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Re: Supplement Your Knowledge materials feedback and invitation for future collaboration

Thank you for the opportunity to provide feedback on how dietary supplements are presented on FDA's website in general and in its recently released Supplement Your Knowledge content for consumers, healthcare professionals, and teachers.

This feedback follows a June Zoom meeting between CRN staff and Office of Dietary Supplement Programs Director Cara Welch, Ph.D. Dr. Welch recommended CRN provide written feedback to facilitate engaging the appropriate FDA personnel so the agency can provide the most accurate information to support public health.

CRN commends the agency for its efforts to provide educational content to key stakeholder groups. We appreciate the targeted messaging with the different groups' needs in mind. For example, at the end of FDA's download, "Talking to Healthcare Professionals About Dietary Supplements," the "Dietary Supplement and Medication Record" reminds consumers to speak with their practitioners about what supplements they take and provides a handy, useful framework for that conversation. However, CRN's members and staff have identified numerous areas of concern that we request FDA consider updating.

CRN's recommendations address ways that FDA's content:

- Overstates the potential risks of taking supplements while downplaying benefits
- Misses opportunities to address public health issues with responsible supplement usage
- Does not communicate the robust regulatory framework in place that gives the agency authority over dietary supplements, leaving a misimpression that the regulation is inadequate
- Could be enhanced by collaboration with the dietary supplement industry through CRN in developing future messaging

CRN offers examples from the overall FDA website's dietary supplements page, as well as from each section of the Supplement Your Knowledge materials for consumers, healthcare professionals, and teachers, plus social media and other resources.

Overall concerns

Main website

A recurring theme CRN identified throughout FDA content is an overstatement of the potential risks of taking supplements and little mention of well-documented health benefits. This distorted presentation leads to missed opportunities to address public health issues (e.g., addressing nutrient deficiencies, supplement usage for specialty populations, supplements that can offset nutrient depletion from prescription medication, and demonstrated ability to reduce the risk of certain diseases) that could be improved with supplementation.

This one-sided presentation contrasts with the way the agency speaks about other categories it regulates, such as cosmetics, medical devices, and traditional food.

Cosmetics, like supplements, are not approved by FDA before going to market. However, this fact is characterized in a decidedly different tone than supplements. With cosmetics, FDA's website states that they do not "need" approval and does not put up bold, red flags about their safety. By contrast, with supplements, the absence of pre-market approval is characterized as the result of a lack of legal authority. FDA inappropriately links this restraint on regulation to concerns over safety and effectiveness.

From FDA's "Cosmetic Products" page:

> "Under U.S. law, cosmetic products and ingredients do not need FDA approval before they go on the market. The one exception is color additives (other than coloring materials used in coal-tar hair dyes), which must be approved for their intended use. Companies and individuals who market cosmetics have a legal responsibility to ensure the safety of their products. In order to take action for safety reasons against a cosmetic on the market, we need reliable information showing that it is unsafe when consumers use it according to the directions in the labeling or in the customary or expected way."

The "Information for Consumers on Using Dietary Supplements" page:

> "The Dietary Supplement Health and Education Act (DSHEA) of 1994, which amended the Federal Food, Drug, and Cosmetic Act, transformed FDA's authority to regulate dietary supplements. Under DSHEA, **FDA is not authorized to approve dietary supplements for safety and effectiveness before they are marketed**. In fact, in many cases, firms can lawfully introduce dietary supplements to the market without even notifying FDA. Since DSHEA was enacted, the dietary supplement market has grown significantly. For example, the number of products has expanded nearly twenty times since 1994."

On the "Overview of Device Regulation" page, FDA states that "FDA's Center for Devices and Radiological Health (CDRH) is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States." Absent is any mention how device regulation compares to drug regulation, which is much more stringent.

On the "Food" page, FDA highlights several agency initiatives including its "Supplement Your Knowledge" campaign currently placed in the arrangement over a section on "Advice about Eating Fish."

