

WHITE PAPER

FDA Statutory Authority To Regulate The Safety Of Dietary Supplements

Prepared by:

Peter Barton Hutt

Covington & Burling LLP

Legal Counsel for the Council for Responsible Nutrition

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Introduction

For almost a century, the Food and Drug Administration (FDA) has regulated nutrients and other dietary supplement ingredients and products¹ under the food provisions initially of the Federal Food and Drugs Act of 1906² and now of the Federal Food, Drug, and Cosmetic Act of 1938³ (FD&C Act), as amended. Congress amended the FD&C Act through the Food Additives Amendment of 1958⁴ and the Color Additive Amendments of 1960⁵ to strengthen the FDA authority over food ingredient safety. In 1976, Congress enacted the Vitamin-Mineral Amendments⁶ to provide that FDA may limit the contents of dietary supplements only for safety reasons.

In 1994, Congress enacted the Dietary Supplement Health and Education Act (DSHEA)⁷ to continue the regulation of dietary supplements under the food provisions of the FD&C Act but to replace the food additive provisions with separate safety requirements for dietary ingredients. In 2002, Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act⁸ to provide additional authority to assure the safety of the food supply. In 2006, Congress enacted the Dietary Supplement and Nonprescription Drug Consumer Protection Act⁹ to require mandatory adverse event reporting systems for dietary supplements. In 2007, Congress enacted the Food and Drug

¹ This White Paper reviews the safety provisions applicable to dietary supplements but does not consider the labeling provisions for these products.

² 34 Stat. 768 (1906).

³ 52 Stat. 1040 (1938), 21 U.S.C. 301 et seq.

⁴ 72 Stat. 1784 (1958).

⁵ 74 Stat. 397 (1960).

⁶ 90 Stat. 401, 410 (1976).

⁷ 108 Stat. 4325 (1994).

⁸ 116 Stat. 594, 662 (2002).

⁹ 120 Stat. 3469 (2006).

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Administration Amendments Act of 2007 (FDAAA)¹⁰ to prohibit the addition of drugs or biologics to food and to authorize the creation of a “reportable food registry” to collect information about articles of food that may pose serious health risks. Most recently, Congress enacted the FDA Food Safety Modernization Act of 2011 (FSMA)¹¹ to improve FDA’s capacity to prevent, detect, and respond to food safety problems.

This White Paper summarizes the safety requirements applicable to dietary supplements under the FD&C Act, as amended, describes the safety requirements applicable to conventional food, and compares these two overlapping regulatory programs.

Executive Summary

Nutrients and other ingredients intended to supplement the daily diet—whether added to a dietary supplement or to a conventional food product—have been regulated by FDA under the food provisions of the 1906 and 1938 Acts for almost a century. The same regulatory requirements have been applied by FDA to these nutrients and related ingredients in whatever type of product they are used. These products have been regulated as drugs only where the labeling or the advertising has specifically represented them for therapeutic use.

It is widely and erroneously believed that DSHEA eviscerated the FD&C Act safety requirements for dietary supplements. In fact, DSHEA did not alter the basic food safety provision in the FD&C Act that has prohibited any poisonous or deleterious substance in food since 1906. For both old (pre-1994) and new dietary ingredients, DSHEA prohibits any significant or unreasonable risk of injury, authorizes an immediate ban of an imminent hazard, and authorizes FDA to impose requirements for good manufacturing practices (GMP). DSHEA excludes new dietary ingredients from the food additive provisions of the FD&C Act, but requires that all new dietary ingredients be the subject of a premarket

¹⁰ 121 Stat. 823 (2007).

¹¹ 124 Stat. 3885 (2011).

notification submitted to FDA with adequate safety information at least seventy-five days before marketing, unless the ingredient has been present in the food supply as an article used for food and in a form in which the food has not been chemically altered. All of the FD&C Act enforcement provisions apply to both old and new dietary ingredients and dietary supplements.

DSHEA contains three procedural provisions that are applicable only to dietary supplements. First, the burden of proof in a civil enforcement action relating to the safety of a dietary supplement is specifically placed on FDA. This is the same rule that applies in litigated court cases involving conventional food adulteration. Second, the court must decide the issue of adulteration of a dietary supplement on a de novo basis. This is the standard rule in any case where FDA institutes litigation against a product or company. As interpreted by the courts, it applies only in an enforcement action and not where a company challenges an FDA regulation, and thus does not change current law. Third, FDA must provide a person an opportunity to present both oral and written views at least ten days before a matter is referred to the Department of Justice for civil court enforcement. This is a new provision, applicable only to dietary supplements, but because of a Supreme Court precedent it is questionable whether it is enforceable. Since they were enacted in 1994, these three procedural provisions have very rarely been invoked in FDA regulatory action, and have had no significant effect.

Conventional food is subject to the same prohibition of poisonous or deleterious substances that applies to dietary supplements, but is not subject to the prohibition of significant or unreasonable risk of illness or injury, or to the immediate ban of an imminent hazard, or to the explicit statutory requirement for compliance with GMP. Conventional food ingredients are subject to the requirements of the Food Additives Amendment of 1958 rather than to the premarket notification requirements applicable to new dietary ingredients. A new conventional food ingredient may therefore be marketed solely on the basis of a manufacturer's own determination that the ingredient is generally recognized as safe (GRAS), and this is in fact the primary basis on which new conventional

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food ingredients are marketed. There is no requirement that FDA be notified or that FDA agree with the GRAS determination. If FDA disagrees, it must bring legal action in the courts and will have the burden of proving that the ingredient is not GRAS.

Thus, DSHEA requires premarket notification for all new dietary ingredients except those that are derived unchanged from food, whereas FDA is not informed about new conventional food ingredients that the manufacturer determines are GRAS. The failure to submit a premarket notification renders the dietary ingredient unlawful. A new dietary ingredient for which there is inadequate information to provide reasonable assurance that it does not present a significant or unreasonable risk of illness or injury is also illegal. If FDA were to make such a determination in response to a premarket notification and the company nonetheless marketed the ingredient, FDA would have the authority to bring legal action in the courts and would have the burden of proof of demonstrating inadequate information. Accordingly, the requirements for initial marketing of a new ingredient are more rigorous for dietary ingredients than for conventional food ingredients.

As the chart attached to the end of this White Paper demonstrates, on balance the FD&C Act, as amended by DSHEA and the Dietary Supplement and Nonprescription Drug Consumer Protection Act, provides somewhat greater FDA regulatory authority over dietary supplements than over conventional food. DSHEA provides greater FDA scrutiny of new dietary ingredients than exists for new conventional food ingredients and adds new safety enforcement authority for all dietary supplements that extends beyond the FDA authority applicable to conventional food. DSHEA adds three additional procedural safeguards for dietary supplement court actions to assure that FDA will act fairly and equitably in its enforcement of safety requirements, but does not substantially change the requirements applicable to court actions involving conventional food. The Dietary Supplement and Nonprescription Drug Consumer Protection Act expands FDA's regulatory authority over dietary supplements by adding postmarket reporting and recordkeeping requirements that are more stringent than those that

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apply to conventional food. Thus, in many ways, the current food safety provisions of the FD&C Act provide FDA with greater substantive authority over dietary supplements than they provide for conventional food, and the modest procedural changes in the court enforcement requirements have had no impact thus far and are unlikely to have a significant impact in the future.

