Council for Responsible Nutrition
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July 14, 2025

By Electronic Submission

Department of Health and Human Services
Office of the Secretary
200 Independence Ave SW
Washington, DC 20201

Re: Request for Information (RFI): Ensuring Lawful Regulation and Unleashing Innovation To Make America Healthy Again. Docket ID. AHRQ-2025-0001. 90 FR 20478 (May 14, 2025).

The Council for Responsible Nutrition (CRN)[1] appreciates the opportunity to provide comments to the Department of Health and Human Services' (HHS) request for information (RFI) to address "regulations that are unnecessary, inconsistent with the law, overly burdensome, outdated, out of alignment with current Executive orders, or otherwise unsound." As the leading trade association representing dietary supplements and functional foods, we submit suggestions regarding the Food and Drug Administration's (FDA) regulations and guidance to advance the implementation of the President's deregulatory initiatives. Dietary supplements are mainstream products that support good nutrition to promote health and wellness and align with the Make America Healthy Again vision. Rescinding existing regulations and guidance that are unnecessary, unduly burdensome, or outdated, would have significant impact on the ability of businesses of all sizes to market dietary supplements and functional foods that help Americans achieve optimal health. However, as the agency aims toward offsetting any new regulation or

[1] The Council for Responsible Nutrition (CRN), founded in 1973 and based in Washington, D.C., is the leading trade association representing dietary supplement and functional food manufacturers and ingredient suppliers. CRN companies produce a large portion of the dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug stores and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. CRN represents more than 180 companies that manufacture dietary ingredients and/or dietary supplements, or supply services to those suppliers and manufacturers. Our member companies are expected to comply with a host of federal and state regulations governing dietary supplements in the areas of manufacturing, marketing, quality control and safety. Our supplier and manufacturer member companies also agree to adhere to additional voluntary guidelines as well as to CRN's Code of Ethics. Learn more about us at www.crnusa.org.

guidance by repealing ten existing ones, it is important that we share our desire for FDA to release anticipated guidance and rulemaking important to our industry, including:

- New Dietary Ingredient Notifications and Related Issues: Identity and Safety Information About the NDI: Guidance for Industry[2]
- Rulemaking to Provide by Regulation that an Ingredient Is Not Excluded From the Dietary Supplement Definition Proposed Rule[3]

The dietary supplement industry has long awaited final guidance from FDA regarding new dietary ingredient notifications. The Food, Drug, and Cosmetic Act (FD&C Act) requires, with some exceptions, manufacturers and distributors of a new dietary ingredient (NDI) to notify FDA with safety information for the NDI at least 75 days before first marketing. Thus, guidance around submission of NDI notifications is crucial to industry's ability to bring ingredient innovations to the market. FDA issued a draft guidance on NDI notifications in 2011 and a revised draft guidance in 2016. CRN expressed concerns through public comments that both documents create significant and unnecessary burdens on the dietary supplement industry without increasing safety for consumers. It has been 31 years since Congress enacted the Dietary Supplement Health and Education Act of 1994 (DSHEA), and 9 years since FDA last issued a complete draft guidance on NDI notifications for industry, albeit rife with issues. The agency has updated parts of final guidance in 2024, but guidance on identity and safety information is still pending. The dietary supplement industry continues to anticipate reasonable guidance on NDI notifications.

CRN also anticipates rulemaking by which FDA provides that an ingredient is not excluded from the dietary supplement definition, thereby allowing the marketing and sale of dietary supplements containing this ingredient. The rulemaking is deregulatory as it would allow companies to lawfully market dietary supplements containing an ingredient that has been unjustly barred previously and then subsequently allowed through enforcement discretion.

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[2] US Food and Drug Administration. Foods Program Guidance Under Development. Available at: https://www.fda.gov/food/guidance-documents-regulatory-information-topic-food-and-dietary-supplements/foods-program-guidance-under-development. Accessed 9 July 2025.

[3] US Office of Information and Regulatory Affairs. Rulemaking to Provide by Regulation that an Ingredient Is Not Excluded From the Dietary Supplement Definition. Available at: https://www.reginfo.gov/public/do/eAgendaViewRule?pubId=202410&RIN=0910-AI91. Accessed 8 July 2025.

This rulemaking would be consistent with FDA's 2022 final guidance[4] on its policy regarding products labeled as dietary supplements that contain N-acetyl-L-cysteine (NAC).

In support of deregulatory initiatives, CRN submits the following suggestions for rescission or revision, in the format of the fillable form provided in the RFI via https://www.regulations.gov/deregulation:

- Investigational New Drug Applications (IND) Guidance: Determining Whether Human Research Studies Can Be Conducted Without an IND and Proposed Rule: Investigational New Drug Applications; Exemptions for Clinical Investigations To Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic
- Certain Types of Statements for Dietary Supplements: DSHEA Disclaimer Placement
- Draft Guidance: Policy on Certain New Dietary Ingredients and Supplements
- Interim Final Rule: Petition for Exemption from 100% Identity Testing of Dietary Ingredients
- Nutrition Labeling of Dietary Supplements: Declaration of the Quantitative Amount of Other Dietary Ingredients
- Nutrient Content Claims for the Calorie Content of Foods – Sugar Content Claims – Sugar Free
- Nutrient Content Claims for the Calorie Content of Foods – Sugar Content Claims – Reduced Sugar

[4] US Food and Drug Administration. Guidance for Industry: Policy Regarding N-acetyl-L-cysteine. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-policy-regarding-n-acetyl-l-cysteine. Accessed 8 July 2025.

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I. Investigational New Drug Applications (IND) Guidance: Determining Whether Human Research Studies Can Be Conducted Without an IND and Proposed Rule: Investigational New Drug Applications; Exemptions for Clinical Investigations To Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

(1) Guidance for Clinical Investigators, Sponsors, and IRBs Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND (September 2013) ("2013 Guidance"), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-new-drug-applications-inds-determining-whether-human-research-studies-can-be.

(2) Proposed Rule — Investigational New Drug Applications; Exemptions for Clinical Investigations To Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic (87 Fed. Reg. 75536 (December 9, 2022)) ("2022 Proposed Rule")

Both the 2013 Guidance and 2022 Proposed Rule implicate 21 C.F.R. Part 312.

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

(1) 2013 Guidance – Interpretive Rule (explains 21 C.F.R. Part 312)

(2) 2022 Proposed Rule – Notice of Proposed Rulemaking

d. What is the name of the regulation being rescinded, if applicable?

(1) Guidance for Clinical Investigators, Sponsors, and IRBs Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND

(2) Proposed Rule — Investigational New Drug Applications; Exemptions for Clinical Investigations To Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic

e. Please provide a short summary of the justifications for the rescission.

CRN believes that the 2013 Guidance and 2022 Proposed Rule should be rescinded because they meet the following criteria identified in Executive Order 14219:

- Establish or interpret regulations that are based on unlawful delegations of legislative power by imposing requirements intended for drugs on dietary supplements and food and allowing FDA to classify food and dietary supplements as drugs based on the end points of a clinical investigation rather than the finished products' intended use, which is also not the best reading of the underlying statutory authority or prohibition;
- Establish or interpret regulations that impose significant costs upon private parties that are not outweighed by public benefits by requiring manufacturers to study the benefits of dietary supplements and food under costly, burdensome INDs;
- Establish or interpret regulations that harm the national interest by significantly and unjustifiably impeding technological innovation and research and development, impose undue burdens on small business, and impede private enterprise and entrepreneurship by discouraging investment in U.S.-based clinical research.

Moreover, the 2013 Guidance and 2022 Proposed Rule should be rescinded because they meet the following general deregulatory considerations under Executive Order 14192:

- Confusing or unnecessarily complicated;
- Impose requirements on the wrong individual or group;
- Impede efforts to innovate; and

- Otherwise interfere with the public or private sector's ability to promote the health and wellbeing of Americans.

Rescinding the 2013 Guidance and 2022 Proposed Rule would result in significant cost savings for U.S. businesses. Both documents impose confusing, burdensome, and costly requirements on FDA, industry, and academia because they require INDs for the research of dietary supplements and foods when Congress did not intend such requirements to extend beyond products intended for use as drugs. These unnecessary regulatory burdens impede innovation, private enterprise, and entrepreneurship, and do not promote the health and wellbeing of Americans. Rather, they would encourage industry and academics to move their valuable and innovative research overseas instead of conducting such research in the U.S. Thus, rescinding the 2013 Guidance and 2022 Proposed Rule would save industry and academia time and resources required to complete and submit an IND for researching the health benefits of dietary supplements and food, while also saving FDA time and resources from having to review unnecessary IND applications or submissions to exempt certain clinical investigations of dietary supplements and food from IND requirements. Rescinding the documents would also encourage cutting edge research in the U.S. on dietary supplements and foods that would promote the health and wellbeing of Americans, thereby supporting U.S. jobs and bolstering the U.S. economy.

f. Please insert the address of the agency. [NPRM, DFR, and IFR only]

Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993–0002

g. Please insert the contact information for the agency.

Contacts for 2013 Guidance:

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h. What is the background for the regulation being rescinded?

(1) Food Drug & Cosmetic Act ("FD&C Act")

Section 505(a) of the FD&C Act prohibits the introduction into interstate commerce of any "new drug" without premarket approval from FDA. A "new drug" is defined as, among other things, "any drug…the composition of which is such that such drug is not generally recognized…as safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereof." 21 U.S.C. § 321(p)(1).

Congress enacted Section 505(i) to allow manufacturers to study the safety and efficacy of "new drugs" without violating Section 505(a). Under Section 505(i), the shipment of "new drugs" into interstate commerce for the purpose of conducting clinical investigations is permitted. Congress tasked FDA with promulgating regulations establishing a framework in which "drugs intended solely for investigational use" could be lawfully studied. FDA promulgated 21 C.F.R. Part 312,

which established the investigational new drug ("IND") application regulations governing the clinical study of drugs.