The overarching tone of each reveals a negative bias when speaking about supplements compared to an almost promotional voice when discussing fish.

- **Conversely, the section on dietary supplements immediately mentions risk** right in the link text ("Resources about dietary supplements, including information about the benefits and risks..." Risk is mentioned again on the landing page right away ("But they may also come with health risks."), only following a tepid acknowledgement that they "can help people improve or maintain their overall health."
- **In contrast, the fish advice section highlights the nutritional value** of fish as noted in the Dietary Guidelines for Americans (DGAs). The risk of mercury consumption is downplayed in contrast to the messaging encouraging women of childbearing age to eat fish, possibly because of the nutritional benefits fish confers outweighs the health risks associated with mercury.

The DGAs also mention nutrient shortfalls and the need for supplementation in some populations—but these facts are not addressed in FDA's content about dietary supplements. This is a missed opportunity to provide important information about the prevalence of nutrient shortfalls.

Americans fall short in many key nutrients.[1] The 2020–2025 Dietary Guidelines for Americans (DGAs) identified that under-consumption of calcium, potassium, dietary fiber, and vitamin D is of public health concern for the general U.S. population because low intakes are associated with particular health concerns.[2] Iron was also identified to be of public health concern in adolescent girls and women of reproductive age, as well as in breastfed infants ages 6 through 11 months.[3,4] In pregnant women, under-consumption of folic acid (in the first trimester), iron, and iodine is also of public health concern.[5,6] The DGAs also state that adolescent females have low dietary intakes of protein, folate, vitamin B6, vitamin B12, choline, and magnesium and that dietary protein and vitamin B12 are more likely to be under-consumed in older adults (60+).

[1] The 2020 Dietary Guidelines Advisory Committee (DGAC). Scientific report of the 2020 Dietary Guidelines Advisory Committee. Washington (DC): USDA, Agricultural Research Service; 2020.

[2] U.S. Department of Agriculture (USDA) and U.S. Department of Health and Human Services (HHS). Dietary Guidelines for Americans, 2020–2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov.

[3] DGAC. Scientific report of the 2020 Dietary Guidelines Advisory Committee. Washington (DC): USDA, Agricultural Research Service; 2020.

[4] USDA and HHS. Dietary Guidelines for Americans, 2020–2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov.

[5] DGAC. Scientific report of the 2020 Dietary Guidelines Advisory Committee. Washington (DC): USDA, Agricultural Research Service; 2020.

[6] USDA and HHS. Dietary Guidelines for Americans, 2020–2025. 9th Edition. December 2020. Available at DietaryGuidelines.gov.

Opportunity to collaborate

We also noticed a section on "The New Nutrition Facts Label" on the "Food" page and would like to again share CRN's "Label Wise" educational materials available at www.BeLabelWise.org. CRN's "Label Wise" content provides information on the new Supplement Facts label. CRN encourages FDA to link to or use this content and would welcome the opportunity to collaborate with the agency and answer any questions or provide customization. CRN appreciates that FDA did include our "Label Wise" video in the materials for educators.

Supplement Your Knowledge

The "Understanding Dietary Supplements" download for consumers in the Supplement Your Knowledge campaign reflects this same over-emphasis of risk and lack of attention to benefits of dietary supplements. Similar verbiage is seen throughout the materials.

- **FDA notes that taking too much** of certain supplements may be harmful; however, some of these same nutrients have been flagged for underconsumption in the DGAs. The FDA download does not identify what amount may be too much (the Upper Level as opposed to the Daily Value) or properly communicate that the Daily Value for many essential nutrients is the level needed to avoid overt symptoms of deficiency. More details for consumers to help them understand where they may fall short, or even how to determine if they are insufficient, are necessary to make the material more balanced and actionable.

- **This same page's bolded admonition to consumers** to "be alert to the possibility of a bad reaction or side effect (also known as an adverse event)" presupposes a level of risk that is incompatible with the reality that the overwhelming majority of dietary supplements are safe. In relation to other FDA-regulated categories, dietary supplements experience one of the lowest rates of adverse events and product recalls. Yet, the page immediately alerts readers to be conscious of potential adverse effects.

