

in collaborative studies often are often cited as "official validated methods." If you modify an officially validated method, you should document the reason for the modification and have data to show that the modified method produced results that are at least as accurate and reliable as the established method for material being tested. Further, you should have complete records of any testing and standardization of laboratory reference standards, reagents, and standard solutions that you use in your laboratory operations. Proposed § 111.25(b)(1) would require calibration of laboratory instruments, apparatus, gauges, and recording devices. Validated methods also exist in official compendia for vitamins, minerals, and several botanicals, so you should use validated methods whenever available. You may use validated methods that can be found in official references, such as AOAC International, USP and others. Other method validations are conducted using two or three laboratories or in a single laboratory by repeating the same test multiple times. Official and nonofficial method validations use similar performance parameters in conducting method validations. If an official validated method does not exist in an official reference, the method you use may be validated by using multiple tests at your laboratory or multiple laboratories performing the same test to document that the intended use of the method is consistently fulfilled. You must validate that the official or nonofficial method works under your conditions of use in your setting. You also should conduct day-to-day validations of the method that you use, whether it is an official validated method or a less-formal validated method, under the conditions of use to ensure that the method will provide the information you need to ensure that your dietary ingredient or dietary supplement has the identity, purity, quality, strength, and composition that it is supposed to have and is thus not adulterated. Consistent, day-to-day test recoveries for the reference material are one indicator that the analytical method is working. There are at least two references that describe test method validation performance parameters: (1) Performance parameters for chromatographic methods are described in "Reviewer Guidance, Validation of Chromatographic Methods" (Center for Drug Evaluation and Research, FDA, November 1994) (Ref. 76); and (2) International Conference on Harmonisation (ICH); Draft Guidance on Specifications: Test Procedures and

Acceptance Criteria for Biotechnological/Biological Products (63 FR 31506, June 9, 1998); and

- Use of test methods in accordance with established criteria. Your process for performing test methods criteria must include sufficient detail, including the material you are testing, the purpose of the test, and the test method. The description of the test method criteria must include any reagents used and preparation instructions, apparatus required, any instructions for preparing the sample to be tested, and instructions for conducting the examination. For example, if you receive components of plant origin from an outside source, your specifications must indicate that you test those components to verify that they are not contaminated with adulterants of vegetable origin and to determine that the microscopic examination method is appropriate for use. Further, you may decide that the AOAC International Official Method 961.01 entitled "Adulterants in Spices" is the appropriate analytical method to detect the contaminant which is a method to detect adulterants of vegetable origin in spices. Your test methods criteria must specify the component, dietary ingredient, or dietary supplement to be tested, and what specifically to test for, *e.g.*, the identity of the component, dietary ingredient, or dietary supplement, or a specific contaminant. The method criteria must provide detailed information about performing the analysis (*i.e.*, the reagent solutions needed and their preparation, the type of microscope and other equipment required, preparing the sample, and examination instructions). The proposed rule would not require that you test for any specific substance and would not require a specific test for a substance, so you would be able to evaluate what the most appropriate test would be for the component, dietary ingredient, or dietary supplement and to use the test methods that are suited to your products and your manufacturing needs. Your test methodology must be specific for the component, dietary ingredient, or dietary supplement and the specifications you have established.

Proposed § 111.60(b)(2) and (b)(3) would apply to documentation and recordkeeping for your laboratory operations. Proposed § 111.60(b)(2) would require the person who conducts the testing and examination to document, at the time of performance, that they followed the laboratory method and the testing and examination results. Proposed § 111.60(b)(3) would require that you keep laboratory testing and examination records in accordance

with proposed § 111.125. Laboratory records are necessary to ensure compliance with established specifications and to demonstrate compliance with the CGMP and quality control processes.

Proposed § 111.60(c) would require that you verify that the laboratory testing methodologies are appropriate for their intended use.

Proposed § 111.60(d) would require that you identify and use the appropriate validated testing method to use for each established specification for which testing is required to determine whether the specification is met. In other words, the proposal would recognize that requiring that you have testing methods is not sufficient alone; you must also use those testing methods to prevent the adulteration of dietary ingredients or dietary supplements.

We invite comment on whether we should require, in a final rule, written procedures for your laboratory operations and should require that the person who performs the laboratory processes document, at the time of performance, that the laboratory processes were performed. 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. Further, we seek comment on whether any of the proposed requirements in this section are not necessary to prevent adulteration and to ensure the identity, purity, quality, strength, and composition of the dietary ingredient or dietary supplement. If comments assert that certain provisions 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. If comments agree that the proposed requirements are necessary for reasons other than those we have provided, the comments should so state and provide an explanation.