Product Testing, Quality Control, and the GMPs

Analysis and testing equipment help the nutraceutical industry gear up for compliance.

BY LEANNA SKARNULIS

The nutraceutical industry has watched FDA labor over a 13-year gestation before delivering its good manufacturing practices (GMPs) in June. Many say the final rules came as no surprise. It is now up to companies to create master manufacturing records (MMRs), perform testing, and provide records to prove that their products meet MMR and label specifications.

In short, the more than 800-page regulation requires manufacturers to prove the identity, purity, strength, and composition of products. What will this mean to manufacturers, testing equipment suppliers, and testing laboratories in terms of providing quality control analysis and incorporating testing equipment into operations?

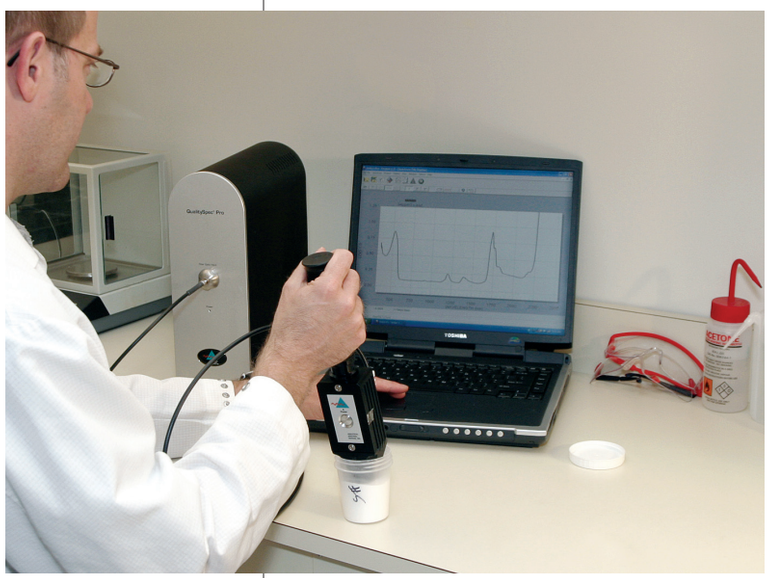

Photo courtesy of Analytical Spectral Devices Inc.

The Vis/NIR Nutraceutical ID system offers a variety of probes and an expandable starter library of more than 65 materials.

IDENTITY OF RAW MATERIALS

Dietary supplement manufacturers, not raw material suppliers, bear the burden of analyzing incoming ingredients. The near-infrared spectrometer (NIR) is a basic piece of equipment for verifying identity.

"With the GMPs' release, our activity has stepped up," says Tom Brown, director of sales and marketing for Analytical Spectral Devices Inc. (ASD; Boulder, CO). "We provide an NIR solution with a starter nutraceutical library that is popular with a lot of people. It's a great tool to start off with and is usable by nontechnical people. It's nondestructive, there's virtually no sample prep, it's flexible, and it's fast."

A portable version can be used for raw material reception, in-process, and for quality control of the finished product. ASD provides two-day training at its facility in Boulder. The system includes Windows-based

software that runs on PCs and integrates into laboratory management systems for recordkeeping.

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GETTING TO COMPLIANCE

With just more than 100 employees, Pacific Nutritional (Vancouver, WA), which currently outsources most testing, must be compliant with GMP rules by June 2009. Dean Bautz, director of quality control, is in the midst of drafting procedures and making recommendations for equipment and personnel needed to outfit an in-house laboratory.

"FDA doesn't require testing of every single lot, but it does require that you have sound justification for reduced lot testing," Bautz says. "When we validate a new vendor, we'll test the first three lots for all specifications. Upon successful testing of the first three lots, we might go to every other lot or every third lot, depending on how critical the material or ingredient is. The same is true of final product testing. After we've demonstrated that our procedures give us the result we need, we may go to testing every second or third lot."

The company has more than 1000 products requiring 1500 different ingredients and receives 10–20 different raw materials daily. "To qualify them all takes time," says Bautz. "Right now we run complete microbiological screening to look for contaminants and establish identity with infrared spectroscopy. That does not work on all raw materials. Every botanical that comes in will have to be identified, probably with TLC (thin-layer chromatography) to prove it really is echinacea or ginseng."

"I'm salivating over all of this," he adds. "As an analytical chemist and lab director, this is what I live for. We'll be adding lots of equipment, and I anticipate our staff will triple. We don't presently have the manpower to run the critical tests we'll need."

He currently has high-performance liquid chromatography (HPLC), atomic absorption spectroscopy (AA), and UV visible spectroscopy (UV/Vis) equipment. He wants to buy two HPLCs, two GC mass spectrometers, and TLC and polymerase chain reaction (PCR) apparatuses.

"We're designing our quality program to qualify raw materials, assure

Photo courtesy of Stable Micro Systems (Godalming, Surrey, UK).