- **And again, consumers are told to "be cautious"** about supplements, second in importance only to reading product labels when it comes to being informed. Even the section titled "What are the Benefits of Dietary Supplements" comes with only one example of a benefit and is followed by the admonition, "Even though dietary supplements can be beneficial, they should not take the place of the variety of foods that are important for a healthy diet." Potential risk always seems to overshadow benefits. At the same time, there is little evidence to suggest that consumers substitute supplement usage as a replacement for a healthy diet and ample evidence that consumers who use supplements are also more likely to try to eat healthy.

Regulation as a category of foods

Throughout the materials, FDA's regulation of dietary supplements is characterized as "less than" with emphasis placed on what the agency does ***not*** do rather than what it ***does*** do.

- The "Dietary Supplements: How FDA Helps Keep You Safe" fact sheet states, in bold, **"FDA does not have the authority to approve dietary supplements for safety and effectiveness or their labeling before they are sold in stores or online."**
- When stakeholders visit the page on "How to Report a Problem with Dietary Supplements," they immediately are hit with a negative, as shown in the sentence CRN highlights below, which is even bolded by the agency for emphasis on other pages, like "Information for Consumers on Using Dietary Supplements."

> "Dietary supplements include vitamins, minerals, herbs, amino acids, whey protein, and creatine. **FDA does not approve dietary supplements before they are sold to the public.** Therefore, it is particularly important for consumers, healthcare professionals, and industry members to report health-related reactions or illnesses (also known as adverse events) to FDA, so we can evaluate the marketplace and take action to protect the public from possibly unsafe products."

It would be worthwhile, in the first example, to rephrase the bolded statement, "FDA does not have the authority to approve dietary supplements..." to "Dietary supplements are regulated by FDA in many respects, but they do not require FDA approval for safety or effectiveness before they are sold in stores or online." It would also be useful to provide context for the consumer that dietary supplements are a category of food, which is also not pre-approved by FDA.

It is easy for consumers to conflate FDA's not approving supplements before they go to market with the idea that the agency does not have authority to regulate supplements at all. These materials should more intentionally and expressly enumerate the many ways dietary supplements ***are*** regulated.

CRN acknowledges that subsequent to the bolded statement, "FDA does not have the authority to approve dietary supplements for safety and effectiveness or their labeling before they are sold in stores or online," there is mention of facilities inspections and adverse event report monitoring. However, these representations of FDA's regulatory authority are downplayed. It would make more sense to lead with the agency's authorities—what it can do— rather than the limits of its authority—what it can't do.

Stakeholders need to know that, when compared to other foods, dietary supplements are in many respects *more* regulated.

- **As with foods, FDA has inspection authority** over dietary supplement facilities.
- **Plus, dietary supplements have their own** GMP requirements under Part 111 that in many respects are more stringent than those for other foods in Part 110 and Part 117.
- **Dietary supplements must submit their structure-function** claims to FDA, whereas foods do not.
- **The serious adverse event reporting** requirement is another example of a regulation specific to supplements and not to other foods.

Serious Adverse Event Reports

An inappropriately alarming tone around adverse events and dietary supplements pervades FDA's content:

- FDA portrays adverse events as much more common than they are.
- Putting the number of serious adverse events related to dietary supplements in context would present a more realistic view of the actual risk, which is low. For instance, if FDA acknowledged the very low incidence of serious adverse events for dietary supplements compared to the number of dosage units sold in the U.S. in any given year, or recognized the number of serious adverse events for supplements as compared to those received for other FDA-regulated categories like drugs, it would paint a decidedly different impression for consumers. By contrast, FDA gets it right in the high school curriculum materials (discussed later in this document) when it acknowledges, "Dietary supplements comprise only a small portion of total FDA recalls: just 2% of more than 800 recalls initiated in 2019 involved dietary supplement products" and that "manufacturers usually voluntarily recall products of concern."
- Adverse events listed include some very frightening but very unlikely examples.