(2) 2013 Guidance

In September 2013, FDA issued the 2013 Guidance to "assist clinical investigators, sponsors, sponsor-investigators, and institutional review boards ("IRBs") in determining whether research studies involving human subjects must be conducted under an IND pursuant to 21 C.F.R. Part 312. Part 312 requires that human research studies be conducted under an IND if all of the following conditions exist:

- The research involves a *drug* as defined in Section 201(g)(1) of the FD&C Act (21 U.S.C. § 321(g)(1)) (i.e., "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease . . ." and "articles (other than food) intended to affect the structure or any function of the body of man or other animals."
- The research is a *clinical investigation* as defined in 21 C.F.R. § 312.3 (i.e., an experiment in which a drug is administered/dispensed to or used on one or more human subjects (except use of a marketed drug in the course of medical practice).
- The clinical investigation is not otherwise *exempt* as described below:
    - Drug product is "lawfully marketed in the U.S.;"
    - Not intended to be reported to FDA as a well-controlled study in support of a new indication;
    - No intent to use study to support any other significant change in the labeling of the drug;
    - Investigation does not involve a route of administration, dose, patient population, or other factor that significantly increases the risk (or decreases the acceptability of the risk) associated with the use of the drug product;
    - Investigation conducted in compliance with the requirements for review by an IRB and the requirements for informed consent;

- Investigation conducted in compliance with the requirements of § 312.7 (i.e., not intended to promote or commercialize the drug product).

With respect to applicability of the IND regulations in Part 312 to foods, including dietary supplements, the 2013 Guidance states that "whether an IND is needed for a clinical investigation evaluating a dietary supplement is determined by the intent of the clinical investigation. Specifically, clinical investigations intended to study the relationship between a dietary supplement's effect on normal structure or function in humans, or to characterize the mechanism by which a dietary supplement acts to maintain such structure or function, are not required to be conducted under an IND. However, an IND is required for clinical investigations intended to evaluate a food or dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease.

Following the issuance of the 2013 Guidance, FDA issued a "Notice of Administrative Stay of Action" regarding certain portions of the guidance ("2015 Stay"). 80 Fed. Reg. 66907 (Oct. 30, 2015). In the 2015 Stay, FDA stated that it did not generally intend to seek INDs for studies in the stayed categories while the stay is in effect, as follows:

- For *conventional foods*:
  - Clinical studies designed to evaluate whether a conventional food may reduce the risk of a disease, intended to support a new or expanded health claim, and conducted in a population that does not include individuals less than 12 months old, those with altered immune systems, or those with serious or life-threatening medical conditions;
  - Clinical studies designed to evaluate a non-nutritional effect of a conventional food on the structure or function of the body.
- For *dietary supplements*:
  - Clinical studies designed to evaluate whether a dietary supplement may reduce the risk of a disease, intended to support a new or expanded health claim, and conducted in a population that does not include individuals less than 12 months old, those with altered

immune systems, or those with serious or life-threatening medical conditions.

The 2015 Stay did not affect clinical investigations of conventional foods or dietary supplements studied for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, evaluating whether the substance reduces the risk of a disease in individuals less than 12 months of age, study populations with altered immune systems or serious/life-threatening medical conditions. The 2015 Stay is still currently in effect.

(3) 2022 Proposed Rule

Following comments regarding the 2013 Guidance, FDA issued the 2022 Proposed Rule. If finalized, the 2022 Proposed Rule would amend IND regulations to provide for two exemptions from the requirement to obtain an IND:

- Self-Determined Exemption – applies if the following criteria are met:
    - Investigation not intended to support a drug development plan for the product or a labeling change that would cause the product to become an unlawfully marketed drug;
    - Investigation conducted in compliance with requirements for IRB review and informed consent;
    - Investigation conducted in compliance with regulations governing promotion and commercial distribution of investigational drugs;
    - Route of administration of product in investigation is the same as in the lawfully marketed product (i.e., oral); and
    - Investigation meets criteria designed to protect health, safety, and welfare of subjects, including that the subjects do not include those with a compromised immune system or a serious or life-threatening disease condition and that the product is used "consistent with its labeled conditions of use or, in the absence of labeled conditions of use, consistent with its ordinary conditions of use (e.g., same dose range and total daily intake, same formulation, same duration of use).
- FDA-Determined Exemption – applies if the following criteria are met:

- Sponsor Requested
  - Study satisfies requirements of a self-determined exemption except one or more of the subject health, safety, and welfare criteria;
  - Must be in writing and include study protocol, information on manufacturer and product to be studied, source of funding, etc.;
  - FDA will grant exemption if it finds the study does not present a potential for significant risk to the health, safety, or welfare of the subject.
    - May be revoked if FDA becomes aware of information suggesting the investigation presents a potential for significant risk to study subjects or does not otherwise meet any other requirement for the FDA-determined exemption.
- Initiated by FDA
  - FDA can also grant an exemption based on a review of an IND that was submitted, if FDA determines that the clinical investigation for which the IND was submitted satisfies the requirements of the self-determined exemption and does not present a potential for significant risk to the health, safety, or welfare of subjects.
  - May be revoked.

i. Explain the reasons for the rescission.

In furtherance of achieving President Trump's goal of Making America Healthy Again ("MAHA"), CRN requests rescission of the 2013 Guidance and 2022 Proposed Rule. As stated in the Request for Information ("RFI"), an important component of MAHA is ensuring that providers and caretakers "focus on preventing and treating chronic diseases instead of having to do unnecessary or burdensome paperwork or otherwise comply with burdensome administrative requirements with no clear health benefit" 90 Fed. Reg. 20478 (May 14, 2025). As explained in more detail below, CRN believes that FDA, industry, and academia can better achieve this goal if the 2013 Guidance and 2022 Proposed Rule are rescinded.

In response to Question 1 from the RFI, the 2013 Guidance and 2022 Proposed Rule should be rescinded because they meet the following criteria identified in Executive Order 14219:

- Establish or interpret regulations that are based on unlawful delegations of legislative power and not the best reading of the underlying statutory authority or prohibition;
- Establish or interpret regulations that impose significant costs upon private parties that are not outweighed by public benefits;
- Establish or interpret regulations that harm the national interest by significantly and unjustifiably impeding technological innovation and research and development, impose undue burdens on small business, and impede private enterprise and entrepreneurship.

In response to Question 3 from the RFI, the 2013 Guidance and 2022 Proposed Rule should be rescinded because they also meet the following general deregulatory considerations under Executive Order 14192:

- Confusing or unnecessarily complicated;
- Impose requirements on the wrong individual or group;
- Impede efforts to innovate;
- Otherwise interfere with the public or private sector's ability to promote the health and wellbeing of Americans.

Rescinding the 2013 Guidance and 2022 Proposed Rule would have significant cost savings. If allowed to remain in place or finalized, both documents would impose confusing, burdensome, and costly requirements on FDA, industry, and academia to obtain INDs for dietary supplements and foods when Congress did not intend such requirements to extend beyond drugs. These unnecessary regulatory burdens impede innovation, private enterprise, and entrepreneurship, and do not promote the Public Health and wellbeing of Americans. Rather, these unwarranted burdens would encourage industry and academics to move their valuable investments in innovative research overseas instead of conducting such research in the U.S. Thus, rescinding the 2013 Guidance and 2022 Proposed Rule would save industry and academia time and resources from completing and submitting an IND for researching the dietary supplements and food, while also saving FDA time and resources from having to review

unnecessary IND applications or submissions to exempt certain clinical investigations from the IND requirements. It would also encourage cutting edge research on dietary supplements and foods that would promote the health and wellbeing of Americans to be conducted on U.S. soil, thereby supporting U.S. jobs and bolstering the U.S. economy.

(1) The 2013 Guidance and 2022 Proposed Rule Establish or Interpret Regulations that are Based on Unlawful Delegations of Legislative Power and NOT the Best Reading of the Underlying Statutory Authority

As noted above, Section 505(a) of the FD&C Act prohibits the introduction into interstate commerce of any "new drug" without premarket approval from FDA. A "new drug" is defined as, among other things, "any drug…the composition of which is such that such drug is not generally recognized…as safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereof." 21 U.S.C. § 321(p)(1). Congress enacted Section 505(i) to allow manufacturers to study the safety and efficacy of "new drugs" without violating Section 505(a). Under Section 505(i), the shipment of "new drugs" into interstate commerce for the purpose of conducting clinical investigations is permitted. Congress tasked FDA with promulgating regulations establishing a framework in which "drugs intended solely for investigational use" could be lawfully studied.

FDA promulgated 21 C.F.R. Part 312, which established the IND regulations governing the clinical study of drugs. However, Part 312 was not promulgated to regulate the clinical study of foods and dietary supplements. In the preamble to the Final Rule establishing Part 312, called the "IND Rewrite," FDA made this purpose clear:

> "This action is one part of a larger effort by FDA to improve the agency's drug approval process . . . The objectives of the IND Rewrite final rule are to establish an efficient investigational drug process in order both: (a) To focus FDA's attention during the early phase of clinical research on protecting the safety of human test subjects . . . and (b) to facilitate consultation between FDA and drug sponsors . . . to help ensure that the design of major clinical trials is acceptable and will support marketing approval if the test results are

> favorable. These changes are also intended to encourage innovation and drug development while continuing to assure the safety of test subjects." 52 Fed. Reg. 8798, 8799 (Mar. 19, 1987).

Part 312 further demonstrates that the IND regulations apply to drugs and not dietary supplements or foods. For example, Section 312.7 states that the intent of the provision is to "restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution." However, dietary supplements and foods are generally permitted to be marketed without premarket approval by FDA. Thus, subjecting dietary supplements and foods to the IND requirements creates confusion and uncertainty with respect to the classification of these products, while also imposing unnecessary burdens on regulators, and dietary supplement and food manufacturers.

In promulgating 21 C.F.R. Part 312, FDA clearly and correctly interpreted the intent of Congress that the regulation of INDs should apply solely to articles being researched as therapeutic drugs for which new drug applications were contemplated. Nowhere does FDA indicate in the promulgation of Part 312 that dietary supplements or foods are within the scope of its existing regulations pertaining to clinical investigations.

Likewise, it is patently clear that the intent of Congress in tasking FDA with establishing the IND regulatory framework was to provide a pathway for the study of "new drugs" given Section 505(a)'s prohibition against the introduction of new drugs in interstate commerce without premarket approval. Nowhere does Congress indicate that this pathway was intended to apply more broadly to the study of dietary supplements or foods.

Moreover, the current IND regulations neither provide legal authority for FDA's Human Foods Program ("HFP") to review INDs nor establish a role for HFP at any stage of the IND process. While the Center for Drug Evaluation & Research ("CDER") and the Center for Biologics, Evaluation & Research ("CBER") could consult with HFP, the Final Guidance does not describe how such a process would

work, and the current IND regulations make no reference to HFP in this regard or otherwise. It is also unclear whether CBER and CDER would harmonize their approaches to reviewing food, food component, and dietary supplement INDs between themselves and with HFP, and how FDA would ensure the various programs apply consistent approaches to reviewing such studies. This provides further evidence of the inapplicability of the IND regulations to dietary supplements or foods as the intent of these regulations are solely focused on drugs.

