FEBRUARY

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3	4	5	6	7	8	9	06
10	11	12	13	14	15	16	07
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24	25	26	27	28			09

2.0.0.3 WEDNESDAY JANUARY 1

Validation

Concept was evolved in 1978 in USA.

→ Validation is Establishing documented evidence, ≤ provides a high degree of assurance that a sp. process will consistently produce a product meeting its pre-determined specifications and Quality characteristics.

Quality includes

- Identity, purity, safety & strength.

→ Validation determines process variables and the acceptable limits for these variables and accordingly sets up appropriate in process controls, ≤ specifies alert and action levels.

Alert level → within certain limits

Action level → ≤ ultimately affect the Quality.

Regulatory requirements:

The requirement of process validation is contained in 21 CFR (code of federal regulation) Published by FDA.

In CGMP (21 CFR)

* Section 211.100 : Written procedure deviation → There shall be a written procedure for prodn & process control design to assure that the drug products have the identity, strength, Quality, & purity they possess or purport or are represented to process.

* Section 211.110 Sampling & testing of Inprocess materials & Drug products.

→ Control procedure should be established to monitor the output and validate the performance of those manufacturing process & that may be responsible for causing variability in the characteristics of in process material and drug product.

Happiness is a wondrous commodity; the more you give, the more you have.

2 | 2 JANUARY THURSDAY 2.0.0.3

JANUARY

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* Section 211.113 Control of microbiological Contamination.

There shall be written procedure Designed to prevent microbial contamination of drug products purporting to be Sterile, shall be established & followed.

* Section 211.165 Testing & release Distribution.

There shall be a written procedure for testing & release distribution.

GMP Regulation for Medical Devices (21 CFR Part 820)

* Section 820.5 : Prepare & Implement a Quality assurance program that is appropriate to sp. device manufacture.

* Section 820.100 : Generally stated requirement for process validation.

Written manufacturing specification & processing procedures shall be established, Implemented and controlled to assure that device confirms to its original design or any approved change in the design.

Benefits of Validation

(1) Reduction in testing
- Raw materials
- Bulk formulation
- finished products

(2) Ultimately reduce Quality cost
- Preventive cost
- Appraisal cost
- Internal failure cost
- External failure cost

Do not bite the hands that feeds you.

Preventive cost: Cost use of to prevent failures, which includes Quality planning, Vendor approval system, Training cost, Documentation SOP, Monographs, preventive damages, calibration, Sanitation, process validation, Q.A. auditing, Self Inspections, Annual review of data

Appraisal cost: Cost of Inspections, testing and Quality Evaluation eg. Inspection of raw & packaging materials, Inspections & testing of In-process materials & finished products, stability testings.

Internal failure cost: Associated c a non-confirming materials, Rejects, Rewards, reinspection, retests, wastage & scraps, Trouble

External failure cost: Recalls, complaints, returns due to Quality related problems.

(3) Improve Q. A.
(4) Rapid trouble shooting
(5) Better system control
(6) Low Inventories.

Types of Validation:

- Prospective validation: Validation protocols is executed before the process is put into commercial use.

  Development phase

  1 x lab scale - 3-5 kg.
  3 x Pilot scale - 30-50 kg
  3x validation batch - 100x (300-500 kg)

- Concurrent validation: On going batch validation
- Retrospective validation: Based on historical datas. (10-20 batches are taken) - No measure change in process.

When money speaks truth remains silent.

4 JANUARY SATURDAY 2.0.0.3

JANUARY

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Conditions for Reterospective validation

(i) Batches manufactured for a defined period.
(Minimum 10 last consecutive batches)

(ii) No. of lots release per year.

(iii) Batch size/ strength / Manufacturing Year.

- Revalidation: After a definite period.

Some important about Concurrent validation.

(a) On-going

(b) When a previously validated process is being transferred to a third party contract manufacture or other manufacturing sites.

(c) Where the product is a different strength of a previously validated product & the same ratio of active or inactive ingredients

(d) When the No. of lots evaluated under the reterospective validation were not sufficient to obtain an high degree of assurance

(e) When the No. of batches produced are limited.

Scope of validation

(i) Analytical test methods (ATM)

Based on accuracy, precision, Linearity, reproducibility, Selectivity, Sensitivity, Limit of detectors, Limit of Quantisation Rubbestness.

5 SUNDAY Accuracy: How much accurate the method as compare to standards.

Precision: Deviation if more - Fail
if less - Pass

Linearity: Batch results must be linear.

There can be no true friendship with

(2) Instrument Calibration:

Calibration is a comparison of a measurement standards or instrument of non-accuracy ī other standard instrument to detect, co-relate, report and eliminate by adjustment by any variation in the accuracy of the item being compared.

