Council for Responsible Nutrition
1828 L Street, NW, Suite 810 • Washington, DC 20036-5114
(202) 204-7700 • fax (202) 204-7701 • www.crnusa.org

March 28, 2023

Dr. Robert McKinnon Califf, FACC, MD
Commissioner
U.S. Food and Drug Administration
United States Department of Health and Human Services
10903 New Hampshire Avenue, White Oak Building One, Room 2217
Silver Spring, MD 20993

Re: Reagan-Udall Report and FDA Foods Programs Reorganization

Dear Commissioner Califf,

The Council for Responsible Nutrition (CRN)[1] appreciated the opportunity to meet with you and your colleagues on January 3rd to discuss the report, "Operational Evaluation of the FDA Human Foods Program," issued by the Reagan-Udall Foundation in December 2022 (Reagan-Udall Report). While dietary supplements were excluded from the scope of the Reagan-Udall Report, many of the issues identified in the report are applicable to dietary supplements and changes that will be implemented as a result of the report will impact the oversight of this category. As such, thank you for initiating our meeting and providing representatives of the dietary supplement industry with a forum to provide input.

We also observed that the Food and Drug Administration's (FDA or Agency) January 31st announcement, "FDA Proposes Redesign of Human Foods Program to Enhance Coordinated Prevention and Response Activities," (the FDA announcement) following the Agency's review of the Reagan-Udall Report did not specifically address dietary supplements either. The Office of Dietary Supplement Programs (ODSP) is currently part of FDA's Center for Food Safety and Applied Nutrition that will be reorganized per the FDA announcement; therefore, the proposed redesign of the FDA's Human Foods Program will significantly

[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 200 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.

affect the dietary supplement category. After our meeting on January 3rd, we were surprised and concerned a month later, that the Agency had no immediate response to questions posed regarding the reorganization's effect on dietary supplement oversight. Future discussions of an updated Human Foods Program should evidence that the Agency has given some consideration to how dietary supplement oversight will fall into this new program.

In follow up to our meeting and review of FDA's recent announcement, we provide the following recommendations and comments.

The Deputy Commissioner for Human Foods should be accountable for dietary supplements.

CRN strongly supports the creation of a Deputy Commissioner for Human Foods position as proposed in the FDA announcement. We agree with the Reagan-Udall Report's findings that "(t)he lack of a single clearly identified person to lead the Human Foods Program has adversely impacted the organizational culture and led to overlapping roles and competing priorities that result in what is perceived as constant turmoil."[2] Further, "(c)lear lines of authority are also essential in establishing and enabling an effective organizational culture."[3] The Reagan-Udall report discusses duplication, confusion, and conflict between the Center for Food Safety and Applied Nutrition (CFSAN) and the Office of Food Policy and Response (OFPR) resulting from the current lack of clarity in authority in the Human Foods Program. Further contributing to this problem is the lack of direct communication between the Office of Regulatory Affairs (ORA), the part of FDA responsible for conducting inspections and investigations, and ODSP, which is responsible for setting agency policy on dietary supplements. CRN emphasizes that this ambiguity is exacerbated for the dietary supplement category within CFSAN because the current Director of CFSAN has been recused from handling dietary supplement issues since January 2015, leaving no clear line of authority for dietary supplements in the agency. So, while there is little opportunity for field personnel in ORA to communicate directly with ODSP, it appears that the heads of these division have little interaction either.

It is critical that any reorganization structure for human foods proposed by FDA include dietary supplements and that the new Deputy Commissioner position is made accountable for the regulation of dietary supplements. Primary in their job responsibilities should be to facilitate a stronger collaboration between that section of FDA charged with developing policy (ODSP) and that section that has the most routine interaction with the industry (ORA). Further, a conflict that would require recusal from overseeing the dietary supplement industry should be considered a disqualifying factor for any candidates for this new position.

