CHAPTER 5: DIETARY SUPPLEMENTS

I. INTRODUCTION

Some in the dietary supplements industry see nanotechnology as a new, more effective method for delivering the benefits of dietary supplements. Others are concerned about the possibility of unintended impacts from ingestion of nanoscale materials. While this debate continues, the use of nanotechnology in dietary supplements increases. The Project on Emerging Nanotechnologies (PEN) has predicted that the dietary supplements industry is one of the biggest potential growth areas for nanotechnology. This chapter looks at the ways that the Food and Drug Administration (FDA) can use its existing authority to regulate nanomaterials in dietary supplements, and the ongoing debates over whether FDA needs new statutory authority to ensure the safety of dietary supplements containing nanomaterials.

II. BACKGROUND ON DIETARY SUPPLEMENTS

Dietary supplements are regulated under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended. A dietary supplement is defined in the FFDCA as a product that is intended to supplement the diet that contains one or more of the listed kinds of dietary ingredients, which include vitamins, minerals, herbs or botanicals, amino acids, or “a dietary substance for use by man to supplement the diet by increasing the total daily intake.” It also must either be labeled as a dietary supplement and must be intended for “ingestion in tablet, capsule, powder, softgel, gelcap, or liquid form,” or, if in another form, not be “represented [for use] as conventional food … or as a sole item of a meal or of the diet.” Topical applications are not considered dietary supplements.

The overlap of the “dietary supplement” category with other categories is somewhat complex. For most purposes, a dietary supplement is also deemed a food. Items approved as new drugs, licensed as biologics, or authorized for clinical investigations under an

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* This chapter was prepared by Sara Beth Watson, Steptoe & Johnson LLP.

1 For example, Health Synergy Group (HGS) markets dietary supplements which use its NanoSynergy™ Delivery System. HGS claims that its Spray for Life® Nano Multivitamin Spray “is the new generation of multivitamins that provides all its benefits plus the highest level of activity, penetration into tissues, organs and cells and metabolic availability never before achievable by any former known technology.” Multi Vitamin, HEALTH SYNERGY GROUP, http://www.sprayforlife.com/products/multivitamin.html.


Investigational New Drug Application (IND) cannot be marketed as dietary supplements, with one exception: if the product was previously marketed as a dietary supplement or food before the approval, licensing, or authorization under an IND, it may be marketed as a dietary supplement afterwards. Claims by a manufacturer that its dietary supplement product will cure, mitigate, treat, or prevent a disease causes the product to cease to be a dietary supplement and become a drug subject to pre-market FDA approval. Claims that a dietary supplement has a relationship to a disease or health-related condition, however, are classified as “health claims” and are subject to prior approval by FDA under the dietary supplement regulations. Claims that a dietary supplement can affect the structure or function of the body are subject to notification and substantiation requirements.

III. EXAMPLES OF DIETARY SUPPLEMENTS CONTAINING NANOMATERIALS

Nanotechnology offers dietary supplements the ability to provide, or at least promise, superior properties such as increased nutrient absorption or biological activity. Dietary supplements which claim to use nanotechnology range from vitamins to herbal extracts to weight-loss drinks. Health Synergy Group markets seven supplements under its Spray for Life® product line, all of which claim to use a NanoSynergy™ Delivery System. The Ma’at Shop sells Crystal Clear Nano Silver, a colloidal silver product claiming that as a result of nanotechnology, the danger of taking too much colloidal silver has been eliminated, since “[t]he silver particles are simply too small to get stuck in our glands and organs.” In all, while the uses of engineered nanoparticles in the dietary supplement market are not fully known, the Project on Emerging Nanotechnologies estimates that more than fifty supplements now on the market claim to contain nanoscale ingredients.

