Dietary Supplements:

Past Compliance & the Future

By Robert Schiff, PhD, RAC, CQA

As we look to the future, an area of regulatory affairs that is expanding dramatically involves dietary supplements. Recently, FDA finalized 21 CFR Part 111 dealing with Good Manufacturing Practices (GMPs) for dietary supplements, which was more than a decade in the making. How is this regulation going to impact the regulatory affairs professional and the dietary supplement or neutraceutical industry in general? To anticipate the future let us look at the recent past through the eyes of an auditor.

According to the FDA website:

> *Congress defined the term "dietary supplement" in the* Dietary Supplement Health and Education Act (DSHEA) *of 1994. A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. They can also be in other forms, such as a bar, but if they are, information on their label must not represent the product as a conventional food or a sole item of a meal or diet. Whatever their form may be, DSHEA places dietary supplements in a special category under the general umbrella of "foods," not drugs, and requires that every supplement be labeled a dietary supplement.*

Many of us take supplements on a daily basis ingesting everything from vitamins to ginkgo biloba, saw palmetto and black cohash. Athletes use various combinations of supplements to improve strength and endurance. Sometimes athletes, both professional and amateur, resort to taking steroids to improve their performance. How do we know this?

Some sports require athletes to be tested after an event to determine whether illegal or unapproved substances have been taken as performance enhancers. If an individual tests positive, he or she may deny taking the restricted substance or may admit to it. Those who deny taking the substance frequently blame an incorrect laboratory test or a mix-up at the manufacturer. Is it possible that the manufacturer may have contaminated a nonrestricted supplement?

If the new dietary supplement GMP regulations are followed, it is very unlikely that contamination would occur. However, prior to the evolution of 21 CFR 211, only the food regulations of 21 CFR 210 and *DSHEA* were applicable.

The author has audited drug, device, biological, food and supplement manufacturers; the latter prior to the enactment of the new regulation. The dietary supplement producers presented unique challenges to the auditor.

Case Study

As part of a lawsuit by an athlete against the manufacturer of a supplement, the auditor was selected by the plaintiff's counsel to determine whether a mix-up could have occurred during production. This particular case was settled during trial and the records are not available for public display. The plaintiff and defendant are masked for the purposes of this article.

The athlete maintained that he had not taken any steroids or steroid-like substances. He simply used an over-the-counter mix of dietary supplements. He tested positive for a restricted substance. Without going into details about the testing, results for both the subject and the supplement mixture were positive. The plaintiff maintained his innocence and the auditor was retained to examine the manufacturing facility and testify to the findings.

During the audit, the auditor was accompanied by several lawyers for both the plaintiff and defendant. The first step was to examine documentation to establish that restricted substances were present in the facility at the time other supplements were produced. Raw-material records for the purchase of the restricted substances were available. However the batch records of the manufacture of the innocuous supplements and the steroids were "lost." It was interesting that batch records for the periods before and after were available. The absence of those records, although product was still in date, violated the food regulations. It was also clear that neither incoming materials—most of which were purchased outside the US—nor finished goods were ever tested to determine whether they actually contained what was presented on the label. This was another violation of *DSHEA*. In fact, the manufacturer did not know what the final product contained. However, these findings do not necessarily indicate product contamination.

The situation became very clear during the facility inspection. As one entered the facility, there was powder everywhere: on the floor, on

containers, on material in the warehouse and in the blending room. Cross-contamination was very probable.

The blending room was most enlightening. Several blenders were in one room and multiple products were being manufactured simultaneously. Air flow in the room to remove dust was minimal, and powder from one blender could easily contaminate another. Restricted substances and routine supplements were mixed using the same blender. Because the batch records were unavailable, it was impossible to determine whether the same equipment was employed on the same day for the various items.

Cleaning now became a critical factor. Cleaning was performed by rinsing and treating with tap water. This was of more than passing interest because while steroids are soluble in organic sosl-vents, they are insoluble in water. Thus, there was a reasonable likelihood that the cleaning process did not totally remove the steroids from the blender.

The audit concluded that there was a reasonable likelihood that cross-contamination could have occurred. This finding was based upon unacceptable blender cleaning, unidentified powder throughout the facility, poor air flow in the blender room, absence of raw material testing, and inadequate cleaning of tableting and capsule equipment.

All of this occurred before the new regulations were enacted. Had they been in effect at the time the original material was manufactured, and had FDA inspected the facility, it is reasonable to suppose that controls to reduce or eliminate the possible cross-contamination would have been in place.

Conclusion

Having inspected several supplement establishments, it is clear to the author that there is a need to test raw materials and finished goods, although it will raise the price of supplements. My experience suggests there are supplement manufacturers now who are not performing this testing. Considering that much of the material used to manufacture supplements comes from outside the US (i.e., China and India), it is prudent to know specifically what our dietary supplements contain.

The current concern about lead in toys and forbidden ingredients in toothpaste requires the implementation of these new rules. *DSHEA* required truth in labeling and has been in place for more than 10 years, so enforcement is a must.

It will be the regulatory affairs professional's responsibility to ensure compliance before the regulations take effect, not afterwards. Dietary supplement manufacturers need to have appropriately experienced staff in place if they are to be compliant. Thus, there is an apparent need for more regulatory affairs professionals in the supplement industry in the immediate future.

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