FDA should present information on how to report serious adverse events without leading consumers to assume these products pose a higher level of risk.

The number of serious adverse events associated with dietary supplements—relatively few—should be included to put the risk in context.

Social Media

CRN appreciates the agency's call to "Spread the Word about Dietary Supplements" with its Supplement Your Knowledge Social Media Toolkit. The messages suggested for posting are more balanced than other FDA content. However, the lead-in language on the toolkit page keeps with the theme of overemphasizing risk. For example, in the section for consumers:

> "Dietary supplements can be beneficial to your health, but they can also involve health risks. When you take too much of a dietary supplement or take supplements with prescription or over-the-counter medicines, you can have a bad reaction—also called an adverse event. And, if you take dietary supplements instead of prescribed medicines, the results potentially could be life-threatening."

The suggested posts then link to the pages mentioned before that do not accurately characterize the benefits and safety profile of dietary supplements.

Content for health care professionals

A third component of FDA's recently released education materials are the video modules developed with the American Medical Association. As a preliminary matter, CRN is surprised and disappointed that FDA would collaborate with a singular partner—the American Medical Association—that is often highly critical of dietary supplements for these health care

professionals' educational modules and not also seek the input of any dietary supplement experts.

We note that CRN repeatedly approached FDA in 2018 and 2019 leading up to the effective dates of the revised regulations for Supplement Facts Labeling and invited collaboration between FDA and CRN to develop consumer-focused education specific to the Supplement Facts changes. FDA allocated significant resources to consumer education on the changing Nutrition Facts label, but none to dietary supplement labeling changes. Each time, CRN was rebuffed and told the agency could not collaborate with industry. Examining any of the AMA's public position statements on dietary supplements, it is difficult to see how it has any less of an agenda than the industry. CRN's own "Label Wise" program demonstrates objectivity and provides valuable tools for consumers to understand and utilize the new information mandated by these changes to the regulations.

With respect to the content of this program, it demonstrates an overall lack of balance in the materials highlighted in several examples from the modules, including:

> **Module 1** examples:
>
> **@3:33** lists common reasons people take dietary supplements, including providing adequate amounts of nutrients the body needs to function. But this seems to be the only brief mention of any potential benefits. At minimum, there is an opportunity here to discuss some of the nutrient gaps in the U.S. population and how dietary supplements can help individuals achieve adequate levels.
>
> **@4:28** compares dietary supplements with drugs. The module highlights, "Unlike drugs, FDA does not have the authority to approve dietary supplements," and **@4:08** mentions that dietary supplements are defined as a category of foods. There is an opportunity **@6:45** for the module to explain it is important for patients to understand that, like foods, FDA does not approve products or product labeling.
>
> **@5:22** notes premarket submissions in limited circumstances. However, this part is very brief and not enough to appreciate FDA's authority in the review of new dietary ingredients (NDIs).

Module 2 could benefit from more context for its warnings. For example:

> **@1:50** the lab test interference discussion notes some supplements interfere with lab tests and provides biotin as an example—but does not specify the high levels of biotin that have caused lab test interference. Providing this contextual information would prevent the misinterpretation that RDA levels of biotin (such as those found in a multivitamin) could cause lab test interference.
>
> **@2:48** the module advises of detrimental effects from taking too much of certain nutrients when it notes taking nutrients above 100% of Daily Value can be harmful (for example, with calcium, iron, vitamin A, vitamin D). This statement displays a complete

lack of appreciation for the appropriate uses of Daily Values, as opposed to Tolerable Upper Intake Levels (ULs). Daily Values are intended to communicate the levels necessary for the majority of the population to achieve sufficient nutrients to avoid deficiency; the ULs are intended to communicate the safe maximum levels of intake. As a result, the module wrongly communicates to doctors that a product exceeding 100% of Daily Value would pose a risk to their patients.

