NATURAL PRODUCTS ASSOCIATION

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CITIZEN PETITION

October 26, 2020

Via Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Citizen Petition Requesting FDA Amend Nutrition Facts and Supplement Facts Labeling Regulations Pertaining to Caloric

Dear Sir or Madam:

The Natural Products Association (NPA) submits this petition, pursuant to Section § 111.75(a)(1) of the Federal Food Drug and Cosmetic Act (FDC Act), to request the Commissioner of Food and Drug Administration (FDA) to amend the Nutrition Facts labeling regulations to allow for a zero calorie calculation on Nutrition Facts and Supplement Facts panels for branched chain amino acids. While the Agency is working through this amendment, we request that the Commissioner grant a formal enforcement discretion to allow the regulated community to follow 21 CFR 101.36(b)(2), rather than 21 CFR 101.9 when providing caloric values on dietary supplement labels for branched-chain amino acids. This enforcement discretion policy would extend until the Agency has time to amend the regulations at 21 CFR 101.9 to align with those in 21 CFR 101.36(b)(2).

Action Requested

NPA specifically requests the following actions take place:

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- NPA requests that 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.
- NPA requests that while the Agency works to make this revision, that an enforcement discretion policy be issued to allow for dietary supplement labels to include BCAAs without specifying caloric values for those ingredients.

Statement of Grounds

This Petition arises out of an area in the regulations that provides industry with conflicting guidelines for the declaration of calories associated with amino acid content on Nutrition Facts labels as compared to Supplement Facts labels. NPA and its member companies are seeking a commonsense approach to this issue in the near-term, in light of increasing private litigation on this topic. Although FDA did not address this issue when it recently updated its Nutrition and Supplement Facts labeling rules, agency action is needed urgently so that determinations about the appropriate declaration of calories associated with amino acid content are appropriately made by the regulatory body authorized by Congress to make such determinations, rather than by the courts.

Argument

NPA urges the Commissioner to grant this Petition because the conflicting regulations applicable to this matter have left reputable companies without adequate guidance to ensure their compliance with the appropriate regulations do not leave them vulnerable to allegations of mislabeling.

1. Discrepancies Between Nutrition and Supplement Facts Labeling.

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FDA regulations covering dietary ingredients spans food and dietary supplements and are primarily covered in two separate sections of the Code of Federal Regulations Title 21. Part 101.9 describes regulations pertaining to nutrition labeling of food (21 CFR 101.9[1]) while Part 101.36 covers regulations pertaining to dietary supplement labeling (21 CFR 101.36[2]).

One component of 21 CFR 101.9 is the description of nutrients that are required to be listed on the Nutrition Facts panel, including protein. For supplement labels, protein and amino acids fall into the (b)(2) category of ingredients as defined in 21 CFR 101.36. According to FDA's Dietary Supplement Labeling Guide,[3] which is the agency's guidance for supplement manufacturers, protein is considered to be a (b)(2)-dietary ingredient; however, dietary supplement labels may not declare protein content in grams on their label if the product contains only individual amino acids. The same section in the regulations provides information pertaining to the calculation of caloric content but does not reiterate the statement that protein, and therefore calories, from amino acids shall not be listed on product labels. This leaves consumers and manufacturers with significant ambiguity regarding the true caloric content of products that only contain amino acids.

Background

There are nine essential amino acids, which include the three BCAAs, leucine, isoleucine, and valine. BCAAs are the most abundant of the essential amino acids and primarily promote protein synthesis in the human body, but they also serve in a multitude of intracellular signaling processes[4]. They cannot be not synthesized in animals, and therefore, must be consumed in

[1] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=101.9
[2] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=101.36
[3] https://www.fda.gov/food/dietary-supplements-guidance-documents-regulatory-information/dietary-supplement-labeling-guide-chapter-iv-nutrition-labeling#4-12
[4] Shimomura Y & Kitaura Y (2018). Physiological and pathological roles of branched-chain amino acids in the regulation of protein and energy metabolism and neurological functions. *Pharmacol Res* 133: 215-217.