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9 See, e.g., Press Release, FDA, FTC and FDA Act Against Internet Vendors of Fraudulent Diabetes Cures and Treatments Measures are Part of Coordinated Effort by United States, Mexico and Canada (Oct. 19, 2006), available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108772 (Among other actions, FDA sent warning letters to 24 firms marketing dietary supplement products with claims to treat, cure, prevent or mitigate diabetes, with threat of further enforcement action, including seizure of the violative products and/or injunctions against the manufacturers and distributors, if violations are not corrected.)
11 FFDCA § 403(r)(6), 21 U.S.C. § 343(r)(6); 21 C.F.R. § 101.93.
13 DrunvaloMelchizedek, The Ma’at Shop, Crystal Clear Nano Silver, http://www.spiritofmaat.com/maatshop/n2_silver.htm. Colloidal silver is an “alternative medicine” claimed by its users to prevent a wide range of diseases, but can cause argyria (permanently blue-gray skin) and other effects if taken in large amounts.
IV. FDA Regulation of Dietary Supplements

A. Pre-Market Regulation of Dietary Supplements

FDA has no general authority to regulate the safety of dietary supplements prior to their introduction to the market. It lacks the authority to review, approve or require testing of, dietary supplements. However, there is one area in which FDA does have pre-market review authority: new dietary ingredients.

Section 413 of the FFDCA defines a “new dietary ingredient” as one not marketed in the United States before October 15, 1994. A dietary supplement which contains a new dietary ingredient “shall be deemed adulterated” unless it meets the requirements of either Section 413(a)(1) or 413(a)(2). Under Section 413(a)(1), a dietary supplement containing a new dietary ingredient is not adulterated if it “contains only dietary ingredients which have been present in the food supply as an article used for food in a form in which the food has not been chemically altered.” If it cannot meet the stringent requirements of Section 413(a)(1), it is deemed adulterated unless it meets the requirements of 413(a)(2).

Section 413(a)(2) has two requirements. First, for the new dietary ingredient, there must be a “history of use or other evidence of safety establishing that the dietary ingredient when used under the conditions recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe.” Second, at least 75 days before marketing the dietary supplement containing the new dietary ingredient, the manufacturer must provide FDA with a new dietary ingredient notification (NDIN) containing “information, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe.” The FFDCA defines “safe” with respect to dietary supplements as not presenting “a
significant or unreasonable risk of illness or injury under—(i) conditions of use recommended or suggested in labeling, or (ii) . . . under ordinary conditions of use.”

Under Section 413(a)(2), the manufacturer is required to present FDA with information which supports the manufacturer’s conclusion that the dietary supplement containing the new dietary ingredient will reasonably be expected to be safe. If a dietary supplement contains a new dietary ingredient and does not meet the requirements of Section 413(a)(1), a manufacturer’s failure to present the information required by Section 413(a)(2), or a finding by FDA that the information submitted is insufficient to establish that the supplement is reasonably expected to be safe, makes the product adulterated. In other words, Section 413(a)(2) places the information burden on the manufacturer, and not on the FDA.

Section 413(a)(2) does not require FDA to take any action in response to a submission. In particular, Section 413(a)(2) does not require FDA to make a finding that a new dietary ingredient for which a notification has been submitted is safe; accordingly, after 75 days, a submitter is free to introduce a dietary supplement containing the new dietary ingredient into commerce. An FDA regulation declares that FDA’s failure to respond, or a statement that it has no further questions, does not constitute a finding by FDA that the new dietary ingredient is safe or that the dietary supplement of which it is a part is not adulterated. On the other hand, FDA guidance indicates that after its review of a new dietary ingredient notification, FDA may notify the submitter that “the information in the notification is inadequate to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.” FDA has used its Section 413 authority to review the information submitted for new dietary ingredients, and has often rejected notifications after finding that the supporting