@7:25 in the doctor-patient consultation, the patient reports taking calcium, melatonin, and a multivitamin. Given this information, the doctor has no reason to discuss all the risks with dietary supplements, for example, interference with medicines, unproven ingredients, accusations of them being falsely marketed, use of supplements in place of prescription drugs, taking too much, and that they are not approved. This evokes a response from the patient that this is "concerning." We agree it is appropriate that the doctor asked how much of the supplements are being taken, recommended the patient discuss the supplements being taken (especially because the patient is taking prescription drugs), and asked the patient to report adverse events. However, the overall exchange creates undue alarm in the patient, especially given the particular supplements the patient has disclosed and presents poor modeling of the kind of dialogue that would make a patient feel comfortable discussing their supplement intake with a doctor.

In Module 3:

- There is no mention of benefits of dietary supplements even though "benefits" are mentioned in the video's description.

Content for educators

The educational materials meant for high school students present an even more alarming picture of dietary supplements and emphasis on risk, so much that they seem designed to scare teens away from taking these products at all.

CRN would like to flag that the "Mystery Powder" image on the cover strongly resembles an actual product's branding—Vital Proteins. (See image, right.)

This overemphasis is apparent in the table of contents where "Risk" appears in large bold letters. The words "Shortcuts" and "Quicksand" also appear in large bold letters on this table of contents page. There is no mention at all of benefits in the table of contents—which, of course, aligns with the fact that, as with the materials for the other stakeholders, benefits are downplayed. An informal count tallied 15 mentions of the word "benefit" versus 65 mentions of "risk" in the teacher's guide for high school classrooms.

CRN does appreciate that FDA included our video, "Understand Changes to Dietary Supplement Labels," in the "Student Procedures" section "Food vs. Supplements."

The introduction, "Why Teach about Dietary Supplements?," raises issues of susceptibility to claims and advertising because of teens' alleged vulnerability due to "their ongoing self-evaluations that revolve around their appearance: they may consider themselves to be too thin, too heavy, or too weak in their search for self-enhancements"—and positions dietary supplements as inherently untrustworthy and inappropriately more concerning than other products.

Module 1, the "Introduction to Dietary Supplements" includes important information about prescription drug interactions. However, saying it is "most important of all" to "be skeptical!" reveals an underlying negative tone.

- **There is a difference** between language that speaks to being an informed, savvy consumer and approaching an entire category of consumer products with "skepticism." This same tone is not evident in the way FDA speaks about other foods, cosmetics, or drugs.
- **The language on pages 12–13** with tips from FDA and NIH (Tip #3) before taking supplements is inflammatory in its use of the word "toxic" and suggests that these risks are more prevalent than they actually are:

> "**Be aware that some dietary ingredients can be toxic in certain circumstances.** Some ingredients and products can be harmful when consumed in high amounts, when taken for a long time, or when used in combination with certain other drugs, dietary supplements, or foods."

Module 2, Dietary Supplements: Risks, Realities, and Reporting, as previously mentioned, raises alarms about risks over benefits.

- **CRN has debunked**[7] the U.S. Centers for Disease Control and Prevention (CDC) data about 23,000 emergency room visits being attributed to dietary supplement use that is cited on page 22. In fact, less than 1% of more than 40,000 adverse events associated with dietary supplement use were serious, according to a study published in the Journal of Dietary Supplements, "Serious Adverse Events Reported with Dietary Supplement Use in the United States: A 2.5 Year Experience."

- **FDA should put more** emphasis on the fact that the illegal products it warns about on page 23 are not actually dietary supplements. FDA advises to "be aware of hidden (and dangerous) ingredients" and warns "you could unknowingly take products marketed as dietary supplements, but actually include prescription drug ingredients, controlled substances, or untested and unstudied pharmaceutically active ingredients. These deceptive products can harm you!"

