DI10. Recommendations for dietary ingredient processors

Facilities that manufacture[[1]](#footnote-1), pack, or hold dietary *supplements* are subject to the regulations in 21 CFR Part 111, while those that manufacture, pack, or hold dietary *ingredients* are technically subject only to the requirements of Part 117. However, in order to ensure their own compliance with the requirements of Part 111, dietary supplement manufacturers often expect their ingredient suppliers to go above and beyond the basic requirements set forth in Part 117, particularly with respect to raw material controls, process controls, recordkeeping, and general quality systems management. Therefore, dietary ingredient processors that do not follow the full requirements of Part 117 may want to consider implementing the additional recommendations set forth below. However, these are only recommendations to be considered; they are not legal or regulatory requirements except as noted in 10.1 (ii)(1) below.

DI10.1 Regulations

i. Companies that process dietary ingredients for distribution in the U.S. are, under U.S. regulations, generally required to comply with 21 CFR Part 117, even if the processing facilities are located outside the US.

ii. However, dietary ingredient processors may be required to comply with the provisions of 21 CFR Part 111 under two circumstances.[[2]](#footnote-2)

1. Under U.S. regulations, a dietary ingredient processor is considered to be a dietary supplement manufacturer, and therefore subject to Part 111, if the dietary ingredient is packaged as a dietary supplement without further processing. For example, if Company A sells cut and sifted ginseng root to Company B who packages the cut and sifted ginseng root in retail packages that are labeled as a dietary supplement, without performing any other processing of the ginseng root, then Company A is a dietary supplement manufacturer and must comply with Part 111.

2. In an effort to ensure product quality, dietary supplement manufacturers and packagers may require their suppliers to comply with Part 111 as a condition of purchase for the dietary ingredient.

iii. Whether or not full compliance with Part 111 is required, dietary ingredient processors should consider implementing various controls that go beyond the requirements of Part 117 to ensure the quality of their products. The following sections outline a number of suggestions to this end. Dietary ingredient processors that are required to comply with Part 111 must consult the full text of Part 111 to determine the applicable additional requirements for their operations.[[3]](#footnote-3)

DI10.2 Component controls

i. For each component (including botanical ingredients, other ingredients, processing aids, packaging materials, and labels), appropriate specifications should be established. These specifications should address the component’s identity, grade, ingredients or materials of construction, limits on impurities, and/or other characteristics as applicable. For botanical components, the specifications should address the applicable quality parameters discussed in Section BQ2 of this document.

ii. Incoming shipments of components should be assigned a lot number and quarantined pending sampling, inspection, testing, and disposition (approval or rejection).

iii. Incoming shipments of components should be properly labeled (e.g., with the buyer’s or seller’s item number, description, and/or lot number) and examined for damage or contamination.

iv. Components should be sampled in accordance with appropriate sampling plans and procedures to ensure representative samples are obtained.

v. Appropriate steps should be taken to ensure each component lot meets its established specifications. These steps may include:

1. Review of certificates of analysis, specifications, guarantees, and other documents provided by the supplier.

2. Tests and examinations performed by the dietary ingredient processor.

3. Tests and examinations performed by an independent laboratory or expert.

vi. All documentation and test results for a lot should be reviewed before the disposition of the lot (e.g., approval or rejection) is decided.

vii. Approved component lots should be stored under appropriate conditions of temperature, humidity, and light so that the quality of the components is not affected.

viii. Rejected components should be moved to a separate storage location from other components.

ix. A retention sample of each component lot should be kept for several years or as long as the records associated with the lot are retained, or as required by regulation. Retention samples should be stored in a manner to protect against insects, microbial growth, moisture, excessive heat, and other sources of degradation. Where the lot consists of fresh plant material or is otherwise likely to spoil, samples may be stored in a frozen or dried state.

x. All documents related to the lot should be marked with the component item number (if used) and lot number, and should be kept on file as a packet for at least several years or as required by regulation.

xi. For each component lot, an inventory control log or other recordkeeping system should be used to document all inventory transactions related to the lot (e.g., usage of the component lot in the manufacture of a particular finished product batch).

DI10.3 Processing operations and finished product controls

i. For each manufacturing and packaging process, comprehensive processing specifications should be established and documented that will ensure finished product quality specifications are reliably met. Such a specification document is called a “master manufacturing record” (MMR). Each batch size of product should have a separate MMR. The MMR should include:

1. The processing steps to be performed. For manual operations this should include:

* The double-checking by a second operator of the weighing or measuring of all components.
* The double-checking by a second operator of each addition of components to the batch.

2. The equipment to be used.

3. The identities and quantities of components to be used, including packaging components and labels.

4. The identities of any processing aids to be used.

5. Equipment settings and other processing parameters.

6. In-process control steps.

7. In-process sampling and testing to be performed.

8. Expected yields after each major process step and at the completion of production.

ii. Where desired, the MMR may include empty spaces for batch-specific data to be recorded.

iii. Each time a cycle of manufacturing or packaging occurs, a document should be created to record the processing of the batch. This document is called a “batch production record” (BPR) and is often created by making or printing a copy of the MMR. The BPR should be used to record the following:

1. The batch number.

2. The dates and where applicable the times at which each step is performed.

3. The identity of operators that perform each step.

4. The identity of actual equipment used.

5. The actual equipment settings used and/or readings obtained.

6. The lot number of each component used.

7. The quantity of each component used.

8. Results of in-process monitoring and/or testing.

9. Actual yields and percent of theoretical yield at appropriate stages of production and after completion of the batch.

10. An example of any finished product label used, preferably coded with the relevant lot or batch number and the date of manufacture and/or expiration.