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22 The FDA Food Safety Modernization Act of 2011, Pub. L. No. 111-353, 124 Stat. 3920 (2011) (FSMA), does require FDA to notify the Drug Enforcement Administration if it determines that a dietary supplement containing a purported new dietary ingredient is unsafe because it may be, or may contain, an anabolic steroid. FSMA § 113, adding a new FFDCA § 413(c), 21 U.S.C. § 350b(c).
24 21 C.F.R. § 190.6(f).
26 FDA receives an average of 71 notifications under Section 413 annually. 73 Fed. Reg. 34,940, 34,941 (June 19, 2008).
studies were inadequate to support a conclusion that the new ingredient will reasonably be expected to be safe. 27

B. LABELING REQUIREMENTS FOR DIETARY SUPPLEMENTS

The basic labeling requirement for dietary supplements is that they must be labeled as “dietary supplements.” 28 Other provisions of the FFDCA govern how dietary supplement labels must list nutritional information and ingredients. 29

In addition, the FFDCA regulates the health claims that can be made with regard to dietary supplements. A claim that a dietary supplement reduces the risk of a disease or health-related condition requires a pre-market petition to and approval from FDA. 30 FDA may take enforcement action against companies making such claims for dietary supplements if FDA becomes aware of the claim. 31

Separate provisions of the FFDCA govern health claims concerning the structure or function of the body, claims of general well-being, and claims of a benefit relating to a classical nutrient deficiency. 32 Dietary supplement manufacturers must notify FDA within 30 days after marketing a product with one or more of these claimed effects. 33 However, once FDA receives notification of the health claim, FDA does not review the claim to determine whether it is supported by scientific evidence. Dietary supplement labels with such health claims must also have a disclaimer that FDA has not evaluated the claims and that the supplement is not intended to “diagnose, treat, cure or prevent any disease.”

C. POST-MARKETING REGULATION OF DIETARY SUPPLEMENTS

Under the FFDCA, FDA has various tools for regulating dietary supplements after they reach the market. FDA can inspect dietary supplement manufacturing facilities. 34 It is

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29 FFDCA §§ 403(q)(5)(F), 403(s), 21 U.S.C. §§ 343(q)(5)(F), 343(s).
30 FFDCA § 403(r)(3), 21 U.S.C. § 343(r)(3); 21 C.F.R. §§ 101.14, 101.70. For an example of an authorized health claim that a nutrient reduces the risk of a condition, see 21 C.F.R. § 101.79 (authorizing claims that “diets adequate in folate may reduce the risk of neural tube defects”).
31 See, e.g., Letter from Jennifer Thomas, Director, Division of Enforcement, Office of Compliance, Center for Food Safety and Applied Nutrition, to Emy San, All Nature Pharmaceuticals, Inc. (Apr. 8, 2009), available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/UCM213832.pdf (warning the company that FDA review of the company website revealed therapeutic claims making the product a drug subject to pre-market approval and the claim a violation of the FFDCA).
33 FFDCA § 403(r)(6), 21 U.S.C. § 343(r)(6); see also 21 C.F.R. § 101.93.
authorized to take action against companies producing adulterated or misbranded dietary supplements. Except for the new dietary ingredient adulteration provisions described above, when taking action against a dietary supplement for adulteration, FDA bears the burden of proof to establish that the product “presents a significant or unreasonable risk of illness or injury.”

FDA has adopted a final rule establishing current Good Manufacturing Practice Requirements (cGMPs) for dietary supplements. Under these cGMPs, before using any component in their dietary supplements, manufacturers must “[c]onduct at least one appropriate test or examination to verify the identity of any component that is a dietary ingredient” unless exempted from doing so. This final rule establishes other quality control measures that manufacturers must follow before marketing dietary supplements.

In addition, manufacturers, packers, and distributors must notify FDA of any serious adverse events associated with their dietary supplements that are reported to them. Dietary supplement firms must keep records of all adverse event reports, both serious and non-serious, and provide FDA access to these records during inspections.