I. Regulation of Dietary Supplements Under the Food Provisions of the FD&C Act

Both the 1906 Act and the 1938 Act define the term “food” broadly to include all articles “used for” food.¹² The term “drug” is defined to include all articles “intended” for the prevention or treatment of disease and, under the 1938 Act, articles (other than food) intended to affect the structure or any function of the human body.¹³

From their origin in the 1920s, dietary supplements were comprised of nutrients or other common food constituents.¹⁴ Cod liver oil—consumed for its vitamin A and vitamin D content—was perhaps the first dietary supplement. As scientists identified and characterized more nutrients, the medical profession urged the food industry to incorporate them into the food supply in order to reduce or eliminate common nutrient deficiencies.¹⁵ Thus, these nutrients were incorporated into the food supply in three ways: (1) as natural constituents of raw agricultural commodities commonly used in the food supply, (2) as separate ingredients added to a processed food, and (3) as separate ingredients added to a dietary supplement.

To the extent that these products were represented in labeling for medicinal purposes, they were regulated as drugs. Indeed, FDA has since the 1940s regulated all parenteral nutrients as prescription drugs¹⁶ and regulated nutrients and any other dietary supplements as drugs if they are labeled for therapeutic use.¹⁷ When represented solely to supplement the daily diet, however, dietary supplements have always been regulated under the FD&C Act as food.¹⁸

¹² 34 Stat. 768, 769 (1906); Section 201(f)(1) of the FD&C Act, 21 U.S.C. 321(f)(1).

¹³ 34 Stat. 768, 769 (1906); Sections 201(g)(1)(B) and (C), 21 U.S.C. 321(g)(1)(B) and (C).

¹⁴ For a more extensive review of the development and FDA regulation of dietary supplements, see Peter Barton Hutt, *Government Regulation of Health Claims in Food Labeling and Advertising*, 41 Food Drug Cosmetic Law Journal 3 (1986).

¹⁵ Peter Barton Hutt, Richard A. Merrill, and Lewis A. Grossman, *Food and Drug Law: Cases and Materials* 198-200 (3d ed. 2007).

¹⁶ TC2-A (November 5, 1945).

¹⁷ E.g., 44 Fed. Reg. 16126 (March 16, 1979).

¹⁸ The last sentence in the definition of a dietary supplement preserves this distinction by providing that a dietary supplement “shall be deemed to be a food” except when it is intended for drug use. Section 201(ff) of the FD&C Act, 21 U.S.C. 321(ff).

Recognizing the unique characteristics of dietary supplements, Congress included in the 1938 Act new authority for FDA to regulate the labeling of food “for special dietary uses.”¹⁹ This provision was intended by Congress to encompass nutrients and dietary supplements, and in fact FDA used this provision to regulate the labeling of nutrients added to both dietary supplements and to the general food supply for many years.

In 1976, Congress took a further step by defining the term “special dietary use” in the FD&C Act.²⁰ Then in 1994, Congress took the final step by defining the term “dietary supplement” in the FD&C Act²¹ and differentiating some—but not all—of the regulatory requirements applicable to dietary supplements from those applicable to conventional food.²² Following 1994, breakfast cereal or any other food product fortified with vitamins and minerals is regulated as a conventional food. A product containing exactly the same vitamins and minerals, labeled as a dietary supplement and not represented as a conventional food, however, falls within the statutory definition of a dietary supplement. Thus, there is a large overlap between what is regulated by FDA as a dietary supplement and as a conventional food. Merely changing the label can, in fact, switch a product from one category to the other.

FDA also regulates dietary supplements under FSMA, a comprehensive food safety statute enacted in 2011 in response to high-profile outbreaks of foodborne illness. Most FSMA provisions apply to “food” or to facilities that manufacture, process, pack, or hold food. Because dietary supplements are defined as “food” under Section 201(ff) of the FD&C Act,²³ all of the provisions of FSMA apply equally to dietary supplements except one. Congress determined that dietary supplements should be required to comply with the GMP provisions of DSHEA and therefore exempted them from the hazard analysis and risk-based preventive control provisions of FSMA.

The remainder of this White Paper discusses the safety provisions of the FD&C Act applicable first to dietary supplements and then to conventional food, and analyzes the similarities and differences.

¹⁹ Section 403(j) of the FD&C Act, 21 U.S.C. 343(j).

²⁰ Section 411(c)(3) of the FD&C Act, 21 U.S.C. 350(c)(3).

²¹ Section 201(ff) of the FD&C Act, 21 U.S.C. 321(ff).

²² E.g., Sections 402(f) and 413 of the FD&C Act, 21 U.S.C. 342(f) and 350b.

²³ Section 201(ff) of the FD&C Act, 21 U.S.C. 321(ff).

II. The Safety Requirements Applicable to Dietary Supplements

For purposes of analysis, this section divides the safety requirements applicable to dietary supplements into those that apply to old dietary supplements, those that apply to new dietary supplements, and the enforcement provisions available to assure compliance with these requirements.

A. Old Dietary Ingredients

A “dietary ingredient” is defined as an ingredient in a dietary supplement that is intended for dietary supplementation.²⁴ Thus, it does not include the functional ingredients in dietary supplements that are intended for such technological uses as fillers, emulsifiers, preservatives, and other similar purposes. A “dietary supplement” is defined as a product that contains one or more dietary ingredients and is labeled as a dietary supplement.²⁵

A “new dietary ingredient” is defined as a dietary ingredient that was not marketed in the United States before October 15, 1994.²⁶ Thus, an “old dietary ingredient” means a dietary ingredient that was marketed before that date.

1. Prohibition of Poisonous or Deleterious Substances

The general food adulteration provision in Section 402(a)(1) of the FD&C Act—which has applied to all food ingredients since it was first enacted in 1906—continues to apply to both old and new dietary supplements and ingredients.²⁷ Section 402(a)(1) prohibits from food “any poisonous or deleterious substance which may render it injurious to health.” DSHEA clarifies this longstanding provision by providing that the food is only deemed to be adulterated, and thus illegal, if it may be injurious to health under the conditions of use recommended or suggested in the labeling.²⁸ This is of no practical importance because the United States Supreme Court had adopted a similar interpretation of the provision as early as 1914²⁹ and that decision has remained unchanged ever since.³⁰

²⁴ Section 201(ff)(1) of the FD&C Act, 21 U.S.C. 321(ff)(1).

²⁵ Sections 201(ff)(1) and (2) of the FD&C Act, 21 U.S.C. 321(ff)(1) and (2).

²⁶ Section 413(d) of the FD&C Act, 21 U.S.C. 350b(d).

²⁷ Section 402(a)(1) of the FD&C Act, 21 U.S.C. 342(a)(1).

²⁸ Section 402(f)(1)(D) of the FD&C Act, 21 U.S.C. 342(f)(1)(D).

²⁹ *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 409 (1914).

³⁰ *Young v. Community Nutrition Institute*, 476 U.S. 974, 982-983 (1986).

2. Prohibition of Contamination with Insanitary or Injurious Substances

Sections 402(a)(3)-(6) of the FD&C Act prohibit food that is filthy, decomposed, held under insanitary conditions whereby it may have been rendered injurious to health, or otherwise unfit for food.³¹ These provisions apply to both old and new dietary supplements.

