

are necessary to demonstrate compliance with the CGMP and quality control procedures.

We invite comment on whether we should require, in a final rule, that you establish and follow written procedures that implement proposed § 111.40(a) and (b). If comments assert that written procedures are necessary, comments should include an explanation of why the requirement is necessary to prevent adulteration including how such a requirement would ensure the identity, purity, quality, strength, and composition of the dietary ingredient or dietary supplement. Conversely, if comments assert that written procedures are not necessary, comments should include an explanation of why the requirement is not necessary including how, in the absence of the requirement, one can prevent adulteration and ensure the identity, purity, quality, strength, and composition of the dietary ingredient or dietary supplement.

4. What Requirements Apply to Establishing a Master Manufacturing Record? (Proposed § 111.45)

Proposed § 111.45 would require that you prepare and follow a written master manufacturing record for each type of dietary ingredient or dietary supplement that you manufacture and for each batch size to ensure uniformity from batch to batch. A master manufacturing record is analogous to a recipe that sets forth the ingredients to use, the amounts of ingredients to use, the tests to perform, and the instructions for preparing the amount the recipe calls for, *e.g.*, 250 mg, 500 mg, vitamin C. This master manufacturing record helps ensure that you manufacture each ingredient or dietary supplement in a consistent and uniform manner. If you neglect to follow the master manufacturing record, you would not add all of the necessary components in the appropriate strength or amount, and this would result in an adulterated ingredient or dietary supplement.

Therefore, proposed § 111.45(a) is necessary to ensure that you prepare and follow a written master manufacturing record for each type of dietary ingredient or dietary supplement to ensure that all the necessary components as specified, and in the amounts specified, are used to manufacture each batch to ensure uniformity from batch to batch and to ensure that the dietary ingredient or dietary supplement is not adulterated. Proposed § 111.45(a)(1) and (a)(2) describe the proposed contents of the master manufacturing record. The master manufacturing record would identify specifications for the points,

steps, or stages in the master manufacturing record where control is necessary to prevent adulteration, and establish controls and procedures to ensure that each batch of dietary ingredient or dietary supplement manufactured meets those specifications. For example, assume that your manufacturing process blends various ingredients in order to make a dietary supplement. Under proposed § 111.45(a), your master manufacturing record would establish controls to look at specific steps in the manufacturing process and evaluate the blends for specific ingredients to ensure that you added the correct ingredients at the correct amounts or concentrations that meet your specifications before the blend proceeds to the next manufacturing step, in accordance with the master production record. Throughout the manufacturing process, you would evaluate, as necessary, any points, steps, or stages where control is necessary to prevent adulteration to ensure that specifications established for those points, steps, or stages are met.

Proposed § 111.45(b) would establish additional requirements for the master manufacturing record. These proposed requirements would include:

- The name of the dietary ingredient or dietary supplement to be manufactured and the strength, concentration, weight, or measure of each dietary ingredient for each batch size. For example, assume you have a million tablet batch size of a vitamin C product in 250 mg tablets and that the only other ingredients in your product are starch, microcrystalline cellulose, and dicalcium phosphate. Under proposed § 111.45(b)(1), your master manufacturing record would state, "Vitamin C 250 mg, 1,000,000 tablets";

- A complete list of components to be used. Again, to continue using the example immediately above, for proposed § 111.45(b)(2), the master manufacturing record also would show that you used starch, microcrystalline cellulose, and dicalcium phosphate in the product;

- An accurate statement of the weight or measure of each component to be used. For example, under proposed § 111.45(b)(3), the master manufacturing record for our hypothetical vitamin C tablet would state the amount of each component used, such as "200 lbs. of Vitamin C, 10 lbs. of microcrystalline cellulose" and the amounts of starch and dicalcium phosphate used. (We would not require that you show the amount using an appropriate English or metric standard in a particular way, but we would expect that you use the most

appropriate weight or measure for the component);

- The identity and weight or measure of each dietary ingredient that will be declared on the Supplement Facts label and the identity of each ingredient that will be declared on the ingredients list of the dietary supplement in compliance with section 403(s) of the act. For proposed § 111.45(b)(4), therefore, the master manufacturing record for our hypothetical product would state that the dietary ingredient is Vitamin C at 250 mg (because Vitamin C would be the dietary ingredient declared on the Supplement Facts label) and identify starch, microcrystalline cellulose, and dicalcium phosphate (because those ingredients would be in the product's ingredient list, but not on the Supplement Facts label); and

- A statement that explains any intentional excess amount of a dietary ingredient. We recognize that some manufacturers intentionally add a specific amount of a dietary ingredient in excess of the declared label amount so that the finished product can meet the label declaration for that dietary ingredient throughout the product's shelf life. For our hypothetical vitamin C tablet, if you added an extra 25 mg of vitamin C to ensure that your product contains at least 250 mg of vitamin C throughout its shelf life, your master manufacturing record would state the component and the actual amount of the component as "Vitamin C, 250 mg, (10 percent excess) 25 mg" or "275 mg of Vitamin C." So, proposed § 111.45(b)(5) would require the master manufacturing record to specify the controlled amount of the excess dietary ingredient necessary to achieve the declared label declaration. This provision is not intended to allow a manufacturer to add excess dietary ingredients in unspecified amounts that would be in excess of the amount actually needed to meet the label declaration.

The agency considered whether to propose requirements in this proposed rule for expiration dating, shelf-life dating, or best if used by dating (hereinafter referred to as expiration dating). Although we recognize that there are current and generally available methods to determine the expiration date of some dietary ingredients, for example vitamin C, we are uncertain whether there are current and generally available methods to determine the expiration dating of other dietary ingredients, especially botanical dietary ingredients. We are not proposing expiration dating at this time because we have insufficient scientific information to determine the biological