In addition, the IND framework is not a suitable model for the study of foods, dietary supplements, and their ingredients. The IND regulations are tailored specifically to research that involves a drug, with little application to food components. The process is designed to investigate molecules for pharmacological activity and acute toxicity potential in animals, in order to assess their diagnostic or therapeutic potential in humans. Drugs are often well-characterized synthetic molecules that are stable over time. In contrast, some dietary supplements and food components are derived from natural material that may have inherent batch-to-batch variability, multiple active ingredients, and other variables that make them unique when compared to drugs.

Even more troubling, the 2013 Guidance and 2022 Proposed Rule would allow FDA to consider what is evaluated in a clinical investigation (i.e., drug/disease endpoint or indication or a structure/function endpoint or indication) of a food or dietary supplement to determine it to be a drug requiring an IND -- even where no representations are made that the food or dietary supplement being studied will have an effect on a disease and the actual intent of the study is to use the data from the clinical study to support lawful structure/function claims. To determine whether a product is a drug or dietary supplement, FDA considers the claims and representations made for a finished product, not how the product is studied. Courts have consistently upheld this approach, which is also supported by past agency statements. *See, e.g., Brown & Williamson Tobacco Corp. v. FDA*, 153 F.3d 155, 163 (4th Cir. 1998) (citing *Coyne Beahm Inc. v. FDA*, 966 F. Supp. 1374, 1390 (M.D.N.C. 1997), *aff'd* 529 U.S. 120 (2000)); *Nat'l Nutritional Foods Assoc. v. Matthews*, 557 F.2d 325, 333 (2d Cir. 1977) (The "vendor's intent in selling the product to the public is the key element" in the FD&C Act drug definition.) *See also* Letter from FDA Chief Counsel Daniel E. Troy, to Jeffrey N. Gibbs (Oct. 17, 2002), at 3. FDA has not explained why, under the guidance, it would instead evaluate a product's intended

use using the intent of a clinical investigation in which a dietary supplement or food is used.

Notably, 21 C.F.R. § 101.93(g), which describes the criteria used by FDA to determine whether a claim about the effects of a product is a disease claim, thereby rendering the product a drug, makes no reference to the intent of the clinical investigation used to substantiate the claim.

Accordingly, the forced application of Part 312 IND requirements to dietary supplements and foods caused by the 2013 Guidance and 2022 Proposed Rule is based on unlawful assumption of legislative power by FDA and not the best reading of the underlying statutory authority provided by Congress. Such overreach creates confusion, unnecessarily complicated regulations, and imposes IND requirements on the wrong group (i.e., those studying dietary supplements and foods but not drugs). For these reasons, the 2013 Guidance and 2022 Proposed Rule should be rescinded.

(2) The 2013 Guidance and 2022 Proposed Rule Establish or Interpret Regulations that Impose Significant Costs Upon Private Parties that are Not Outweighed by Public Benefits, Harm the National Interest by Significantly and Unjustifiably Impeding Technological Innovation and Research and Development, Impose Undue Burdens on Small Business, and Impede Private Enterprise and Entrepreneurship

Robust clinical studies are essential for providing efficacious and safe dietary supplements and ensuring that dietary supplement claims are adequately substantiated. If allowed to remain in place, the 2013 Guidance and 2022 Proposed Rule would impose significant costs on industry looking to research innovative dietary ingredients and academics looking to conduct research on dietary supplements and foods, especially the type of research needed to address chronic disease as part of MAHA. The undue regulatory burdens imposed by these two documents would likely cause research to be conducted overseas where such unnecessary regulatory obstacles to innovative research do not exist or discourage such research altogether. This would, in turn, impede technological innovation and research and development in the U.S. as such innovation, research, and development would instead benefit other countries, while also having a detrimental impact on the public health here at home.

Moreover, the regulatory burdens imposed by the 2013 Guidance and 2022 Proposed Rule would impose undue burdens on small businesses as the IND process is costly and time-consuming. This would, in turn, impede private enterprise and entrepreneurship.

For instance, using the example in the 2013 Guidance regarding the role of broccoli sprouts in cancer prevention, the 2013 Guidance would require an academic researcher conducting such a study to dedicate a significant amount of time to filling out the IND application; conducting or paying for analytical testing to determine the characteristics, potency, purity, and stability, as well as safety, of the broccoli sprout test agent (assuming these characteristics are even determinable); and, likely engaging other professionals experienced with the IND process – all in addition to meeting the research institution's requirements. Further, ***even if the broccoli sprout preparation is already sold as a food or dietary supplement***, he/she would need to partner with the manufacturer to obtain information for the chemistry, manufacturing, and controls ("CMC") section of the IND application or ask the manufacturer to dedicate its own resources to establishing a product master file that can be reviewed by FDA. Although this type of expertise is common among those in the drug industry, that is not the case for academic researchers wishing to explore the benefits of commonly consumed foods and dietary supplements, who might as a result be significantly delayed or unable to complete their research. To avoid the burdens imposed by the 2013 Guidance, these researchers may instead take advantage of less onerous and confusing clinical investigation requirements in other countries.

The 2013 Guidance also thwarts the intent of MAHA by discouraging research aimed at preventing and treating chronic disease. Upon publication of the 2013 Guidance, several heads of university departments of nutrition and food science who are affected by the guidance subsequently contacted FDA to express concerns about its impact on a wide range of clinical research. They stated that applying the IND requirements to the research of supplements and foods "would have a paralyzing effect on research in the U.S. and stifle innovation and product development." They also highlighted the "confusing and contradictory" nature of the 2013 Guidance. *See* Letter from Connie M. Weaver et al., to Janet Woodcock, Director, CDER (Nov. 13, 2013), accessed July 14, 2025, from https://www.regulations.gov/comment/FDA-2010-D-0503-0019. A consortium of organizations representing the nutrition, medical, and science communities expressed similar concerns to FDA regarding the 2013 Guidance and its

implications for nutrition research. *See* Letter from American Society of Nutrition et al., to Janet Woodcock, Director, CDER (Nov. 26, 2013), accessed July 14, 2025, from https://www.regulations.gov/comment/FDA-2010-D-0503-0039.

Overall, the requirement for an IND for the clinical study of a food or dietary supplement may be viewed by researchers and industry as a costly and confusing regulatory barrier. For example, from FY 2019 to EOY 2024, about 31% of Warning Letters issued to those conducting FDA-regulated research related to the investigator's failure to submit an IND application prior to commencing research. The most common reason for filing to submit an IND was that investigators argued they were not obligated to submit an IND because the test article was a food or dietary supplement. *See* Beth Weinman, David Peloquin, and Jessica DeLalio, *Compliance Challenges for Clinical Research Cites*, FDLI – Update Magazine, Winter 2025, https://www.fdli.org/2025/02/compliance-challenges-for-clinical-research-sites/.

Moreover, by requiring an IND for supplements that are not intended to be marketed as drugs, the 2013 Guidance acts in opposition to the spirit of the Dietary Supplement Health and Education Act of 1994 ("DSHEA"). DSHEA notes the "benefits of dietary supplements to health promotion and disease prevention" and the use of supplements to "limit the incidence of chronic diseases and reduce long-term health care expenditures." DSHEA also mandates that "the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers." However, the 2013 Guidance would require an IND to study many types of dietary supplements that have been safely consumed by millions of Americans for years, as well as many food ingredients that have GRAS status, even when the research is conducted on a healthy population and is already subject to existing requirements for clinical trial safety. Thus, instead of advancing public health, which is an integral part of FDA's mission, the 2013 Guidance threatens future research opportunities, discourages investment in health promotion studies, and impedes the development of and access to safe and lawful supplements.

The confusing and unduly burdensome regulatory requirements imposed by the 2013 Guidance will also hamper research and innovation in the U.S. with respect to New Dietary Ingredients ("NDIs"). Section 201(ff)(3)(B)(ii) of the FD&C Act (21 U.S.C. § 321(ff)(3)(B)(ii)) states that a dietary supplement may not include "an article authorized

for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations have been made public." Under the 2013 Guidance, however, many potential NDIs might no longer qualify as lawful NDIs because many NDI studies would be required to be conducted under an IND. Once the existence of these newly required INDs for these potential NDIs becomes public, however, the article will no longer be a lawful NDI, notwithstanding the fact that the NDI would not be marketed for any drug purpose.

Requiring INDs for NDI research is also particularly problematic because a significant amount of dietary supplement and food component research is conducted independently and is not industry-initiated. As a result, a supplement company that is collecting data to submit an NDI notification to FDA may be unaware that independent studies are concurrently being conducted under an IND. If the independent investigator makes his or her study public before the product that would contain the NDI under investigation is marketed as a dietary supplement, however, then the product or ingredient being studied under the IND can no longer be marketed as a dietary supplement, or any food product. This is true even if the investigator conducted the IND with no commercial intent, as the 2013 Guidance makes clear that "[w]hether the IND regulations apply to a planned investigation does not depend on whether the intent of the clinical investigation is commercial or noncommercial." Instead, the NDI or a product containing the NDI previously studied under the IND would require FDA drug approval before it may be legally marketed. This creates a significant obstacle to ingredient innovation for the dietary supplement industry.

The 2022 Proposed Rule, if finalized, will lead to similar confusion and regulatory burdens for the food and dietary supplement industry. Although its purpose is to "make it easier for sponsors and sponsor-investigators to conduct certain clinical investigations evaluating drug uses of foods" by establishing exemptions from the IND requirements, the rule fails to clearly articulate what products are eligible for an exemption while also creating a burdensome exemption process. Specifically, the 2022 Proposed Rule limits IND exemptions to dietary supplement and food products that are "lawfully marketed" in the U.S., creating uncertainty as to what food and dietary supplement ingredients are subject to the exemption and limiting innovation on ingredients under development.

Determining what FDA would consider to be "lawful" is not clear in many situations, particularly in recent years due to inconsistent FDA applications of the FD&C Act and FDA regulations, as well as the lack of finalized guidance around important dietary supplement requirements. For example, companies have marketed n-acetyl-L-cysteine ("NAC") as a dietary supplement in the U.S. for decades under the assumption that FDA considered the marketing to be legal. In 2020, however, FDA issued warning letters suggesting that NAC was not a legal dietary ingredient due to the alleged timing of NAC drug approval and NAC's first use in a dietary supplement under Section 201(ff)(3)(B) of the FD&C Act, which, as discussed above, prevents an ingredient's use in food or supplements if the ingredient was approved as a drug or subject to an IND authorization and had undergone substantial, public clinical investigations before the ingredient is used in a supplement or food (i.e., "drug preclusion"). Prior to 2020, FDA had not objected to NAC's use and even noted in one public document that the agency considered it to be an appropriate dietary ingredient. FDA created similar confusion with another ingredient – nicotinamide mononucleotide ("NMN") – when it permitted new dietary ingredient notifications to move forward based on an FDA determination that NMN is an appropriate dietary ingredient. The agency later revoked this determination citing drug preclusion and the existence of IND authorization and clinical studies that purportedly predated the date of NMN's use in supplements.

