1310 L Street, NW, 7th Floor
Washington, DC 20005
cei.org

202 331 1010 main
202 331 0640 fax

November 9, 2021

Lauren K. Roth,
Associate Commissioner for Policy
Office of the Commission of the FDA
U.S. Department of Health and Human Services
5630 Fishers Ln
Rockville, MD 20852
Via Email: lauren.roth@fda.hhs.gov

Re: Information Quality Act Correction Request Regarding Voluntary Sodium Reduction Goals: Target Mean and Upper Bound Concentrations for Sodium in Commercially Processed, Packaged, and Prepared Foods (86 FR 57156) (Oct. 14, 2021)

The Competitive Enterprise Institute (CEI) submits this request for correction of this agency's 2021 re-evaluation of sodium in food. We submit this under the Information Quality Act (IQA), 114 Stat. 2763, section 515, as implemented through HHS and Office of Management and Budget (OMB) guidelines. These guidelines were expanded by OMB in a memorandum issued on April 24, 2019. In accordance with FDA's quality guidelines, we are following the dispute resolution process "beginning with the employee or division that disseminated the information, or by contacting the center, the Agency, or an ombudsman." FDA also asks that we additionally send a copy to the FDA's Ombudsman at OMBUDS@oc.fda.hhs.gov, which we will do. If appeals are necessary, they are to follow the process of internal agency review of decisions specified in 21 C.F.R. § 10.75.

This request concerns FDA's failure to conduct a peer review of its scientific evaluation of sodium, contrary to OMB guidelines. The Federal Register notice, 86 FR 57156, was signed by Lauren K. Roth, Associate Commissioner for Policy, on October 8, 2021. As such, she appears to be the initial employee at FDA who disseminated the information and for that reason we are beginning the request for correction process with her.

Under HHS guidelines, "**The agency will respond to all requests for correction within 60 calendar days of receipt.**" https://aspe.hhs.gov/reports/hhs-guidelines-ensuring-maximizing-quality-objectivity-utility-integrity-information-disseminated. For this reason, we expect a response to this request for correction (RFC) within 60 calendar days.

In addition, the new OMB guidelines require that, "The agency response should contain a point-by-point response to any data quality arguments contained in the RFC and should refer to a peer review that directly considered the issue being raised, if available." Furthermore, "Agencies should share draft responses to RFCs and appeals with OMB prior to release to the requestor for

assessment of compliance with the above norms." Thus, responses to correction requests now need to be reviewed in advance by OMB sufficiently in advance of the 60-day deadline.

FDA's Scientific Evaluation of Salt Does Not Meet the Information Quality Act Requirements

As shown below, the document titled "Voluntary Sodium Reduction Goals: Target Mean and Upper Bound Concentrations for Sodium in Commercially Processed, Packaged, and Prepared Foods: Guidance for Industry" does not meet the requirements of the Information Quality Act.

The document was disseminated to the public via the Federal Register at 86 FR 57156 and online at https://www.fda.gov/media/98264/download.

This document is based upon FDA having "reviewed the publicly available scientific literature on potential opportunities and technologies for reducing sodium."

This scientific evaluation by FDA made the following statements:

- "sodium intake should be reduced in order to reduce the risk for hypertension and cardiovascular disease; lower levels are recommended for children younger than 14 years of age."
- "Research shows that excess sodium consumption is a contributory factor in the development of hypertension (Refs. 4, 13-15), which is a leading cause of heart disease and stroke, the first and fifth leading causes of death in the United States, respectively (Ref. 16)"
- "Decreasing population sodium intake is therefore expected to reduce the rate of hypertension."
- "Research also shows that the increase in blood pressure seen with aging, common to most Western countries, is not observed in populations that consume low sodium diets (Ref. 17) and that the U.S. population consumes far more sodium than recommended (Refs. 3 and 18)."
- "Moreover, dietary reduction of sodium can lower blood pressure, as has been demonstrated in the Dietary Approaches to Stop Hypertension (DASH)-Sodium trial (Ref. 19) and other experimental studies (Refs. 4 and 20)."
- "Multiple studies have estimated the public health and economic benefits associated with broad reduction in sodium intakes in the U.S."
- "Those studies have shown that reductions in average intake (modeled at a variety of intake levels below current intake, down to an average level of roughly 2,200 mg/day) have been estimated to result in tens of thousands fewer cases of heart disease and stroke each year, as well as billions of dollars in health care savings over time."
- "One study (Ref. 27) used three epidemiological datasets to estimate the separate public health benefits of reducing the population's average sodium intake to 2,200 mg/day over 10 years."

