

## The cGMP Final Rule for Dietary Supplements

### *Product Safety*

#### **GMP Compliance Deadlines**

Companies with 20–499 full-time equivalent employees.....June 25, 2009

Companies with fewer than 20 full-time equivalent employees.....June 10, 2010

#### **Product Safety**

Under the Dietary Supplement Health and Education Act (DSHEA), manufacturers have an essential responsibility to substantiate the safety of their products. Any representations or claims made about products are substantiated by adequate evidence to show that they are not false or misleading. The cGMPs will help to ensure manufacturers produce unadulterated and properly labeled dietary supplements.

While there are many possibilities that could render a product unsafe for consumption, they are generally categorized into six sources of contaminations/adulterations. These contaminations and adulterations must be tested to ensure product safety. Because it is a complex issue and difficult to understand, customers should develop a program that fits their specific needs.

- I. Pesticides – Hundreds of pesticides have been used worldwide over the last several decades, with many still being used today. FDA/EPA have set guidelines for the limits of many of pesticides in various foods, water and supplements. The methods for pesticides testing in the US are frequently referred to as “Pesticide Analytical Manual” (PAM). EPA has several methods for various pesticides such as EPA 608, 8080, 625 and 8270. Both PAM and EPA methods use similar sample extraction procedures followed by analysis using one or more analytical techniques including GC, GC/MS, HPLC and LC/MS. Therefore, these methods are similar and somewhat interchangeable.
  - (1) Pesticide screen- this is can accommodate up to several hundreds of pesticides by GC/MS or LC/MS. When screening finds suspected pesticides at appreciable concentrations, further tests are required to obtain better quantification. It should be recognized that this screening method is expensive and may not provide the detection limit for certain pesticides.
  - (2) Chlorinated pesticides – this is a group of the most toxic pesticides. The test method is frequently performed by GC-ECD with low detection limits (i.e.EPA 8081) and GC/MS (EPA 8270). This same method can be used for PCNB analysis.
  - (3) Phosphorous and nitrogen pesticides – the method for this group is usually quoted as EPA 8140, GC/MS can also be used for them.
  - (4) Carbamate pesticides – This is a group of insecticides with nitrogen attached to the carboxyl group. The test methods are often quoted as EPA 531 (water) or 8318 (waste). Both methods are HPLC. If a lower detection is required, post column derivatization is required for detection of low limits of carbamate.
- II. Solvent Residues (or Organically Volatile Impurities, OVI) – There are many possible solvent residues in a product. USP method 467 describes three classes of OVI according to their toxicities. Analytical techniques are head-space GC for relatively low detection limits, and direct injection into GC for polar OVI that allow relatively high detection limit. GC/MS is also frequently used for more conclusive determination of OVI, especially when non specific residue solvents are targeted or unknown. Therefore, it is better for customers to have basic info about the possible solvents used for producing the product.
- III. Heavy Metals – Heavy metals are frequently referred to lead, arsenic, mercury and cadmium. There are others such as aluminum and antimony. There are specific limits required for heavy metals by Prop 65. The technologies for testing them are atomic absorption spectrophotometer (AA) with graphite furnace, ICP-IES and ICP-MS. Due to the complexity of sample matrices, AA method is limited due to interference. ICP-MS becomes the method of choice. No matter which method is used, the sample must be digested thoroughly by a microwave digester.
- IV. Pathogens – There are many possible pathogens in food and supplement products. The most frequent pathogens are E. Coli, Staphylococcus and salmonella, and along with these three, total bacterial populations and yeast are often tested to gauge the microbial contamination. Other pathogens may also be required depending on the suspected contamination.
- V. Adulteration – This has become an important issue during the last a few years. The major examples are (1) melamine adulteration, (2) impotency drugs and other drugs adulteration, and (3) adding less expensive ingredients to higher priced items such as Chondroitin sulfate by dextrins, ginkgo extract by rutin and saw palmetto by common oils, etc.
- VI. Antibiotics and drugs – FDA has stepped up effort to control products imported that contain various antibiotics and animal drugs used in feeds.

This newsletter concludes our three parts of technical Newsletter for cGMP compliance.