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We are submitting this comment on behalf of the Global Food Research Program (GFRP) at the University of North Carolina at Chapel Hill. The GFRP is a project of the Carolina Population Center. Our researchers and staff collaborate with diverse partners across the globe to evaluate food and nutrition policies and to develop research aimed at reducing diet-related disparities in health and creating a healthful food system. We commend the FDA for engaging in efforts to develop a uniform definition of ultra-processed foods (UPFs) for policy and regulation purposes in the US. Our team has been deeply engaged in scientific research on UPFs for many years and is involved in efforts to develop operational definitions of UPFs for use in policies that aim to reduce their consumption in the US and in other countries. Our responses to the FDA's questions below are rooted in our extensive experience in this area.

Intake of UPFs is very high in the United States, corresponding to over 50% of the calories consumed in the country.[1–4] Given the links between UPF intake and adverse health outcomes, population-level interventions to reduce UPF consumption in the United States are urgently needed. Importantly, **the available evidence base linking UPF consumption to health harms is more than sufficient to warrant regulatory action**.[5–15] This evidence base includes high-quality randomized controlled trials showing that diets composed of UPFs lead to higher energy intake than diets composed of minimally processed foods,[16–18] as well as epidemiological evidence linking higher UPF intake with increased risk of several chronic health issues, especially cardiovascular disease, type 2 diabetes, and mental health disorders.5 While knowledge gaps still exist, clear precedents for regulatory action based on epidemiological and mechanistic evidence exist – for example, from the regulation of tobacco, alcohol, and opioids, which were initially targeted based on incomplete evidence and ultimately saved millions of lives.

Obtaining an operational definition of UPFs is a key initial step for regulatory action. **The goal of such an operational definition must be, first and foremost, identifying products for intervention in a manner that maximizes population health benefits. To achieve this goal, the FDA must ground its efforts in the evidence linking UPFs to health harms and, as closely as possible, mirror the methods by which this evidence identified UPFs.**

While it is true that different conceptual definitions of UPFs exist, **the scientific evidence linking UPFs to adverse health outcomes almost exclusively uses the Nova classification system to identify UPFs.[5–15]** Therefore, the available evidence base would only support policies that identify UPFs in manner sufficiently consistent with the Nova system. **While certain concessions may be necessary to develop an operational UPF definition that is suitable for policy and regulation within the United States' complex food supply, there is no scientific evidence suggesting that definitions that substantially depart from the Nova system would yield meaningful health benefits.**

- The Nova classification system divides foods into four groups: (1) unprocessed or minimally processed foods, (2) processed culinary ingredients, (3) processed foods, and (4) UPFs — defined, in summary, as industrial formulations containing few or no whole-food ingredients that are assembled into edible products using intense processing methods and often enhanced with additives to improve their sensory properties. While this definition encompasses a wide range of foods whose degree of healthfulness may vary, a recent review of conceptual definitions of UPFs in the scientific literature found that most are less specific and less functional than Nova's, failing to provide markers unique to UPFs.[19]
- To date, the Siga system seems to be the only conceptual definition of UPFs that not only provides detailed information on UPF markers (as Nova does) but also builds on Nova's approach and classifies UPFs into categories more granular than those of the Nova system. In summary, this system's categorization considers how many markers of processing are present in a product, how much health risk each marker seems to pose individually, and the product's overall nutrient content.[19] **While Siga's approach may seem promising from a conceptual standpoint, it is important to note that this system has not yet been used in any studies linking UPFs to ill health.** Therefore, it is unclear whether Siga's greater granularity, which would likely lead to more implementation challenges and higher regulatory burden, would translate into larger health benefits if used for policy purposes.
- Multiple systematic reviews and meta-analyses reveal that **evidence linking UPFs to health outcomes overwhelmingly relies on Nova**, with studies that do not use Nova to identify UPFs being so uncommon that they generally are not included in reviews.[5–15]

Given that Nova should serve as the foundation for operational UPF definitions, the major challenge to be addressed is the fact that **information about industrial processing methods employed in the manufacturing of specific products is not readily available.** This is a challenge that researchers have faced for over a decade and have addressed by **using food groups and ingredients to identify UPFs**. Current research shows that the ingredients lists and nutrition facts panels required in countries like the US, United Kingdom, Brazil, and Chile provide excellent information for identifying UPFs.[20–24]
We provide details about this approach below in response to questions 2a-2d.

Crucially, adapting this ingredients-based approach developed by researchers for application in policy and regulation contexts would be the best way to ensure that (a) interventions are based on data consistently available for all packaged foods, (b) interventions are consistent with the scientific evidence linking UPFs to ill health, and (c) interventions can be readily monitored and evaluated.

The ingredients-based approach developed by researchers to identify UPFs uses certain ingredients as proxy indicators (or "markers") of UPF status.[25,26] Below we provide more information about such ingredients. Importantly, the types of ingredients discussed in 2a and 2b below equally represent UPF markers – they are only commented on separately here given the structure of the FDA's questions.

