

The cGMP Final Rule for Dietary Supplements *Potency (Label-Claim) Testing*

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

Strength and Potency

For strength or potency indicated in the supplement facts of each product, the cGMP rule require all claims to be substantiated by laboratory testing data using established methods. The rule requires testing all lots for all active ingredients claimed. The test results must support the amounts indicated in the label.

The initial step for a comprehensive testing program is to establish a detailed product specification which is used to set the testing specification. When preparing the specification, one must take into consideration the variation of an ingredient in the final product. This variation could come in a number of ways: purity of the raw material, accuracy and variation of the test results of the raw material, water content of the raw material, test variation of finished products, and the methods used in the raw material and final product testing, etc. For example, a chondroitin sulfate at 90% purity is on a dry-basis, but if it contains 8-10% moisture, a formulator must make adjustment to this moisture content. Failure to recognize these factors may result in an incorrect formulation that will ultimately lead to the failure of the final products for not meeting the label claims.

After product and testing specifications as well as the formulation has been established, a vigorous testing program must be carried through the whole process, starting from the raw material to finished goods. The following are critical elements:

1. Define product specifications: The specifications may be set at $\geq 100\%$ or 90-110% of label claims. Marketing people like to use 100% or above the claim, while QA/QC units are more scientifically-based and use 90-110% for well-defined ingredients, which is more in line with USP OTC products. For certain products such as herbal products with undefined standards and methods plus complex matrices, the specification may be 80-120%. It is critical to have proper specifications set appropriately.
2. Define methods of testing for each ingredient. The methods may differ between raw material and the finished products due to the difference in matrices. As we all know, one method will not work for all types of products, including USP or AOAC methods. This is why a considerable effort should be made to develop specific methods for given products. The most common methods are HPLC, GC, AA or ICP, UV-VIS, Titration and other wet chemistry methods. Titration methods may be suitable for raw material and single ingredient products, but unfit for many different finished products. FT-IR and TLC are more for ID tests.
3. Providing label claims to the laboratory is very useful because this information will help chemists not only to set their calibration to meet the method requirements, but also to produce more accurate results and speed up the delivery time. We all know that each instrument and method has its detection and quantification limits. Without knowing the claims, there are chances that the concentrations of sample preparation are too high or too low, falling outside the calibration range. The test results will not be as accurate in this case, or the test has to be repeated with time wasted. It is acceptable that certain customers don't want the labs to know the claims for various reasons, but please keep in mind the potential pitfalls involved.
4. Providing sample matrices information is just as important as providing claims. Certain customers are reluctant to provide such information due to the confidential formulation. In this case, minimal information will still help. For example, a dietary fiber test by traditional fiber AOAC method will not work for resistant maltodextrin (RMD) and modified cellulose. Carotenoids coated and uncoated will also required different methods for preparation, etc.
5. Shelf-life or the stability of a product is an integral part of the cGMP. Any claims for shelf-life of a product should be backed-up with study data. Because the test by an accelerated method requires six months, we must plan ahead in order to obtain on-time data for a product launch. Similarly, disintegration, dissolution and extended release of products also require testing as well.
6. Selecting a qualified laboratory partner is important. There are many laboratories to choose from, but several things stand out to be most important: a rigorous quality system and program in place, using established and validated methods, willingness to work with customers on questions in a timely manner, providing quality and consistent data, reasonable turnaround time, and reasonable cost. Professional integrity, accredited and audited labs are also major factors of consideration.