

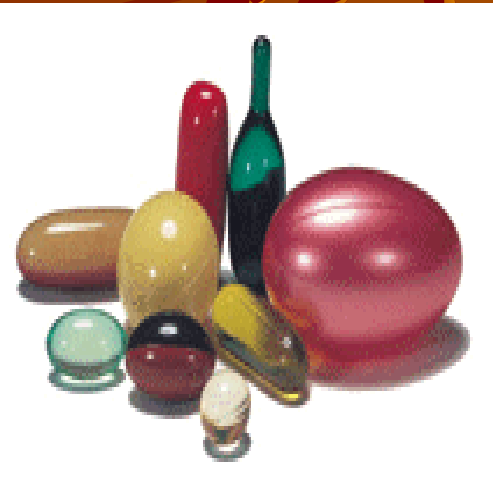
Understanding DS cGMP Requirements for Testing

Dietary Supplement cGMPs Final Rule- 21 CFR Part 111

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AOAC MEETING

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Hot Topics

Raw Materials Vendor Qualification
and Testing

Finish Product Testing and
Exemption from Testing

Expiration Dating

Supplier Qualifications

- ◆ Raw Materials
- ◆ Procedures SOP)
- ◆ Documentation
- ◆ Re-qualifications
- ◆ Audits



Production and Process controls

- ◆ What is the purpose of adding :
- ◆ Production and Process Controls to our GMP's
- ◆ To facilitate reduced testing

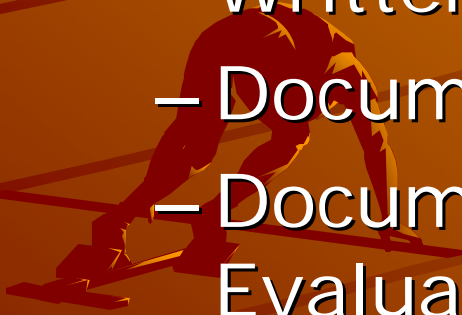


Production and Process Controls

✦ Why is Reduced Testing Acc



- Establishing Critical Control Points
- Written Procedures
- Documentation of Process Controls
- Documentation of Results of Test and Evaluations
- Quality Review and Approval



Production and Process Controls

◆ How and Where Does it all begin?



Raw Materials

Production and Process Controls

- ◆ Specifications for Dietary Ingredients
 - Identity, Quality, Strength and Composition
 - ◆ Identity Test, plus COA-Qualified Vendor
 - ◆ Qualified by confirmation of results
- ◆ Specifications for other Components (Excipients)
 - All established Specs
 - ◆ Accepted on COA, qualified vendor
 - Approved by Quality



Raw Materials

Production and Process Controls

- ✦ How to determine whether specifications are met.
- ✦ Components:
 - Before use
 - Conduct test or COA for qualified vendors
 - Documentation and Quality Review



In Process Materials Production and Process Controls

c. Specifications for In-Process Production

(how this requirement supports
finish product testing
requirements)

✦ In process specifications

- Materials and Control Points
- Adequate documentation to support process specifications
- Review and approve by Quality



Finished Batches

Production and Process Controls

- ✦ Specifications for:
 - Finished batches of Dietary Supplements
 - Subset Sampling and Testing
 - No valid analytical methods
 - ✦ Test Component and Test in-process
 - ✦ QC Unit must determine absence of valid test methods



Finish Product Testing



✦ The Final Rule:

✦ You must test every batch of finish product to determine whether specifications are met

✦ or:

✦ You may test sub sets of finish product batches based upon a statistical sampling plan with documented basis for determining compliance

Finish Product Testing

✦ You may exempt one or more ingredients

✦ from verification if:

– Specifications can not be verified

– No valid test method

Documentation for basis of assurance

Quality Control Review and Approval



Production and Process Controls

Written Procedures for all specifications

Documentation that controls were implemented and monitored.

Documentation of the basis for qualification of vendors and re-qualification.

