

concerned, persons who market dietary ingredients and dietary supplements always remain responsible for their products. If the manufacturer markets the product, it would have to meet all proposed CGMP requirements, if the agency finalizes the rule as proposed. If another person buys a product (such as bulk dietary ingredients) from a manufacturer and distributes the product under its own name, that person must meet all applicable CGMP requirements.

**Question 7.** We invited comment on whether specific controls are necessary for computer-controlled or assisted operations and how best to ensure that the software programs and equipment used to direct and monitor the manufacturing process are properly designed, tested, validated, and monitored.

Comments generally supported specific controls for computer-controlled or computer-assisted operations. One comment suggested requiring manufacturers to confirm, by adequate and documented testing, that their computer software programs perform their intended functions when computers are used as part of an automated production system having a significant and direct impact on product safety. Another comment suggested requiring that software programs and equipment used to direct and monitor manufacturing processes are properly designed, tested, evaluated, and monitored. The comment added that, if we consider imposing specific requirements on how firms document the adequacy of their computer-controlled or assisted operations, we should address those recommendations through a guidance document instead of issuing regulations.

We agree that computer-controlled or computer-assisted operations need to be properly designed, tested, evaluated, and monitored to ensure that the computers do what they are supposed to do. Manufacturers should confirm, by adequate and documented testing, that their computer software programs perform their intended functions because computer use as part of an automated production system has a significant and direct impact on product safety. Computers are an important controlling piece of equipment in the manufacture of dietary supplements because they often direct and control key steps or processes in the manufacture of dietary supplements. If computers do not operate correctly, the dietary supplements manufactured using those computers may be adulterated.

Several comments supported requirements for specific controls, but opposed using validation-of-operation mandates like those in the CGMP regulations for drugs. One comment suggested that we regulate computer-controlled and computer-assisted operations for dietary supplements in the same way that we regulate such operations in the pharmaceutical industry, but only where an operation is directly related to the product's concentration or purity. One comment suggested that we consider adopting the computer-controlled and computer-assisted procedures specified in the proposed infant formula CGMP.

We propose general requirements to ensure that equipment is suitable for its intended use. However, we seek comment, in the proposed rule, about whether we should include requirements, written procedures, and records for equipment verification and re-verification. We request comment on what verification manufacturers should be using in their computer-controlled or computer-assisted operations to ensure that a dietary ingredient or a dietary supplement that is produced is not adulterated during manufacturing. In addition, we request comment on whether we should issue guidance documents on verification procedures for use with computer-controlled or computer-assisted operations. Guidance documents generally represent FDA's advice or current thinking on a particular matter and are not binding on any person. In contrast, regulations create enforceable requirements that apply to all persons engaged in the same action or who make the same product.

As discussed in greater detail later in this document, certain processes are necessary to ensure that computer-controlled or computer-assisted equipment functions properly. This is because of the important role of such equipment in manufacturing. For example, if computer-controlled or computer-assisted equipment is used to control components, in-process materials, and rejected materials unsuitable for use, the operation must function as expected to ensure that components suitable for use in manufacturing dietary ingredients and dietary supplements are not mixed up with components held under quarantine such as those components that have been rejected as unsuitable for use. If computer-controlled or computer-assisted operations are used for the addition and mixing of components, they must function properly to ensure that the correct components are added and appropriately mixed to avoid producing a dietary ingredient or

dietary supplement that is adulterated. Computer-controlled or computer-assisted operations are not perfect; computers are subject to malfunctions and "bugs" (errors) in the software they use. Problems with data entered into the computer may produce unreliable results. For these reasons, specific controls for computer-controlled or computer-assisted operations are necessary to prevent the manufacture of an adulterated dietary ingredient or dietary supplement.

A few comments stated that no specific requirements for computer-controlled or computer-assisted operations are needed because computer hardware and software are simply specialized plant equipment so that no special regulations are needed.

We agree that computers are specialized pieces of plant equipment and, therefore, should be subject to additional requirements beyond those which would apply to plant equipment. Computers are specialized pieces of equipment because they are subject to malfunctions and "bugs" (errors) in the software, they are reliant upon data entered into a computer, and they may be used to perform important roles such as component or dietary ingredient identification, measuring components and dietary ingredients, and quarantining materials. Consequently, proposed § 111.30 would establish requirements for automatic, mechanical, or electronic equipment. The proposed requirements would cover, among other things, automatic equipment design, and routine calibration, inspection, and checks to ensure proper performance. As stated previously, we are seeking comment on whether we should include requirements for verification and re-verification of automatic, mechanical, or electronic equipment and processes and whether we should include requirements for computerized systems that are separate from requirements for other mechanical or automatic equipment. We discuss proposed § 111.30 in greater detail later in this document.

**Question 8.** We asked for comments on whether certain, or all, of the requirements for manufacturing and handling dietary ingredients and dietary supplements may be more effectively addressed by a regulation based on the principles of Hazard Analysis and Critical Control Point (HACCP), rather than the system outlined in the industry submission.

In the ANPRM, we noted that, because of the wide variety of dietary ingredients and dietary supplements and because of the heterogeneous composition of the dietary supplement