3. Exclusion from the Food Additive Provisions

DSHEA amended the definition of a food additive in Section 201(s) of the FD&C Act to exclude both old and new dietary ingredients.³² To replace the food additive provisions, DSHEA established a separate set of safety requirements for dietary ingredients. The food additive provisions continue to apply to the functional components of a dietary supplement that do not fall within the definition of a dietary ingredient.

4. Prohibition of Unapproved Color Additives

Section 721 of the FD&C Act requires specific FDA approval of all color additives used in food.³³ This requirement applies to both old and new dietary supplements.

5. Prohibition of Significant or Unreasonable Risk of Illness or Injury

DSHEA establishes new food safety requirements for both old and new dietary supplements and dietary ingredients, in place of the food additive provisions.³⁴ Section 402(f)(1)(A) of the FD&C Act, as added by DSHEA, prohibits any dietary supplement or dietary ingredient, whether old or new, that presents a “significant or unreasonable risk of illness or injury” either under conditions of use recommended or suggested in the labeling or, if no conditions of use are suggested or recommended, under ordinary conditions of use. Unlike conventional food ingredients, there is no exclusion for old or new dietary ingredients that are generally recognized as safe (GRAS) or that were subject to a prior FDA or USDA approval (prior sanction). The safety standard of significant or unreasonable risk of illness or injury is comparable to the broad safety standard

³¹ 21 U.S.C. 342(a)(3)-(6).

³² Section 201(s)(6) of the FD&C Act, 21 U.S.C. 321(s)(6).

³³ 21 U.S.C. 379e.

³⁴ Section 402(f) of the FD&C Act, 21 U.S.C. 342(f).

imposed under the Consumer Product Safety Act³⁵ and the Toxic Substances Control Act.³⁶ It is a new standard for food safety under the FD&C Act and does not apply to conventional food.

The standard of significant or unreasonable risk of illness or injury provides substantial discretion for FDA to take appropriate regulatory action against a dietary supplement or dietary ingredient that represents a risk of illness or injury. FDA may use its judgment in determining what is a significant risk or an unreasonable risk. In 2004, for example, FDA promulgated a regulation banning dietary supplements that contain ephedra after conducting a risk-benefit analysis and concluding that ephedra at any dose presents an “unreasonable risk of illness or injury” under Section 402(f)(1)(a) of the FD&C Act.³⁷ When industry challenged this agency action, the appellate court held that FDA’s use of discretion in weighing the effects of ephedra was appropriate because “Congress unambiguously required the FDA to conduct a risk-benefit analysis” in implementing the “unreasonable risk” standard.³⁸ Thus, in determining the reasonableness of a risk, the agency may take into account the scientific basis for the use of the dietary ingredient in human health and nutrition and the potential benefit and risk of such use.³⁹ This standard is broader in scope than the food additive requirements because there is no exclusion for GRAS and prior sanctioned ingredients. It thus provides greater discretion and authority for FDA to enforce food safety requirements for dietary ingredients than the agency has for a conventional food ingredient.

6. Prohibition on Marketing Food to Which Drugs or Biological Products Have Been Added

Section 301(ll) of the FD&C Act, as added by FDAAA, prohibits the introduction into commerce of any food that contains an approved new drug or a licensed biologic or a drug or biologic for which substantial clinical investigations were initiated and made public.⁴⁰ This provision appears to prohibit the same substances already prohibited from use in a dietary supplement under Section 201(ff)(3)(B),⁴¹ which specifically excludes from the dietary

³⁵ 86 Stat. 1207 (1972), 15 U.S.C. 2051 et seq.

³⁶ 90 Stat. 2003 (1976), 15 U.S.C. 2601 et seq.

³⁷ 69 Fed. Reg. 6788, 6794 (February 11, 2004).

³⁸ *Nutraceutical Corp. v. Von Eschenbach*, 459 F.3d 1033, 1038 (10th Cir. 2006), *cert. denied*, 550 U.S. 933 (2007).

³⁹ *Id.* at 1040 (“[T]he potential risk is more ‘unreasonable’ if the potential benefit is smaller.”).

⁴⁰ Section 301(ll) of the FD&C Act, 21 U.S.C. 331(ll).

⁴¹ Section 201(ff)(3)(B) of the FD&C Act, 21 U.S.C. 321(ff)(3)(B).

supplement definition approved new drugs or biologics and articles subject to substantial clinical investigations.⁴²

7. Immediate Ban of an Imminent Hazard

Section 402(f)(1)(C) of the FD&C Act, as added by DSHEA, provides authority for the Secretary of Health and Human Services to declare any old or new dietary supplement or dietary ingredient to be an illegal imminent hazard to public health or safety.⁴³ This administrative determination results in an immediate ban of the ingredient or product. There is no comparable authority for conventional food.

This provision is modeled on the imminent hazard authority added to the FD&C Act by the Drug Amendments of 1962⁴⁴ for all new drug products.⁴⁵ Like the new drug imminent hazard authority, this power may not be delegated by the Secretary.

Following an imminent hazard determination by the Secretary, a dietary supplement or dietary ingredient must immediately cease marketing. One element of the existing FDA definition of an imminent hazard is that the situation should not be permitted to continue while a hearing or other formal proceeding is being held.⁴⁶ The DSHEA provision therefore requires that, once the dietary supplement or dietary ingredient is banned and cannot be marketed, the Secretary must promptly initiate an administrative proceeding to affirm or withdraw the ban. This is the same way that the imminent hazard provision has been applied to new drugs.⁴⁷ Because the concept of an imminent hazard is so broad, this authority provides substantial discretion to ban any dietary supplement or dietary ingredient that presents a safety risk that should not reasonably be allowed to continue pending the usual rulemaking or court enforcement action.

8. Requirement of Good Manufacturing Practices

Section 402(g) of the FD&C Act was added by DSHEA to provide explicit statutory authority for FDA to prescribe GMP requirements for dietary supplements.⁴⁸ There is no comparable statutory authority for conventional food,

⁴² FDA published a proposed regulation on Section 301(l), but has not promulgated a final regulation. 73 Fed. Reg. 43937 (July 29, 2008).

⁴³ Section 402(f)(1)(C) of the FD&C Act, 21 U.S.C. 342(f)(1)(C).

⁴⁴ 76 Stat. 780, 782 (1962).

⁴⁵ Section 505(e) of the FD&C Act, 21 U.S.C. 355(e).

⁴⁶ 21 C.F.R. 2.5(a)(2).

⁴⁷ *Forsham v. Califano*, 442 F. Supp. 203, 208 (D.D.C. 1977).

⁴⁸ 21 U.S.C. 342(g).

but FDA nonetheless established GMP regulations for the entire food supply, including dietary supplements, in the late 1960s.⁴⁹

The GMP regulations that FDA has promulgated for dietary supplements under the explicit statutory authority in DSHEA are substantially more rigorous than the current GMP regulations for conventional food.⁵⁰ These GMP requirements apply to all domestic and foreign companies that manufacture, package, label, or hold dietary supplements.⁵¹ Among other requirements, these comprehensive regulations require the creation of a master manufacturing record⁵² and production and process controls,⁵³ verification of the components used in manufacturing,⁵⁴ designation of quality control personnel,⁵⁵ review of product complaints,⁵⁶ and maintenance of written records.⁵⁷ A facility that complies with the robust dietary supplement GMP requirements is exempt from the comparable FSMA provisions pertaining to hazard analysis and risk-based preventative controls.⁵⁸

9. Requirement of Adverse Event Reporting

Section 761 of the FD&C Act, added by the Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006, requires a manufacturer, packer, or distributor whose name appears on the label of a dietary supplement—known as the “responsible person”—to report a serious adverse event to FDA within 15 days of receipt of the information.⁵⁹ The “responsible person” must also maintain records of all adverse reports, whether serious or not, for six years.⁶⁰ As discussed below, the mandatory adverse event reporting requirements for dietary supplements are more stringent than the comparable reporting requirements for conventional food under the reportable food registry.