- "The researchers estimated that this pattern of reduction would prevent between 280,000 and 500,000 premature deaths over 10 years and that sustained sodium reduction would prevent additional premature deaths."

Based on its evaluation, the agency recommended lowering the average intake of salt per day from 3,400 to 3,000 mg/day.

This conclusion was reached despite the fact that none of the scientific studies cited discuss 3,000 mg/day.

The FDA Scientific Evaluation of Salt Is a Highly Influential Scientific Assessment

This FDA document does not discuss IQA compliance at all. However, the document is a "highly influential scientific assessment" (HISA), and this triggers a number of IQA requirements that FDA failed to follow. But even if the document was not a HISA and contained only "influential scientific information," FDA still would have failed to follow the OMB guidelines.

The FDA Scientific Evaluation of Salt is a Scientific Assessment.

According to OMB's *Final Information Quality Bulletin for Peer Review*, 70 FR 2664 (2005), ("OMB 2005 Final Memo"), the "term 'scientific assessment' means an evaluation of a body of scientific or technical knowledge, which typically synthesizes multiple factual inputs, data, models, assumptions, and/ or applies best professional judgment to bridge uncertainties in the available information. These assessments include, but are not limited to, **state-of-science reports**; technology assessments; **weight-of-evidence analyses**; **meta-analyses**; **health, safety, or ecological risk assessments**; **toxicological characterizations of substances**; integrated assessment models; **hazard determinations; or exposure assessments**." *Id.* at 2666 (emphasis added).

Under the OMB definition, the document is a scientific assessment because it:

1. purports to be based on FDA's review of "the publicly available scientific literature,"
2. claims it is evaluating the state-of-the-science as to sodium, and
3. claims of health risks caused by sodium.

The FDA Scientific Evaluation of Salt is a Highly Influential Scientific Assessment due to its social and economic impacts and its controversial nature.

The OMB 2005 Final Memo defines a "highly influential scientific assessment" (HISA) as a scientific assessment which "(i) Could have a potential impact of more than $500 million in any year, or (ii) Is novel, controversial, or precedent-setting or has significant interagency interest." 70 FR 2671, 2675.

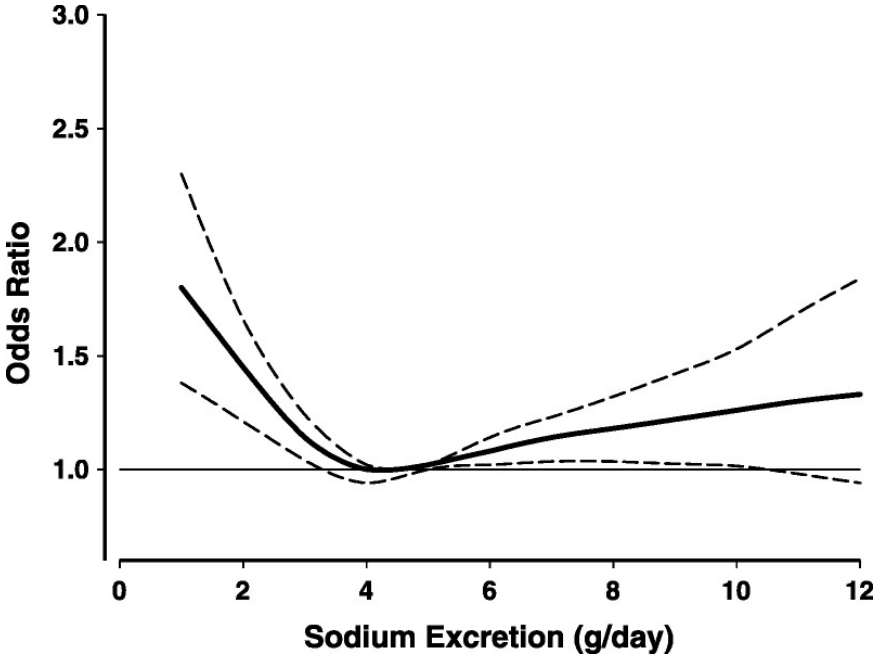
FDA's recommendations are designed to affect the entire food industry, which is a $1.79 trillion dollar industry (according to the USDA https://www.ers.usda.gov/topics/food-markets-prices/food-service-industry/market-segments/). FDA seeks to cut the salt intake of foods by 12 percent. The food salt market alone in the United States is a $4.5 billion dollar industry which would be deliberately restricted by FDA's recommendation. Even assuming a naive analysis of a 12% reduction in the food salt market, that would still mean a $540 million reduction that surpass the $500 million requirement for a HISA. But, of course, changing food ingredients doesn't just involve less salt purchasing but also requires reformulation of product ingredients, retooling manufacturing of such products, changes to labeling and other advertising, and could substantially affect the entire food industry. The result is likely to be billions spent changing what is in most food products on the market today.