V. Applying Existing Regulations to Dietary Supplements Containing Nanomaterials

A. New Dietary Ingredients

1. New Dietary Ingredient Notification for a Nanomaterial

A manufacturer of dietary supplements known to have notified FDA of its use of a nanoscale material as a new dietary ingredient is Nano Port (USA) Inc. Nano Port submitted information to FDA that it intended to market dietary supplements containing Nano Red Elemental Selenium (under the trade name Nano-Se). Nano Port claimed that the size of selenium in Nano-Se was between 20 and 60 nanometers, and that the selenium exhibited “different biological properties” compared to non-nanoscale selenium.

38 Id. § 111.75(a)(1)(i)-(ii).
41 FFDCA § 761(e), 21 U.S.C. § 379aa-1(e).
42 Letter from Yu Har Fei, President, Nano Port (USA) Inc., to Division of Standards and Labeling Regulations, FDA (May 20, 2003), available at http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0196-01-vol144.pdf.
43 Id.
FDA’s responses stated that Nano Port’s submission did not “provide an adequate basis to conclude that Nano Red Elemental Selenium (Nano-Se), when used under the condition recommended or suggested in the labeling of your product, will reasonably be expected to be safe.”\textsuperscript{44} FDA based its conclusion on two main deficiencies in Nano Port’s submission: first, Nano Port failed to provide adequate information on the chemical identity of Nano-Se; second, Nano Port’s health and safety studies did not use Nano-Se as the test substance.\textsuperscript{45}

Nano Port then submitted additional information to FDA.\textsuperscript{46} In response, FDA noted that Nano Port had not provided any additional information on the chemical identity of Nano-Se, including how Nano-Se was manufactured.\textsuperscript{47} Likewise, Nano Port had not included health and safety studies which used Nano-Se as the test substance, as FDA had requested. As a result, FDA once again concluded that Nano Port’s submission did not “provide an adequate basis to conclude that Nano Red Elemental Selenium (Nano-Se), when used under the condition recommended or suggested in the labeling of your product, will reasonably be expected to be safe.”\textsuperscript{48}

It is worth noting that FDA has often concluded that manufacturers of dietary supplements which do not contain nanoscale ingredients have failed to provide adequate information to establish that the product will reasonably be expected to be safe. Moreover, FDA often bases its conclusion on the same concerns that it expressed in the letters to Nano Port.\textsuperscript{49}

2. \textit{Determining Whether a Nanoscale Dietary Ingredient is “New”}

The application of the reasonable expectation of safety standard to NDINs for nanoscale dietary ingredients, as in the case of Nano-Se, is only a concern when manufacturers of dietary supplements containing nanomaterials actually submit NDINs. There is a larger debate,

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\item \textsuperscript{44} Letter from Susan J. Walker, Acting Division Director, Division of Dietary Supplement Programs, FDA, to Yu Har Fei, President, Nano Port (USA) Inc. (Aug. 19, 2003), \url{available at http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0196-01-vol144.pdf}; Letter from Susan J. Walker, Acting Division Director, Division of Dietary Supplement Programs, FDA, to Yu Har Fei, President, Nano Port (USA) Inc. (May 7, 2004) at 2, \url{available at http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0234-02-Fei-vol166.pdf}.
\item \textsuperscript{45} Letter from FDA to Yu Har Fei (Aug. 19, 2003), \textit{supra} note 44.
\item \textsuperscript{46} Letter from Yu Har Fei, President, Nano Port (USA) Inc., to Division of Standards and Labeling Regulations, FDA (Feb. 9, 2004), \url{available at http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0234-03-NanoPort-vol166.pdf}.
\item \textsuperscript{47} Letter from FDA to Yu Har Fei (May 7, 2004), \textit{supra} note 44, at 2.
\item \textsuperscript{48} Id.
\item \textsuperscript{49} See, \textit{e.g.}, letter from Linda S. Pellicore, Senior Toxicologist, Division of Dietary Supplement Programs, FDA, to Mark L. Dreher, Vice President, Pom Wonderful, LLC (July 7, 2006), \url{available at www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0349-01-vol270.pdf} (concluding that the company Pom Wonderful had failed to provide sufficient information on the chemical identity and safety of a proposed new dietary ingredient, Pom:, a pomegranate fruit polyphenol extract); letter from Linda S. Pellicore, Senior Toxicologist, Division of Dietary Supplement Programs, FDA, to Robert McKay, Vice President, Seppic, Inc. (July 20, 2006), \url{available at www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0353-vol270.pdf} (stating that the submission for the proposed new dietary ingredient Extramel did not provide a description of how the ingredient was manufactured, and did not supply information establishing the safety of Extramel).
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However, regarding whether nanoscale dietary ingredients must be subject to that requirement. Several commentators have recommended that FDA explore the option of declaring nanoscale versions of ingredients to be new dietary ingredients.\textsuperscript{50} Some have gone a step further and have urged FDA to use its Section 413 authority to regulate all nanomaterials in dietary supplements as new dietary ingredients.\textsuperscript{51}

