CARDINAL
Nutrition

Comments on the Proposed FDA Dietary Supplement GMP Regulations
Docket No. 96N-0147

Tom Freeman, Technical Manager

Section 111.10 (b) (5)
Maintaining gloves used in handling components, dietary ingredients, or dietary supplements in an intact, clean, and sanitary condition. The gloves must be of an impermeable material;

This section refers to gloves, but does not say that gloves are mandatory.

There are some situations in which gloves are ineffective and/or cumbersome. If a person is packaging a bulk material in fiberpacks with metal ring lids, bulky gloves can interfere with the finer work such as attaching security tabs, and thin, flexible gloves can be easily damaged by the sharp edges of the metal rings on the lid.

Please clarify the requirement for the use of gloves.

Subpart C – Physical Plant

Subpart C does not address the grounds around the physical plant. There should be some minimum requirement for sanitation and cleanliness in the area surrounding the plant. Drainage and trash removal should be adequate.

One of the hoped-for results of this regulation by our company is the general upgrading of the quality of dietary supplements and the elimination of products that fail to meet minimum quality standards. Requiring a minimum cleanliness standard of plant grounds is a necessary small step toward those goals.

Section 111.20 (d) (5)
... Be designed and constructed in a manner that prevents contamination of components, dietary ingredients, dietary supplements, or contact surfaces. The design and construction must include, but not be limited to: (5) Equipment that controls temperature and humidity ...

Some dietary supplements, such as methylsulfonylmethane (MSM), are not affected by temperatures or humidity within normal environmental

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ranges. Temperature and humidity controls should only be required where necessary to protect product quality.

Section 111.25 (b) (1)& (2)
(1) You must calibrate instruments and controls you use in manufacturing or testing a component, dietary supplement, or dietary supplement

This section does not specify which instruments and controls must be calibrated. In most manufacturing facilities there are many instruments and controls that do not directly affect the quality of the product. Calibrating all instruments and controls could easily become unduly burdensome. The requirement for periodic calibration of instruments and controls should be limited to those directly involved in the critical control parameters of the process. Obviously, critical control parameters would have to be established. All other instrumentation could be labeled as "for information only".

(2) You must calibrate before first use ...

Calibrating before first use should not be required for precalibrated instrumentation, as long as it is certified to be precalibrated and is installed correctly. Precalibrated instrumentation is much more expensive than non-calibrated instrumentation and the additional expense is sometimes justified so that calibration won't be necessary.

Section 111.35 (i) (4) (iii)
You must not reprocess any component, dietary ingredient, or dietary supplement if it is rejected because of contamination with microorganisms or other contaminants, such as heavy metals.

Exceptions should be allowed for this section. Our company makes a product which is distilled then prilled. After prilling, additives are added. The final product is tested. Minor hits of heavy metals have shown up in the analyses, which have been shown to come from the additives. Redistillation of the product will remove the additive and accompanying heavy metal. Subsequently using a different lot of additive will usually solve the heavy metal contamination situation. Any heavy metal that was originally present in the product is now in the distillation bottoms. This section of the regulation would prevent this redistillation to remove the heavy metal.

Section 111.37 (b) (13) (i)
Perform appropriate tests and examinations of ... ***Components,*** *dietary ingredients, dietary supplements, packaging, and labels received to ensure that they meet specifications.*

There should be some allowance for accepting the certificate of analysis for incoming raw materials, if said raw materials are chemicals and are supplied by a certified (audited) supplier. For instance, in making of MSM (methylsulfonylmethane), hydrogen peroxide and dimethyl sulfoxide are used. If those suppliers are ISO certified and periodically audited, testing of the incoming raw materials from those companies should not be required.

Section 111.50 (c) (4)

(c)The batch production record must include, but is not limited to: ... (4) The date and time of the maintenance, cleaning, and sanitizing of the equipment and processing lines used in producing the batch.

Maintenance and cleaning records should not be included in batch records. Typically, batch records, once reviewed and approved, are filed away so that quick reference to maintenance or cleaning information would be difficult and time to find. Maintenance and cleaning information should be filed in separate files or log books, so the specific information can be easily accessed.

Section 111.50 (f)

Same as Section 111.35 (i) (4) (iii) above.

Section 111.65 Manufacturing Operations

This section does not appear to have a requirement for Standard Operating Procedures (SOP's). This should be required, because SOP's are a very good way to improve quality and consistency in a manufacturing operation. Management of change for the SOP's should also be included.

Section 111.85 (b) (1)

(b) You must not salvage returned dietary ingredients and dietary supplements, unless: (1) Evidence from their packaging (or, if possible, an inspection of the premises where the dietary ingredients and dietary supplements were held) indicates that the dietary ingredients and dietary supplements were not subjected to improper storage conditions ...

This section would be very difficult to comply with. First most customers are many miles away (sometimes in another country), so it would be very difficult and costly to "inspect the premises" where the material was held. Also, although container inspection should be done, inspection alone cannot ascertain whether the product was subjected to improper storage conditions.

Section 111.85 (b) (2)
Tests demonstrate that the dietary ingredients or dietary supplements meet all specifications for identity, purity, quality, strength, and composition.

This should not include all returned product. If the product is stable a material and the original container security seals are still intact, the Quality Unit should have the option of returning the material to inventory.

Additional Comments

- Expiration dating should be required on all containers.
- For the benefit of the American public and for the future of the dietary supplement industry this regulation must be strongly enforced once it is put into place.
- There should be some way of certifying that a company complies with these FDA GMPs so that customers can differentiate between suppliers and chose a GMP compliant company as a supplier. This might help drive the noncompliant companies out of business and lessen the enforcement load on the FDA.

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