There are also scientists who disagree with FDA's conclusions. Here are just a few examples many of which are peer-reviewed studies in respected medical journals:

- A recent peer-reviewed study "Sodium Intake and Health: What Should We Recommend Based on the Current Evidence?" which was published in the 2021 edition of Nutrients by: Andrew Mente, Principal Investigator for the Epidemiology Program at the Population Health Research Institute, McMaster University; Martin O'Donnell, Associate Director of the HRB-Clinical Research Facility, National University of Ireland; Salim Yusuf, Marion W. Burke Chair in Cardiovascular Disease, Department of Medicine, McMaster University. https://www.mdpi.com/2072-6643/13/9/3232/htm.

  This study found the ideal sodium intake is between 3 and 5 grams per day, and that the U.S. is below the global average of 3.95. Furthermore, they found that the U.S. is currently closer to the too-low amount (less than 3 g/day) than the too-high amount (5 g/day). With an overall conclusion that "At present, recommendations to reduce sodium intake in whole populations to low levels is premature. This conclusion was repeated in two recent reviews by a group of experts (with diverse opinions and backgrounds)." It went on that "We suggest that, until new data emerge (ideally from large clinical trials), the optimal sodium intake should be in the range between 3 and 5 g/day. Most Americans (i.e., about four out of five people) have sodium intakes below 5 g/day, and in these individuals there is little evidence that lowering sodium will reduce cardiovascular events or death. Therefore, efforts to reduce sodium intake in entire populations cannot be justified." *Id.*

- A 2016 study found that high sodium is only a problem in hypertensive population, but that there is an "association of low sodium intake with increased risk of cardiovascular events and death is observed in those with or without hypertension." Mente, Andrew et al. *Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies*, The Lancet vol. 388 (2016). Their conclusion was that "lowering sodium intake is best targeted at populations with hypertension who consume high sodium diets." *Id.*



Robert P. Heaney, *Making Sense of the Science of Sodium*, Nutrition Today (2015). This study suggests that intake between 4 g/day and 6g/day is ideal for minimizing the risk of cardiovascular events. This study means FDA's proposed reduction of sodium in this guidance is likely to result in increased risk of cardiovascular events.

- Another group of researchers have found the same thing. A 2014 Meta-study which examined 25 different studies with a total of 274,683 participants, were grouped cohorts into three groups: (1) low sodium, meaning as <2,645 of sodium, (2) high sodium was > 4,954 mg of sodium, and (3) medium Sodium was between these two. The results were that "Both low sodium intakes and high sodium intakes are associated with increased mortality, consistent with a U-shaped association between sodium intake and health outcomes." *Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis,* American Journal of Hypertension, Vol. 27, No. 9 (2014), https://academic.oup.com/ajh/article/27/9/1129/2730186.

  The 2014 study, acknowledged that "The optimal range of sodium intake for cardiovascular health is controversial." And its findings were such that "estimated sodium intake between 3 g per day and 6 g per day was associated with a lower risk of death and cardiovascular events than was either a higher or lower estimated level of intake." Martin O'Donnell, et al., *Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events*, (August 14, 2014) https://www.nejm.org/doi/full/10.1056/nejmoa1311889.

- Another study wrote that "Few issues in medicine received more attention and raised more controversy." The study examined the results of many different meta-analysis and experimental results concluding that: "Taken together, available evidence does not support the current recommendations of a generalized and indiscriminate reduction of salt intake at the population level." Katarzyna Stolarz-Skrzypek, Yan-Ping Liu, Tatiana Kuznetsova, et al, *Blood pressure, cardiovascular outcomes and sodium intake, a critical review of the evidence*, Acta Clinica Belgica, Vol. 67, No. 6 (2012), https://www.ncbi.nlm.nih.gov/pubmed/23340145.

- In the Journal of the American Medical Association, a 2011 study found that high sodium "did not translate into a higher risk of hypertension or CVD complications," but that lower sodium "was associated with higher CVD mortality." Stolarz-Skrzypek K, Kuznetsova T et al., *Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion*. Journal of the American Medical Association 305 (2011), https://pubmed.ncbi.nlm.nih.gov/21540421/.

- In 2008 a study by Hillel W. Cohen, Susan M. Hailpern, Michael H. Alderman found that the results of their "data are consistent with the hypothesis that lower sodium intake is associated with increased CVD and all-cause mortality." *Sodium Intake and Mortality Follow-Up in the Third National Health and Nutrition Examination Survey (NHANES III),* Journal of General Internal Medicine, Vol. 23, No. 9 (2008), pp. 1297–1302, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2518033.