⁴⁹ 21 C.F.R. part 110.

⁵⁰ 72 Fed. Reg. 34752 (June 25, 2007).

⁵¹ 21 C.F.R. 111.1.

⁵² 21 C.F.R. 111.205 and 111.210.

⁵³ 21 C.F.R. part 111, subparts E-L.

⁵⁴ 21 C.F.R. part 111, subpart G.

⁵⁵ 21 C.F.R. 111.105.

⁵⁶ 21 C.F.R. part 111, subpart O.

⁵⁷ 21 C.F.R. part 111, subpart P.

⁵⁸ 21 U.S.C. 350g note.

⁵⁹ Section 761 of the FD&C Act, 21 U.S.C. 379aa-1.

⁶⁰ Section 761(e)(1) of the FD&C Act, 21 U.S.C. 379aa-1(e)(1).

10. FSMA Requirements

FSMA significantly expanded FDA's authority to regulate food safety in response to outbreaks of foodborne illness. This increased regulatory authority over the food supply includes additional recordkeeping requirements and record access provisions,⁶¹ more frequent inspections of domestic and foreign facilities,⁶² and more stringent restrictions on the importation of food,⁶³ among other requirements. With the exception of the hazard analysis and risk-based preventive control provisions of FSMA, which are discussed below, all of the provisions in FSMA apply to old and new dietary supplements as well as conventional food.

⁶¹ Section 414 of the FD&C Act, 21 U.S.C. 350c.

⁶² Section 421 of the FD&C Act, 21 U.S.C. 350j.

⁶³ Sections 805-808 of the FD&C Act, 21 U.S.C. 384a-384d.

B. New Dietary Ingredients

As already noted, a new dietary ingredient is a dietary ingredient that was not marketed in the United States before October 15, 1994. DSHEA exempted new dietary ingredients (along with old dietary ingredients) from the food additive provisions of the law, but not from the general adulteration provisions of the law, and established a separate new set of safety requirements for new dietary ingredients.⁶⁴

1. Prohibition of Poisonous or Deleterious Substances

The prohibition against a poisonous or deleterious substance in food, that has existed since 1906, continues to apply to new dietary ingredients as well as old dietary ingredients.

2. Prohibition of Contamination with Insanitary or Injurious Substances

All of the prohibitions against contamination with insanitary or injurious substances apply to new dietary ingredients as well as to old dietary ingredients.

3. Exclusion from the Food Additive Provisions

The exclusion of dietary ingredients from the food additive provisions of the FD&C Act applies to both new ingredients and old ingredients. This exclusion does not apply to components of dietary supplements that are not dietary ingredients.

4. Prohibition of Unapproved Color Additives

The prohibition against use of any unapproved color additive applies to new dietary supplements as well as to old dietary supplements.

5. Prohibition of Significant or Unreasonable Risk of Illness or Injury

The authority of FDA to prohibit a dietary ingredient that presents a significant or unreasonable risk of illness or injury applies to new dietary

⁶⁴ To clarify the obligations under DSHEA, FSMA required FDA to issue guidance on the regulatory requirements for new dietary ingredients and the premarket notification process. FDA issued draft guidance in July 2011, which the agency has stated is not to be implemented until it is issued in final form. 76 Fed. Reg. 39111 (July 5, 2011).

ingredients as well as old dietary ingredients. It does not apply to conventional food.

6. Premarket Notification for New Dietary Ingredients

Section 413(a) of the FD&C Act, as added by DSHEA, imposes the requirement of premarket notification to FDA of a new dietary ingredient unless the ingredient has been present in the food supply as an article used for food and in a form in which the food has not been chemically altered.⁶⁵ For all new dietary ingredients that do not meet this exception, the premarket notification must be submitted to FDA at least seventy-five days before the new dietary ingredient is marketed. The premarket notification must contain a history of use or other evidence of safety establishing that the ingredient will reasonably be expected to be safe and must include information, including published articles, that support a reasonable expectation of safety. FDA has promulgated regulations to implement this provision.⁶⁶

Section 402(f)(1)(B) of the FD&C Act, as added by DSHEA, provides that a new dietary ingredient for which there is inadequate safety information to provide reasonable assurance that it does not present a significant or unreasonable risk of illness or injury is deemed to be adulterated and thus illegal.⁶⁷ Accordingly, if a premarket notification under Section 413(a)(2) fails to contain adequate information to establish that a new dietary ingredient will reasonably be expected to be safe, the ingredient becomes illegal under Section 402(f)(1)(B). As added by FSMA, if FDA determines that there is inadequate safety information under Section 413(a)(2) because the article may be or may contain an anabolic steroid or steroid analogue, FDA must notify the Drug Enforcement Administration of its determination.⁶⁸

Following enactment of this provision, FDA has informed some people who have submitted premarket notifications for new dietary ingredients that the agency has concluded that the submission does not establish a reasonable expectation of safety. There is no comparable premarket notification requirement for a new conventional food ingredient that has been the subject of a self-determination of GRAS status or a prior sanction.

⁶⁵ 21 U.S.C. 350b(a)(1).

⁶⁶ 21 C.F.R. part 190.

⁶⁷ 21 U.S.C. 342(f)(1)(B).

⁶⁸ Section 413(c) of the FD&C Act, 21 U.S.C. 350b(c).

7. Prohibition on Marketing Food to Which Drugs or Biological Products Have Been Added

Section 201(ff)(3)(B) and Section 301(l) of the FD&C Act prohibit any dietary supplement or conventional food that contains an approved or investigational new drug or biologic unless the supplement or food was marketed first.

8. Immediate Ban of an Imminent Hazard

The imminent hazard provision described above applies to new dietary ingredients as well as old dietary ingredients. It does not apply to conventional food.

9. Requirement of Good Manufacturing Practices

The GMP requirements described above apply to new dietary ingredients as well as old dietary ingredients.

10. Requirement of Adverse Event Reporting

The mandatory adverse event reporting requirements described above apply to new dietary ingredients as well as old dietary ingredients. The reportable food registry requirements applicable to conventional food are less stringent.

11. FSMA Requirements

FDA's authority to enhance food safety requirements generally applies to new dietary ingredients as well as old dietary ingredients, with one exception. Dietary supplements must comply with the GMP provisions of DSHEA rather than the hazard analysis and risk-based preventive control provisions of FSMA.

C. Enforcement

It is equally important to understand the FDA enforcement authority under the FD&C Act with respect to the food safety requirements for both old and new dietary ingredients.

1. Rulemaking Authority

The authority of FDA to promulgate regulations under Section 701(a) of the FD&C Act “for the efficient enforcement of this Act” applies to both old and new dietary supplements and dietary ingredients.⁶⁹ For example, FDA asserted this authority in a regulation banning dietary supplements containing ephedra.⁷⁰

2. Federal Court Enforcement

The formal court enforcement powers authorizing product seizure,⁷¹ an injunction against illegal activity,⁷² and criminal prosecution of individuals and companies⁷³ are applicable to both old and new dietary supplements and dietary ingredients.