While we have noted our support for the creation of a Deputy Commissioner role overseeing food (including dietary supplements), we are concerned that the plan to keep the Office of Regulatory Affairs' (ORA's) core food activities separate from the proposed Human Foods Program will not achieve the

[2] Henney, et. al; 2022. Operational Evaluation of the FDA Human Foods Program: A Report of the Human Foods Independent Expert Panel. 12. https://reaganudall.org/operational-evaluation-fdas-human-foods-programs. Accessed March 28, 2023.
[3] Henney, et. al; 2022. Operational Evaluation of the FDA Human Foods Program: A Report of the Human Foods Independent Expert Panel. 13. https://reaganudall.org/operational-evaluation-fdas-human-foods-programs. Accessed March 28, 2023.

clear line of authority that the Reagan-Udall report deemed essential for an effective organizational culture. Instead, authority will be divided, causing confusion, and hindering timely decision-making.

Dietary supplement issues should be prioritized

Absent leadership from the CFSAN Director, we believe important issues for dietary supplements have not been prioritized and have been overlooked or marginalized. For example, more than six years after issuance of FDA's revised draft guidance on New Dietary Ingredients (NDIs) in August 2016, the agency has still not released final guidance or given any indication of when it will be issued. The lack of final guidance leaves many issues related to NDIs unresolved.

FDA has also lagged in moving forward with other rulemaking and guidance promised by the Agency or requested by industry stakeholders, such as a rulemaking regarding an exemption from the drug preclusion provision of the Food, Drug, and Cosmetic Act (FDCA) for the dietary ingredient n-acetyl-l-cysteine (NAC) and responding to several citizen petitions filed by the industry related to ingredient legality and labeling. [4, 5]

Dietary supplement facility inspections are also lacking. In FY22, FDA conducted less than 500 domestic and foreign dietary supplement facility inspections, representing approximately only 5% of facilities.[6] While the COVID-19 pandemic impacted the number of facility inspections in recent years, in a typical year, FDA still only conducts about 500 to 600 dietary supplement inspections.[7] At that rate, it will take FDA more than 20 years to conduct at least one inspection of every dietary supplement facility that is currently registered with the Agency under FSMA.

Inspectional findings and what appears to be a lag between inspections/testing and enforcement actions also compromise consumer safety and suggest a great need for increased collaboration between ORA, ODSP, and other relevant offices. For example, according to a warning letter dated January 9, 2023, FDA inspected a manufacturing facility in June 2022 and obtained a sample and labeling of a male sexual enhancement product during the inspection.[8] Based on the inspection, review of the product labeling (including the firm's website), and laboratory analysis of the sample, FDA determined that the product in question is an unapproved new drug and a misbranded drug. FDA acknowledged in the warning letter that the firm initiated a voluntary recall of a single lot of the product in August 2022. Subsequently, the Agency issued a warning to consumers not to use the product in November 2022. Finally, the warning

---

[4] Center for Food Safety and Applied Nutrition. FDA releases final guidance on Enforcement Discretion for NAC. U.S. Food and Drug Administration. https://www.fda.gov/food/cfsan-constituent-updates/fda-releases-final-guidance-enforcement-discretion-certain-nac-products. Accessed March 28, 2023.

[5] Requests that the FDA revise the Nutrition Facts regulations to address the discrepancy between 21 CFR 101.36(b)(2) and 21 CFR 101.9 pertaining to providing caloric values for branched chain amino acids (BCAAs) on supplement labels and that an enforcement discretion policy be issued to allow for dietary supplement labels to include BCAAs without specifying caloric values for those ingredients. U.S. Food and Drug Administration. Regulations.gov. https://www.regulations.gov/docket/FDA-2020-P-2134/document. Accessed March 28, 2023.

[6] Josh Long. FDA audits climb in FY22 for dietary supplement facilities. Natural Products INSIDER. https://www.naturalproductsinsider.com/regulatory/fda-audits-climb-fy22-dietary-supplement-facilities. Published October 13, 2022. Accessed March 28, 2023.

[7] Id.