The Capsule Tensile Rig measures strength and stability of hard gel capsules, enabling manufacturers to identify the effects of fillings on the mechanical strength of the capsule shell.

that specifications for the product will hold up throughout the manufacturing process, and provide any needed overages for shelf-life testing." (The GMPs require shelf-life testing only if the label carries an expiration date.) "Whatever input goes in had better not degrade before the expiration date," says Bautz.

UP TO SPEED

Some manufacturers, such as Robinson Pharma (Santa Ana, CA) and Synergy Production Laboratories (Moab, UT), say they already were ready for the GMPs.

"A lot of companies did quite a bit to get to a certain level of compliance prior to release of the GMPs," says Gary Callahan, senior vice president of operations for Robinson Pharma's drug division. "We have a drug license, in part to make us more ready for the dietary supplement rules."

He says the company has a very good and well-equipped laboratory and currently does identity testing on raw materials. "We'll add equipment to do quantitative testing," he says. "We rely on vendors' certificates of analysis partially now, but we will have to validate what we're getting from them and will do extended testing on every shipment that comes in."

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The effect of the GMP rules on Synergy Production Laboratories will be minimal and will mainly involve modification of reporting and documentation, says CEO and founder Mitchell M. May, PhD. "We're already essentially compliant, as are a lot of the companies we know, and our current system exceeds the new GMPs."

May welcomes the regulations. "There's a segment of the industry that will be highly impacted and rightly so," he says. "The public has a right to assurances that what they're buying is what the label says it is."

THE GMPs' IMPACT ON TESTING LABS

Nutraceutical testing by Nelson Laboratories (Salt Lake City) involves microbiological methods such as plate counts, coliform testing, and organism identification. Jeff Nelson, president and CEO, says it will take time before testing labs feel the impact from the regulation. "We might pick up more raw material screening to make sure incoming materials have low bacterial counts and possibly more final product testing to see that the product is microbiologically safe or even do more pathogen screenings postproduction to make sure there's nothing that's a threat for customers," says Nelson. "It's hard to say exactly."

Nelson is waiting to see how the regulation will be enforced. "This particular regulation is fairly vague, and I'm not certain how it's going to be interpreted at the point of enforcement," he says. "There will start to be private letter rulings from FDA with independent firms, word will spread, and manufacturers will take defensive measures to respond to the enforcement approach. That will drive business for laboratories more than anything."

Callahan says Robinson Pharma occasionally outsources testing, and he expects outsourcing to initially increase with the GMP rules. "Some tests we feel an outside lab may be better qualified to do, at least until we have those tests developed," he says. "We'll also use outside labs to validate our test methods."

Synergy uses both in-house and third-party labs for testing. "We'll send certain highly specialized ingredients, such as a particular flavonoid, to a lab that's much better equipped to test than we are," says May. The company also augments its in-house testing with third-party validation.

"If we claim a standardization and verify it ourselves, we will also use an outside lab to make sure that our in-house results are reliable," he says. "Prior to a finished product being released from quarantine we'll have it tested by a third party, and if there's incongruence we'll send it to another lab. It's how we monitor our own system."

INLINE TESTING

Dr. Schleuniger Pharmatron (Manchester, NH) is a supplier of automated tablet testing systems. Walter Friesendorf, national salesman, says the GMPs require manufacturers to create MMRs that include a formula for every product and also be able to prove that the finished product's identity, purity, strength, quality, and composition comply with the MMR formula and label.

A lot can go wrong in blending products that have multiple ingredients. "There's an optimum blending time when everything is evenly distributed," says Friesendorf. "Each tablet must contain a homogeneous blend of ingredients and have the proper dosage and size. Measurements must be done at critical control points, such as when the powder is transformed to a tablet."

The GMPs leave it up to manufacturers to write test protocols, such as testing 10 tablets every 10 minutes as they come off the press. "Weight is the key measurement," says Friesendorf. "If the weight is off, something is wrong. But the weight can be correct and there could still be something wrong with the blend, so you test for deviations in hardness and thickness. To meet the GMPs, you have to make tests that can yield scientifically acceptable data, which means electronic testing."

ON THE HORIZON

May predicts that some equipment manufacturers may be inspired to develop new equipment or modify existing equipment to be more specific to what the GMPs require. "I look forward to new offerings in the next nine to 12 months that will zero in precisely on what the GMPs require," he says. "Some of the current equipment is overbuilt and some is underbuilt for analyzing a raw material and the finished good."

One such adaptation that might appeal to nutraceutical manufacturers is the inline StepOne system from Dr. Schleuniger Pharmatron. It combines an automatic tablet tester for measuring weight, thickness, diameter, and hardness, with an NIR spectrometer system from Bruker Optics Inc. (Billerica, MA) for measuring tablet potency and uniformity of content. StepOne is currently in use by pharmaceutical companies in Europe and the United States. ❖

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