FDA Releases Long-Awaited Dietary Supplement Current Good Manufacturing Practices Final Rule

Nearly thirteen years after Congress granted the Federal Food and Drug Administration ("FDA") the authority to prescribe regulations setting forth current good manufacturing practices ("CGMPs") for dietary supplements,¹ and four years after FDA published its proposed rule,² FDA released its Final Rule on Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements ("Final Rule").³ The Final Rule establishes, at 21 C.F.R. Part 111, the minimum CGMPs required for manufacturing, packaging, labeling, or holding dietary supplements to ensure the quality of the dietary supplements.

The Final Rule's sixteen subparts, described in detail in the 208-page Federal Register document, are driven by a few major themes that FDA reiterates throughout the preamble to the Final Rule:

- **CGMPs are needed to ensure the quality of dietary supplements.** Ensuring quality means that a company consistently and reliably manufactures what it intends and that it establishes process controls to prevent the dietary supplement from becoming adulterated.

- **CGMPs require written procedures detailing the specifications a manufacturer establishes for its dietary supplements and the production processes needed to achieve those specifications.** CGMPs require the creation of written documentation substantiating that these procedures are satisfied and the specifications are met.

- **The key steps towards ensuring the quality of dietary supplements are ensuring the identity and quality of components used to manufacture a dietary supplement, and utilizing in-process controls to ensure that the product specifications are met.** These two requirements permit testing of only a subset of finished batches of product, rather than testing of each finished batch.

- **CGMPs do not address the inherent safety of the ingredients used in dietary supplements, which is covered by other statutory provisions.** Similarly, adverse event reporting requirements are not comprehensively encompassed within CGMPs.⁴

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¹ 21 U.S.C. § 402(g)(2).
⁴ The recently-enacted “Dietary Supplement and Non-Prescription Drug Consumer Protection Act” (Public Law 109–462) requires mandatory reporting to FDA of serious adverse events associated with the use of a dietary supplement in the U.S., effective December 22, 2007.
While the “effective date” of the Final Rule is August 24, 2007, the actual compliance dates are phased in over the next three years. Companies with more than 500 employees have until June 2008 to comply, companies with less than 500 employees have until June 2009 to comply, and companies with fewer than 20 employees have until June 2010 to comply with the Final Rule.

Part I of this document briefly summarizes the key requirements established in the Final Rule. Part II raises issues of potential importance for dietary supplement companies that will be subject to the CGMP requirements and for food companies monitoring FDA’s thinking as the agency considers revising the food CGMPs in 21 C.F.R. Part 110.

I. Key Requirements of the Final Rule

A. Scope

The CGMPs apply to all domestic and foreign companies that manufacture, package, label or hold dietary supplements, including those involved with the activities of testing, quality control, packaging and labeling, and distributing them in the United States (referred to herein as “companies”). Each company involved in manufacturing, packaging, labeling, or holding dietary supplements is responsible for only those CGMPs that relate to its activities.

The Final Rule is limited to only those involved with dietary supplements – it does not extend to entities that manufacture, package, label, or hold only dietary ingredients, or to persons engaged only in activities associated with the harvesting, storage, or distribution of raw agricultural commodities that will be incorporated into dietary supplements by other persons. Additionally, the Final Rule does not apply to retail establishments holding dietary supplements only for purposes of direct retail sale to individual consumers, although this exception does not include a retailer’s warehouse or other storage facility, nor does it extend to warehouses or storage facilities that sell directly to individual consumers.

B. Master Manufacturing Record

The creation of a master manufacturing record is central to the CGMP scheme, as this record serves as the touchstone for most of the other CGMP requirements to ensure the quality and uniformity of all dietary supplements a company produces. FDA analogizes the master manufacturing record to a recipe, setting forth the ingredients to use, the amounts to use, the tests to perform, and the instructions for preparing the quantity the recipe calls for.

C. Production and Process Controls

Production and process controls are the means by which the master manufacturing record is implemented. The Final Rule requires companies to establish, through written procedures, a specification for any point, step, or stage in the manufacturing, packaging, labeling, and holding process where control is necessary to ensure the quality of the dietary supplement. Companies must provide adequate documentation for why meeting these specifications will help ensure the quality of the dietary supplement, and then adequate documentation that all controls were implemented and

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5 If those dietary ingredients are subsequently only packaged, labeled, and sold to consumers as a dietary supplement without further processing, however, then the supplier of the dietary ingredients will be deemed a manufacturer of a dietary supplement and subject to the CGMP requirements.
specifications met. While not denominated a “hazard analysis and critical control point” (“HACCP”) requirement, it contains analogous elements.

D. Identity Verification of Components

The CGMPs require companies to verify the identity of all components used to manufacture dietary supplements. “Component” is defined as “any substance intended for use in the manufacture of a dietary supplement, including those that may not appear in the finished batch of the dietary supplement. Component includes dietary ingredients (as described in section 201(ff) of the act) and other ingredients.”