In addition, the 2022 Proposed Rule fails to define the term "marketed," and, even if defined, could stifle innovation by limiting research for new product development. There are numerous reasons why a food or dietary supplement that is "lawful" in the U.S. may not have been advertised and made available to consumers. For example, a company may not have identified the right sales channels, or the company may still be conducting research to support potential claims. The "marketed" requirement may also create an unnecessary burden for investigators intending to study a product containing a combination of existing ingredients, as it would require investigators to establish the legal status of each ingredient.

IRBs would have difficulty discerning when an IND is or is not required. Erring on the side of caution, however, IRBs would likely interpret the 2013 Guidance and 2022 Proposed Rule as requiring an IND for most clinical studies, even if an IND is not needed and/or the self-determined exemption applies. Such a large volume of IND applications would create obstacles to conducting clinical research as investigators struggle to provide the necessary information, in addition to the increased workload for

an agency with already limited resources. And although the IND regulations provide a process for a sponsor to request a waiver from FDA, this request must be submitted to the agency either in an IND or in an information amendment to an IND. Moreover, under the 2022 Proposed Rule, there is no time limit for FDA to grant an exemption request, which further delays progress. Rather than navigate the waiver or exemption process or attempt to draft study protocols that avoid the need for an IND, researchers may abandon their efforts altogether – in direct contravention to the goals of MAHA by stifling research of food and dietary supplements to prevent and treat chronic disease.

Accordingly, the extension of Part 312 IND requirements to dietary supplements and foods by the 2013 Guidance and 2022 Proposed Rule impedes efforts to innovate and otherwise interferes with the public and private sector's ability to promote the health and wellbeing of Americans through clinical investigations on dietary supplements and foods. By imposing confusing and unduly burdensome regulatory requirements on clinical investigations involving dietary supplements and foods, such research is at risk of being conducted overseas and benefiting other countries, while also undermining the goals of MAHA. Thus, the costs imposed by these documents far outweigh any benefits to Americans. For these reasons, the 2013 Guidance and 2022 Proposed Rule should be rescinded.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

The text of 21 C.F.R. Part 312 would remain the same after the rescission of the 2013 Guidance and 2022 Proposed Rule.

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

II. Certain Types of Statements for Dietary Supplements: DSHEA Disclaimer Placement

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

The phrase "on each panel and page where there is such a statement" from the second sentence of 21 C.F.R. § 101.93(d) should be rescinded and modified to state:

Section 101.93(d) Placement. The disclaimer shall be placed adjacent to the statement with no intervening material or linked to the statement with a symbol (e.g., an asterisk) at the end of each such statement that refers to the same symbol placed adjacent to the disclaimer specified in paragraphs (c)(1) or (c)(2) of this section. **On product labels where such a statement is made, the disclaimer shall appear on one label panel. In labeling (e.g., pamphlets, catalogs), the disclaimer shall appear on the page where such a statement is made.** The disclaimer shall be set off in a box where it is not adjacent to the statement in question.

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

The proposed rescission/modification is a part of a Final Rule: Food Labeling; Requirements for Nutrient Content Claims, Health Claims, and Statements of Nutritional Support for Dietary Supplements.

d. What is the name of the regulation being rescinded, if applicable?

21 C.F.R. § 101.93(d), "Certain types of statements for dietary supplements, placement" (rescinding and modifying from the second sentence the phrase "on each panel or page where there is such a statement")

e. Please provide a short summary of the justifications for the rescission.

CRN proposes rescinding the phrase "on each panel or page where there is such a statement" from 21 C.F.R. § 101.93(d) and replacing it with modified language proposed above and below in sections (II)(b) and (II)(j). As currently written, Section 101.93(d) requires a disclaimer to appear on every panel of a dietary supplement label where a structure/function statement is made. The rescission of this language would allow firms the flexibility to place the disclaimer on a single label panel of a dietary supplement product that they consider appropriate.

The rescission would maintain adequate levels of consumer protection while reducing unnecessary, redundant regulatory burdens on companies. In the 27 years since 21 C.F.R. § 101.93(d) was finalized, dietary supplements have become a routine part of many consumers' wellness practices, and consumers are more knowledgeable about the differences between dietary supplements and drug products. Rescinding the phrase "on each panel or page where there is such a statement" from 21 C.F.R. § 101.93(d) will not change the requirement to provide the mandatory disclaimer in a prominent manner in a box and in bold type on the product label, when such disclaimer is not made adjacent to the statement in question. Further, a single disclaimer on a dietary supplement product's label linked to a structure/function claim by a symbol adequately informs consumers of the existence of additional information and satisfies the legislative intent to have a structure/function statement "contain" the disclaimer. The basis for the rescission is supported by relevant recent case law.

Thus, in response to Question 1 from the RFI, CRN believes that the phrase "on each panel or page where there is such a statement" should be rescinded from 21 C.F.R. §101.93(d) and modified as proposed above and below in sections (II)(b) and (II)(j) for the following reasons:

- It imposes restrictive labeling requirements for dietary supplements, which are not based on the best reading of the underlying statutory authority or prohibition.
- It hinders the streamlined use of the disclaimer on labels and reduces efficiency, thereby imposing significant costs upon private parties and imposes undue burdens on small business that are not outweighed by any public benefits.

In response to Question 3 from the RFI, the above-mentioned phrase from Section 101.93(d) should be rescinded and modified as proposed above and below in sections (II)(b) and (II)(j) for the following reasons:

- It requires information to be placed on the label that is not needed or used efficiently, by forcing dietary supplement labels to repeat the disclaimer on every panel with a structure/function claim.
- It is based on FDA's belief of consumer perception of dietary supplements in 1997, and therefore obsolete.
- It otherwise interferes with the public or private sector's ability to promote the health and wellbeing of Americans by taking up space on a product's label that could otherwise be used to include important health information about the product.

The above-mentioned rescission and requested modification satisfy the legislative intent of the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), while also reducing unreasonable regulatory burdens on businesses, reducing compliance costs, and supporting labeling efficiency – therefore advancing the goals of the Executive Order and the RFI.

f. Please insert the address of the agency.

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g. Please insert the contact information for the agency.

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Phone: 301–436–1696

h. What is the background for the regulation being rescinded?

Passed in October 1994, DSHEA amended Section 403(r) of the Federal Food, Drug, and Cosmetic Act to include Section 403(r)(6), which established requirements for nutritional statements made for dietary supplements, including structure/function claims. Section 403(r)(6)(C) provides that a structure/function statement for a dietary supplement may be made if "the statement contains, prominently displayed and in boldface type, the following: 'This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.'" 21 U.S.C. § 343(r)(6)(C).

In September 1997, FDA issued the Final Rule "Food Labeling; Requirements for Nutrient Content Claims, Health Claims, and Statements of Nutritional Support for Dietary Supplements" ("Final Rule"), which implemented the requirements in Section 403(r)(6)(C) and established placement requirements for the disclaimer under 21 C.F.R. § 101.93(d). 62 Fed. Reg. 49859 (Sept. 23, 1997).

i. Explain the reasons for the rescission.

CRN requests rescission and modification of a part of 21 C.F.R. § 101.93(d) that requires a disclaimer to appear on every panel where there is a structure/function claim, i.e., the phrase "on each panel or page where there is such a statement" Congress enacted DSHEA to establish a regulatory framework for the dietary supplement industry, aiming to balance consumer access to supplements with ensuring their safety. As explained in more detail below, CRN believes that FDA and the dietary supplement industry can better achieve this goal if the above-mentioned phrase is rescinded from 21 C.F.R. § 101.93(d) and replaced with the modified language proposed in sections (II)(b) and (II)(j).

In response to Question 1 from the RFI, CRN believes that the phrase "on each panel or page where there is such a statement" should be rescinded from 21 C.F.R. § 101.93(d) and modified for the following reasons:

- It imposes restrictive labeling requirements for dietary supplements, which are not based on the best reading of the underlying statutory authority or prohibition.

- It hinders the streamlined use of the disclaimer on labels and reduces efficiency, thereby imposing significant costs upon private parties and imposing undue burdens on small business that are not outweighed by any public benefits.

In response to Question 3 from the RFI, the above-mentioned phrase from Section 101.93(d) should be rescinded and modified for the following reasons:

- It requires information to be placed on the label that is not needed or used efficiently, by forcing dietary supplement labels to repeat the disclaimer on every panel with a structure/function claim.
- It is based on FDA's belief of consumer perception of dietary supplements in 1997, and therefore obsolete.
- It otherwise interferes with the public or private sector's ability to promote the health and wellbeing of Americans by taking up space on a product's label that could otherwise be used to include important health information about the product.

CRN requests rescission of the above-mentioned phrase from Section 101.93(d) to allow flexibility with respect to placement of the disclaimer, especially given consumers' current knowledge and familiarity with the dietary supplement category and the disclaimer, the benefits to industry efficiency, and the current lack of regulatory enforcement by FDA when a disclaimer is made in the manner proposed here.

The statutory requirement under Section 403(r)(6)(C) that a structure/function claim "contain" the required disclaimer does not specify that the disclaimer must appear on the same panel as the claim. Rather, the term "contain" may reasonably be interpreted to allow the use of a symbol that clearly links the claim to a prominently displayed disclaimer on the label. So long as the disclaimer draws consumer attention, it remains functionally "contained" within the claim as required by the statute. In practice, this approach still ensures the disclaimer is seen and understood by consumers.

The current regulation implementing Section 403(r)(6)(c), 21 C.F.R. § 101.93(d), was originally established in the 1997 Final Rule. In the 1997 Final Rule, the agency concluded that consumers are accustomed to asterisks or other symbols to associate two discrete pieces of information, but the agency further suggested that the claim and statement must be in the same field of vision, requiring a disclaimer on every panel where a statement was made. 62 Fed. Reg. 49865. However, in the 27 years since the rule was enacted, to our knowledge, FDA has never enforced any such requirement that the disclaimer appear on every panel, suggesting that the agency views a single, well-placed disclaimer as sufficient to fulfill the intended purpose of Section 403(r)(6)(c).