- Yet another example is James DiNicolantonio, a research scientist at Saint Luke's Mid America Heart Institute and associate editor of the journal BMJ Open Heart. According to this scientist, salt consumption "does not seem to be a problem for most people." Hannah Sparks, *FDA wants to radically reduce salt in the nation's food supply*, New York Post (Oct 13, 2021) https://nypost.com/2021/10/13/fda-wants-to-radically-reduce-salt-in-nations-food-supply/. As Dr. DiNicolantonio wrote, "approximately 80% of people with normal blood pressure … are not sensitive to the blood-pressure-raising effects of salt at all." According to Dr. DiNicolantonio, those without rare kidney diseases, could have up to 6,000 milligrams of sodium a day with no ill effects.

OMB describes "most controversial issues," as one in which "there exists a range of respected scientific viewpoints regarding interpretation of the available literature." 70 FR 2669. The above published articles by experts in the field, including most of which that are peer-reviewed by other experts, qualify as "respected scientific viewpoints regarding interpretation of the available literature" that differ from FDA's conclusion. This demonstrates that these guidelines by FDA are, at the very least, controversial and contrary to some published peer-reviewed studies. As one of the above peer-reviewed studies states, "Few issues in medicine received more attention and raised more controversy." Stolarz-Skrzypek, *supra*, https://www.ncbi.nlm.nih.gov/pubmed/23340145. Another that "The optimal range of sodium

intake for cardiovascular health is controversial." Martin O'Donnell, *supra*, https://www.nejm.org/doi/full/10.1056/nejmoa1311889.

Being controversial is not a requirement to be a HISA, but an influential scientific evaluation which is controversial is considered a HISA under OMB guidelines regardless of the monetary impacts.

In short, FDA's evaluation will have a huge potential impact and is controversial. Either of these factors alone makes this evaluation a Highly Influential Scientific Assessment according to the OMB guidelines. But given that both factors are present, there can be no question about its status as a HISA.

Even if it is not a HISA, the FDA Evaluation Is Clearly Influential Scientific Information

A lower standard set of peer review requirements is applied to information that is not a HISA, but is instead categorized as "influential scientific information." The definition of this is "scientific information the agency reasonably can determine will have or does have a clear and substantial impact on important public policies or private sector decisions." OMB 2005 Final Memo, Section I, Part 6. Even if FDA properly determined that the Evaluation is not a HISA, it clearly is "influential scientific information" because it was specifically designed to influence the food industry's use of salt which, as explained above, is a $4.5 billion dollar industry.

FDA Failed to Follow the OMB Guidelines By Ignoring the Peer Review Requirement

We know of no evidence that FDA performed the peer review which is required for all HISA and ISI information. OMB 2005 Final Memo, Section II, Part 1 ("To the extent permitted by law, each agency shall conduct a peer review on all influential scientific information that the agency intends to disseminate."); Section II, Part I ("To the extent permitted by law, each agency shall conduct peer reviews on all information subject to this Section."). As such, none of the peer review requirements for HISA or ISI by OMB were followed by HHS.

Because no peer review was done, OMB's requirements concerning selection of reviewers, independence, choice of peer review mechanism, opportunity for public participation in the peer review process, and certification of compliance were all violated by FDA.

The failures by FDA to do a proper peer review as required by the OMB and HHS guidelines for the FDA Scientific Evaluation of Salt undermine the quality of the information disseminated.

FDA Should Withdraw the FDA Scientific Evaluation of Salt Due To Lack to Lack of Peer Review

The Information Quality Act guidelines require an agency to follow the proper peer review process *before* a scientific assessment can be disseminated. No valid peer review process was done for the FDA's scientific evaluation of salt. Until such a peer review process is validly completed, under the OMB guidelines, HHS should formally withdraw the document through a

notice in the Federal Register inform the public that the information disseminated should not be relied upon for regulatory or other purposes until a proper peer review has been completed.

FDA should then start the process of peer reviewing FDA's scientific evaluation of salt. Lastly, FDA will have to reconsider the evaluation's findings in light of this new peer review process, taking into account objections and problems raised by the peer reviewers and the public. The public is required to be involved in a HISA peer review through the opportunity to submit comments for evaluation by the peer reviewers under OMB guidelines.

By withdrawing the FDA Scientific Evaluation of Salt and then restarting the peer review process for it, it can ensure that there is confidence in the quality of the information being disseminated.

Sincerely,

Devin Watkins, Attorney
devin.watkins@cei.org
Sam Kazman, General Counsel
sam.kazman@cei.org
Competitive Enterprise Institute
1310 L Street NW, 7th Floor
Washington, DC 20005
(202) 331-1010