This argument is based on the view, acknowledged by FDA, that a nanoscale version of a substance can have very different properties than macroscale substance of identical chemical composition.\textsuperscript{52} Nanomaterials have a much higher surface area to mass ratio than non-nanoscale materials; this increased surface area can lead to greater chemical reactivity.\textsuperscript{3} The shape of nanoparticles may differ from non-nanoscale particles, and the shape alone may influence toxicity. Furthermore, particle size can influence the absorption and transport of substances in the body. This is not an exhaustive list of the ways in which nanoscale particles may have novel properties, but rather is intended to illustrate the scientific basis for asserting that a nanoscale version of an ingredient should be treated as a new dietary ingredient.

These commenters have asked under what circumstances FDA will consider a nanotechnology-based dietary ingredient to be a “new dietary ingredient” under the FFDCA. FFDCA Section 413 defines a new dietary ingredient as an ingredient that has not been marketed in the United States prior to October 15, 1994.\textsuperscript{53} One can argue that nanoscale dietary ingredients were not marketed prior to that date, and accordingly all nanoscale dietary ingredients are new dietary ingredients.

On the other hand, one could argue that if a macroscale dietary ingredient was marketed prior to that date, a nanoscale version of that ingredient would not be a new dietary ingredient. In what amounts to the same thing, one could also argue that a new nanoscale dietary ingredient is not subject to the Section 413(a)(2) requirement to submit safety information to FDA as it meets the provisions of Section 413(a)(1): “The dietary supplement contains only dietary ingredients which have been present in the food supply as an article used for food in a form in

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\textsuperscript{51} See, e.g., FRIENDS OF THE EARTH, supra note 14, at 3 (“All deliberately manufactured nanomaterials must be subject to new safety assessments as new substances, even where the properties of their larger scale counterparts are well-known.”).
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\textsuperscript{53} FFDCA § 413(c), 21 U.S.C. § 350b(d).
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which the food has not been chemically altered.” 54 Under this argument, if a nanoscale substance has the same chemical composition as a macroscale substance which has been part of the food supply, then the nanoscale substance is not subject to the NDIN requirement.

Legislative history supports the view that a chemical change, but not a physical change, in food makes the new dietary ingredient subject to the safety information submission requirement. The legislative history of the Act which added the new dietary ingredients provision 55 states that “the term ‘chemically altered’ does not include the following physical modifications: minor loss of volatile components, dehydration, lyophilization, milling, tincture or solution in water, slurry, powder, or solid in suspension.” 56 If a food ingredient which has been milled down to the nanoscale has not been “chemically altered,” arguably it is not subject to the submission requirement. On the other hand, some nanoscale new dietary ingredients are likely to be chemically different from macroscale materials used in food; these would presumably be subject to the NDIN requirement.