In the Final Rule's discussion about the standard for prominence, FDA also emphasized readability and the signaling of importance by type size and a box around the disclaimer. 62 Fed. Reg. 49866. When the disclaimer appears in a bold type size and enclosed in a box, as required by other subsections of Section 101.93, the prominence and visibility required by the statute is already achieved. Combined with a symbol such as an asterisk linking structure/function claims to the disclaimer, and, given the small packaging size of many dietary supplements and common use of small round bottles with continuous labels that wrap around the bottle, consumers can easily see the disclaimer and understand what claims it qualifies. Thus, the use of one disclaimer, even when placed on a different panel, effectively communicates the disclaimer to consumers.

Importantly, courts have supported this approach and determined that use of an asterisk effectively notifies consumers that more information is available regarding the claim. See *McWhorter v. The Procter & Gamble Co*., No. 24-cv-00806-AMO, 2025 WL 948061 (N.D. Cal. Mar. 28, 2025) (citing *Whiteside v. Kimberly-Clark Corp*., 93 F.4th 1127 (9th Cir. 2024)). In *McWhorter v. The Procter & Gamble Co*., the court affirmed that the presence of an asterisk on a front-label claim reasonably directs consumers to consult the back panel for further information. Citing the Ninth Circuit Court of Appeals' reasoning in *Whiteside v. Kimberly-Clark Corp*., the court explained that an asterisk signals to a reasonable consumer that a claim is qualified elsewhere, and therefore, the consumer cannot ignore the asterisk and claim to have been misled. Accordingly, when a structure/function claim is linked to a disclaimer via a symbol, consumers read the corresponding panel to understand the claim in full.

Class action plaintiffs have taken advantage of the unnecessary burdens imposed by the current regulation and demanded costly settlements from companies for failing to strictly comply with Section 101.93(d). Thus, by rescinding the above-mentioned redundant requirement to place the disclaimer on every label panel, companies can focus their attention on providing innovative products that promote public health, rather than defending against litigation that does nothing to protect the public health. Rescinding the requirement would also benefit businesses by streamlining label design and reducing packaging complexity. Allowing a single, clearly placed disclaimer minimizes redundant text, simplifies production workflows, and lowers associated compliance costs. It also provides more space for dietary supplement companies to include other information that would better benefit public health, such as the beneficial effects consumers can expect from the product. These advantages align with the broader goals of the RFI to reduce unnecessary regulatory burdens and support more cost-effective operations for dietary supplement companies, while also promoting public health.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

The phrase, "on each panel or page where there is such a statement" will be removed from 21 C.F.R. § 101.93(d). After the rescission, the text of 21 C.F.R. § 101.93(d) should be modified to state:

Section 101.93(d) Placement. The disclaimer shall be placed adjacent to the statement with no intervening material or linked to the statement with a symbol (e.g., an asterisk) at the end of each such statement that refers to the same symbol placed adjacent to the disclaimer specified in paragraphs (c)(1) or (c)(2) of this section. **On product labels where such a statement is made, the disclaimer shall appear on one label panel. In labeling (e.g., pamphlets, catalogs), the disclaimer shall appear on the page where such a statement is made.** The disclaimer shall be set off in a box where it is not adjacent to the statement in question.

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

III. Draft Guidance: Policy on Certain New Dietary Ingredients and Supplements

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

Draft Guidance – Policy Regarding Certain New Dietary Ingredients and Dietary Supplements Subject to the Requirement for Premarket Notification: Guidance for Industry (May 2022) ("2022 Late NDIN Draft Guidance"), available at https://www.fda.gov/media/158369/download.

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

Interpretive Rule

d. What is the name of the regulation being rescinded, if applicable? This could be the name of the part of the C.F.R. or the name of a previous rulemaking.

Draft Guidance – Policy Regarding Certain New Dietary Ingredients and Dietary Supplements Subject to the Requirement for Premarket Notification: Guidance for Industry

e. Please provide a short summary of the justifications for the rescission.

In response to Question 3 from the Request for Information ("RFI"), the 2022 Late NDIN Draft Guidance is obsolete as industry is unlikely to utilize the FDA's 180-day grace period to submit late New Dietary Ingredient Notifications ("NDINs"). The 2022 Late NDIN Draft Guidance also requires information that would not be used effectively by FDA while key issues remain unresolved regarding what dietary ingredients or products require submission of an NDIN. FDA has not made significant progress in developing tools, including the issuance of final guidance that would resolve existing confusion concerning the NDIN process, which would help companies determine their notification obligations and incentivize participation in the NDIN process. Thus, until these concerns are resolved, it is likely that only few NDINs, if any, will be submitted under the 2022 Late NDIN Draft Guidance. Even for the NDINs it does receive within the grace period, FDA would not be able to use the information effectively without first addressing the concerns from industry regarding whether the NDIN was necessary in the first place. Due to the lack of FDA final guidance on the topic, there is still significant confusion in the industry as the when an NDIN is required. Accordingly, rescission of the 2022 Late NDIN Draft Guidance is appropriate.

f. Please insert the address of the agency. [NPRM, DFR, and IFR only].

Not applicable.

g. Please insert the contact information for the agency.

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h. What is the background for the regulation being rescinded?

The Federal Food, Drug, & Cosmetic Act ("FD&C Act") requires that the manufacturer or distributor of a "new dietary ingredient" ("NDI") that has not been present in the food supply as an article used for food in a form in which the food has not been

chemically altered, or a dietary supplement that contains an NDI, must submit an NDIN to FDA at least 75 days before introducing the product into interstate commerce. 21 U.S.C. § 350b(a). NDINs must contain information providing the basis on which the manufacturer or distributor of the NDI, or dietary supplement containing the NDI, has concluded that the dietary supplement containing the NDI is reasonably expected to be safe. 21 C.F.R. §190.6.

In May 2022, FDA issued the 2022 Late NDIN Draft Guidance stating that the agency is aware that some manufacturers and distributors have marketed products for which a premarket NDIN may be required but was not submitted. The guidance further states that FDA intends to exercise enforcement discretion for a limited time and in limited circumstances to encourage firms to submit NDINs. The enforcement discretion would last for 180 days following the publication in the Federal Register of a final version of the guidance, and submitters must show that the dietary supplement subject of the NDIN was marketed in the U.S. as of May 20, 2022. The guidance also indicates that, while FDA would be able to confirm receipt of a NDIN within 75 days of receipt, the agency does not anticipate completing its scientific evaluation and providing a response to the NDIN within that time period.

i. Explain the reasons for the rescission.

In response to Question 3 from the RFI, the 2022 Late NDIN Draft Guidance is obsolete as industry is unlikely to utilize the FDA's 180-day grace period to submit late NDINs, as further discussed below. The 2022 Late NDIN Draft Guidance also requires information that would not be used effectively by FDA given key issues regarding NDINs remain unresolved. Stated differently, if the 2022 Late NDIN Draft Guidance is finalized, FDA would be exercising enforcement discretion in an area that it has not fully conceptualized—i.e., what constitutes an NDI and whether submission of a late NDIN is even required.

FDA first issued its Draft Guidance for Industry on New Dietary Ingredient Notifications and Related Issues ("NDIN Draft Guidance") in July 2011. 76 Fed. Reg. 39111 (July 5, 2011). The NDIN Draft Guidance was issued with the stated purpose of helping manufacturers and distributors of dietary ingredients and dietary supplements to determine what qualifies as an NDI, when an NDIN is required, what information

should be provided in the NDIN, and related issues. After receiving numerous industry comments citing concerns with 2011 Guidance, in August 2016, FDA issued a revised version of the NDIN Draft Guidance that superseded the 2011 Guidance. 81 Fed. Reg. 53486 (August 21, 2016). Once again, industry stakeholders stated concerns with the NDIN Draft Guidance, noting that it would create significant and unnecessary burdens on the dietary supplement industry without increasing safety for consumers, cause significant confusion about when an NDIN is required, and is wholly inconsistent with Dietary Supplement Health and Education Act of 1994 ("DSHEA"). See Council for Responsible Nutrition. Comment from Council for Responsible Nutrition (Received on Dec. 12, 2016). https://www.regulations.gov/comment/FDA-2011-D-0376-1994. Among other issues, in the NDIN Draft Guidance FDA narrowly interprets "dietary substance" to substances that have a history of "common use" as food or drink, despite Congress not imposing such "common use" requirements. In addition, FDA stated in 2016 that it was willing to establish an authoritative list of pre-1994 dietary ingredients that are not subject to the NDIN requirement. Other than holding a public meeting in 2017, no progress has been made to create an authoritative list of pre-DSHEA dietary ingredients that would be exempt from the NDIN requirements. As a result, there is confusion and uncertainty in industry as to what ingredients would be considered "old dietary ingredients" and therefore not require an NDIN.

Numerous other questions remain with respect to the 2016 NDIN Draft Guidance, and nearly a decade later, the guidance remains in draft form with the sole exception of Section V, which pertains to NDIN procedures and timeframes. However, this section was only finalized in March 2024. This lack of progress continues to discourage industry from submitting NDINs, despite FDA's expressed intent to exercise enforcement discretion per the 2022 Late NDIN Guidance.

Moreover, FDA states in the 2022 Late NDIN Guidance that it may not be able to review notifications within 75 days after the notification is submitted. This uncertainty of when submitters may receive a response from FDA, and whether they have time to respond to FDA comments before their notification becomes public, further discourages manufacturers and distributors from submitting NDINs.

Overall, FDA made minimal progress in developing tools that would help companies determine their notification obligations and incentivize participation in the NDIN

process. Thus, while some companies may be prepared to submit late NDINs within FDA's 180-day grace period, much of the industry is waiting for FDA to address major concerns related to the confusion caused by the 2016 NDIN Draft Guidance. Until these concerns are resolved, it is likely that only a few NDINs, if any, will be submitted under the 2022 Late NDIN Draft Guidance. Even for the NDINs it does receive within the grace period, CRN believes FDA would not be able to use the information effectively without first addressing the concerns from industry regarding whether the NDIN was necessary in the first place. Accordingly, CRN believes that rescission of the 2022 Late NDIN Draft Guidance is appropriate.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

Rescission of the 2022 Late NDIN Guidance would not affect the text of any regulation. The text of 21 C.F.R. § 190.6, which describes the NDIN requirements, will remain unchanged.

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

IV. Interim Final Rule: Petition for Exemption from 100% Identity Testing of Dietary Ingredients

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

The petition exemption referenced in the latter part of 21 C.F.R. § 111.75(a)(1)(i) (i.e., "unless you petition the agency under paragraph (a)(1)(ii) of this section and the agency exempts you from such testing") and described under 21 C.F.R. § 111.75(a)(1)(ii).