11. A record of any deviations or variances that occur during processing of the batch.

12. Approval by Quality personnel of any deviations or variances that occur.

13. Approval at appropriate stages of production and after completion of production by supervisors, managers, and Quality personnel as appropriate.

iv. The allocation of components or issuance of labels for use in manufacturing or packaging should be appropriately controlled to ensure that (a) the components and labels are the proper ones for the product to be made, and (b) only approved lots are used.

v. Finished product batches should be sampled in accordance with appropriate sampling plans and procedures to ensure representative samples are obtained.

vi. Appropriate steps should be taken to ensure each finished product batch meets its established specifications. These steps may include:

1. Review of the batch production record.

2. Tests and examinations performed by the dietary ingredient processor.

3. Tests and examinations performed by an independent laboratory or expert.

vii. All documentation and test results for a batch should be reviewed before the disposition of the batch (e.g., approval or rejection) is decided.

viii. Approved finished product batches should be stored under appropriate conditions of temperature, humidity, and light so that the quality of the product is not affected.

ix. Rejected finished product batches should be moved to a separate storage location from other finished products.

x. All documents related to the batch should be marked with the product item number (if used) and batch number, and should be kept on file as a packet for at least several years or as required by regulation.

xi. For each finished product batch, an inventory control log or other recordkeeping system should be used to document all inventory transactions related to the batch (e.g., distribution of the batch to various customers).

xii. A retention sample of each finished batch should be kept for several years or as long as the records associated with the lot are retained, or as required by regulation. Retention samples should preferably be stored in the same packaging and under the same storage conditions used for the distributed product, or else in similar packaging and conditions.[[4]](#footnote-4) Where the finished product is not shelf stable, samples may be stored in a frozen or dried state.

DI10.4 Laboratory operations

i. Test methods should be maintained in writing and should be suitable for their intended purpose. Test methods should be appropriately accurate, precise, and specific. Chemical and physical test methods used for purely internal purposes such as in-process monitoring may not need the same degree of scientific validity as methods used for other purposes.

ii. Appropriate analytical standards should be used for laboratory testing. Primary chemical standards should be properly qualified either in-house or by the vendor, to ensure the purity is accurately known. Botanical reference standards should be authoritatively authenticated, either in-house or by the vendor.

DI10.5 Personnel

i. Personnel should be qualified by training or experience for the tasks to be performed.

ii. Personnel qualifications and training should be documented and maintained on file.

iii. Personnel training should include:

1. Health, safety, and environmental protection procedures.

2. Personal hygienic practices.

3. Food safety procedures.

4. Good manufacturing practices.

5. Job-specific information.

DI10.6 Equipment

i. Processing, packaging, and testing equipment should be suitable for its intended purpose and capable of operating satisfactorily as required by the process.

ii. Processing, packaging, and testing equipment should be properly cleaned, and sanitized where appropriate. In general, processing and packaging equipment should be cleaned (and sanitized where appropriate) either in between each batch or between products, or (for continuous processing operations) on a daily basis or at another suitable frequency.

iii. Processing, packaging, and testing equipment should be properly maintained. In general, preventive maintenance should be performed in accordance with the equipment manufacturer’s instructions.

iv. Processing, packaging, and testing equipment should be properly verified or calibrated at suitable frequencies to ensure proper performance. Calibration standards should be traceable to an authoritative reference standard (e.g., NIST[[5]](#footnote-5)) where possible.

DI10.7 Quality management

i. Appropriate quality assurance practices should be implemented to ensure product quality and GMP compliance.

ii. Standard operating procedures should be written for manufacturing, packaging, laboratory, warehousing, and quality management operations.

iii. Records should be kept of all activities performed in the facility that may have direct or indirect bearing on product quality or GMP compliance. All records should be made contemporaneously with the operation performed and should be maintained on file for several years or as required by regulation.

iv. A system should be implemented for receiving, documenting, and investigating product-related customer complaints, including but not limited to adverse events.

v. A system should be implemented for receiving, quarantining, and determining the disposition of returned goods.

vi. Quality management personnel should approve or reject all specifications, controls, tests, examinations, standard operating procedures, master manufacturing records, labels, and other documents or procedures that may affect the quality of the botanical product, and also approve or reject all deviations from these documents and procedures, including any reprocessing or repackaging.

vii. Quality management personnel should approve or reject all component lots, finished product batches, and returned goods.

viii. Quality management personnel should review records of facility and equipment cleaning and sanitization; pest control; equipment verifications and calibrations; employee training; sampling records; and customer complaints.

ix. Quality management personnel should approve or reject all changes to facilities, equipment, specifications, controls, tests, examinations, standard operating procedures, master manufacturing records, labels, and any other changes that may affect the quality or GMP compliance of the botanical product.

1. “To manufacture” in this context includes “to process,” and vice versa. U.S. food regulations generally do not distinguish between “processing” and “manufacturing”; see the definition of “manufacturing/processing.” However, there is a subtle but important distinction between “manufacturing/processing” (as used in FDA food regulations) and “processing” (as used in U.S. law). (See the definition of “processed food” for more information.) [↑](#footnote-ref-1)
2. Firms that comply with Part 111 are exempt from Part 117 Subparts C and G; see Appendix 4 for more information. [↑](#footnote-ref-2)
3. Dietary ingredient manufacturers may also consider other certification models, such as from the Global Food Safety Initiative (GFSI). [↑](#footnote-ref-3)
4. For product distributed in bulk (e.g., 50-lb bags), it is often not possible to keep retention samples packed in precisely the same manner as the distributed product. [↑](#footnote-ref-4)
5. “NIST” is the National Institute of Standards and Technology, a U.S. government agency that provides authoritative reference standards for physical, chemical, and other measurements. [↑](#footnote-ref-5)