Because dietary ingredients are the central defining ingredients of a dietary supplement, the Final Rule requires each manufacturer to perform its own testing or examination to verify the identity of each dietary ingredient prior to use in the manufacturing process. The identity testing requirement applies to manufacturers who purchase dietary ingredients from a dietary ingredient supplier as well as to those who manufacture their own dietary ingredients. For components that are not dietary ingredients, a manufacturer may rely on a certificate of analysis from the supplier if certain criteria are met.

Concurrently with the publication of the Final Rule, FDA also published in the Federal Register an Interim Final Rule (“IFR”) establishing procedures for requesting an exemption from this 100 percent identity testing requirement for dietary ingredients, provided certain conditions are met and required records are maintained. Under the IFR, a dietary supplement manufacturer may petition FDA under 21 C.F.R. § 10.30 for an exemption to the 100 percent identity testing requirement based upon appropriate data and information establishing an alternative identity testing system that results in no material diminution of assurance compared to the 100 percent identity testing. The approval of such a petition will cover only those dietary ingredients and suppliers identified in the petition and/or approval. The IFR becomes effective and will be implemented with the Final Rule, but FDA seeks comment on its provisions. In addition, FDA intends to issue guidance on the information and type of data that should be included in an exemption petition.

E. Quality Control

In the Final Rule, FDA clarifies that the CGMPs do not require the creation of an independent quality control unit. Requirements are imposed upon “quality control personnel,” defined as “any person, persons, or group, within or outside of your organization, who you designate to be responsible for your quality control operations.” Quality control personnel essentially have ultimate oversight authority over CGMP compliance.

F. Product Complaints

The Final Rule requires that a “qualified person” must review all product complaints to determine whether the product complaint involves a possible failure of a dietary supplement to meet any of its specifications or other CGMP requirements, and if so, to investigate that complaint. Quality

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6 21 C.F.R. § 111.3.
8 21 C.F.R. § 111.3.
9 21 C.F.R. § 111.560.
control personnel must review and approve decisions about whether to investigate a product complaint and review and approve the findings and follow-up action of any investigation performed. These reviews and investigations must extend to all relevant batches and records. Product complaints that represent adverse events, covered by the Dietary Supplement and Non-Prescription Drug Consumer Protection Act, need to be analyzed, recorded, preserved, and made available for inspection in accordance with the provisions of that Act.

G. Recordkeeping and Records Access

The Final Rule requires companies to keep written records required by the Rule for one year past the shelf life date (if used), or two years beyond the date of distribution of the last batch of dietary supplements associated with those records. FDA clarifies that shelf life dating includes “best if used by” dating as well as expiration dating. Records may be kept as original records, true copies, or as electronic records if compliant with 21 C.F.R. Part 11. All records required by the Final Rule must be “readily available” during the retention period for inspection and copying by FDA “when requested.”

H. Other Provisions

The Final Rule also establishes CGMPs for: personnel, physical plant and grounds, equipment and utensils, laboratory operations, manufacturing operations, packaging and labeling operations, holding and distributing, and returned dietary supplements.

Notably, FDA deleted its highly troublesome proposed requirement that any claim that a non-dietary ingredient component is generally recognized as safe (“GRAS”) must be supported by a citation to the agency’s regulations or by an explanation for why there is general recognition of the safe use of the substance in a dietary ingredient or a dietary supplement. In the preamble to the proposed rule, FDA had stated that a company could not use the agency’s response to a GRAS notification as its basis for asserting compliance with this proposed requirement because an FDA response letter to a GRAS notification is not the same as a company’s explanation for why an ingredient is GRAS. Finalization of that proposed requirement would have substantially undermined the value of FDA’s current GRAS notification process.

II. Issues of Potential Concern or Meriting Careful Consideration

A. FDA Records Access Authority

1. Legal Authority for FDA’s Access to Dietary Supplement Records

Despite FDA’s historical and long-standing acknowledgement that it has only very limited records inspection authority for food (including dietary supplements), which would not extend to records access to confirm compliance with CGMP requirements generally, FDA has maintained that it does have authority to mandate agency access to CGMP records. FDA asserts that it is not relying on its factory inspection authority under Section 704 of the Federal Food, Drug, and Cosmetic Act (“FDCA”), which plainly does not extend to records inspection authority for food (including dietary supplement) facilities. Rather, FDA states that its records access authority derives from its authority to promulgate dietary supplement CGMPs at Section 402(g) and the general grant of agency authority to

See note 4, supra.

21 C.F.R. § 111.610.
promulgate regulations for the “efficient enforcement” of the FDCA at Section 701(a). The agency claims that records access is “imperative to the efficient enforcement of the dietary supplement CGMP final rule.”