The ingredients-based approach developed by researchers to identify UPFs considers non-culinary ingredients to be UPF markers. Non-culinary ingredients are sources of carbohydrates (i.e., varieties of sugars and modified starches), fats (i.e., varieties of modified oils), or proteins (i.e., varieties of protein isolates) that are not typically used in home kitchens.[25,26] Because these ingredients are used in larger amounts in a product's formulation, they normally appear in the beginning or middle of a product's ingredient list — however, it is worth noting that "beginning" and "middle" are not objectively defined positions, and thus should not be used as a defining criterion.

The ingredients-based approach to identify UPFs developed by researchers considers additives with critical "cosmetic" functions to be UPF markers regardless of their placement along the ingredient list. Additives with "cosmetic" functions are those that improve the sensory properties (e.g. appearance and texture) of products and thus do not encompass all food additives. "Cosmetic" additives are necessary because the ultra-processing of grains and proteins result in products that lack the sensory properties of desirable foods, such as color and taste. Additives return such properties to final products, so that they look and taste appealing to consumers.

- The following functional classes of additives from the UN Codex Alimentarius are considered as "cosmetic," and thus constitute UPF markers: anti-foaming agents, foaming agents, bulking agents, gelling agents, thickeners, carbonating agents, colors, emulsifiers, emulsifying salts, flavor enhancers, glazing agents, and sweeteners. Flavors do not constitute a Codex functional class but are also considered as cosmetic additives.[25–27] A forthcoming special issue of The Lancet suggests that using the presence of cosmetic additives is the best strategy to identify UPFs for policy interventions globally.[28]
- The following technical effects as classified by the FDA closely correspond to the aforementioned cosmetic functions: **(1) surface-active agents, (2) stabilizers and thickeners, (3) propellants, aerating agents, and gases, (4)**

color and coloring adjuncts, (5) emulsifiers and emulsifying salts, (6) flavoring agents and adjuvants, (7) flavor enhancers, (8) surface-finishing, (9) non-nutritive sweeteners.[20] Thus, the presence of additives with these technical effects could constitute one basis for an operational definition of UPFs in the US.

- While using the full aforementioned list of FDA technical effects would be the most comprehensive approach to identifying UPFs, we recognize that it still constitutes a complex set of criteria. Fortunately, recent work suggests that a substantial portion of UPFs in the food supply may be captured for intervention through simplified criteria.[20,22,23] We are currently conducting a study to assess how reliably different sets of simplified criteria would approximate Nova's full criteria in the US food supply. Our previous study with a nationally representative sample of US households' food purchases over a year found that the use of colors and flavors would allow for the identification 98% of UPFs in the food supply, while full list of "cosmetic" FDA classes of additives (plus flavors) would allow for the identification of 100% of UPFs in the food supply.[20]

While it is true that additives are used in small amounts and contribute minimally to the composition and weight of the finished food – leading them to normally appear towards the end of a product's ingredient list – they still **substantially alter foods' sensory properties, making them more palatable, visually appealing, and transforming industrial formulations of edible components into food-like products.** This enhanced palatability and appeal, in turn, can accelerate food absorption and reinforce cravings, resulting in products thar are less satiating overconsumed compared to minimally processed foods,[16–18] and considered potentially addictive by many psychologists and neuroscientists.[29,30] **Importantly, natural or artificial additives can both have this functional impact on foods' sensory properties, and thus should not be considered separately**.

As stated above, the rationale for using certain types of food additives to identify UPFs is the additive's functional impact on the texture and appearance of foods (i.e., "cosmetic" function). **This impact can be achieved even if the additive is used in very small amounts.** Thus, the amount of cosmetic additive used in a food should not influence whether the food should be characterized as UPF.

A focus on ingredients for identifying UPFs derives from the aforementioned lack of readily available information about processing methods, not from specific ingredients being the sole or main source of the health harms linked to UPFs. **Ingredients are used as proxy indicators (or "markers") of UPFs in the absence of more precise information about processing methods, but individual UPF markers may or may not pose individual health concerns.** Therefore, UPF definitions should not be based on how harmful the specific UPF markers included may be. The available scientific evidence links UPFs to ill health as a category, so **ingredients should only be used as a tool to identify if a given product is or is not part of the UPF category**.

- The mechanisms underlying the links between UPFs and ill health are multifaceted and not yet fully understood. Currently, hypothesized mechanisms (supported by varying levels of evidence) include UPFs' poor nutrient profile,[31–34] hyperpalatability,[35–41] the degree and the presence of xenobiotics42–46 and other potentially harmful compounds used or formed during intense processing.[47–50] These mechanisms operate simultaneously and likely in synergy, making it extremely difficult to isolate them. As a result, efforts focusing on any single mechanism in isolation (e.g., specific ingredients) are unlikely to meaningfully mitigate the potential harms of UPFs.
- **While regulating ingredients that pose individual health concerns is a commendable effort, this type of effort should be separate and distinct from efforts to regulate UPFs.** Defining UPFs based on the presence of a narrow set of ingredients that may individually cause harm, as several states currently propose, would likely lead to a vast underestimation of true UPFs in the food supply.
- The amounts of different ingredients used in UPFs are not examined in the literature linking UPFs to adverse health outcomes, so there is no evidence to support a UPF definition based on ingredient amounts.