3. Informal Enforcement Mechanisms

All of the existing informal mechanisms that FDA uses to enforce the FD&C Act are applicable to both old and new dietary supplements and dietary ingredients. These include a warning letter,⁷⁴ request for recall,⁷⁵ adverse publicity,⁷⁶ and other similar agency action.

4. Bioterrorism Enforcement Provisions

Title III of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 provided FDA with additional statutory enforcement powers to increase food security in order to reduce the threat of

⁶⁹ 21 U.S.C. 371(a).

⁷⁰ 69 Fed. Reg. 6788, 6794 (February 11, 2004).

⁷¹ Section 304 of the FD&C Act, 21 U.S.C. 334.

⁷² Section 302 of the FD&C Act, 21 U.S.C. 332.

⁷³ Section 303(a) of the FD&C Act, 21 U.S.C. 333(a).

⁷⁴ Section 309 of the FD&C Act, 21 U.S.C. 336.

⁷⁵ 21 C.F.R. part 7, subpart C.

⁷⁶ Section 705 of the FD&C Act, 21 U.S.C. 375.

bioterrorism. FDA was provided with increased regulatory authority over the food supply, including administrative detention,⁷⁷ registration of food facilities,⁷⁸ recordkeeping requirements and records inspection authority,⁷⁹ and prior notice of imported food shipments,⁸⁰ to name just a few of these new authorities. All of the provisions in the Bioterrorism Act apply to dietary supplements as well as conventional food.

5. Suspension of Facility Registration

Section 102 of FSMA expands the facility registration requirement in Section 415 of the FD&C Act by requiring food facilities to renew their registration every two years.⁸¹ FSMA also increases FDA's enforcement authority by authorizing the agency to suspend a facility's registration if (1) the holder was responsible for an adulteration that creates a reasonable probability of causing serious adverse health consequences or death or (2) the holder knew or should have known that a food product it held, packed, or received posed a risk of causing serious adverse health consequences or death.⁸² A suspension order would prohibit the facility from importing food into the United States or introducing food into the stream of domestic commerce.⁸³ These provisions apply to dietary supplements as well as conventional food.

6. Administrative Detention Orders

Under Section 207 of FSMA, FDA may order the administrative detention of an article of food if there is "reason to believe" that the food article is adulterated or misbranded.⁸⁴ Section 207 introduces a less demanding standard than the previous standard under the FD&C Act, which allowed an administrative detention order only upon "credible evidence or information" of "a threat of serious adverse health consequences or death." These provisions apply to dietary supplements as well as conventional food.

⁷⁷ Section 304(h) of the FD&C Act, 21 U.S.C. 334(h).

⁷⁸ Section 415 of the FD&C Act, 21 U.S.C. 350d.

⁷⁹ Section 414 of the FD&C Act, 21 U.S.C. 350c.

⁸⁰ Section 801(m) of the FD&C Act, 21 U.S.C. 381(m).

⁸¹ Section 415(a)(3) of the FD&C Act, 21 U.S.C. 350d(a)(3).

⁸² Section 415(b) of the FD&C Act, 21 U.S.C. 350d(b).

⁸³ Sections 415(a) and (b) of the FD&C Act, 21 U.S.C. 350d(a) and (b).

⁸⁴ Section 304(h) of the FD&C Act, 21 U.S.C. 334(h).

7. Mandatory Recall Authority

Section 206 of FSMA gives FDA the authority to issue an order requiring a mandatory recall of adulterated or misbranded food.⁸⁵ If FDA finds a reasonable probability that food is adulterated or misbranded and will cause “serious adverse health consequences or death to humans or animals,” FDA may ask the responsible party to voluntarily recall the food.⁸⁶ If the responsible party refuses, FDA may issue an order requiring the responsible party to immediately cease distribution and notify recipients.⁸⁷ The responsible party then has the opportunity for an informal hearing within two days of the cease distribution order.⁸⁸ After the hearing, FDA can amend the cease distribution order to require a recall.⁸⁹ Refusal or failure to follow a cease distribution or recall order under this section is a prohibited act⁹⁰ and could result in civil fines.⁹¹ These provisions apply to dietary supplements as well as conventional food.

8. Burden of Proof in Civil Enforcement Actions

Section 402(f)(1) of the FD&C Act, as added by DSHEA, provides that, in any proceeding under this specific subparagraph (but not any other provisions in the FD&C Act), FDA bears the burden of proof to show that a dietary supplement is adulterated.⁹² This is the same rule that applies in litigated court cases involving conventional food adulteration. If FDA contends that a food contains a poisonous or deleterious substance, or is not GRAS, the agency bears the burden of proof in a court enforcement action. In a challenge to the FDA ephedra regulation, the appellate court held that this burden may be met by the FDA risk-benefit analysis supporting the regulation.⁹³

9. De Novo Judicial Review

Section 402(f)(1) of the FD&C Act also provides that, in a court enforcement action under this specific subparagraph (but not any other provisions in the FD&C Act), the court shall decide the issue of adulteration of a dietary

⁸⁵ Section 423 of the FD&C Act, 21 U.S.C. 350l.

⁸⁶ Section 423(a) of the FD&C Act, 21 U.S.C. 350l(a).

⁸⁷ Section 423(b) of the FD&C Act, 21 U.S.C. 350l(b).

⁸⁸ Section 423(c) of the FD&C Act, 21 U.S.C. 350l(c).

⁸⁹ Section 423 (d)(1) of the FD&C Act, 21 U.S.C. 350l(d)(1).

⁹⁰ Section 301(xx) of the FD&C Act, 21 U.S.C. 331(xx).

⁹¹ Section 303(f)(2)(A) of the FD&C Act, 21 U.S.C. 333(f)(2)(A).

⁹² 21 U.S.C. 342(f)(1).

⁹³ *Nutraceutical Corp.*, note 38 *supra*, at 1039.

supplement “on a de novo basis.” This is how FDA litigation has always been conducted with respect to adulteration issues, and presents no new policy issue.

If FDA takes enforcement action based on violation of a statutory provision, FDA would need to meet its burden by submitting evidence of the risks of illness or injury posed by the product. But where FDA has already conducted an exhaustive rulemaking procedure taking into account the risks, benefits, and uses of a product, as well as stakeholder comments and evidence, the courts have held that it is sufficient for FDA to present evidence that (1) the regulation exists and (2) it applies to the product that is the subject of the enforcement action.⁹⁴ The court would use a de novo standard of review, but the regulation itself would satisfy the evidentiary burden.

Where there is a court challenge to a regulation, as there was for ephedra, under standard administrative law principles the regulation must be upheld unless it is unlawful or is arbitrary and capricious. In the ephedra case, the appellate court held that the de novo standard of review is limited to enforcement proceedings.⁹⁵ If FDA promulgates a regulation, as it did with ephedra, and private parties challenge the regulation in court, “the normal rules for judicial deference regarding agency action apply.”⁹⁶ Therefore, the court would not make its own de novo determination.⁹⁷

10. Opportunity to Present Views Before a Civil Proceeding is Instituted

Section 402(f)(2) of the FD&C Act provides that, before FDA may report a violation of Section 402(f)(1)(A) to the Department of Justice for a civil court enforcement action, the person against whom such proceeding would be initiated shall be given appropriate notice and the opportunity to present both oral and written views, at least ten days before such notice.⁹⁸ This is a new provision, that does not apply to any other civil court action under the FD&C Act. It is questionable, however, whether this provision will be applied in the way it is written. Section 305 of the FD&C Act contains a comparable provision requiring that, before any violation of the FD&C Act is reported by FDA for institution of a criminal proceeding, the person against whom the proceeding is contemplated “shall” be given appropriate notice and an opportunity to present views either orally or in writing. Nonetheless, the United States Supreme Court has held that

⁹⁴ *Hi-Tech Pharmaceuticals, Inc. v. Crawford*, 544 F.3d 1187, 1191 (11th Cir. 2008).