Currently, nearly all manufacturers of dietary supplements made using nanomaterials appear to take the position that nanoscale versions of existing food ingredients are not new dietary ingredients. 57 In July 2011, FDA issued guidance calling for an evidence-based inquiry as to whether a nanoscale dietary ingredient is new, in light of an Obama Administration principle that “[n]anomaterials should not be deemed or identified as intrinsically benign or harmful in the absence of supporting scientific evidence, and regulatory action should be based on such scientific evidence,” 58 and its own implementing position that it “does not categorically judge all products containing nanomaterials or otherwise involving application of nanotechnology as intrinsically benign or harmful.” 59 The guidance advised companies to contact FDA prior to submitting an NDIN for a nanomaterial or product that involves the application of nanotechnology, since “there is little scientific literature discussing the safety of nanomaterials in dietary supplements.” 60 It focused on whether a change in particle size to the nanoscale would alter chemical properties; if so, then the dietary ingredient would be considered to be chemically altered. 61 This will involve a case-by-case analysis. This guidance responds to a 2009 report by the Government Accountability Office that found that FDA should prepare guidance on what kinds or degrees of changes to grandfathered ingredients trigger NDIN.

55 The new dietary ingredients provision in FFDCA § 413, 21 U.S.C. § 350b, was added by Section 8 of DSHEA. For a discussion of the legislative history of DSHEA, see supra note 23.
60 See NEW DIETARY INGREDIENT GUIDANCE, supra note 25, § VI.
61 Id., § IV.
requirements. In addition, the FDA Nanotechnology Task Force recommended that FDA issue guidance as to whether, and when, a nanoscale version of an existing ingredient would be considered a new dietary ingredient.

B. LABELING

While the health claims and disclaimer rules for dietary supplements apply to dietary supplements containing nanomaterials, as in other areas, controversies have arisen regarding whether companies should be required to alert consumers to the presence of nanomaterials in their products. Some advocacy groups stress that without mandatory labeling to indicate the presence of nanomaterials in foods and dietary supplements, “there is no way for anyone to choose to eat nano-free.” Under the FFDCA, dietary supplement labels are required to list ingredients by their common names and to not be false or misleading, lest they be deemed misbranded. However, FDA has not declared that the presence of nanomaterials is a material fact, the absence of which on a label would render the label misleading.

C. POST-MARKET REGULATION

Post-market regulation of dietary supplements can be applied to dietary supplements containing nanomaterials products in a relatively straightforward way. Inspections of facilities are authorized. The rules regarding good manufacturing practices may benefit from modification, in part, to reflect changes in the manufacture of supplements containing nanomaterials. However, FDA already possesses the necessary statutory authority to adapt its cGMP rules to the manufacture of dietary supplements containing nanomaterials. Likewise, the requirement to keep records of, and report to FDA, serious adverse events should apply to dietary supplements containing nanomaterials, though some commenters advocate expanding FDA’s authority to include mandatory reporting of adverse events that do not qualify under the current standards as “serious.”

VI. REGULATION OF DIETARY SUPPLEMENTS IN THE EUROPEAN UNION

To gain perspective on the regulation of dietary supplements containing nanomaterials in the United States, it is helpful to examine the regulatory framework in the European Union (EU). The basic regulatory approach to dietary supplements, or food supplements, as they are termed in the EU, is to maintain a “positive list.” The European Commission has asked agencies to


63 FDA NANOTECHNOLOGY TASK FORCE REPORT, supra note 52, at 34.

64 FRIENDS OF THE EARTH, supra note 14, at 3.

65 See, e.g., SCHULTZ & BARCLAY, PEN, supra note 14, at 24.

provide scientific opinions on the risks of nanomaterials in food.\textsuperscript{67} These opinions have emphasized that much remains unknown about the health risks of nanomaterials, and that the toxicity of nanoscale materials generally cannot be inferred from the toxicity of macroscale materials of identical chemical composition.\textsuperscript{68} Having assessed current legislation that could regulate nanotechnology, the Commission concluded that “[c]urrent legislation covers in principle the potential health, safety and environmental risks in relation to nanomaterials.” The Commission recommended regulating nanotechnology by improved implementation of existing laws; the Commission did not suggest the need for new nano-specific legislation.\textsuperscript{69} 