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the diet and are thus considered essential. They are commonly found in eggs and meats but are also found in vegetable sources such as potatoes, maize or rice[5]. They are rapidly absorbed upon consumption, reaching peak blood concentration within thirty minutes[4].

The RDA for general protein consumption in healthy adults is 0.8 mg/kg body weight/day[6], however, individuals that are exercising should ingest higher levels of protein daily in the range of 1.4-1.7 g/kg body weight/day. A World Health Organization (WHO) publication entitled "Protein and Amino Acid Requirements in Human Nutrition" described the daily requirements for proteins and amino acids, including daily requirements for BCAAs. The authors described the daily requirements for BCAAs as being: 39 mg/kg for leucine; 26 mg/kg for valine; 20 mg/kg for isoleucine based upon indispensable amino acid requirement values for adults[5]. These values were reassessed in follow-up studies, which determined that total BCAA requirements for adults should be closer to 144 mg/kg/day with an upper limit of 210 mg/kg/day[7]. Therefore, there are generally accepted daily requirements for BCAAs which conflict with the language in 21 CFR 101.9 that state that ingredients without RDIs or DRVs are not permitted to be on the label, including amino acids.

Lack of Clear Guidance from the Agency

In comments received to the docket at "Food Labeling: Revision of the Nutrition and Supplement Facts Label"[8], several questions were posed to the Agency regarding how it determined protein quality, which could influence its inclusion on a label. FDA responded,

[5] https://apps.who.int/iris/bitstream/handle/10665/43411/WHO_TRS_935_eng.pdf;jsessionid=600D8951C75417C52E2CE09F2A77EA26?sequence=1

[6] Campbell B, Kreider RB, et al. (2007). International Society of Sports Nutrition position stand: protein and exercise. *Journal of the International Society of Sports Nutrition* 4:8.

[7] Riazi R, Wykes LJ, Ball RO, Pencharz PB (2003). The total branched-chain amino acid requirement in young healthy adult men determined by indicator amino acid oxidation by use of L-[1-13C]phenylalanine. *J Nutr* 133(5): 1383-1389.

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"There is also no definition of protein that is generally accepted by the scientific community that could be applied to a regulatory framework. The development of validated analytical methods for the determination of non-protein nitrogen containing compounds to match a scientifically sound regulatory definition of protein will take time. Therefore, we plan to revisit the determination of protein on the label once validated analytical methods and/or a regulatory definition for protein can be established[8]."

We are unsure why the Agency made this determination, as methods for assessing protein quality have been established for quite some time. An FAO/WHO Expert Consultation on Protein Quality and Evaluation was held in 1990 and determined that protein quality was a measure of the protein digestibility-corrected amino acid score (PDCAAS)[9]. PDCAAS is calculated as the ratio of the first limiting amino acid in the (test) protein compared to the concentration of that amino acid in a reference pattern and then corrected by the true fecal digestibility of the test protein. Complete proteins would contain all nine essential amino acids and would have a higher PDCAAS score as compared to incomplete proteins. If a protein does not provide all of the essential amino acids, then it is not allowed to be listed on a nutrition fact panel as a percent daily value (%DV) for protein because it is not considered to be a complete protein. The Agency's own response to comments covered appropriate measurement of protein quality. FDA stated that the PDCAAS method was the not going to be changed, as it was a valid assessment tool.

The Agency's response to comments on the docket for the changes to the Nutrition Facts rules also touched on the required statement "not a significant source of protein." This

[8] https://beta.regulations.gov/document/FDA-2012-N-1210-0875
[9] G Schaafsma (2000). The protein digestibility-corrected amino acid score. *J Nutr*130(7): 1865S-7S.

statement indicates to consumers that are less knowledgeable in human nutrition that the product does not contain "enough" protein because the product does not contain all of the essential amino acids therefore it is considered to "not be a significant source of protein." A commenter suggested that the Agency amend the language contained in the required statement to include the text, "not a source of complete protein," when the product contains protein with a low PDCAAS score. Comments to this docket argued that the former statement discounts the value of proteins to the diet when they are insignificant simply due to the omission of one or two essential amino acids. The Agency declined to make the change in language and based its reason for that decision on the premise that consumers would not understand or appreciate the difference between a significant source of protein as compared to a complete protein. This is another reason that FDA should revise the Nutrition Facts rules; if BCAAs are not a significant source of protein then they should not be required to report caloric values as if they were.

