



# The supportive relationship between current Good Manufacturing Practices (cGMPs) and quality specifications for dietary supplements/dietary ingredients

Gabriel I. Giancaspro and James C. Griffiths  
U.S. Pharmacopeia, Rockville, MD

## ABSTRACT

Dietary supplement consumers are nervous about the products they are using, and skittish regarding the frenetic introduction of innovative, “hot” new products. FDA has released the long awaited current Good Manufacturing Practices (cGMPs), and the purveyors are coming to terms with how to comply and of course, how to gain a marketing advantage. Perhaps to compliment and complete these quality-driven cGMPs, dietary supplement manufacturers, at both the ingredient and final product level, need to embrace a new paradigm for quality and safety - consistent accurately identified ingredients. The old terms of art - unique, new and improved - are ripe for replacement with terms such as analyzed, characterized, standardized and specified, as derived from harmonized public standards agreeable by practitioners, manufacturers and government.

## INTRODUCTION

FDA’s new dietary supplement cGMPs provide standards that affect the products, processes, and people involved in dietary supplement manufacturing. These standards support the overall quality of the finished dietary supplement.

Quality means that the dietary supplement consistently meets the established specifications for identity, purity, strength, and composition, and limits on contaminants, and has been manufactured, packaged, labeled and held under conditions to prevent adulteration under 402(a) (1-4), of the FFD&CA

The rule requires the establishment of specifications for:

Identity, Purity, Strength and Composition and absence of contaminants of

- components including dietary ingredients,
- in-process
- finished products

## DSGMPs AND QUALITY SPECIFICATIONS

### REQUIRE

- 100% Identity testing is required for every dietary ingredient, unless an FDA exemption is obtained pursuant to the petition procedure in the accompany Interim Final Rule.
- An identity specification is required for every component, including dietary ingredients. For non-dietary ingredient components, instead of testing, a manufacturer can rely upon a supplier’s Certificate of Analysis. A manufacturer must “qualify” its supplier, periodically reconfirm the findings in the Certificate of Analysis, and have knowledge of the tests upon which the Certificate relied.
- The rule requires calibration of analytical equipment, for which reference materials are needed. GMPs gives freedom to manufacturers to set their own Reference Materials but supports the use of Compendial Reference Standards where they are available.
- FDA specifies that manufacturers must establish adequate controls over the production process and specifications for their product to ensure that they “consistently and reliably manufacture what [they] intend.” In other words, “the focus of CGMP is on process controls to ensure that the desired outcome is consistently achieved, and not on the inherent safety of the ingredients used.”

### DO NOT REQUIRE

- Complete finished batch testing, instead only one measure is allowed as a proxy for the complete quality of the finished product.
- Specific microbiological/toxicity testing protocols and reference standards, manufacturers have the flexibility and responsibility to set their own.
- Performance Testing: There are no requirements for testing dissolution or disintegration of oral solid dosage forms.
- These CGMPs establish no common or minimum requirement for quality. Although the CGMPs will help ensure that one manufacturer’s product is similar from batch to batch, the specifications for similar articles can vary widely from manufacturer to manufacturer.



## CONCLUSIONS

New current good manufacturing practices (cGMP) regulations for dietary supplements require manufacturers to establish their own standards of identity and quality. The resulting standards are not subject to public review and remain private after finalization. The consumer will not know the standards to which each product is held and will be unable to determine whether two products sharing the same name or bearing the same ingredients are similar or how they differ. Widespread use of public standards created by The United States Pharmacopeial Convention (USPC) for dietary supplements and dietary ingredients, in conjunction with the new cGMPs, could help ensure the quality and consistency of these products while conserving resources both on the part of the U.S. Food and Drug Administration (FDA or

Agency) and manufacturers. Reliance on USPC standards—public specifications containing tests, procedures, and acceptance criteria—would eliminate the need for repetitive development and review of validation and other data for procedures to ensure the identity and quality of a specified dietary ingredient or dietary supplement. Manufacturers will need to set up a system of supervision for their suppliers and the FDA will step up inspections to check compliance with the rule. In this system, a public standard that can be accessed and shared by suppliers, manufacturers and FDA inspectors is of paramount value. Pharmacopeial methods, specifications and reference materials are well positioned to serve as reliable source of these public standards.

## USPC PUBLIC DOCUMENTARY STANDARDS AND REFERENCE MATERIALS

- USPC now publishes two compendia in a single volume: USP and the National Formulary (NF). NF contains monographs for excipients, and USP mainly contains monographs for active ingredients, finished products.
- A monograph sets out the name and definition of an article; any packaging, storage, and labeling requirements; and a specification: List of tests, one or more analytical procedures for each test, and acceptance criteria.
- USPC provides specifications for other ingredients that may be included in a dietary supplement in the Food Chemicals Codex (FCC), a compendium of public standards for food ingredients.
- Soon, USPC will publish the USP Dietary Supplements Compendium, a reference that will combine dietary ingredient standards both from USP and FCC together with supplemental information specific to dietary supplement industry.
- USPC also establishes reference materials through a rigorous process of collaborative testing that includes government laboratories and independent scrutiny from the USP Counsel of Experts, resulting in an unbiased source of reference standards for quality testing.

## THE VALUE OF USPC PUBLIC STANDARDS

- cGMPs call for standards without standardization: Multiple manufacturers may establish different standards of identity, strength, quality, and purity for dietary ingredients and dietary supplements that are introduced into commerce under the same name.
- Use of USPC’s standards for dietary ingredients and dietary supplements, would serve manufacturers, regulators, and the public because these standards can be used by all actors in the marketplace, conserving FDA and manufacturer resources.
- If manufacturers choose to build proprietary specifications “from scratch,” FDA would need to assess the manufacturer’s compliance to those proprietary specifications. Public standards may serve as common guidance both for the manufacturers and inspectors, the former to set their specifications and latter to check whether these specifications are sufficient to warrant consistent quality.
- Uniform standards allow comparisons of products in clinical trials. With one quality standard in use for a particular substance, researchers can eliminate certain unknowns from their research, and, as a result, may be better able to reach conclusions about the safety and efficacy of the material.