⁹⁵ *Nutraceutical Corp.*, note 38 *supra*, at 1037.

⁹⁶ *Id.* (internal citation omitted).

⁹⁷ *Id.*

⁹⁸ 21 U.S.C. 342(f)(2).

this is not a requirement.⁹⁹ It therefore appears likely that the same result would apply here.

⁹⁹ *United States v. Dotterweich*, 320 U.S. 277, 278-279 (1943).

III. The Safety Requirements Applicable to Conventional Food

For purposes of this analysis, the term “conventional food” will be used to encompass all food that is subject to FDA jurisdiction under the FD&C Act except for dietary supplements and dietary ingredients. Thus, it includes what are commonly referred to as “functional food” and “medical food” as well as other special dietary food products. These products commonly contain many of the same nutrients, botanical substances, herbs, and other ingredients that are also used as dietary ingredients in dietary supplements.

Thus, most of the substances that are used as dietary ingredients in dietary supplements are also used as ingredients in conventional food. The final food product is classified either as a dietary supplement or as a conventional food solely on the basis of the representations and claims made for the product, not on the basis of the nature of the ingredients, the composition of the product, its safety, or its nutritional value. The statute provides that a dietary supplement must explicitly be labeled as a dietary supplement and may not be represented as a conventional food.¹⁰⁰ All other food is classified as a conventional food. A product that is explicitly labeled as a dietary supplement must bear the “Supplement Facts” box on the label, in accordance with FDA regulations promulgated under the authority of DSHEA.¹⁰¹ A food that is not explicitly labeled as a dietary supplement on the principal display panel of the label must instead bear the “Nutrition Facts” box in accordance with regulations promulgated by FDA¹⁰² under the authority of the Nutrition Labeling and Education Act of 1990.¹⁰³

In this context, the safety provisions of the FD&C Act that apply to conventional food are now reviewed, first for both old and new ingredients and then the enforcement provisions available to assure compliance.

¹⁰⁰ Sections 201(ff)(2)(B) and (C) and 411(c)(1)(B)(ii) of the FD&C Act, 21 U.S.C. 321(ff)(2)(B) and (C) and 350(c)(1)(B)(ii). DSHEA amended Section 411(c)(1)(B) to delete the limitation imposed by the Vitamin-Mineral Amendments of 1976 that a dietary supplement may not simulate a conventional food.

¹⁰¹ 21 C.F.R. 101.36.

¹⁰² 21 C.F.R. 101.9.

¹⁰³ 104 Stat. 2353 (1990).

A. Conventional Food Ingredients

1. Prohibition of Poisonous or Deleterious Substances

As noted above, Section 402(a)(1) of the FD&C Act prohibits the use of any poisonous or deleterious substance in conventional food that may render the food injurious to health. This is solely a risk-based standard. It does not permit FDA to balance benefit against risk.

2. Prohibition of Contamination with Insanitary or Injurious Substances

Sections 402(a)(3)-(6) of the FD&C Act, described above, apply to all conventional food.

3. Food Additive Provisions

Under the Food Additives Amendment of 1958, which added Section 409 to the FD&C Act,¹⁰⁴ a new ingredient may lawfully be used in conventional food only under any of the following three alternative criteria. First, it may be used without FDA premarket approval if it was approved by FDA or USDA between 1938 and 1958 for the intended use (commonly referred to as a “prior sanction”).¹⁰⁵ Second, it may be used without FDA premarket approval if it is generally recognized as safe (GRAS) for its intended use.¹⁰⁶ GRAS status may be based either on common use in food prior to 1958 or on scientific procedures.¹⁰⁷ Unlike for drugs, there is no requirement that a food ingredient be used “to a material extent or for a material time” before it may attain GRAS status.¹⁰⁸ Third, if it is not prior sanctioned and not GRAS, it may only be used in compliance with a food additive regulation promulgated by FDA in response to a premarket food additive petition submitted by the sponsor.¹⁰⁹ A food additive petition must demonstrate that the additive is safe under its intended conditions of use, i.e., that there is a “reasonable certainty in the minds of competent scientists that the substance is not harmful.”¹¹⁰

Because prior sanctions, by their nature, do not exist for new substances or new uses of old ingredients, and because the cost and time to obtain

¹⁰⁴ 21 U.S.C. 348.

¹⁰⁵ Section 201(s) of the FD&C Act, 21 U.S.C. 321(s).

¹⁰⁶ *Id.*

¹⁰⁷ *Id.*; 21 C.F.R. 170.30(a).

¹⁰⁸ Compare Section 201(p)(2) of the FD&C Act, 21 U.S.C. 321(p)(2).

¹⁰⁹ Section 409(b) of the FD&C Act, 21 U.S.C. 348(b).

¹¹⁰ 21 C.F.R. 170.3(i); Section 409 of the FD&C Act, 21 U.S.C. 348.

FDA approval and promulgation of a food additive regulation is prohibitive,¹¹¹ virtually all new conventional food substances and new uses of old conventional food substances occur under a determination of GRAS status. Accordingly, the “significant or unreasonable risk of illness or injury” standard applies to all old and new dietary ingredients but the “reasonable certainty of no harm” standard applies to only a minority of old and new conventional food ingredients.

Nothing in the FD&C Act requires a manufacturer or distributor to obtain the opinion of FDA about the GRAS status of any substance prior to using it in conventional food. FDA has confirmed that there is no legal obligation to request an opinion of the agency or to inform the agency prior to using a new ingredient that is subject to a self-determination of GRAS by a company.¹¹² FDA has published lists of GRAS substances¹¹³ but the agency has stated that those lists “do not include all substances that are generally recognized as safe for their intended use in food.”¹¹⁴ Unlike new dietary ingredients, there is no premarket notification requirement for new GRAS substances for use in conventional food. Accordingly, the FD&C Act and FDA regulations recognize that companies may use new food ingredients in conventional food based solely on a self-determination of GRAS status.

FDA has taken the position that GRAS status requires “common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances” and thus that a determination of GRAS status “shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data and information.”¹¹⁵ Publication of the scientific studies supporting a GRAS publication—either in traditional scientific journals or through the internet—is therefore sufficient to underpin a self-determination of GRAS.

FDA at one time established a voluntary GRAS affirmation petition procedure to facilitate FDA review of self-determinations of GRAS status by the regulated industry.¹¹⁶ This was a voluntary, not a mandatory, process and there was no requirement to follow it. Because of a rising backlog of GRAS affirmation petitions, FDA proposed in 1997 to replace the GRAS affirmation petition procedure with a simpler GRAS premarket notification system.¹¹⁷ Although this proposed regulation has not yet been promulgated in final form,

¹¹¹ Peter Barton Hutt, *Regulation of Food Additives in the United States*, in A. Larry Branen et al., editors, *Food Additives*, Chapter 8 (2d ed. 2002).

