

formulas, and to perform tests for its manufacturing activities.

In another example, several consumers and employees at spas in Massachusetts and Arizona complained of dizziness, vomiting, or lightheadedness after consuming several dietary supplements. We did an inspection and found that, in the case of two products, the manufacturer's formula called for the use of a product having 0.2 percent selenium by weight, but the manufacturer's records showed that it used a product that had 5 percent selenium by weight. This difference meant that the supplements, instead of containing 200 µg of selenium, contained between 400 to 4,699 µg of selenium. After further investigation, we determined that the error occurred when the quantity of selenium to be used was printed in kilograms (kg), instead of g. The change in unit measurement represents a change from the master manufacturing record. Had the manufacturer's quality control unit reviewed the change in the master manufacturing record, it probably would not have approved the change to include use of the product containing the higher percent of selenium.

One comment to the ANPRM opposed a requirement that would have a quality control unit review and approve the master manufacturing record. The comment stated that this review and approval process is overly restrictive because other units can perform this function and only need be audited or periodically verified by the quality control unit. The comment suggested that the quality control unit assure that a master production and control record must be prepared for the manufacture of each dietary ingredient and dietary supplement, rather than review and approve such records.

We do not agree that the review and approval process is overly restrictive and decline to adopt the comment's suggestion. The quality control unit can be composed of individuals from various parts of the organization. Removing this responsibility from the quality control unit would diminish the quality control unit's responsibility and authority. As stated earlier, the manufacturing process of a dietary ingredient or a dietary supplement can be a sophisticated process, and we understand that all organizational units that are involved in critical formulation and manufacturing steps, such as production, engineering, research, and regulatory affairs, should review and approve a master production order and changes to it. However, the responsibility for reviewing and approving the master manufacturing

record and modifications to that record properly rests with the quality control unit because the individuals in the quality control unit would have the expertise to make a decision whether the master manufacturing record, if followed, will result in an unadulterated dietary ingredient or dietary supplement and does not mean that the manufacturer needs a large number of employees.

You should note that, while the quality control unit is responsible for reviewing and approving the master manufacturing record and changes to that record, this does not mean that the quality control unit must prepare the master manufacturing record itself or act without any involvement from other parts of your manufacturing operation. Other individuals or groups may help prepare, review, and approve drafts of a master manufacturing record and draft changes to an existing master manufacturing record, but the quality control unit is responsible for reviewing and approving the final master manufacturing record and modifications to that record.

Proposed § 111.45(d) would pertain to written documentation and recordkeeping. Proposed § 111.45(d) would require that you keep your master manufacturing records in accordance with proposed § 111.125. The master manufacturing record in addition to the batch production records will ensure that a complete history of each batch of dietary ingredient or dietary supplement is available for your review in the event that a problem arises with a particular batch. These records also are necessary to demonstrate compliance with the CGMP and quality control procedures.

We invite comment on whether a written procedure for preparing the master manufacturing record and making any modifications to the record, consistent with the requirements in this section, should be required 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 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.

5. What Requirements Apply to Establishing a Batch Production Record? (Proposed § 111.50)

Proposed § 111.50(a) would require that you prepare a batch production record every time you manufacture a batch of dietary ingredient or dietary supplement. This requirement would apply to any batch, including a batch approved for reprocessing by the quality control unit. The proposal also would require the batch production record to include complete information relating to the production and control of each batch. The batch production record is necessary to document that you followed the master manufacturing record to make each batch of dietary ingredients or dietary supplements. It is important to document such information for each batch because it serves as a check that the master manufacturing record was followed. If you later discover problems with a particular batch of dietary ingredients or dietary supplements, you could look at the batch production record for that batch, compare it to the master manufacturing record, and see whether the problems occurred because of a failure to follow the master manufacturing record. These records, in conjunction with your master manufacturing records, will create a written system which, when followed, will result in a reproducible, high-quality, and uniform dietary ingredient or dietary supplement.

Proposed § 111.50(b) would require the batch production record to accurately follow the appropriate master manufacturing record and also require that you perform each step in producing the batch. Even if you have someone else (such as a contractor) perform a particular step, you would remain responsible for ensuring that each step is done that complies with the