[8] Center for Drug Evaluation and Research. Warning Letter - Distributor RFR, LLC - 643724 . https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/distributor-rfr-llc-643724-01092023. Accessed March 28, 2023.

letter was issued in January 2023. It is unclear why over 6 months elapsed between the inspection and warning letter, and why stronger enforcement measures have not been taken, particularly for violations that impact consumer safety. Unfortunately, this one example is emblematic of the long delays that routinely occur between the agency's discovery of a potential health concern and meaningful enforcement activity. CRN is concerned that delayed action and the lack of strong enforcement actions to remove blatantly illegal products from the market pose a risk to consumer safety.

Further progress on FDA's Program Alignment is needed

FDA's Program Alignment includes implementation of a program-based management structure that aligns Office of Regulatory Affairs (ORA) staff by FDA-regulated product, replacing a structure based on geographic regions in which employees, regardless of their area of expertise, may do work in more than one program area.[9] FDA indicated that specializing by FDA-regulated product type will ultimately "result in a high level of technical expertise and more uniform application of ORA's policies and processes."

While some progress in Program Alignment has been made since the initiative was announced in May 2017, as acknowledged in the Reagan-Udall Report, much more is needed for efficient and effective field operations. Although dietary supplements are regulated as a category of food, Good Manufacturing Practices (GMP) regulations for dietary supplements are very different from those for conventional food.[10] A thorough understanding of dietary supplement GMP regulations and specialized training for dietary supplement facility inspections are needed for investigators. In the nearly five years since the program was launched, little progress has been made to instruct investigators in the unique aspects of dietary supplement regulation and to concentrate a corps of investigators dedicated to dietary supplement inspections. Too often, an inspector arrives at a dietary supplement facility with less appreciation for the unique aspects of Part 111 than the quality assurance executives in the facility.

Increased communication and collaboration within FDA are necessary for an effective Human Foods Program

The Reagan-Udall Report indicates that FDA staff often operate in silos and that "staff are not actively encouraged to broaden their thinking and work with individuals outside of their division, office, or center. Such a narrow range of engagement can inhibit staff from identifying or embracing the over-arching goals of the Program."[11] Examples provided above regarding lags in rulemaking, responses to citizen petitions, and enforcement actions following inspections/testing, demonstrate the need for increased collaboration and communication within the Agency related to dietary supplement issues.

Collaboration with external stakeholders, including regulated industry, will improve the efficiency and effectiveness of the Human Foods Program

In addition to fostering a collaborative culture within FDA, collaborating with external stakeholders such as industry members whose products are regulated under the Human Foods Program will benefit the

[9] Office of Regulatory Affairs. Program Alignment and ORA. U.S. Food and Drug Administration. https://www.fda.gov/about-fda/ora-program-areas/program-alignment-and-ora. Updated April 4, 2019. Accessed March 28, 2023.
[10] Code of Federal Regulations. The National Archives. 21 CFR Part 111 and 21 CFR Part 117. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B. Accessed March 28, 2023.
[11] Henney, et. al; 2022. Operational Evaluation of the FDA Human Foods Program: A Report of the Human Foods Independent Expert Panel. 12. https://reaganudall.org/operational-evaluation-fdas-human-foods-programs. Accessed March 28, 2023.

program. As stated in the Reagan-Udall Report, "an effective FDA Foods Program cannot operate in a vacuum: collaboration across the federal government, with states and state government, international regulatory bodies, and with the many food stakeholders is crucial to leveraging best practices, eliminating redundancy, and optimizing efficiencies."[12]

CRN agrees with the Reagan-Udall Report's assessment about collaboration with stakeholders, including regulated industry. In an effort to explore potential opportunities to improve the efficiency, frequency, and utility of Good Manufacturing (GMP) inspections for dietary supplement facilities, members of the dietary supplement industry have worked to develop proposals to help reduce the backlog of facility inspections, allow FDA to prioritize its resources based on risk, and address inconsistencies in how inspections are conducted. CRN and other dietary supplement trade associations have initiated meetings with FDA to share these proposals, and discussions are ongoing with the hope of achieving the shared goal of improving GMP compliance and bolstering dietary supplement safety across the industry.