This issue remained unclarified by FDA's 2016, guidance entitled: "FDA's Policy on Declaring Small Amounts of Nutrients and Dietary Ingredients on Nutrition Labels: Guidance for Industry[10]". This guidance was issued to address the discrepancies between the Nutrition Facts and Supplement Facts regulations. The guidance provided FDA's thinking on how manufacturers of both conventional food and dietary supplements should declare nutrients and dietary ingredients that are present in small quantities on nutrition labels. The intention was to describe an enforcement discretion exercise when a conflict arises between references in the regulations on this topic. Requirements pertaining to nutrient values for conventional foods are found in 21 CFR 101.9(c)(1)-(8). Certain dietary ingredients are often incorporated

[10] https://www.fda.gov/media/98834/download

into food and dietary supplements, and therefore, the regulations that govern their presence in food overlap with the nutrient value regulations that are required for dietary supplements. Regulations pertaining to nutrient declarations in dietary supplements are found at 21 CFR 101.36(b)(2)(ii). Dietary ingredients that are listed in 21 CFR 101.36(b)(2) and are referred to as "(b)(2)-dietary ingredients." Unlike nutrients in conventional food, the (b)(2)-dietary ingredients can only be declared when they are present in dietary supplements in amounts that exceed the amount that can be declared as zero in nutrition labeling according to 21 CFR 101.9(c) (see 21 CFR 101.36(b)(2)(i)). This guidance was intended to address instances where the regulations conflicted with one another, however, it did not touch on the issue of BCAA labeling. This incongruity leaves manufacturers with unclear guidelines regarding whether they should label their products with a caloric value for BCAAs when they are unable to list them as protein. Consumers may not understand the nuance of complete versus incomplete proteins, however, they do realize that macronutrients (protein, carbohydrates, and fat) contribute to calories. If a manufacturer were to provide caloric values for a product that only contained BCAAs, as many amino acid supplements do, then a savvy consumer would question the source of the calories since many people assume that an amino acid would be considered a protein for the purpose of inclusion on a label.

For these reasons, we request that FDA provide clarity on this issue and revise the Nutrition Facts rules to state that a manufacturer should not report caloric value for BCAAs.

2. While the Agency works to provide clarity on this issue, we request that a formal enforcement discretion guidance be issued. The process for revising the Nutrition Facts rules would take a significant period of time, during which companies would be left without appropriate clarification. This ambiguity could potentially leave reputable companies open to frivolous lawsuits due to the incongruities in the regulations. An enforcement discretion policy or

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guidance would allow reputable manufacturers to list amino acids on their labels without listing calories without being in violation of labeling regulations.

Conclusion

The Agency should revise the Nutrition Facts rules so that they allow for labels that contain BCAAs to do so without listing caloric values for those ingredients. Furthermore, the Agency should issue an enforcement discretion guidance while they revise the Nutrition Facts rules that would allow manufacturers to list BCAAs on product labels without being required to also list caloric values for those amino acids. This enforcement discretion guidance should continue until the Agency addresses the discrepancy in the regulations related to calculating protein content and the associated caloric value when a product only contains amino acids.

Environmental Impact Statement

NPA maintains that the actions requested in this Petition are exempt from the requirement to provide an environmental impact statement pursuant to 21 C.F.R. § 25.30(h).

Economic Impact

Information on the economic impact of this proposal can be provided if requested.

Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to NPA which are unfavorable to the petition.

Sincerely,

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