Production and Process Controls

Monitor In-process points to:

- ◆ a. Determine whether specs are met
- b. Detect deviations

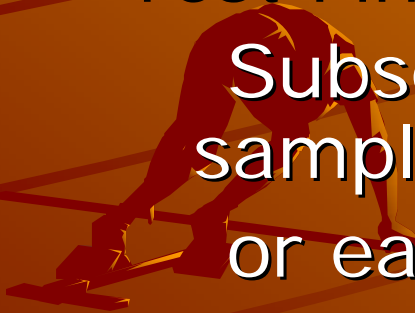
Test Finished Product

Subset of batches based on statistical sampling

or each batch

Test for one or more specs for identity, purity, strength and composition

Limits on contamination



Production and Process Controls

- ✦ Test must be appropriate and scientifically valid.
- ✦ Exemption from specifications testing
- ✦ Document basis for exemption
- ✦ Quality Control review and approval



Production and Process Controls

- ✦ If Specs are not Met:
- ✦ Quality Control must reject
- ✦ QC conducts Material Review
- ✦ QC approval to rework or treatment that will ensure quality



Production and Process Controls

- ✦ Establish Corrective Action Plan
- ✦ Conduct Material Review and
- ✦ Make a Material Disposition Decision when
 - Specifications failures
 - Established steps in Master Record is not completed
 - Unanticipated adulteration
 - Calibration not performed
 - Returned goods



Production and Process Controls

- ✦ Written Standard Operating Procedures

 - to assure consistency in handling receipt, sampling, testing of raw materials, testing and release of process and/or finished

- ✦ Deviations

- ✦ Rejected In-Process Material

- ✦ Master Formula

 - not less than 100 % label claim



Production and Process Controls

◆ Handling of Adulterated Materials

- Must be Rejected
- Materials Contaminated with Microorganisms or Heavy Metals –Reject
- QC review of all of the above
- Investigation and Corrective Action Must be Documented



Production and Process Controls

✦ Documentation Must Contain:

- Established Specifications
- Actual Results
- Deviations and Unexpected Occurrences
- Corrective Action
- Disposition Decision and Follow –up
- Identity of Individual who conducted investigation and QC reviewer



Expiration dating

- ◆ NLEA Requirements
- ◆ Stability Studies
- ◆ Interim Expiration dating



Bulk Manufacturers

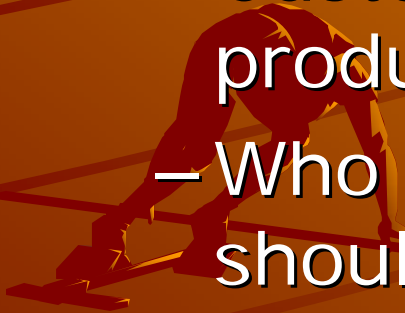
✦ How to Meet the non-requirements?:

- Suggestions:

- Shipping Containers and Storage

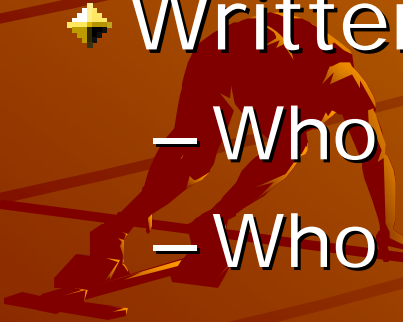
- Customers Request/you made the product

- Who should conduct studies and who should pay



Finished Goods Manufacturers and Packers

- ✦ Container Closure Systems
- ✦ Recommended Storage Conditions
- ✦ Whose responsible
- ✦ Written Agreements
 - Who test
 - Who pays



Suggested Interim Dating

- ◆ Scientific Data
- ◆ Accelerated studies
- ◆ Side by Side studies
- ◆ Similar product data
- ◆ Stability Protocol Records
- ◆ Commitment to remove from marketplace

Thank You

✚ Questions??

