

# Top 3 GMP Violations in Dietary Supplement Companies

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- Failure to establish and follow master manufacturing and batch production records.
- Failure to test for identity of all ingredients before use.
- Failure to document corrective actions undertaken

In the four years since FDA released its final rule on dietary supplement GMPs (good manufacturing practices) and began a staggered start for compliance, from large companies to the smallest firms, the supplement industry has exerted great energy into preparing for FDA GMP inspections. Experts in all things FDA, GMP, quality control (QC) and supplements wrote articles, spoke at seminars and workshops, and offered one-on-one consulting. Industry organizations created or furthered third-party GMP certification programs and compliance training in an effort to give supplement companies some hands-on experience in bringing their firms into compliance.

Despite these great efforts, early results from the first few years of inspections have highlighted some common violations of the GMP regulation (21 CFR 111). Whether a sign of the breadth of the supplement industry or of a lack of urgency among numerous companies, the failures during these first rounds of inspections offer the greater industry some potentially useful lessons in helping those yet-uninspected companies prepare for a visit from FDA's inspectors. Given the recent wave of FDA warning letters for inadequate responses to the 483 inspection reports, the lessons learned may also help those recently or currently undergoing inspection to more appropriately respond to 483s.

Bradford Williams, manager of the Division of Dietary Supplement Programs at FDA's Center for Food Safety and Nutrition (CFSAN), confirmed FDA has significantly increased its inspection rate, from just one inspection in 2008 to 84 inspections in 2010; as of May 2011, there were 66 supplement GMP inspections conducted, with a projected 2011 total of around 191 or more.

Alarmingly, he reported fiscal year 2010 violation rates were nearly 25 percent, which was higher than FDA expected. He explained the agency expected noncompliance to grow as firm size decreased, but noncompliance has been across the board of company sizes and types, including own-label distributors, contract manufacturers and re-packers and -labelers.

The chronology of GMP inspection events goes generally like this: FDA sends GMP inspectors to a facility to conduct investigations. All records relevant to GMPs must be available for inspectors. After the inspection, a form 483 inspection report is delivered to the inspected firm, detailing any violations found and what FDA expects from the company in response to these violation notices. It is advisable to try to respond adequately—detailed written plans for corrective action, including a timeline—within 15 days of receiving the 483. If FDA decides the response to the 483 report is inadequate, it can issue a warning letter to the company, which usually comes with a requirement to respond within 15 days of the letter. If the company's

response is still inadequate, or even defiant, FDA can take further enforcement action such as product seizure, injunction and prosecution. However, for some corrective actions reported by those responding to 483s, FDA seems to be content to promise a close inspection of these items in its next inspection of those facilities.