Before a food supplement can be marketed in the EU, the supplement ingredients must appear on a positive list of approved ingredients.\textsuperscript{70} The EU has a separate regulatory scheme for “novel foods.” The current Novel Foods Regulation requires pre-market testing and approval of all foods defined as novel.\textsuperscript{71} The EU tried for three years to pass a new novel foods legislation that would set a legal definition for “nanomaterials” and require food using such materials to be labeled as such. Other issues led to a collapse of negotiations in March 2011.\textsuperscript{72} However, parts of the legislation were salvaged and implemented into the Food Information Regulation, published in the Official Journal in October 2011.\textsuperscript{73} The regulation provides a transition period


\textsuperscript{69} \textit{Commission Directive 2002/46/EC, supra note 66, Art. 4(8).}


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with the first requirements applicable in 2014. The Food Information Regulation establishes information requirements for food, also covering food supplements as per the definition of “food” under the EU Food Law Regulation. 74 The Food Information Regulation establishes labeling requirements for all food ingredients, including engineered nanomaterials. “Engineered nanomaterials” are defined as any intentionally produced material that has one or more dimensions of the order of 100 nm or less or that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale. 75 All ingredients in the form of engineered nanomaterials must be clearly indicated on the ingredients list by listing the ingredient name followed by the word “nano” in brackets. 76 However, section 3 on “nutrition declaration” requirements specifically excludes food supplements. 77 This is a developing area of EU regulation.

VII. CALLS FOR EXPANDED REGULATION OF DIETARY SUPPLEMENTS CONTAINING NANOMATERIALS

In addition to urging FDA to use its existing authority to better regulate nanotechnology, some commentators have proposed that the FFDCA be amended to provide FDA with greater regulatory power over dietary supplements containing nanomaterials. These recommendations to amend the FFDCA fall into three main categories: pre-market approval of dietary supplements containing nanomaterials; mandatory labeling of dietary supplements containing nanomaterials; and increased reporting of health data to FDA and consumers.

A. PROPOSALS TO GIVE FDA PRE-MARKET APPROVAL AUTHORITY

According to some commentators, FDA does not possess adequate legal authority to regulate nanoscale ingredients in dietary supplements. To remedy this problem, they have proposed amending the FFDCA to require FDA to approve dietary supplements containing nanomaterials before they could be marketed. 78 Under this view, new risk assessments should be done for all dietary supplements containing nanomaterials, even if the macroscale version of the dietary ingredient is deemed safe. 79 For example, a 2009 report by the Project on Emerging Nanotechnologies recommended that Congress provide FDA with authority to require manufacturers of dietary supplements containing nanomaterials to conduct studies demonstrating

75 Regulation 1169/2011, supra note 73, at 26 (Art. 2(t)).
76 Id. at Art. 18(3).
77 Id. at Art. 29(1)(a).
79 See, e.g., FRIENDS OF THE EARTH, supra note 14, at 3.
the products’ safety prior to FDA’s approving the products for sale. These proposals would represent a significant departure from the existing regulation of dietary supplements and be more akin to the way that FDA currently regulates drugs. These proposals have not gained widespread support to date. FDA’s Nanotechnology Task Force Report does not include a recommendation that FDA seek statutory authority to conduct pre-market safety assessments of dietary supplements containing nanomaterials.

### B. PROPOSALS TO REQUIRE MANDATORY LABELING OF DIETARY SUPPLEMENTS CONTAINING NANOMATERIALS

In echoes of the debates over genetically modified food, some consumer advocates have called for mandatory labeling of products, including dietary supplements, which contain nanomaterials. They believe that without mandatory labeling of products containing nanomaterials, consumers cannot make informed choices. FDA has not been sympathetic to this argument. The Nanotechnology Task Force stated that it “does not believe there is a basis for saying that, as a general matter, a product containing nanoscale materials must be labeled as such. Therefore the Task Force is not recommending that the agency require such labeling at this time.” The Report’s recommendations, including the recommendation for labeling, were endorsed by the Commissioner of the FDA.

