

equipment in production. Automated equipment is often used to ensure proper formulation, mixing, and processing or to test a batch of dietary ingredient or dietary supplement. Such automated equipment frequently consists of a computer or system of computers that control many or all stages of production, inprocess sampling, and testing. It is important that such systems and equipment function as expected to ensure that the dietary ingredient or dietary supplement contains the correct ingredients in the appropriate amounts and is manufactured according to these CGMP proposed requirements, and thus, is not adulterated under section 402(g) of the act.

Proposed § 111.30 sets forth requirements for automatic, mechanical, or electronic equipment. These types of equipment include, for example, mechanical equipment such as a scale used to weigh bulk components and electronic equipment such as a computerized blending machine.

Proposed § 111.30(a) would allow you to use automatic, mechanical or electronic equipment to manufacture, package, label, and hold a dietary ingredient or dietary supplement. Thus, the proposal would let you decide what type of equipment meets your needs. Proposed § 111.30(a)(1) would require that you must design or select equipment to ensure that dietary ingredient or dietary supplement specifications are consistently achieved. Equipment used in dietary ingredient or dietary supplement manufacturing, packaging, and label operations must be, for example, of an appropriate size and installed properly in order to produce an unadulterated product. If not designed or installed properly, the equipment can lead to a variety of problems. For example, a mixer for the blending of powdered ingredients will not properly perform its function if the blade is too small relative to the size of the mixer or not properly placed inside of the mixer. Such a mixer may produce an adulterated product because the dietary supplement, for example, is not of uniform composition and therefore would not be able to meet the specifications for purity, quality, strength, or composition in the final product. Thus, equipment design and selection is critical to ensure that you manufacture an unadulterated dietary ingredient or dietary supplement.

Proposed § 111.30(a)(2) would require that you determine the suitability of your equipment. The equipment that you use must be capable of operating satisfactorily within the operating limits required by the process. The equipment

must function as intended. Some systems may work properly only within a narrow range of environmental conditions, such as temperature and humidity, and some might be particularly sensitive to electromagnetic interference. The actual conditions of use of a system should be considered as early as possible in its design and development. Systems need to be installed in a manner that takes into account the inherent limitations of the system, tested under conditions that reflect actual conditions of use, and properly maintained to ensure that they continue to function as expected during their lifetime.

Moreover, the incorporation of software into the operation of automatic equipment has not only increased the complexity of such equipment but also has resulted in a process that may operate differently for each execution because a software-based control system can be configured at will by the operator or by the system itself. Therefore, proposed § 111.30(a) would require that you exercise appropriate controls over systems and, in particular, over the software used in the systems.

Proposed § 111.30(b) would require, for any automatic, mechanical, or electronic equipment that you use, that you must:

- Routinely calibrate, inspect, or check to ensure proper performance.
- Make and keep written records of equipment calibrations, inspections, or checks;
- Establish and use appropriate controls to ensure that your quality control unit approves changes in master manufacturing record, batch control records, packaging operations and label operations, or changes related to the equipment that you use and that only authorized personnel institute the changes;
- Establish and use appropriate controls to ensure that the equipment functions in accordance with its intended use and have your quality control unit approve these controls; and
- Make and keep backup file(s) of software programs and of data entered into your computer system. Your backup file may be a hard copy of data you have entered, diskettes, tapes, microfilm, or compact disks but must be an exact and complete record of the data you entered. We also propose to require that you keep your backup software programs and data secure from alterations, inadvertent erasures, or loss. In this way, you have a record of changes to your software program and of your current software program used in manufacturing. This information is important to both identify any

production errors or discrepancies and to make necessary corrections. Such records will allow you to troubleshoot and to operate these systems with a minimum of interruption when problems occur because the records will include a copy of all software used and a backup file of data entered into the computer or related system which can be used to reload the system. The records also will provide information that you can use in trying to determine why a problem with the system is occurring or why the system is not producing a dietary ingredient or dietary supplement that complies with your specifications for the product.

Appropriate controls that you establish and use for automated measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions will minimize the potential for growth of microorganisms, for contamination, or for adding too much or too little of a dietary ingredient. Observations, inspections, and checks of the equipment will help you to determine if critical factors such as revolutions per minute, temperatures, pressures, process times, and automatic documentation are being controlled by the system. Under proposed § 111.30(b), examples of controls to ensure that the equipment functions in accordance with its intended use include:

- Determining the extent and frequency of calibration, inspections and checks to ensure proper performance;
- Determining and using predetermined action plans when an alarm sounds indicating an out-of-limits situation or malfunction;
- Checking in-put and out-put on a sufficient basis to provide a high degree of assurance that input and output is accurate;
- Comparing manual calculations of data with the automated calculations on a sufficient basis to provide a high degree of assurance that the automated calculations are accurate; and
- Determining the adequacy of automated cleaning and residue elimination.

We invite comment on whether we should require, in a final rule, that you establish and follow written procedures for the calibration, inspection, and checking of automatic equipment. In addition, we invite comment on whether there are procedures, other than those mentioned, that we should include in a final rule. If comments assert that written procedures are necessary, comments should include an explanation of why the requirement is necessary to prevent adulteration