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

Interim Final Rule

d. What is the name of the regulation being rescinded, if applicable? This could be the name of the part of the C.F.R. or the name of a previous rulemaking.

Certain portions of 21 C.F.R. § 111.75(a)(1)(i) ("unless you petition the agency under paragraph (a)(1)(ii) of this section and the agency exempts you from such testing;") and subsection (ii) in its entirety and 21 C.F.R. § 111.95(b)(6).

e. Please provide a short summary of the justifications for the rescission.

In response to Question 3 from the Request for Information ("RFI," 90 FR 20478 (May 14, 2025)), it is CRN's opinion that the portions of 21 C.F.R. § 111.75(a)(1)(i) ("unless you petition the agency under paragraph (a)(1)(ii) of this section and the agency exempts you from such testing;") and the entirety of subsection (ii) allowing for the submission of a petition to exempt a manufacturer from 100% identity testing on dietary ingredients, and 21 C.F.R. § 111.95(b)(6) establishing related recordkeeping requirements are obsolete and should be rescinded. Since the Interim Final Rule permitting the submission of this exemption petition was issued in June 2007 (72 Fed. Reg. 34959 (June 25, 2007)), CRN understands that only one such petition has been submitted to FDA. This sole petition was ultimately withdrawn as it was submitted by the ingredient supplier rather than the manufacturer as mandated by regulation, and the petition was never resubmitted. Rescinding these regulations would have minimal impact on industry as it has not been used by industry in the almost two decades it has been in place. It would also result in significant cost savings for the government as FDA would not have to allocate resources for evaluating such exemption petitions should they be submitted.

f. Please insert the address of the agency. [NPRM, DFR, and IFR only].

Food and Drug Administration
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Silver Spring, MD 20993–0002

g. Please insert the contact information for the agency.

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h. What is the background for the regulation being rescinded?

As required by the Dietary Supplement Health and Education Act of 1994, in 2007 FDA finalized Current Good Manufacturing Practice ("CGMP") regulations under 21 C.F.R. Part 111 that establish minimum requirements related to the manufacturing, packaging, labeling, or holding of dietary supplements to ensure the quality of dietary supplements. Section 111.75 of the CGMPS ("What must you do to determine whether specifications are met?") requires manufacturers to perform their own identity testing to verify the identity of all dietary ingredients prior to use in the manufacturing process (i.e., 100 percent identity testing of dietary ingredients), regardless of whether the dietary ingredient is manufactured in house or purchased by the manufacturer from a dietary ingredient supplier.

In addition to the final CGMP rule, FDA also issued an Interim Final Rule ("IFR") that added language Section 111.75(a)(1)(i) and (ii) that would allow a manufacturer to submit a petition to FDA under Section 10.30 for an exemption from the requirement of 100 percent identity testing. The petition, if granted by FDA, would allow the manufacturer to reduce the frequency of identity testing of components that are dietary

ingredients from 100 percent to some lower frequency. In the preamble to the Interim Final Rule, FDA noted its position that "it may be possible for a manufacturer to demonstrate, through various methods and processes in use over time for its particular operation, that a system of less than 100 percent identity testing would result in no material diminution of assurance of the identity of the dietary ingredient as compared to the assurance provided by 100 percent identity testing." 72 Fed. Reg. at 34959-60. The IFR also added 21 C.F.R. § 111.95(b), which requires that a manufacturer keep FDA's response to a petition submitted under § 111.75(a)(1)(ii) as a record.

i. Explain the reasons for the rescission.

In response to Question 3 from the RFI, it is CRN's opinion that the portions of 21 C.F.R. § 111.75(a)(1)(i) and subsection (ii) in its entirety allowing for the submission of a petition to exempt a manufacturer from 100 percent identity testing on dietary ingredients and 21 C.F.R. § 111.95(b)(6) establishing related recordkeeping requirements are obsolete and should be rescinded. As noted above, the IFR permitting the submission of this petition was issued in June 2007. In the almost 20 years that the rule has been in place, CRN understands that only one such petition has been submitted to FDA, which was ultimately withdrawn as it was submitted by the ingredient supplier rather than the manufacturer as mandated by the regulation. The petition was never resubmitted.

Rescinding these regulations would result in significant cost savings for the government as FDA would not have to allocate resources to evaluating such exemption petitions should they be submitted. If the regulations remain in place, FDA would be required to dedicate considerable resources to establish a review process for any petitions that are ultimately properly submitted under Section 111.75(a)(1)(ii) as it does not currently have such a review process in place (again, it has never reviewed a completed petition pursuant to this regulation). This would be a wasteful allocation of resources for a petition that appears to be rarely, if ever, utilized by industry.

Moreover, given that the exemption petition has not been utilized by industry in almost 20 years, rescinding the rule allowing for the petition would have minimal impact on industry. Based on the above, CRN believes the IFR is obsolete and would be a prime

candidate for repeal to make room for a new, more consequential regulation that would better protect the public health.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

The petition exemption referenced in the latter part of 21 C.F.R. § 111.75(a)(1)(i) (i.e., "unless you petition the agency under paragraph (a)(1)(ii) of this section and the agency exempts you from such testing") and the entirety of 21 C.F.R. § 111.75(a)(1)(ii) would be removed from the regulations. The rest of Section 111.75(a)(1) would remain the same. In addition, 21 C.F.R. § 111.95(b)(6) establishing related recordkeeping requirements associated with submission of a petition under § 111.75(a)(1)(ii) would be removed.

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

V. Nutrition Labeling of Dietary Supplements: Declaration of the Quantitative Amount of Other Dietary Ingredients

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

21 C.F.R. § 101.36(b)(3)(ii) and 101.36(c)(3) should be revised as proposed in below section (j). If these regulations are revised, the draft guidance, "Policy Regarding Quantitative Labeling of Dietary Supplements Containing Live Microbials: Draft Guidance for Industry" (Draft Guidance) (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-policy-regarding-quantitative-labeling-dietary-supplements-containing-live) should be rescinded.

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

21 C.F.R. § 101.36(b)(3)(ii) and 101.36(c)(3) are final rules, and "Policy Regarding Quantitative Labeling of Dietary Supplements Containing Live Microbials: Draft Guidance for Industry" is draft guidance.

d. What is the name of the regulation being rescinded, if applicable? This could be the name of the part of the C.F.R. or the name of a previous rulemaking.

21 C.F.R. 101.36 - Nutrition Labeling of Dietary Supplements. Specifically, 21 C.F.R. § 101.36(b)(3)(ii) and 21 C.F.R. 101.36(c)(3) should be revised.

e. Please provide a short summary of the justifications for the rescission.

In response to Questions 3 and 5 in the RFI, CRN believes the nutrition labeling of dietary supplements regulation requiring declaration of the quantitative amount of live microbials by metric weight should be revised for the following reasons:

- The regulation is obsolete as the requirement for declaring the quantitative amount of dietary ingredients in metric weight did not consider application to live microbials.
- The regulation interferes with the private sector's ability to promote the health and wellbeing of Americans by not permitting information that helps consumers and healthcare providers make informed choices about dietary supplements containing live microbials.

- The regulation no longer reflects the current state of technology because the scientifically accepted unit of measure for live microbials is CFUs and not metric weight.

Currently, 21 C.F.R. § 101.36(b)(3)(ii) requires that the quantitative amount of "other dietary ingredients," which include probiotics, be declared by weight per serving. However, probiotics are live microorganisms and declaration of weight does not indicate the viability of the probiotics in the product throughout shelf life. The quantity in CFUs represents the amount of viable microorganisms in the product and is the scientifically accepted unit of measure for probiotics. Providing science-based, accurate labeling information will help consumers and healthcare professionals to make informed choices. Therefore, 21 C.F.R. § 101.36(b)(3)(ii) should be amended to require the quantitative amount of probiotic dietary ingredients to be declared in CFUs.

For proprietary blends, 21 C.F.R. § 101.36(c)(2) indicates that "other dietary ingredients" contained in the proprietary blend shall be declared in descending order of predominance by weight. Further, 21 C.F.R. § 101.36(c)(3) requires that the quantitative amount by weight specified for the proprietary blend shall be the total weight of all other dietary ingredients contained in the proprietary blend. FDA should similarly amend these regulations to require the quantity of a probiotic blend of probiotics to be declared in CFUs, and to require the probiotic dietary ingredients in the proprietary blend to be declared in descending order of predominance by CFUs.

FDA announced in the Draft Guidance the agency's intention to exercise enforcement discretion when supplement marketers use CFUs when declaring the quantity of live microbials on a Supplement Facts label. However, the draft guidance states that supplements must also list the quantitative amount of live microbial dietary ingredients by metric weight, as is required by current regulation applicable generally to other dietary supplements, in addition to an expression of CFUs; supplements must also list live microbial dietary ingredients in a proprietary blend in descending order of predominance by weight. CRN is concerned that the listing of the quantitative amount in CFUs and by metric weight is not feasible because CFUs are not correlated directly to weight. In fact, FDA states in the Draft Guidance that "(t)he weight of microbial dietary ingredient in a product represents the product's total cellular mass, consisting

of both live and dead microorganisms, and therefore does not necessarily correlate with the number of viable microorganisms in that product."

f. Please insert the address of the agency. [NPRM, DFR, and IFR only].

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g. Please insert contact information for the agency.

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5100 Paint Branch Pkwy.
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Phone: 301–436–1696

h. What is the background for the regulation being rescinded?

In proposed rule, "Food Labeling: Revision of the Nutrition and Supplement Facts Labels" (79 Fed. Reg. 11879 (March 3, 2014)), FDA proposed to revise its labeling regulations for conventional foods and dietary supplements to provide updated nutrition information on the label to assist consumers in maintaining healthy dietary practices. In response, CRN submitted comments to request that, among other things, FDA consider providing flexibility regarding units of measure for dietary ingredients that are more accurately labeled with units of measure specific to the ingredient, such as colony forming units (CFUs) for probiotics. In the final rule, "Food Labeling: Revision of the Nutrition and Supplement Facts Labels" (81 Fed. Reg. 33742 (May 27, 2016)), FDA declined CRN's request and indicated it will address the issue separately from the final rule, stating:

"We recognize that manufacturers are using a number of different units of measure for probiotics, enzymes, and other dietary ingredients. We need to fully evaluate each unit of measure for dietary ingredients to determine if it is appropriate for use on the Supplement Facts label, and if there are any implications to allowing for the use of such

units of measure on the label. Because of the complexity of these labeling concerns, we plan to issue information related to this subject at a later date."