Trade groups have opposed calls for mandatory labeling of products containing nanomaterials. For example, the Food Products Association (FPA) and Grocery Manufacturers Association (GMA) have stated that FDA should use its approach to biotechnology as a model for handling nanotechnology; just as food products using biotechnology are not required to be labeled as containing genetically modified ingredients, so too, food products containing nanomaterials should not have to be labeled as such. On the other hand, presumably for commercial reasons, some manufacturers and retailers have prominently stated that their dietary supplements contain nanomaterials; indeed, the names of some dietary supplements include the word “nano.”

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80 SCHULTZ & BARCLAY, PEN, supra note 14, at 24. Under this proposal, FDA would have the authority to “waive pre-market review of safety data for specific classes of dietary supplements containing engineered nanoparticles where it finds that such a waiver is consistent with the protection of public health.” Id.

81 See, e.g., Consumers Union Comment, supra note 79, at 10.

82 See id. A 2009 report issued by the Project on Emerging Nanotechnologies does not call for mandatory labeling of dietary supplements containing nanomaterials, but does recommend that Congress give FDA the authority to require the registration of all dietary supplements containing engineered nanoparticles. See SCHULTZ & BARCLAY, PEN, supra note 14, at 24.

83 FDA NANTECHNOLOGY TASK FORCE REPORT, supra note 52, at 35.


85 Comments from Craig Henry, Senior Vice President, FPA, & Mary Sophos, Senior Vice President, GMA, on FDA Docket No. 2006N-0107, FDA-Regulated Products Containing Nanotechnology Materials at 5 (Nov. 9, 2006), available at http://www.fda.gov/ohrms/dockets/dockets/06n0107/06N-0107-EC25-Attach-1.pdf.
C. PROPOSALS TO INCREASE THE INFORMATION PROVIDED TO FDA ON DIETARY SUPPLEMENTS CONTAINING NANOMATERIALS

Under the FFDCA, the manufacturer of a dietary supplement containing nanomaterials has no legal obligation to notify FDA that its product contains nanomaterials, or to provide FDA with any studies on the health effects of its dietary supplement, provided that the nanomaterials are not deemed new dietary ingredients under Section 413 and do not make a health claim. However, if a manufacturer of a dietary supplement containing nanomaterials sought to make a health claim requiring a pre-market petition, FDA’s review of the petition would likely uncover the presence of nanomaterials in the product (if they were not already disclosed by the manufacturer).

Some commentators have expressed concern that FDA is not receiving the data necessary to evaluate the safety of nanomaterials in dietary supplements. The proposals for remedying this perceived information gap tend to be part of proposals for pre-market safety assessments and mandatory labeling. According to this argument, if FDA had legislative authority to perform pre-market safety assessments of dietary supplements containing nanomaterials, it would then have the authority to require health information on nanomaterials in dietary supplements. Additionally, a report by the Project on Emerging Nanotechnologies has recommended increasing the information provided to FDA on dietary supplements containing nanomaterials by proposing that Congress expand the adverse reporting requirement to include all adverse events, not just serious adverse events.

VIII. CONCLUSION

FDA has limited authority over dietary supplements, particularly those that do not make health claims. The pre-market review authority for new dietary ingredients is potentially relevant for nanoscale dietary ingredients, but its use in practice is likely to depend on FDA providing guidance on whether it considers nanoscale versions of macroscale dietary ingredients to be “new” for purposes of that authority.

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86 Claims that a product reduces the risk of a disease or health-related condition requires a pre-market petition to the FDA. See supra notes 9-11, 30-33, and accompanying text.
87 DAVIES, supra note 79, at 15, 22; Consumers Union Comment, supra note 78, at 3, 9; FRIENDS OF THE EARTH, supra note 14, at 3, 46; SCHULTZ & BARCLAY, PEN, supra note 14, at 24.
88 SCHULTZ & BARCLAY, PEN, supra note 14, at 24.