

Therefore, for natural products it may be appropriate to perform tests of finished product to confirm that, of the microorganisms present, those of public health significance did not survive processing and those that remain that are not of public health significance do not contaminate the dietary ingredient or dietary supplement.

Although the proposal does not specify microbial limits for undesirable microorganisms, other non-FDA sources have established acceptable, general limits of microbial levels for dietary ingredients and dietary supplements (Refs. 66 and 67). These often include limits for total aerobic microbial count, which ranges from  $10^4$  to  $10^7$  per g, depending on source and nature of components; a total combined yeast and molds count, which can range from  $10^3$  to  $10^5$  per g, again depending on source and nature of components; and the absence of *Salmonella* species, *E. coli* and *Staphylococcus aureus*. We establish microbial limits for undesirable microorganisms based on scientific information such as literature surveys and laboratory analyses. At this time, however, we do not have sufficient information to support establishing microbial limits for undesirable microorganisms for dietary ingredients. Therefore, the proposed rule does not establish microbial limits for dietary ingredients. However, you must be aware of potential contamination, regardless of whether it is due to filth, insects, microorganisms, or toxins, and you must test or examine as appropriate components, dietary ingredients, or dietary supplements for those types of contamination that may adulterate or may lead to adulteration.

Proposed § 111.35(l) would explain that the tests you use to determine whether your components, dietary ingredients, and dietary supplements meet specifications must include at least one of the following tests: Gross organoleptic analysis, microscopic analysis, chemical analysis, or other appropriate test. These tests may vary in detail or complexity depending on the purposes of the test and the material being tested. For example, if your component is raw cranberries, and you are trying to verify that a shipment of red berries consists of raw cranberries, an organoleptic (visual test) may be sufficient (assuming that you recognize cranberries). However, if your component is a chemical substance, and you are trying to verify that a shipment of bulk powder is that chemical substance, chemical analysis may be more appropriate than an organoleptic analysis.

Proposed § 111.35(m) would require that you must record the results of all testing and examinations performed in accordance with this section. If a test or examination is performed on a production batch, you must record the test or examination result in the batch production record in accordance with § 111.50(c)(10). Your records must document whether the testing and examination demonstrates that specifications are met.

Proposed § 111.35(n) would require for any specification that is not met, that you must conduct a material review and disposition decision under § 111.35(i).

Proposed § 111.35(o) would require that you make and retain records, in accordance with proposed § 111.125, to ensure that you follow the requirements of this section. The proposal would require these records to include, but would not limit them to:

- The specifications established;
- The actual results obtained during the monitoring operation;
- Any deviation from specifications and any unanticipated occurrences;
- Any corrective actions taken;
- The disposition decisions and followup; and
- The identity of the individual qualified by training and experience who investigated any deviation from specifications or unanticipated occurrence and the identity of the individual from the quality control unit who reviewed the results of that investigation.

These records would enable you to show, and for us to determine, your compliance with proposed § 111.35. We generally determine CGMP compliance by conducting inspections, so records play an important role during those inspections in determining CGMP compliance.

## 2. What Requirements Apply to Quality Control? (Proposed § 111.37)

Proposed § 111.37(a) would require that you use a quality control unit to ensure that your manufacturing, packaging, label, and holding operations in the production of dietary ingredients and dietary supplements are performed in a manner that prevents adulteration and misbranding, including ensuring that dietary ingredients and dietary supplements meet specifications for identity, purity, quality, strength, and composition. This requirement does not mean that the manufacturer needs a large number of employees. The manufacturing process for an ingredient or a dietary supplement can be a sophisticated process, and all organizational units that are involved in critical formulation and manufacturing

steps, such as production, engineering, research, and regulatory affairs, may be included in quality control functions.

Proposed § 111.37(b) would require that your quality control unit must do the following:

- Approve or reject all process, procedures, specifications, controls, tests, and examinations, and deviations from or modifications to them that may affect the identity, purity, quality, strength, and composition of a dietary ingredient or dietary supplement;
- Determine whether all components, dietary ingredients, dietary supplements, packaging, and labels conform to their specifications;
- Approve or reject all components, dietary ingredients, dietary supplements, packaging, and labels;
- Review and approve all master manufacturing records and all modifications to the master manufacturing records;
- Review and approve all batch production-related records which include, but are not limited to, cross-referencing receiving and batch production records, approval of a material review and disposition decision, approval for reprocessing, and approval for releasing for distribution. Cross-referencing receiving and batch production records means that the quality control unit must verify that the batch record includes certain documentation of the receiving records for the components and dietary ingredients such as the unique identifier assigned to the shipment lot of components, testing results, a material review and disposition decision, if conducted, and approval for use by the quality control unit.
- Review and approve all processes for calibrating instruments or controls;
- Review all records for calibration of instruments, apparatus, gauges, and recording devices;
- Review all records for equipment calibrations, inspections, and checks;
- Review and approve all laboratory control processes and testing results;
- Review and approve all packaging and label records which include, but are not limited to, cross-referencing receiving and batch production records, approval for repackaging and relabeling, and approval for releasing for distribution;
- Collect representative samples of:
  1. Each shipment lot of components, dietary ingredients, dietary supplements, packaging, and labels received for testing or examination, as needed, to determine whether the component, dietary ingredient, dietary supplement, packaging, or labels meet specifications before use or for testing,