¹¹² 62 Fed. Reg. 18938, 18941-18942 (April 17, 1997).

¹¹³ 21 C.F.R. parts 182 and 184.

¹¹⁴ 21 C.F.R. 170.30(d).

¹¹⁵ 21 C.F.R. 170.30(a) and (b).

¹¹⁶ 21 C.F.R. 170.35.

¹¹⁷ 62 Fed. Reg. 18938 (April 17, 1997).

FDA informally abandoned the GRAS affirmation petition process shortly after the proposal was published and has been implementing the GRAS premarket notification system ever since. Like the GRAS affirmation process, the GRAS premarket notification system is entirely voluntary and is not required by the FD&C Act or FDA regulations.

Most ingredients used in conventional food today are used on the basis of a self-determination of GRAS status. Some of the self-determinations have been submitted for confirmation by FDA through a GRAS affirmation petition before 1997 or a GRAS premarket notification since 1997. Many of them, however, have not been submitted to FDA and thus have not been subject to FDA review. There is presently no list of ingredients used in conventional food on the basis of a self-determination of GRAS status because there is no requirement under the FD&C Act that these determinations be reported to FDA.

4. Prohibition of Unapproved Color Additives

The prohibition of unapproved color additives under Section 721 of the FD&C Act applies to all conventional food.

5. Prohibition of Significant or Unreasonable Risk of Illness or Injury

The safety provisions of the FD&C Act applicable to conventional food contain no prohibition against a significant or unreasonable risk of illness or injury.

6. Premarket Notification for New Ingredients

The safety provisions of the FD&C Act applicable to conventional food do not contain a requirement of premarket notification to FDA of new food ingredients except for those that are not subject to a prior sanction and are not GRAS and thus are food additives that require premarket approval.

7. Prohibition on Marketing Food to Which Drugs or Biological Products Have Been Added

Section 301(ll) of the FD&C Act, as added by FDAAA,¹¹⁸ prohibits the introduction into commerce of any food that contains an approved drug or licensed biologic, or a drug or a biologic for which substantial clinical investigations were initiated and made public, unless the food was marketed first.¹¹⁹ This provision applies to both conventional food and dietary supplements.¹²⁰ Based on the similarities between Sections 301(ll) and 201(ff) of

¹¹⁸ 121 Stat. 823, 951-952 (2007).

¹¹⁹ Section 301(ll) of the FD&C Act, 21 U.S.C. 331(ll).

¹²⁰ Section 201(ff)(3)(B) of the FD&C Act, 21 U.S.C. 321(ff)(3)(B).

the FD&C Act, Congress likely meant to expand the prohibitions in Section 201(ff)(3)(B) for dietary supplements to conventional food.

8. Immediate Ban of an Imminent Hazard

The safety provisions of the FD&C Act applicable to conventional food do not authorize FDA to impose an immediate ban of an imminent hazard to public health or safety.

9. Requirement of Good Manufacturing Practices

Although the safety provisions of the FD&C Act applicable to conventional food do not provide explicit statutory authority to prescribe GMP requirements, FDA established GMP regulations for the entire food supply in the late 1960s. Section 418 of FD&C Act, as enacted by FSMA, requires facilities to identify hazards that are reasonably likely to occur and implement preventative controls to provide assurances that the identified hazards would be significantly minimized and that food would not be adulterated.¹²¹ These preventative controls may include existing GMP requirements in addition to other procedures, practices, and processes.¹²² Section 418 does not apply to dietary supplements if the facility is in compliance with the new dietary supplement GMP requirements.¹²³

10. Requirement of Adverse Event Reporting

Under FDAAA, Congress granted FDA the authority to create a “reportable food registry” to which registered food facilities must report if the use of or exposure to an article of food has a reasonable probability of causing serious adverse health consequences or death to humans.¹²⁴

The FDA reportable food registry for conventional food imposes a more limited set of obligations than the mandatory adverse event reporting requirements for dietary supplements.¹²⁵ For conventional food, a responsible party must file a report to the registry only if there is a link between exposure to a food and a serious health risk. A report is not required if the adulteration was corrected or the food was destroyed.¹²⁶ For dietary supplements, the responsible

¹²¹ Section 418 of the FD&C Act, 21 U.S.C. 350g.

¹²² Section 418(o)(3)(F), 21 U.S.C. 350g(o)(3)(F).

¹²³ Section 418 of the FD&C Act, 21 U.S.C. 350g.

¹²⁴ Section 417 of the FD&C Act, 21 U.S.C. 350f.

¹²⁵ Section 761 of the FD&C Act, 21 U.S.C. 379aa-1.

¹²⁶ Section 417(d)(2)(C) of the FD&C Act, 21 U.S.C. 350f(d)(2)(C).

person must report any serious adverse event associated with a dietary supplement regardless whether that event can be causally linked to the dietary supplement.

The reportable food registry requirements do not apply to dietary supplements because the latter were already subject to the more rigorous mandatory adverse event reporting requirements.¹²⁷

11. FSMA Requirements

FSMA significantly expanded FDA's authority to regulate the safety of all food. Its provisions generally apply to both dietary supplements and conventional food, with one exception. Dietary supplements are subject to the GMP requirements of DSHEA and all other food is subject to the hazard analysis and risk-based preventive control provisions of FSMA.

¹²⁷ Section 201(ff) of the FD&C Act, 21 U.S.C. 321(ff).

B. Enforcement

The following provisions described above that are applicable to enforcement of the FD&C Act with respect to the food safety requirements for dietary supplements and dietary ingredients are also applicable to conventional food: rulemaking authority, federal court enforcement, informal enforcement mechanisms, the bioterrorism enforcement provisions, suspension of facility registration, administrative detention orders, and mandatory recall authority. Accordingly, there is no need to discuss these further.

Three provisions of the FD&C Act, as added by DSHEA, are by their terms applicable only to dietary supplements and dietary ingredients: the burden of proof in a civil enforcement action under Section 402(f), de novo judicial review in such a court action, and an opportunity to present views before a civil proceeding is instituted under that subsection. Allocating the burden of proof to FDA in a civil enforcement action, however, merely restates current law and thus has no practical impact. De novo judicial review applies to FDA enforcement actions, but not to judicial review of a challenge to an agency regulation. The requirement for an opportunity to present views before a civil proceeding is instituted for violation of the specific subsection is a new provision that does not apply to any other civil court action under the FD&C Act, but it is questionable whether this provision will be applied in the way it is written because of prior Supreme Court precedent. Accordingly, these three provisions provide for only limited change from the way that conventional food court actions are conducted. These provisions have been used only very rarely since enactment of DSHEA, and without significant impact.

II. Analysis of the Similarities and Differences Among the FD&C Act Safety Provisions Applicable to Dietary Supplements and Conventional Food

As the preceding summaries of the safety requirements under the FD&C Act applicable to dietary supplements and conventional food demonstrate, the statutory provisions applicable to both categories of food are far more similar than they are different. This is shown graphically in the two tables attached at the end of this White Paper.

A. The Substantive Safety Requirements

The bedrock food safety requirement that has been the foundation for protection of the American food supply since 1906—the prohibition of poisonous or deleterious substances in food—applies equally to dietary supplements and conventional food. The prohibition of contamination with insanitary or injurious substances, the prohibition of unapproved color additives, and the prohibition of the addition of drugs or biologics similarly applies to both categories of food products. The requirements recently established by FSMA, such as restrictions on importation and increased facility inspections, also apply generally both to dietary supplements and conventional food. Conventional food is subject to the hazard analysis and risk-based preventive control provisions of FSMA and dietary supplements must comply with the GMP requirements of DSHEA.