Industry initiatives may complement FDA activities as well. After FDA updated the regulations for Nutrition Facts and Supplement Facts labeling in 2016, the agency developed materials to educate consumers about changes to the nutrition labels (i.e., for conventional food). While the changes to supplement labels were not as extensive or prominent as those for conventional food, updates to the daily values and new units of measure for various nutrients impacted both categories. However, FDA declined to provide educational materials for dietary supplements. CRN filled this void by developing LabelWise, an online guide to understanding Supplement Facts and repeatedly offered to partner with the agency in various ways to provide this information to consumers. CRN's invitations were rebuffed each time, despite multiple examples where the agency collaborates with industry on education in other regulated categories.

Separately, FDA released its own consumer education for dietary supplements "Supplement Your Knowledge" in June 2022[13] without seeking the input of industry stakeholders prior to its release. CRN subsequently met with FDA personnel to discuss its concerns and submitted reactions[14] that the educational materials overly focus on perceived risk versus potential benefits from supplement usage, and over emphasis on ways supplements are not regulated rather than ways that they are. These missteps could have been avoided with consultation from the regulated industry.

And finally, in 2018, CRN launched an online public registry of dietary supplement labels called The Supplement Online Wellness Library (OWL).[15] This online resource provides product labels, ingredient listings, label claims and other information about more than 12,000 dietary supplements in the U.S. market. CRN requires participation in the Supplement OWL among our members, and many nonmember companies also voluntarily submit their product labels to this registry. FDA has recently called for a

---

[12] Henney, et. al; 2022. Operational Evaluation of the FDA Human Foods Program: A Report of the Human Foods Independent Expert Panel. 10. https://reaganudall.org/operational-evaluation-fdas-human-foods-programs. Accessed March 28, 2023.
[13] Center for Food Safety and Applied Nutrition. FDA Launches New Dietary Supplement Education Initiative. U.S. Food and Drug Administration https://www.fda.gov/food/cfsan-constituent-updates/fda-launches-new-dietary-supplement-education-initiative. Published June 2, 2022. Accessed March 28, 2023.
[14] CRN. Re: Supplement Your Knowledge materials feedback and invitation for future collaboration. https://www.crnusa.org/sites/default/files/pdfs/comments-pdfs/CRN-feedback-FDA-DietarySupplement-Content-091322.pdf. Published September 13, 2022. Accessed March 28, 2023.
[15] The Supplement Owl. https://supplementowl.org/. Accessed March 28, 2023.

mandatory product listing of dietary supplements[16,17] and the Supplement OWL could easily serve as a template for what a mandatory system might look like, as well as serve as a resource in investigations. Nevertheless, repeated efforts by CRN to provide education on the Supplement OWL to field investigators and other FDA personnel at ODSP and elsewhere in the agency have been declined. Given the acknowledgement that FDA is understaffed and underresourced with respect to many aspects of its food program, and especially with respect to the burgeoning dietary supplement marketplace, FDA would be well-served to seek collaboration from established industry stakeholders like CRN.

Again, thank you for the opportunity to share our perspective with you. CRN wishes the agency much success in its reimagination of the Human Foods Program and stands ready to assist in areas where we have overlapping interests in building a stronger, safer dietary supplement industry.

Sincerely,

Steve Mister

President & CEO

Andrea Wong, Ph.D.

Senior Vice President

Scientific & Regulatory Affairs

[16] Center for Food Safety and Applied Nutrition. FDA releases final guidance on Enforcement Discretion for NAC. U.S. Food and Drug Administration. https://www.fda.gov/food/cfsan-constituent-updates/fda-releases-final-guidance-enforcement-discretion-certain-nac-products. 42. Accessed March 28, 2023.

[17] Cara Welch. FDA makes the case for dietary supplement product listing requirement. Natural Products INSIDER. https://www.naturalproductsinsider.com/regulatory/fda-makes-case-dietary-supplement-product-listing-requirement. Published February 7, 2023. Accessed March 28, 2023.