(3) Process utility services:

Water, Gas, air, steam, Drainage

HVAC → Heating ventilation Air conditioning System.

(4) Raw & Packaging materials.

(5) Equipments:

All Equipments should be passed in

DQ - Design Qualification

IQ - Installation Qualification

OQ - Operational Qualification

PQ - Performance Qualification

(6) Facilities

(7) Manufacturing process

(8) Product Design: First stage in P'ceuticals.

- formulation Design
- Primary package compatibility studies.
- Specification of raw & packaging material
- Process & utility services
- Pilot plant services.
- Trial Commercial batches.
- Commercial Production
- Concurrent validation
- Revalidation

7 JANUARY TUESDAY 2.0.0.3

JANUARY

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(9) Cleaning : Covers 3 areas.
- Equipment & process containers.
- Product Containers & closures.
- Facilities.

Following points should be considered
- Cleaning limits
- Material used for cleaning
- Cleaning Methods
- Trace analysis methods & Limits.

(10) Operators.

Documents necessary in a validation
1. Validation Master Plan (VMP)
2. Validation Protocols
   - IQ
   - OQ
   - PQ
   - Computer Systems
   - Equipment facility, utility, Qualifications.
   - Process
   - Packaging
   - cleaning
   - Standard Operating procedures.
3. Optimization batch Testing Guideline.
4. Validation Reports
5. change control systems.

Validation Master Plan (VMP)

It is an internally approved document that describes in clear & consise wording, the General expectations, intentions

The wealthy man is a slave of his wealth.

methods and approaches to be used during entire validation effects.

Importance:

It provides to all the concern people & also the FDA Inspectors.

A Complete scope of the activities which is to be planned.

(a) What activity are to be performed.
(b) Who is going to perform the activity.
(c) When the activity get start & when they should get finalized (Time frame)
(d) How the activity will be performed.
(e) What documents will be generated.
(f) Policy for revalidation.
(g) Who is the authorised person to initiate & review the activity

* A VMP describes clearly the company philosphy, expectations & approaches to be followed.
* It Identify the System & Controls to be validated & the level of testing required
* It covers all aspects of project eg. Equipment Qualification, Training, Maintenance & change control.

Contents of typical VMP:

1. Introduction. 2. Purpose 3. Scope 4. Overview [Description of the system to validated]
5. Responsibilities 6. Validation Methadology 7. Acceptance Criteria & Validation Reports 9. Change Controls. 10. Deliverables.

Benefits of VMP

1. It provides a total picture of project.
2. It is a management tool for tracing progress.
3 Assignment of responsibilities & promotes team work.
4. It identify the acceptance criteria before the start of Validation.

Validation Protocols:

It is a written plan & states that how validation will be conducted.

9 JANUARY THURSDAY 2.0.0.3

JANUARY

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FORMAT
- On Cover page : Approval.
- Scope of projects : Description of departments covered.
- Objectives
- Description
- IQ, OQ, PQ
- Roll of responsibilities
- Prevalidation activities
- SOP requirements.
- Process monitoring
- Sampling & Testing
- Acceptance Criteria (Limits)
- Documents required
- Additional Information
  * Flow chart of process.
  * Sampling methods to be used.
  * In-process sampling - To collected & tested
  * Testing to be conducted on collected samples.
  * Sample size
  * Type of containers
  * Precautions.

OBJECTIVES

If you lend, you either lose the money or gain an enemy.

Facility Design & Construction

Accomplished by

(a) Filtering the air supply to reduce or Eliminate particulate Contamination.

(b) Maintaining high air pressure

(c) Providing smooth, easily cleanable surface on equipments floors, walls.

Principles of sterilization

Method

Microbial Destruction

Utility Qualification

(A) HVAC system

(1) HEPA filter Integrity

(2) Airborne particle control

(3) Air flow direction

(4) Room air pressure differential

(5) Temperature & humicity control

(B) Water

(C) Compressed Gases

Equipment Qualification/Validation

1. IQ, DQ, PQ, OQ

2. Cleaning Operation

filling Equipment

- Liq. filling
- Powder filling

Sealing/Capping Equipment

1. Vial capping Equipment

- Ampoule sealing Equipment.

How poor are they, that have no patience.

10 11 JANUARY SATURDAY 2.0.0.3

JANUARY

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Filtration System

- Bubble point test
- Diffusion flow testing
- Bubble point - pressure hold test.

Environmental Qualification

Area decontamination

- Sanitizing agent
- Nonviable particulate Monitering
- Surface sampling
  - Replicate Organism Detection & counting
  - swab test
- Airborne viable particulate Monitering
- Aseptic filling
- Documentation.

12 SUNDAY