Nutritional OUTLOOK

What Does High-Quality Ingredient Testing Look Like?

Justin Bath, June 25, 2018

Trends & Business, Regulatory, Science

Test. The word itself can raise blood pressure and bring back unbidden memories of unprepared students awaiting the scores of their high school chemistry exams. Out in the "real" world, particularly in the natural products industry, the word *test* means something completely different. It means trust; it means quality; and above all, it means safety.

Nutraceutical and dietary supplement makers are responsible for manufacturing the highest-quality products possible. As more companies recognize the need for heightened quality assurance, there has been a widespread shift wherein more firms are choosing to partner with contract manufacturers who can help handle and manage the manufacturing and testing of high-quality products.

Partnering with contract manufacturers brings several benefits, not least of which is that these companies are, or should be, familiar with the proper processes and procedures required to comply with the regulations governing these products. Such compliance should be second nature to them.

Good Manufacturing Practices

As part of its dietary supplement current good manufacturing practices (cGMPs; 21 *CFR* 111), the U.S. Food and Drug Administration (FDA) says that to ensure the quality of the finished product, manufacturers are responsible for establishing specifications for identity, purity, strength, and composition related to components of dietary supplements (21 *CFR* 111.70). They are also responsible for establishing limits for the types of contamination that may adulterate or lead to adulteration of the finished batch of the dietary supplement.

These cGMPs are designed to prevent the inclusion of the wrong ingredient, the addition of too much or too little of an ingredient, the possibility of contamination, and the improper packaging and labeling of a product. The manufacturer must then ensure that the tests and examinations they use to determine whether these specifications are met are based on appropriate, scientifically valid methods. (21 *CFR* 111.75)

Defining Test

What is interesting is that these cGMPs do not dictate which specific tests and examinations a company should use to substantiate that established specifications are met, only requiring that test methods be appropriate (fit for purpose) and scientifically valid. Perhaps unsurprisingly, because margins can be thin and competition fierce, some manufacturers, even contract manufacturers, take half-measures or skip critical tests in an effort to save money.

What to Test For

For those responsible companies seeking high-quality, fit-for-purpose test methods, the following are examples of what is involved when testing for identity, purity, strength, and composition.

Identity

Identity testing means testing to make sure the raw material in hand is what it's claimed to be. The way to test for identity is to compare a sample of the raw material against a reference standard of that raw material. This is often accomplished by using Fourier-transform infrared spectroscopy (FTIR).

FTIR is used to make a qualitative match. A beam comprising many frequencies of light at once is shined at the sample. FTIR measures how much of that beam is absorbed by the sample. Next, the beam is modified to contain a different combination of frequencies, yielding a second data point. This process is repeated several times to infer what the absorption is at each wavelength.

This process compares the sample's test results with the test results from a reference standard. The reference standard can either be an internally provided standard or be obtained from an outside, independent standard provider, such as the United States Pharmacopeia (USP). The USP standardizes many types of raw material samples, which manufacturers can use to verify the identity of the sample raw materials they have.

Other tests that can satisfy the Dietary Supplement cGMP identity-verification requirements include:

- HPLC (high-pressure liquid chromatography)
- TLC (thin-layer chromatography)
- NIR (near infrared spectroscopy)
- Organoleptic testing
- ELISA (enzyme-linked immunosorbent assay)
- SNIF-NMR (site-specific natural isotope fractionation–nuclear magnetic resonance)
- IRMS (isotope ratio mass spectrometry)
- Wet-chemistry methods

Purity

If a contaminated product makes its way into consumers' hands, a number of problems can arise, some potentially harmless and some potentially deadly. When the contamination could cause a

product to result in harm if consumed, the product is deemed adulterated. According to the Dietary Supplement Health Education Act (DSHEA) of 1994, adulteration of a dietary supplement occurs when:

- A product presents a significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or even if no conditions of use are suggested or recommended in the labeling but when the consumer uses the product under ordinary conditions of use;
- Contains a new dietary ingredient (NDI) for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury;
- Regulators declare that a product poses an imminent hazard to public health or safety
- The product is or contains a dietary ingredient that renders it adulterated

Purity tests look for contamination to ensure there are no micro contaminations or metals. These include tests for yeast, mold, chloroform, salmonella, *E. coli,* and heavy metals.