This end-run around FDA’s lack of records inspection authority for food and dietary supplement facilities under section 704 is vulnerable to challenge, on a number of grounds. First, the history of the statutory provisions relating to records access and CGMPs for drugs and devices demonstrates that FDA’s authority to mandate CGMPs does not necessarily mean agency authority to access records. While FDA was given statutory CGMP authority in 1962 for all drugs, it was only given record inspection authority with respect to new drugs and prescription drugs. From 1962 until record inspection authority was expanded to over-the-counter (“OTC”) drugs in 1997, FDA had to determine OTC drug manufacturer compliance with drug CGMPs without authorized access to their records. In the case of devices, two statutory provisions – one dealing with CGMPs and the other with mandatory record keeping – were used by FDA to craft the device quality system regulation.

Second, FDA’s assertions that records access is needed to determine whether a dietary supplement is adulterated and to enable the agency to enforce the dietary supplement CGMPs are belied by FDA’s acknowledgement that other provisions of the FDCA guard against adulteration, and that the CGMPs are focused primarily upon ensuring the “quality” of dietary supplements. While “quality” does mean that a dietary supplement has been produced under conditions that are designed to prevent adulteration, strong arguments could be mustered against an agency need for CGMP records relating to “quality” in order to determine whether a dietary supplement is adulterated, since the agency presumably was able to determine whether a dietary supplement was adulterated prior to the promulgation of this Final Rule. Moreover, FDA will be entitled to the most “necessary” records – those relating to adverse event reports – under the Dietary Supplement and Non-Prescription Drug Consumer Protection Act, effective December 22, 2007.

Third, the Fourth Amendment offers a degree of protection against FDA’s assertion of records access authority here even though dietary supplement manufacturers are willing participants in a regulated industry, given the agency’s weak arguments for the “need” for records access. These issues are particularly sensitive because the records required to be created will undoubtedly include trade secrets and confidential commercial information. Agency vigilance will be required to ensure that no such protected information is released if documents FDA has copied are made available to the public under the Freedom of Information Act.

A related open question relates to the discoverability of the mandatory records in any litigation relating to a dietary supplement, and what privileges or protections may attach to those records.


The Final Rule provides only that required records be “readily available” during the retention period for inspection and copying by FDA “when requested.” The Rule does not clarify when FDA may request the records (i.e., only during regular business hours? only during the course of a facility inspection? only upon “credible evidence” that a dietary supplement may be adulterated?) or how quickly they must be produced in response to an FDA request in order to be compliant with this requirement.

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12 72 Fed. Reg. at 34785.
B. Potential Consequences of Recordkeeping Failures

Because Section 402(g)(1) of the FDCA provides that a dietary supplement shall be deemed adulterated if it has been prepared, packed, or held under conditions that do not meet CGMP regulations, this provision could be read to mean that violations of the recordkeeping requirements of the CGMPs render a dietary supplement adulterated even if the product itself is unblemished.

The consequences seem even more uncertain for violations of recordkeeping requirements relating only to specifications for ensuring that a manufacturer produces the product it intends to make. Would a failure to comply with recordkeeping requirements render the product labeling “unsubstantiated” and the product misbranded? Is there now an affirmative legal duty for a company to prove compliance with its own “recipe” and manufacturing plans on demand? If so, if a company’s records are deemed inadequate, may FDA act against the company even without evidence of a non-compliant product? What would be the burden of proof and with whom would it lie – is the company proving it followed its recipe or is the agency proving it did not?

C. Implications of Consumer Complaints

The requirements surrounding the need to investigate consumer complaints could be particularly sensitive. While reviews and investigations of such complaints must extend to all “relevant batches and records,” it may be difficult to determine with certainty which batches and records may be “relevant.” If an investigation follows procedures but does not catch other products or processes that might be implicated, questions could arise as to the integrity of the overall quality control system for a company. At the same time, a finding that a consumer complaint does relate to CGMPs could also raise questions about the adequacy of quality control. In sum, while the CGMPs require comprehensive procedures to be established, justified, and documented, following those procedures may not offer a “safe harbor” if any error ultimately occurs.

D. Comparison to Drug CGMPs

The dietary supplement CGMPs established by the Final Rule, given their detail and emphasis on controls over every element of production, bear a stronger resemblance to drug CGMPs than they do to the rather general food CGMPs, although the low-acid canned food and acidified food CGMPs are also detailed in the processing aspect of production. Nonetheless, the dietary supplement CGMPs still remain far less onerous than the drug CGMPs. A key difference is that the dietary supplement CGMPs do not require process validation, which is mandated by the drug CGMPs. Rather, the emphasis in the dietary supplement CGMPs is on documentation that relates back to the master batch record in terms of product composition and processing steps. For companies manufacturing both drugs and dietary supplements, if all operations are performed in accordance with the drug CGMPs, then the dietary supplement CGMPs would be satisfied for those products. Following the dietary supplement CGMPs for all operations, however, would not satisfy the CGMP requirements for drugs.

Covington & Burling LLP has extensive experience and expertise with all aspects of the regulation of dietary supplements and compliance with CGMP regulations for the full range of FDA-regulated products. We would be pleased to provide counsel for clients affected by or otherwise interested in the Final Rule.
This information is not intended as legal advice, which may often turn on specific facts. Readers should seek specific legal advice before acting with regard to the subjects mentioned herein.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our food & drug practice group:

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