Two new provisions added by DSHEA and applicable only to dietary supplements provide important new food safety requirements. The first prohibits any new or old dietary supplement or dietary ingredient that presents a significant or unreasonable risk of illness or injury. The second authorizes FDA to impose an immediate administrative ban on the marketing of any dietary supplement or dietary ingredient that presents an imminent hazard to public health or safety. There are no comparable provisions applicable to conventional food.

The Dietary Supplement and Nonprescription Drug Consumer Protection Act requires the submission of reports to FDA relating to any serious adverse event associated with a dietary supplement within 15 business days of the responsible party's receipt of the information. Although conventional food is subject to compliance with the reportable food registry if the food has a reasonable probability of causing serious adverse health consequences or death, the reporting and recordkeeping requirements for dietary supplements are more stringent than those for conventional food.

Finally, conventional food ingredients are subject to the food additive provisions of the FD&C Act whereas dietary ingredients are subject to the new safety requirements added by DSHEA. The analysis of these provisions reveals that a new conventional food ingredient that is the subject of a self-determination of GRAS status is not subject to mandatory premarket notification and review by FDA, whereas all new dietary ingredients are required to be the

subject of a premarket notification and review by FDA unless they contain only dietary ingredients that 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.¹²⁸

From this analysis, it is apparent that FDA has adequate statutory authority to assure the safety of both dietary ingredients and conventional food ingredients. Because mandatory premarket notification exists for new dietary ingredients, but not for new GRAS conventional food ingredients, and because of the statutory power given to FDA to require comprehensive adverse event reporting, to prohibit a significant or unreasonable risk of illness or injury, and to impose the immediate ban of an imminent hazard, the statutory safety provisions under the FD&C Act applicable to dietary supplements would appear to be stronger than those applicable to conventional food.

B. The Enforcement Provisions

The following enforcement provisions under the FD&C Act are equally applicable to dietary supplements and conventional food: rulemaking authority, federal court enforcement, informal enforcement mechanisms, the bioterrorism enforcement provisions, suspension of facility registration, administrative detention orders, and mandatory recall authority.

Three procedural provisions added to the FD&C Act by DSHEA apply only to dietary supplements: the burden of proof in a civil enforcement action under Section 402(f)(1) of the FD&C Act, de novo judicial review in a court enforcement proceeding under that section, and an opportunity to present views before a civil court proceeding under that section. As a practical matter, however, these three provisions have little importance. First, these provisions have very rarely been used since enactment of DSHEA, and they have had no practical impact. Second, FDA always has the burden of proof in a civil enforcement action. Third, de novo judicial review always occurs in a court enforcement action, but not on judicial review of promulgated regulations. Fourth, the opportunity to present views before a civil court proceeding is counter to Supreme Court precedent and would, in any event, only delay court enforcement for ten days. During that time, FDA could impose an immediate ban through administrative action if there was an imminent hazard to public health or safety. Finally, these procedural provisions apply only to Section 402(f)(1) of the FD&C Act, as added by DSHEA, and do not apply to Section 402(a)(1) or other applicable food safety provisions.

Accordingly, the procedural safeguards applicable to Section 402(f)(1) of the FD&C Act do represent a modest change from the requirements applicable to conventional food, but they have been of no importance as a practical matter. The stronger substantive food safety requirements applicable to dietary supplements as a result of the enactment of DSHEA and the Dietary

¹²⁸ Section 413(a)(1) of the FD&C Act, 21 U.S.C. 350b(a)(1).

Supplement and Nonprescription Drug Consumer Protection Act would appear greatly to outweigh these modest procedural changes.

Peter Barton Hutt

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Peter Barton Hutt has specialized in food and drug law for more than forty years. He served as Chief Counsel to FDA during 1971-1975. He is the coauthor of the casebook used to teach food and drug law throughout the country and he teaches a full course on this subject each Winter Term at Harvard Law School.

**Application of the FD&C Act
Safety Requirements to Dietary Supplements and Conventional Food**

Applicable Safety Requirement Statutory Authority	Dietary Supplements		Conventional Food	
	Old	New	Old	New
Prohibition of Poisonous or Deleterious Substances § 402(a)(1)	Yes	Yes	Yes	Yes
Prohibition of Contamination with Insanitary or Injurious Substances §§ 402(a)(3)-(6)	Yes	Yes	Yes	Yes
Prior Sanction Exclusion from Food Additive Requirements § 201(s)	No	No	Yes	No
GRAS Exclusion from Food Additive Requirements § 201(s)	No	No	Yes	Yes
Food Additive Requirements § 409	No	No	Yes	Yes
Prohibition of Unapproved Color Additives § 721	Yes	Yes	Yes	Yes
Prohibition of Significant or Unreasonable Risk of Illness or Injury § 402(f)	Yes	Yes	No	No
Prohibition on Food to Which Drugs or Biological Products Have Been Added §§ 201(ff)(3)(B), 301(l)	Yes	Yes	Yes	Yes
Immediate Ban of an Imminent Hazard § 402(f)(1)(C)	Yes	Yes	No	No
Requirement of GMP § 402(g)	Yes	Yes	Yes	Yes
Requirement of Hazard Analysis and Risk-Based Preventive Controls § 418	No	No	Yes	Yes
Premarket Notification §§ 413(a), (c)	No	Yes	No	No

Reportable Food Registry § 417	No	No	Yes	Yes
Mandatory Adverse Event Reporting § 761	Yes	Yes	No	No
Increased FDA Record Inspection Authority § 414	Yes	Yes	Yes	Yes
Increased FDA Inspections of Domestic and Foreign Facilities § 421	Yes	Yes	Yes	Yes
Establishment of Foreign Supplier Verification Program § 805	Yes	Yes	Yes	Yes
Accreditation of Third-Party Auditors § 808	Yes	Yes	Yes	Yes

**Application of the FD&C Act
Enforcement Authority to Dietary Supplements and Conventional Food**

Applicable Statutory Enforcement Authority	Dietary Supplements		Conventional Food	
	Old	New	Old	New
Federal Court Enforcement §§ 302-304	Yes	Yes	Yes	Yes
Informal Enforcement Mechanisms §§ 309 & 705 21 C.F.R. part 7	Yes	Yes	Yes	Yes
Bioterrorism Enforcement Provisions §§ 304(h), 414, 415, 801(m)	Yes	Yes	Yes	Yes
Suspension of Facility Registration § 415	Yes	Yes	Yes	Yes
Administrative Detention Order § 304(h)	Yes	Yes	Yes	Yes
Mandatory Recall Authority § 423	Yes	Yes	Yes	Yes
Government Has the Burden of Proof in Civil Enforcement Actions § 402(f)(1)	Yes	Yes	Yes	Yes
De Novo Judicial Review of Enforcement Actions § 402(f)(1)	Yes	Yes	Yes	Yes
De Novo Judicial Review of Challenges to Rulemaking § 402(f)(1)	No	No	No	No
Opportunity to Present Views Before Civil Court Proceeding § 402(f)(2)	Yes	Yes	No	No
Rulemaking Authority § 701(a)	Yes	Yes	Yes	Yes