InstantGMP Compliance Series for Dietary Supplements

Improving Batch Production Records

Problems with Batch Records

- Lack of detail on procedures
- Inadequate information on decisions for changes during production
- Failure to show specifications and test results
- No Master Manufacturing Records
- Batch records did not follow the Master
- QC did not properly disposition batch

Why Batch Records are Important

- Shows when product was produced
- Documents
- Assures consistency in how processes are followed
- Enforces uniformity and quality
- if adulteration occurs, records will show the source of the material so that its use can be stopped

Basics of cGMP Manufacturing

- Instructions and procedures are clear and unambiguous
- Manufacturing processes are clearly defined and controlled
- Facilities designed to minimize cross-contamination and mix-ups
- Operators are trained
- Records demonstrate that all required steps were taken
- Deviations investigated and resolved

Definitions

- Component
  - Any substance used in manufacturing
  - Some may not appear in finished batch
- Ingredient
  - Any component that becomes part of the finished batch
  - E.g. dietary ingredient or raw material
- In-Process Material
  - Any material that undergoes its own process before becoming part of the final product

Definitions

- Batch
  - Specific quantity of a product that is uniform
  - Intended to meet full set of specifications
  - Made on a single batch production record during one manufacturing cycle
- Batch Number
  - Lot or control number which refers to complete manufacturing history of batch

Definitions

- Theoretical Yield
  - Quantity of product to be made
- Actual Yield
  - Total quantity of product measured at the end of manufacturing a batch
- Percent Yield
  - Actual Yield / Theoretical Yield X 100
- Percent Loss
  - 100 – Percent Yield

Master Manufacturing Record

- Must prepare and follow a ``master manufacturing record'' for:
  - Manufacturing
  - Packaging
  - Labeling
- One MMR for each unique formulation and each batch size
- Ensures uniformity in the finished product from batch to batch

Batch Production Record

- Must have a new batch record for each new batch
- Include:
  - Unique identifier for each batch
  - Identity and weight of each component
  - Identity of equipment and processing lines
  - Date and time of equipment maintenance and cleaning
  - Statement of actual and % theoretical yield

In-Process Controls

- Must monitor the steps where control is necessary to ensure quality
- Determine whether the in-process specifications are met
- Controls include COA from qualified vendors
- Dietary ingredients need identity testing
- Use scientifically valid method for each specification

Batch Production Records

- Also include:
  - All results obtained during the operation
  - For tablets and capsules – add steps to prevent metal or foreign materials from equipment from getting into the batch
  - Reference to location of the label
  - Proof that quality control reviewed the BPR and dispositioned the batch

Deviations

- Triggered by any unanticipated occurrence could result in adulteration
- May not reprocess a batch that deviates unless approved by Quality
- Quality must conduct a material review
- Then make a disposition decision
- Corrective and Preventative Actions (CAPA) needed for deviations

Batch Record Review

- Quality personnel must conduct all reviews and make disposition decisions
- Review receiving records
- Determine if all specs are met
- Make sure no contamination occurred
- Resolve all manufacturing deviations

Production Controls

- Cannot use only end-product testing to ensure quality
- Start with high quality components that meet well defined specifications
- Confirm the identity of each component
- Detect problems through in-process controls and specs
- Prevent contaminates from entering the batch
- Test every batch unless a sampling and testing program is combined with good controls
- Quality Control reviews all documentation

In-Process Controls

- Monitor the steps where control is necessary to ensure quality
- Perform in-process checks like capsule weights or tablet hardness
- Determine whether the in-process specifications are met - If not, record a deviation
- Meeting in-process specs helps ensure final product will meet requirements

Control Point Specifications

- Needed for any point where control in the manufacturing process ensures quality, for example:
  - Heating steps
  - Cooling steps
  - Specific sanitation procedures to protect product
  - Points where cross-contamination might occur
  - Where environmental hygiene is necessary

How Long Must Master Records be Kept?

- Length of time product complaints are likely to arise
- Generally 2 years after date of distribution (not date of manufacture)
- If shelf life dating is used, 1 year past the shelf life date
- Packagers and labelers that return the product to the manufacturer for distribution do not need separate records

How Must Master Records be Kept?

- Records are the backbone of a quality system
- FDA must have the means to examine them during an inspection
- If microfilming is used, a suitable reader must be available
- If electronic, must meet 21 CFR Part 11 requirements

Batch Production Record – Manufacturing Instructions

Benefits of Electronic Manufacturing

- More efficient than manual systems
- Shrink or eliminate redundant processes and forms
- Trim time and overhead costs
- Reduce errors, omissions and deviations
- Provide opportunities to reorganize and update processes
- Increases throughput, quality and margins

InstantGMP™

- Electronic cGMP Manufacturing Execution System
- Seamlessly incorporates everything necessary for cGMP manufacturing in one place
- Web-based application makes all data visible to everyone at all times
- Uses built-in quality procedures to make cGMP compliance easy
- Provides opportunities for more flexibility, visibility and productivity

InstantGMP™

Find more presentations and videos on cGMP Manufacturing and Dietary Supplements in the Resource Center at

www.instantgmp.com