21 C.F.R. § 101.36(b)(3)(ii) and 21 C.F.R. § 101.36(c)(2) require the declaration of dietary ingredient quantity by weight. For live microbials, weight does not provide any information about the quantity of live microbials in a product. Declaring quantity by weight does not provide consumers with accurate information about the amount of viable microorganisms present in a product throughout shelf life.

In 2018, FDA issued Draft Guidance, Policy Regarding Quantitative Labeling of Dietary Supplements Containing Live Microbials, indicating the agency's intent to exercise enforcement discretion for products containing live microbials that declare quantity in CFUs, but requires quantity to also be declared by weight. CRN is concerned that the listing of the quantitative amount in CFUs and by metric weight is not feasible because CFUs are not correlated directly to weight. In fact, FDA states in the Draft Guidance that "(t)he weight of microbial dietary ingredient in a product represents the product's total cellular mass, consisting of both live and dead microorganisms, and therefore does not necessarily correlate with the number of viable microorganisms in that product." To achieve a consistent live microbial quantity in CFUs, the weight of a particular CFU count may vary from batch to batch. As such, it is not practical to label the weight of each batch individually or to list individual live microbial ingredients within a blend in descending order by weight for each batch. Further, listing different weights on product labels that contain the same CFU counts would confuse consumers. Therefore, it is practical to declare live microbial ingredient quantities in either CFU or total cellular mass as weight, but not both. However, it is the CFU, and not weight, that is the scientifically accepted unit of measure for declaring quantitative amounts of live microbial ingredients.

i. Explain the reasons for the rescission.

The reason for the proposed revision of 21 C.F.R. § 101.36(b)(3)(ii) and 101.36(c)(3) and subsequent recission of the Draft Guidance is twofold: the regulation no longer reflects the current state of technology, and the regulation is bad policy, unreasoned, or unsound.

Current regulation requires the quantity of dietary ingredients to be listed by weight. However, weight is not an appropriate unit of measure for live microbial ingredients because it represents the total cellular mass of an ingredient, including live and dead

microorganisms. Within a microbial dietary ingredient, it is not possible to distinguish the weight of live microorganisms from that of dead microorganisms. Consequently, dietary supplement manufacturers cannot measure and label the weight of the live microorganism component of a microbial dietary ingredient. If quantity were to be labeled in weight, both live and dead microorganisms would be included and would not provide consumers with information about the amount of the relevant, beneficial ingredient (i.e., live microorganisms).

While the Draft Guidance indicates FDA's intent to exercise enforcement discretion when supplement marketers use CFUs when declaring the quantity of live microbials on a label, the Draft Guidance states that supplements must also list the quantitative amount by metric weight. To achieve a consistent live microbial quantity in CFUs, the weight of a particular CFU count may vary from batch to batch. As such, it is not practical to label the weight of each batch individually or to list individual live microbial ingredients within a blend in descending order by weight for each batch. Further, listing different weights on product labels that contain the same CFU counts would confuse consumers. Therefore, it is practical to declare live microbial ingredient quantities in either CFU or total cellular mass as weight, but not both. However, it is the CFU, and not weight, that is the scientifically accepted unit of measure for declaring quantitative amounts of live microbial ingredients.

Declaration of dietary ingredients in a Supplement Facts label should provide the most meaningful information to consumers and, to that end, FDA has previously ruled that the claimed amount of certain nutrients should be expressed in units that are most helpful to consumers and that do not necessarily match the weight of the source ingredient. For example, vitamin E claims are based on the equivalent amount of alpha tocopherol and different conversion factors are used to determine the vitamin E weight claim that corresponds to the type of vitamin E used in the product. Similarly, vitamin A claims are based on retinol activity equivalents and therefore the amount of vitamin A claimed from non-retinol ingredients such as beta-carotene is different from the weight of the source ingredient. Likewise, a mineral claim does not reflect the total weight of the mineral salt, but only the active elemental mineral component. In the case of probiotics, live microorganisms are the beneficial and relevant portion of the ingredient. As such, only live microorganism quantity should be declared on a Supplement Facts label.

FDA recognizes in the Draft Guidance that "the labeled weight of the microbial ingredient may not accurately reflect the number of live microorganisms throughout the range of times a product is expected to be consumed because live microorganisms are susceptible to cell death throughout the shelf life of a product." Similarly, vitamins and other dietary ingredients are subject to degradation throughout the product lifecycle (e.g., warehouse, shipping, retail, and consumer shelves). To meet the claimed amount at end of shelf life, the addition of an overage at time of manufacture may be required. Just as the amount of a vitamin declared on a Supplement Facts label does not include an intentional overage, the claimed amount of a live microbial ingredient should not include an overage that is included to compensate for cells that die during the product's shelf life. The labeled quantity should reflect only the amount of live, viable cells at the end of shelf life. This is not possible if quantity is declared by weight.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

21 C.F.R. § 101.36 (b)(3) Information on dietary ingredients for which RDI's and DRV's have not been established" should be revised as follows:
"(ii) The quantitative amount by weight per serving of other dietary ingredients shall be presented in the same manner as the corresponding information required in paragraph (b)(2)(ii) of this section or, when a linear display is used, shall be presented immediately following the name of the other dietary ingredient. For other dietary ingredients that are live microbials, the quantitative amount shall be presented using colony forming units (CFU), the appropriate unit of measure to indicate the amount of live microbial organisms. The quantitative amount by weight shall be the weight of the other dietary ingredient listed and not the weight of any component, or the source, of that dietary ingredient."

Additionally, 21 C.F.R. § 101.36(c)(3) should be amended as follows:

"The quantitative amount by weight, or by CFUs for proprietary blends of live microbials as described in paragraph (b)(3)(ii) of this section, specified for the proprietary blend shall be the total weight (or CFUs) of all other dietary ingredients contained in the proprietary blend…A symbol…or immediately following the quantitative amount by weight (or by CFUs) for the proprietary blend."

If the final rule is revised as proposed, the Draft Guidance on Policy Regarding Quantitative Labeling of Dietary Supplements Containing Live Microbials: Guidance for Industry should be rescinded.

k. Please insert the name of the current agency head

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

VI. Nutrient Content Claims for the Calorie Content of Foods – Sugar Content Claims – Sugar Free

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

21 C.F.R. § 101.60(c)(1)(iii) should be rescinded and modified as proposed in below section (j).

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

The proposed rescission is a final rule.

d. What is the name of the regulation being rescinded, if applicable?

21 C.F.R. § 101.60 – Nutrient content claims for the calorie content of foods – Sugar content claims. Specifically, 21 C.F.R. § 101.60(c)(1)(iii) addressing "sugar free" and similar terms.

e. Please provide a short summary of the justifications for the rescission.

In response to Question 3 from the RFI, CRN believes the regulation's requirements for dietary supplements that meet the "sugar free" criteria to bear the statement "not a low calorie food" should be rescinded and revised for the following reasons:

- The regulation interferes with the private sector's ability to promote the health and wellbeing of Americans by requiring confusing statements on certain dietary supplements that use the term "sugar free" or similar terms.

FDA regulations prohibit dietary supplements from bearing claims about calories. As a result, dietary supplements that meet the criteria for the "low calorie" claim are not permitted to use the term "low calorie" or similar terms in the product label or labeling, with a few exceptions. Dietary supplements are permitted to use the term "sugar free" and similar terms if they meet the criteria; however, those dietary supplements that are not low calorie and are sugar free must include the statement, "not a low calorie food." The requirement for this statement is confusing because consumers do not encounter many dietary supplements that use the term "low calorie" so when consumers see "not a low calorie food" on dietary supplements, they may misunderstand that all dietary supplements are "not a low calorie food" when, in fact, most dietary supplements are low calorie.

Additionally, most dietary supplements are prohibited from using the term "low calorie" by 21 C.F.R. § 101.60(a)(4). Therefore, although many dietary supplements meet the definition of "low calorie," it would be rare for a consumer to encounter a dietary supplement bearing the term "low calorie." Consumers may instead find dietary supplements with the term "sugar free" and no statement about calorie content even when they meet the definition of "low calorie."

To avoid this contradiction and consumer confusion, the regulation pertaining to sugar free content claims should be amended to exempt dietary supplements from the requirement to bear the statement "not a low calorie food." This statement deters consumers from dietary supplements that use the term "sugar free," even those that

are “low calorie” (but cannot state that fact) if they misperceive that all dietary supplements are not a low calorie food.

f. Please insert the address of the agency. [NPRM, DFR, and IFR only]

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g. Please insert the contact information for the agency.

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Phone: 301–436–1696

h. What is the background for the regulation being rescinded?

In the final rule, “Food Labeling; Requirements for Nutrient Content Claims for Dietary Supplements of Vitamins, Minerals, Herbs, and Other Similar Nutritional Substances” (59 Fed. Red. 354 (January 4, 1994)), FDA amended its nutrient content claims regulations to (1) include dietary supplements under the coverage of the general principles for nutrient content claims; (2) provide for the use of expressed and implied nutrient content claims on labels or in labeling of dietary supplements; and (3) provide for petitions for nutrient content claims for dietary supplements. The final rule was promulgated in response to the Nutrition Labeling and Education Act of 1990 and to the Dietary Supplement Act of 1992.

21 C.F.R. § 101.60(a)(4) prohibits dietary supplements from bearing claims about calories unless there is a similar dietary supplement that normally exceeds the definition of “low calorie.” The regulation states:

> "For dietary supplements, claims regarding calories may not be made on products that meet the criteria in § 101.60(b)(1) or (b)(2) for "calorie free" or "low calorie" claims except when an equivalent amount of a similar dietary supplement (e.g., another protein supplement) that the labeled food resembles and for which it substitutes, normally exceeds the definition for "low calorie" in § 101.60(b)(2)."

Although most dietary supplements are prohibited from bearing claims about calories, they are permitted to bear claims about sugar content, such as "sugar free" if they meet the definition for the claim. As part of the criteria for use of the term "sugar free" and similar terms, a product must meet the conditions described in 21 C.F.R. § 101.60(c)(1)(iii):

> (A) It is labeled "low calorie" or "reduced calorie" or bears a relative claim of special dietary usefulness labeled in compliance with paragraphs (b)(2), (b)(3), (b)(4), or (b)(5) of this section, or, if a dietary supplement, it meets the definition in paragraph (b)(2) of this section for "low calorie" but is prohibited by §§ 101.13(b)(5) and 101.60(a)(4) from bearing the claim; or
>
> (B) Such term is immediately accompanied, each time it is used, by either the statement "not a reduced calorie food," "not a low calorie food," or "not for weight control."

Accordingly, those dietary supplements that <u>do not</u> meet the definition of "low calorie" but otherwise meet the definition for "sugar free" must bear a disclaimer "not a low-calorie food" or other statements as prescribed in the regulation.

i. Explain the reasons for the rescission.

