

and utensils to guard against contamination.

Proposed § 111.25(a)(4) would require your equipment and utensils to have seams that are smoothly bonded or maintained to minimize accumulation of component, dietary ingredient, or dietary supplement particles, dirt, filth, organic material, or any other extraneous material or contaminants.

We are proposing this requirement because equipment and utensils containing breaks, pits, cuts, or grooves can be difficult to clean, and the pores or crevices in those breaks, pits, cuts, or grooves can become a breeding ground for microorganisms and insulate them from cleaning and sanitizing agents.

Proposed § 111.25(a)(5) would require freezers and cold storage compartments that hold components, dietary ingredients, or dietary supplements to be fitted with accurate thermometers or other temperature-measuring or temperature-recording devices and would recommend automatic devices for regulating temperature or for sounding an alarm to indicate significant temperature changes in a manual operation. These devices are necessary to ensure that you are able to monitor the temperatures where you hold your components, dietary ingredients, or dietary supplements and to indicate whether they were held at appropriate temperatures to minimize the growth of pathogens and to prevent deterioration.

While we patterned proposed § 111.25(a)(5) after a provision in the food CGMPs (§ 110.40(e)), we invite comment on whether we should require specific target temperatures for dietary ingredients or dietary supplements held in freezers or cold storage, and if so, what those temperatures should be and why.

Proposed § 111.25(a)(6) would require instruments or controls used in the manufacturing, packaging, or holding of a dietary ingredient or dietary supplement to be accurate and precise, adequately maintained, and adequate in number for their designated uses. By using the words, “accurate and precise,” we mean that the instruments or controls must be accurate—the recorded measurements are equal to the true value of the thing being measured—and precise—individual measurements should be close to each other when made under the same conditions. For example, if the temperature inside a particular piece of equipment is 100 °F, and your thermometer for that piece of equipment reads a temperature of 100 °F, the thermometer is accurate. If multiple temperature readings for that thermometer ranged from 99.7 °F to

100.4 °F, and the variation in temperature was not significant statistically, you could say the thermometer is precise. The proposed requirement identifies examples of such instruments and controls, such as instruments or controls you use to measure, regulate, or record:

- Temperatures;
- pH;
- Water activity; or
- Other conditions that control or prevent the growth of microorganisms or other contamination.

Instruments or controls that affect the environment, such as instruments that regulate temperature, pH, and water activity, are important because environmental factors can influence microorganism growth and deterioration. For example, changes in water activity (a_w) can have a dramatic impact on microorganism growth. A population of *Salmonella typhimurium* is reduced tenfold in 0.18 minutes at 60 °C if the a_w for the suspending medium is 0.995. If the a_w is 0.94, it takes 4.3 minutes (or nearly 24 times as long) at 60 °C to achieve the same tenfold reduction (Ref. 58).

Adequate maintenance is an important part of proposed § 111.25(a)(6). If you fail to properly maintain your instruments and controls, they may produce unreliable readings and contribute towards the contamination and adulteration of your dietary ingredients and dietary supplements. For example, assume that you refrigerate a particular dietary ingredient to prevent microorganism growth. If your refrigerator gives you the wrong temperature readings so that the actual temperature inside your refrigerator is too high, you may be unaware of microorganism growth that has occurred on your dietary ingredient. Similarly, if the actual temperature inside your refrigerator is too low so that you unintentionally froze the dietary ingredient, the freezing process may have produced a chemical change in your dietary ingredient that will cause it to be out of specification.

Note, too, that the proposal also would require that your instruments and controls be adequate in number for their designated uses. For example, if the temperature of a large piece of equipment needs to be monitored, several temperature-indicating devices may be needed to accurately monitor the temperature in all parts of the equipment.

A comment to the ANPRM objected to requiring all instruments and controls used in all aspects of dietary supplement manufacturing be accurate. The comment said such a requirement

would imply strongly a need for validation, but that validation is a standard applicable to drug CGMPs, but not to food CGMPs. The comment said that a dietary supplement CGMP rule should not require validation of instruments and controls.

We disagree with the comment's objection to requiring all instrument and controls be accurate because, as we stated earlier, inaccurate instruments and controls may generate inaccurate readings, and those readings may adulterate your dietary ingredients and dietary supplements. We believe that all instruments and controls used in the manufacture, packaging, and holding of dietary ingredients and dietary supplements be accurate and precise, adequately maintained, and adequate in number for their designated uses.

We further disagree that the principles of validation are applicable to drugs, but not to foods. We stated in a previous FDA publication (Ref. 59) that the “computerized system used to control critical functions in food processing should be validated in its entirety.” We have no basis to conclude that validation of instruments and controls is a standard applicable to drugs and not to foods, nor did the comment provide a reason for its assertion that validation does not apply to foods. We invite comment in this proposal on whether we should include requirements in a final rule, that would address the same or similar concerns that the principles of validation would address. We also invite comment on whether there are other procedures that we should include in a final rule.

Proposed § 111.25(a)(7) would require compressed air and other gases that are introduced into or onto a component, dietary ingredient, dietary supplement, or contact surface or that are used to clean contact surfaces to be treated in a way so that they do not contaminate the component, dietary ingredient, dietary supplement or contact surface. Air or other gases that are not properly treated and filtered, or air that is not of the proper purity, can introduce contaminants into the dietary supplement product and adulterate it. Also, compressed gases can be contaminated with oil from the equipment (such as an air compressor) or with filth or microbiological contaminants from the compression, storage, or distribution equipment. So, if left untreated, the compressed air can deposit those contaminants onto your components, dietary ingredients, dietary supplements, and contact surfaces. Filtration at the air intake and after compression, storage, and distribution may be an effective means of reducing