Full-panel tests for microorganisms like *E. coli,* yeasts, molds, etc., are well advised. Tests can be carried out to determine a total number of organisms on a surface, device, or instrument, or in a product. A surface is swabbed to collect bacteria. The collected material is measured (counted) against a standard. A count lower than the standard indicates no danger; a count higher than the standard indicates the opposite. Tests include, but are not limited to, sterility, general microbiology, and bioburden testing.

For heavy-metal testing, one method used is inductively coupled plasma mass spectrometry, or ICP-MS. This is an analytical technique used for elemental determinations. It is performed by ionizing a sample with inductively coupled plasma and then using a mass spectrometer to separate and quantify those ions.

Strength

Testing for strength is testing to determine how much of the active ingredient is present in a particular dosage. Testing for strength is performed by HPLC. HPLC measures how much of an active ingredient is present.

Composition

Each component of a dietary supplement needs to be verified to ensure what is listed on the label matches what's in the bottle. There are two categories of supplement component: 1) dietary ingredients, and 2) non-dietary ingredients.

DSHEA defines the five categories of substances that qualify as dietary ingredients: a vitamin; mineral; herb or other botanical; amino acid; or a dietary substance used to supplement the diet to increase the total dietary intake of a nutrient; as well as a concentrate, metabolite, constituent, extract, or combination of any of the above ingredients. Non-dietary ingredients, on the other hand, include ingredients like fillers, artificial colors, sweeteners, flavors, or binders.

Testing requirements for dietary and non-dietary ingredients are different. Non-dietary ingredient suppliers must be validated and approved by a manufacturer. Dietary ingredients are generally tested in a qualified laboratory to ensure they meet standards and specifications.

Testing Processes

It is important to note that cGMPs require testing at the beginning and at the end of manufacturing, as well as in-process. Also, while contract manufacturers should be following the testing protocols listed above, nutritional supplement brand owners are ultimately responsible for confirming that products produced under its label conform to FDA's requirements. The brand owner can be held responsible for selling non-conforming and/or adulterated product, so it is important that companies choose a contract manufacturer carefully.

Understanding the requirements as outlined in 21 *CFR* Part 111 is essential for anyone producing a nutritional supplement. Choosing the right manufacturer is an important part of the process, and all brands should ensure they are properly educated on the FDA requirements. Below is a list of some of the most basic testing requirements a brand should understand when producing nutritional supplements. (Note: this list is not intended to be all-inclusive.)

- Raw material validation and testing (purity, potency, strength, and composition)
- Production testing to ensure all equipment is clean and properly calibrated
- In-line checks at regular intervals to confirm lots and batches are being produced to specification
- Finished-goods validation and testing (purity, potency, strength, and composition)

Finally, it is important for a brand to ensure that its chosen manufacturer follow all cGMP processes before releasing finished goods. Understanding and auditing how products are released at multiple stages in the manufacturing process will help any brand provide the highest-quality product possible.

The Future of Testing

Just like in high school, more tests are on the way. For instance, NSF International recently launched an independent testing protocol and verification program for raw botanical ingredients used in the dietary supplement industry. This protocol not only utilizes advanced DNA authentication of the target species, the testing program also screens for contamination, including common adulterants, toxic adulterants, allergens, and fillers.

Moving forward, tests such as DNA sequencing with real-time (qualitative) polymerase chain reaction testing (PCR) will help to continue to propel individual products as well as the entire industry towards greater levels of safety and quality.

Justin Bath is president of Biovation Labs, a contract manufacturing, formulation, private label, and supplier company serving the natural products industry. The company works within the life science space, manufacturing products for supplement and nutraceutical companies worldwide. Its new 104,000-sq-ft corporate headquarters houses a state-of-the-art, high-capacity manufacturing facility serving the needs of both large and early-stage companies. Biovation Labs follows cGMP standards. For more information, visit www.biovationlabs.com.

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