Dietary Supplement cGMPs

Staying Ahead of the FDA

NIA WEST
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Presented by:
Joys Quality Management Systems
Who is Subject

- Dietary Supplement Manufacturers
- Packers, Holders / Warehouses
- Foreign Firms That Export Dietary Supplements to the US
Subpart E
Requirements to Establish a Production and Process Control System
Production and Process Controls

• System of controls for all stages of manufacturing, packaging, labeling, and holding

• Designed to ensure product quality as specified in master manufacturing records

• Reviewed and approved by Quality Unit
Production and Process Control (cont.)

• Implement:
  - Quality Control Operations in manufacturing, packaging, labeling, and holding Dietary Supplements
Production and Process Controls (cont.)

- Establish Specifications For:
  - Identity, purity, quality, strength, composition and limits of contamination for components
  - In-process controls for manufacturing
  - Dietary supplement labeling and packaging
Production and Process Controls (cont.)

• Specifications for Packaging Components must Assure:
  - That packaging is safe and suitable for its intended use
  - It must not be reactive or absorptive so as to react with the Dietary Supplement
Establish specifications for:

a. Points, steps, or stages where quality may be compromised

b. Dietary Ingredients and other Components

   including limits on contamination

* DI - Identity Test - minimum

* Other Components - COA /Verification
c. In-Process Production

- In process specifications
- Adequate documentation to support in-process specifications
- Review and approve by Quality
Production and Process Controls (cont.)

d. Labels
   specs for labels and packaging

e. Finish product
   specs and limits for contaminants

f. Products from suppliers
   specs for ID

g. Packaging and labeling
   specifications for finished product
Production and Process Controls (cont.)

• Establish Specifications for:
  - Finished batches of Dietary Supplements
  - Subset Sampling and Testing
  - No valid analytical methods
    • Test in-process
    • QC must determine absence of valid test methods
Production and Process Controls (cont.)

How to determine whether specifications are met:

For Dietary Ingredients:

Before Use
- Conduct one identity test, if
- Verify COA from Qualified Vendors, or
- Test for all specifications
Production and Process Controls (cont.)

How to determine whether specifications are met.

Other Components:

Before use
- Conduct test or COA for qualified vendors
- Documentation and Quality Review
Production and Process Controls (cont.)

Establish 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 (cont.)

Test must be appropriate and scientifically valid

Exemption from specifications testing

Document basis for exemption

Quality Control review and approval
Production and Process Controls (cont.)

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 (cont.)

- 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 (cont.)

Handling of Adulterated Materials
- Must be Rejected, unless approved by QC for reprocessing or adjustment
- 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 (cont.)

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
Production and Process Controls (cont.)

Calibration of Gauges, Scales

Equipment Cleaning and Sanitation

Hazard Analysis and Critical Control Points (HACCP)

Proper Identification of Containers, Lines and Equipment
Production and Process Controls (cont.)

Representative Samples
- Each new lot of components, packaging and labels
- In Process materials
- Sub sets of finished products (statistical sampling plan)
- Each lot of packaged and labeled DS
Production and Process Controls (cont.)

Reserve Samples
- Must be held in same container closure system
- Be identified with lot number
- Be retained for 1 year after Exp date or 2 years from the date of distribution
- Must be stored under conditions consistent with labeling
Subpart F
Quality Control Requirements
Quality Control Organization

Q C Responsibilities

- approve or reject procedures, specifications, controls, tests, examinations, deviations
- approve or reject raw materials, packaging materials, labeling and finished products
QC Unit Responsibilities

- Approve all Master Manufacturing Records
- Approve all Batch Records
- Review and approve all processes for calibrations
- Review all records for Calibration of instruments, apparatus
QC Unit Responsibilities (cont.)

- Review and Approve all laboratory control processes and testing results
- Review and Approve all packaging and labeling records
- Collect representative samples of all incoming materials, in-process materials, labeling, finish products, and packaging
QC Unit Responsibilities (cont.)

• Keep reserve samples for 3 years from date of manufacturing for complaints and investigations

• Reserve Samples Must be:
  - Properly Identified
  - 2x amount needed for testing
QC Unit Responsibilities (cont.)

- Perform appropriate Test and Examinations
- Review and approve all material review and dispositions
- Approve reprocessing or distribution of returned goods
- Maintain signed and dated documentation of all activities performed; documentation prepared at the time of actual performance
Subpart J
Laboratory Operations
Laboratory Controls

• Written Procedures
  - Laboratory operations
  - Laboratory Tests and Evaluations
  - Records shall be made and maintained

• Equipment Validation/Calibration
Laboratory Controls (cont.)

• **Scientifically Validated Methods**
  - Scientific journals, text books, references

• **Modified Official Methods**
  - Documented reasons and data

• **Standards Control**
  - Secondary Standards, Botanical Standards
Laboratory Controls (cont.)

- Documentation that methods were followed
- Deviations and Methods Revisions
- OOS investigations
- Product Release
- Reserve Samples
- Stability Studies / Expiry Dating
Subpart H
Master Manufacturing Record
Master Manufacturing Records

• Master records must be prepared for each Dietary Supplement for each batch size.

• The Master must identify specifications for points and steps necessary to prevent adulteration.

• The Master must establish controls to ensure specifications are met.
Master Manufacturing Records (cont.)

• Master records must include:
  - Name of DI or DS
  - Strength, concentration, weight, or measure
  - Complete list of components
  - Accurate statement of weight or measure of each component
  - Identity and weight or measure of each dietary ingredient
Master Manufacturing Records (cont.)

• Must contain (cont.)
  - Statement of intentional excess
  - Statement of theoretical yield
  - Description of packaging
  - Written Instructions for each processing step
  - Specifications
  - Special Notations
Master Manufacturing Records (cont.)

- Sampling and Testing
- Corrective Action Plans
- QC Review and Approval
- Must be kept maintained
Wrap Up

• Questions and Answers