21 C.F.R. § 101.60(c)(1)(iii) should be rescinded and revised because it is unreasoned and causes confusion. Most dietary supplements are prohibited from using the term "low calorie" by 21 C.F.R. § 101.60(a)(4), so it would be rare for a consumer to encounter a dietary supplement bearing the term "low calorie" even when many dietary supplements meet the definition of "low calorie." Consumers may find dietary supplements with the term "sugar free" and no statement about calorie content even when they are indeed "low calorie."

Under 21 C.F.R. § 101.60(c)(1)(iii), dietary supplements that are not "low calorie" and otherwise meet the definition of "sugar free" are required to include a disclaimer "not a low calorie food." This requirement for a disclaimer is confusing because consumers rarely see the "low calorie" claim on dietary supplements in the first place and may misperceive that all dietary supplements are "not a low calorie food" when they encounter dietary supplements that contain both statements of "sugar free" and "not a low calorie food." Yet, most dietary supplements contain insignificant calories. The regulations allow most conventional foods to use the term "low calorie" and "sugar free" when they meet the definition, so consumers may encounter food products that are labeled "low calorie" and "sugar free." Food product labeling can also convey options that are not low calorie and are sugar free. The same is not afforded for dietary supplements which are generally not permitted to use the term low calorie. Hence, the statement "not a low calorie food" required for certain sugar free dietary supplements is confusing and implies that all dietary supplements are not low calorie (which is contrary to fact). Therefore, 21 C.F.R. § 101.60(c)(1)(iii)(B) should exempt dietary supplements from the requirement to include the statement "not a reduced calorie food," "not a low calorie food," or "not for weight control."

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

21 C.F.R. § 101.60(c)(1)(iii)
...
B) Such term is immediately accompanied, each time it is used, by either the statement "not a reduced calorie food," "not a low calorie food," or "not for weight control" **except if the product is a dietary supplement**.

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

VII. Nutrient Content Claims for Calorie Content of Foods – Sugar Content Claims – Reduced Sugar

a. Which agency/agencies promulgated the regulation?

U.S. Food and Drug Administration

b. Which title, parts, and/or sections of the Code of Federal Regulations (C.F.R.) should be rescinded?

The phrase "and dietary supplements of vitamins and minerals" should be rescinded from 21 C.F.R. § 101.60(c)(5), which states, in part:

"The terms "reduced sugar," "reduced in sugar," "sugar reduced," "less sugar," "lower sugar" or "lower in sugar" may be used on the label or in labeling of foods, except meal products as defined in § 101.13(l), main dish products as defined in § 101.13(m), and dietary supplements of vitamins or minerals, provided that . . . ."

c. Is your proposed rescission a notice of proposed rulemaking, final rule, direct final rule, interim final rule, or interpretive rule?

The proposed rescission is a final rule.

d. What is the name of the regulation being rescinded, if applicable?

21 C.F.R. § 101.60 – Nutrient content claims for the calorie content of foods - Sugar content claims. Specifically, 21 C.F.R. § 101.60(c)(5) addressing "reduced sugar" and similar terms.

e. Please provide a short summary of the justifications for the rescission.

In response to Question 1, 2, and 3 from the RFI, CRN believes that the regulation's prohibition of dietary supplements of vitamins and minerals from using the term "reduced sugar" and similar terms should be removed by rescinding the phrase "and dietary supplements of vitamins and minerals" from 21 C.F.R. §101.60(5) for the following reasons:

- The regulation imposes an unjustifiable prohibition of dietary supplements of vitamins and mineral only, which is not based on the best reading of the underlying statutory authority or prohibition.
- The regulation prohibits the communication of truthful and non-misleading information about a product's sugar content, thereby hindering the policy goals of Executive Order 14212 to focus on reversing chronic disease.
- The regulation is obsolete because it is based on a prohibition in the Food, Drug, and Cosmetic Act (FD&C Act) that no longer exists.
- The regulation interferes with the private sector's ability to promote the health and wellbeing of Americans by using terms on product labels such as "reduced sugar" when it is truthful.

21 C.F.R. § 101.60(c)(5) allows use of the terms "reduced sugar" and similar terms on food product label or labeling if criteria are met but prohibits dietary supplements of vitamins and minerals. This prohibition is not justified because it is inconsistent with the FD&C Act as amended by the Dietary Supplement Health and Education Act of 1994 (DSHEA). The FD&C Act currently does not prohibit the labeling or advertising of dietary supplements of vitamins and minerals from giving prominence to or emphasizing ingredients that are not vitamins or minerals. This prohibition was struck from the FD&C Act after the final rule, but FDA has not updated the rule to reflect the change in the statute. As it currently stands, the regulation prohibiting dietary supplements of vitamins and minerals from using the terms "reduced sugar" and similar terms is obsolete and inconsistent with the statute.

The regulation currently states, in part:

> "The terms "reduced sugar," "reduced in sugar," "sugar reduced," "less sugar," "lower sugar" or "lower in sugar" may be used on the label or in labeling of foods, except meal products as defined in § 101.13(l), main dish products as defined in § 101.13(m), and dietary supplements of vitamins or minerals, provided that…"

f. Please insert the address of the agency. [NPRM, DRF, IFR only]

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Silver Spring, MD 20993–0002

g. Please insert the contact information for the agency.

Cara Welch
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5100 Paint Branch Pkwy.
College Park, MD 20740
Phone: 301–436–1696

h. What is the background for the regulation being rescinded?

In its proposed rule, "Food Labeling; Requirements for Nutrient Content Claims for Dietary Supplements of Vitamins, Minerals, Herbs, and Other Similar Nutritional Substances" (58 Fed. Reg. 33744 (June 18, 1993)), FDA proposed to include (1) dietary supplements under the coverage of the general principles for nutrient content claims; (2) provide for the use of expressed and implied nutrient content claims on labels or in labeling of dietary supplements; and (3) provide for petitions for nutrient content claims for dietary supplements. The proposed rule was in response to the Nutrition Labeling and Education Act of 1990 and to the Dietary Supplement Act of 1992. The proposed rule explains that it does not permit the label or labeling of dietary supplements of vitamins and minerals from bearing the terms "reduced sugar" or similar terms because of specific language in the FD&C Act Section 411(21 U.S.C. § 350(b)(2)). FDA states:

> "Section 101.60(c)(4), which FDA is proposing to redesignate as § 101.60(c)(5), defines "reduced sugar," "less sugar," and "lower sugar" as a reduction of at least 25 percent per reference amount. FDA tentatively concludes that these terms cannot be made on dietary supplements of vitamins and minerals because section 411 of the act states that labeling and advertising for dietary supplements of vitamins and minerals cannot give prominence to or emphasize ingredients that are not vitamins or minerals. Therefore, FDA is proposing to amend § 101.60(c)(5) by adding dietary supplements to the list of foods on which the use of the term "reduced" or its synonyms to describe the sugars content is not permissible. However, under this proposal, these terms may be used on dietary supplements that are not subject to section 411 of the act, such as dietary supplements of fiber, of herbs, and of other similar nutritional substances. Section 411 does not preclude such claims and, as stated above, the agency has tentatively concluded that the definition of terms should be consistent for all foods at least to the extent permitted by law."

In its final rule, "Food Labeling; Requirements for Nutrient Content Claims for Dietary Supplements of Vitamins, Minerals, Herbs, and Other Similar Nutritional Substances," (59 Fed. Red. 354 (January 4, 1994)), FDA finalized 21 C.F.R. § 101.60(c)(5) as proposed, prohibiting dietary supplements of vitamins and minerals from bearing the "reduced sugar" and similar terms. The final rule was issued prior to the passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA), which among other things, defined dietary supplements and amended the FD&C Act. One such amendment "struck out former subpar. (B), which read as follows: ''Notwithstanding the provisions of subparagraph (A), the labeling and advertising for any food to which this section applies may not give prominence to or emphasize ingredients which are not— ''(i) vitamins, ''(ii) minerals, or ''(iii) represented as a source of vitamins or minerals.'' (See "Editorial Notes" for FD&C Act Section 411(21 USC 350)). Hence, the subpart of FD&C Act Section 411 referenced in FDA's 1993 proposed rule justifying the prohibition of dietary supplements of vitamins and minerals from bearing the "reduced sugar" and similar terms no longer exists in the FD&C Act. FDA should have amended 21 C.F.R. § 101.60(c)(5) to reflect the amendment of FD&C Act Section 411 but has not done so, leaving this obsolete regulation in the C.F.R.

i. Explain the reasons for the rescission.

The phrase "and dietary supplements of vitamins and minerals" should be rescinded from 21 C.F.R. § 101.60(c)(5) because it causes the regulation to be obsolete and inconsistent with statute. The FD&C Act, as amended, by DSHEA, no longer prohibits the labeling and advertising of dietary supplements of vitamins and minerals from giving prominence to or emphasizing ingredients which are not vitamins, minerals or represented as a source of vitamins or minerals. To be consistent with the FD&C Act, FDA's regulation at 21 C.F.R. § 101.60(c)(5) should permit dietary supplements of vitamins and minerals to bear "reduced sugar" and similar terms so long as criteria are met. In addition, the regulation is unreasonable as it permits dietary supplements that do not contain vitamins or minerals, e.g., dietary supplements of fiber, herbs, or other nutritional substances, to bear "reduced sugar" or similar terms while prohibiting dietary supplements of vitamins and minerals. There is no justification for separate treatment of the types of dietary supplements regarding the ability to bear the term "reduced sugar" if criteria are met. Further, by unjustly prohibiting "reduced sugar" claims on dietary supplements of vitamins and minerals, even when truthful, the regulation interferes with dietary supplement marketers' ability to convey information about the sugar content of products that could help Americans make informed choices to promote health and wellness.

j. Describe the text of the relevant C.F.R. provisions as it will exist after the rescission.

21 C.F.R. § 101.60(c)(5)

The terms "reduced sugar," "reduced in sugar," "sugar reduced," "less sugar," "lower sugar" or "lower in sugar" may be used on the label or in labeling of foods, except meal products as defined in § 101.13(l) and main dish products as defined in § 101.13(m), provided that...

k. Please insert the name of the current agency head.

Martin A. Makary

l. Please insert the title of the agency head.

Commissioner of Food and Drugs

Thank you for considering our comments.

Sincerely,

Andrea Wong
Senior Vice President, Scientific & Regulatory Affairs

Megan Olsen
Senior Vice President and General Counsel

Haiuyen Nguyen
Vice President, Regulatory & Nutrition Policy