- Steam quality
- Heat distribution

Validation

Dry heat sterilization

- Parameters
- Air circulation, positive air pressure, HEPA filter
- Advantages
  - *microorganisms destroyed*
  - *depyrogenation possible*
- Disadvantages
  - *poor heat transfer*
  - *higher temperatures for long periods*

Validation

Process variation

Controllable causes of variation may include:

- Temperature, humidity
- Variations in electrical supply
- Vibration
- Environmental contaminants
- Light
- Human factors
- Variability of materials
- Wear and tear of equipment

Validation

Change control

- Must be a review procedure for validated processes
- From time to time changes may be necessary
- Documented change control procedure needed
- “Like for like" changes do not require re-validation

Validation

Mixing validation liquid and solid dose change control and scale up

- Mixer type and size
- Batch size
- Pilot study scale up
- Limit on the proportion of the scale up

Validation

Finalization of validation process

- Final report required
- Summarize and reference protocols and results
- Conclusion required: "Is the process valid"
- Final report should be reviewed and approved by
  - *the validation team*
  - *"authorized person"*

Validation

Group Session

- You are given a tablet manufacturing flow chart to study
- List the critical steps that are required to be validated
- List the critical equipment required to be qualified
- Identify the variables and construct a table as directed