- **CRN appreciates** that FDA notes it "actively works to identify and remove from the market over-the-counter products, frequently represented as dietary supplements, that contain undeclared ingredients that could be harmful." However, as mentioned there

[7] Context Is Key to Analyzing Results of New Study on Dietary Supplements in New England Journal of Medicine, Says CRN," Oct. 14, 2015

should be more emphasis that these products are not legal supplements marketed by the mainstream industry.

- **The warnings about "high doses"** of protein are vague because they do not say what a high dose is, but at the same time overstate the possible side effects.

The "HEALTH ALERT" that says, "It is especially difficult to know whether sports supplements are safe because it is unusual to have long-term studies that focus on teens. Products marketed as sports supplements also may contain harmful drugs or additives that are not listed on the label" also paints "sports supplements" with too broad a brush. More specificity is needed for this to be useful information.

CRN appreciates on page 27, "Dietary Supplement Recalls: At a Glance," FDA putting recalls into context, noting, "Dietary supplements comprise only a small portion of total FDA recalls: just 2% of more than 800 recalls initiated in 2019 involved dietary supplement products" and that "manufacturers usually voluntarily recall products of concern."

In the list of credible sources on page 29, we suggest FDA include the Council for Responsible Nutrition: www.crnusa.org.

The activity for students on page 40 has an underlying negative view of supplements and presents "leading" statements that portray supplements as inherently problematic. These and other statements are overly broad:

- "Dietary supplements can cause serious harm or even death."
- "Dietary supplements may cause harm because they may contain dangerous, unlabeled ingredients."

CRN acknowledges the danger of concentrated caffeine and would like to spotlight our voluntary guidelines, updated in response to a 2018 FDA guidance, which calls for restraint against marketing caffeine in combination with alcohol and cautions against the sale and marketing of bulk amounts of pure or highly concentrated caffeine.

The section on Energy/Performance Supplements on page 49 names a list of notable safe ingredients with an overly risk-focused series of warning language following:

- "Dietary supplements marketed as energy/performance supplements can contain many ingredients such as vitamins and minerals, protein, amino acids, and herbs, and the amounts of these ingredients in the products can vary."

CRN appreciates the value of flagging that energy and performance supplements can interact with medications. However, the overarching and overly alarmist tone detracts from the information being actionable in the real world, as it is too dismissive of supplements:

- "Like all dietary supplements, performance supplements can have negative effects. Dietary supplements marketed for energy/performance can be especially problematic when mixed with prescription medicine or used before and after medical procedures. These are examples of some supplements and the negative reactions that can occur from their use…"

More detail should be provided as to quantities that would interfere. As previously noted, the biotin example would take a large amount of biotin.

- "Supplements may interfere with some blood tests, and they may also interfere with other laboratory tests. For example: biotin can significantly interfere with certain lab tests and cause incorrect test results that may leave health issues undetected."

CRN acknowledges the importance of FDA providing information about dietary supplements to these stakeholders—consumers, health care professionals, and educators. In addition, journalists and policymakers may access the content for background when reporting on dietary supplements, so it is key that the fact FDA regulates dietary supplements is very clearly stated.

We still see too many journalists reporting that supplements are not regulated by FDA. This is one reason why we are asking for FDA to more prominently state what it does to regulate supplements so the robust framework is better understood.

CRN reiterates that there is a difference between encouraging constituents to be smart consumers of safe, beneficial products and painting an entire industry and category of consumer packaged goods as deserving of skepticism.

CRN seeks to open a more active dialogue with the right contacts at the agency so FDA staff has a trusted resource for factual, science-backed details about dietary supplements they can contact and engage as updates are made to educational content or new content is developed in the future.

Please let us know the best way to move forward in that direction if there are specific contacts in the agency's communications or education departments our staff should reach out to directly. CRN would welcome the opportunity to connect with key FDA staff on a regular basis to build a working relationship and be in closer touch to facilitate the ongoing sharing of information.

Sincerely,

Steve Mister
President & CEO
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