March 7, 2022

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Sent via email to: Dave@chinovabioworks.com

Dear Petitioner:

Your submission requesting that the Commissioner of Food and Drug amend their *Guidance for Industry: Scientific Evaluation of the Evidence on the Beneficial Physiological Effects of Isolated or Synthetic Non-Digestible Carbohydrates Submitted as a Citizen Petition (21 CFR 10.30)* (hereinafter also referred to as the "Guidance Document") (U.S. FDA, 2018), as indicated below in bold font, to consider meta-analyses in their evaluations, provided that the meta-analysis includes all studies from which scientific conclusions can be drawn, and sufficient detail on each individual study included in the meta-analysis is provided as part of the submission.

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> "*Reports, such as review articles, which summarize the findings of individual studies, and meta-analyses, that discuss a number of different studies, do not provide enough information on critical elements of the individual studies, such as the study population characteristics and the composition of the products used. Similarly, the lack of detailed information on the individual studies prevents us from determining whether the studies are flawed in critical elements such as design, conduct of studies, and data analysis. Reviewing the critical elements of each study is necessary to determine whether any scientific conclusions can be drawn from it. Therefore, we intend to use review articles and similar publications only to identify reports of additional studies that may be useful to our scientific review and as background information about the beneficial physiological effect of added non-digestible carbohydrates*. ***As part of the scientific review, a high quality meta-analysis that is conducted and included in the petition may be considered in evaluating the strength of the evidence, provided that all publicly available studies from which scientific conclusions can be drawn are included in the meta-analysis, and sufficient detail on each individual study included in the meta-analysis is provided as part of the petition***".

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"*We intend to evaluate the strength of the evidence to determine whether there is a beneficial physiological effect of an added non-digestible carbohydrate using the publicly available studies from which scientific conclusions can be drawn. We intend to conduct this evaluation by considering the number of studies and sample sizes of each study, the dose response data, the types of foods tested, the relevance of the body of scientific evidence to the U.S. population or target subgroup, and the overall consistency14,15 of the total body of evidence.*
A high-quality meta-analysis that is conducted and included in the petition may also be considered in evaluating the strength of the evidence. *These factors are considered when determining whether the evidence is sufficient to support a conclusion that there is a beneficial physiological effect. Our evaluation of the strength of the evidence considers:*

- Number of studies and number of subjects per group/study.

- *Doses provided across studies and dose-response analyses conducted within a study.16*

- *The type of foods, for example, solid foods, beverages, or dietary supplements, to which the non-digestible carbohydrate was added.*

- *Outcome (i.e., a beneficial effect, no effect, or an adverse effect) and method used to measure the physiological endpoint. For the outcome of an intervention study to demonstrate a beneficial physiological effect, the results of the treatment group would need to be statistically significantly different from the control group ($P < 0.05$).* ***In cases where a meta-analysis is appropriate, the pooled effect size would need to be statistically significant ($P<0.05$).***

- *Consistency of findings. In general, the greater the consistency among the studies in showing a beneficial physiological effect, the higher the level of confidence that a relationship between an added non-digestible carbohydrate and a beneficial physiological effect exists. Conflicting results do not disprove an association because the elements of the study design may account for the lack of a beneficial effect in negative studies, but conflicting results tend to weaken confidence in the strength of the association.*

- ***A high-quality meta-analysis that is conducted as part of the petition, using all publicly available studies from which scientific conclusions can be drawn. To be considered a high-quality meta-analysis, transparent and adequate documentation of the objective, study eligibility criteria, statistical methodology, and sub-group analyses should be prepared prior to the conduct of the meta-analysis and provided in the petition; as well, sufficient detail on each individual study included in the meta-analysis must be provided as part of the petition***".

This citizen petition was received and processed under CFR 10.30 by this office on 03/04/2022. It was assigned docket number FDA-2022-P-0293. Please refer to this docket number in future correspondence on this subject with the Agency.

Please note, the acceptance of the petition for filing is a procedural matter and in no way reflects the Agency's decision on the substantive merits of the petition.

Sincerely,

Dynna Gorham-bigby -S

Digitally signed by Dynna Gorham-bigby -S
Date: 2022.03.07 15:10:56 -05'00'

Dynna Bigby
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