As nutrition and public health researchers, this is not our area of expertise. Food scientists are better qualified to provide information on this topic. However, as mentioned above, **information about food processing methods is not readily available, and we are not aware of any scientific articles or studies linking UPFs to ill health in which processing methods were used to identify UPFs.** Additionally, processing methods are constantly changing and evolving. Thus, relying on information about processing methods to identify UPFs would be a misguided approach.

We believe that the term "ultra-processed" fits the foods described well. The term is necessary because these foods — which, per Nova, are distinct from processed foods – are uniquely altered at the cellular level by industrial processes, unlike foods that have undergone traditional and less intense processing (e.g. fermentation, preservation, basic milling).[51] Additionally, in our experience interacting with many different stakeholders, from students to the lay public to policymakers, the average consumer now seems to understand what an ultra-processed food is – a perception corroborated by recent studies.[52–58]

Nutritional composition is one of the mechanisms underlying the link between UPFs and ill health, but not the only one. While policies and interventions may benefit from considering UPFs' nutritional composition, **centering Nova-based ingredient criteria would be the best way to ensure**

that interventions target products in a manner consistent with the scientific evidence linking UPFs to ill health.

- **While most UPFs are high in sugar, sodium, and/or saturated fats, this is not universally true.** Our research group has conducted a study using data on all purchases from 100,000 US households over a year, which showed that 84% of UPFs (as defined by Nova) purchased by US households were high in sugar, sodium, and/or saturated fats. While this is a large portion, the study also showed that, **by using nutrient content (i.e., high sugar, sodium, or saturated fat content) and simplified UPF marker ingredients (i.e., colors and flavors) as criteria to identify UPFs, interventions would be able to capture almost 100% of UPFs purchased by US households**.[20]
- In previous randomized controlled trials, diets composed of UPFs led to higher caloric intake compared to diets composed of minimally processed foods with identical macronutrient and energy compositions.[16–18] Importantly, one of these trials designed both the minimally processed and the ultra-processed diets following macronutrient and food group recommendations from the United Kingdom's dietary recommendations, thus offering participants a "healthy" ultra-processed diet. Researchers found that while both diets resulted in weight loss, this loss was significantly larger on the minimally processed diet.[18]
- One recent randomized controlled trial found that, independently of both macronutrient content and caloric intake, diets composed of UPFs led to compromised metabolic and reproductive health markers compared to diets composed of minimally processed foods.[59]
- Epidemiological evidence finds associations between UPF intake and adverse health outcomes, including all-cause mortality, adiposity, cardiovascular disease, type 2 diabetes, some cancers, gastrointestinal disorders, chronic kidney disease, non-alcoholic fatty liver disease, and mental health disorders to be partially independent from nutrient content.[60–69]
- Some evidence suggests that certain additives present in UPFs may act as xenobiotics and have detrimental effects on the microbiome, contributing to inflammatory processes and adverse health outcomes.[42–46] These effects may be independent from nutrient content.
- **Previous policies targeting foods based exclusively on their nutrient content have been shown to lead manufacturers to reformulate products in ways that may not be beneficial to health.** For example, in Chile, a policy implementing mandatory warning labels on products high in added sugars led food manufacturers to increase their use of non-nutritive sweeteners, which may pose health concerns.[70–72] **Targeting all UPFs as a category could help avoid potentially harmful reformulations, as most reformulations of UPFs would be unlikely to change their UPF status.**

Therefore, nutritional composition and ultra-processing represent distinct concepts that should not be equated. **However, nutritional composition could serve as a useful supplemental criterion in approaches for targeting UPFs, provided that the presence of key UPF-marker ingredients remains central to the UPF definition.** As our aforementioned work has shown,[20] layering added sugar, sodium, and saturated fat thresholds onto an approach for identifying UPFs **could simplify the set of ingredients that would need to be targeted** (and periodically updated) to capture the majority of UPFs in the US food supply, mitigating regulatory burdens. Additionally, nutritional composition could be used as a **criterion to differentiate between types of UPFs for policy purposes**, as some policies may need to prioritize subsets of UPFs with multiple harmful attributes (i.e., both ultra-processing and unbalanced nutritional composition).

Lastly, an approach for targeting UPFs that incorporates supplemental nutritional composition criteria should **build on well-established regulatory precedents**. The Pan American Health Organization (PAHO) nutrient profile model, now used for policy purposes by several jurisdictions around the world, would be the strongest of such precedents. The state of California now provides an example of how to leverage the PAHO nutrient profile model to create a comprehensive policy framework for targeting UPFs. **California's AB 1264 of 2025 defines UPFs through ingredient- based criteria and layers on thresholds for added sugar, sodium, and saturated fat based on the PAHO model**. Our team worked with representatives from California and demonstrated that, compared with the PAHO model, the FDA model presented in the January 2025 proposed rule on front-of-package labeling — which sets nutrient thresholds at more than 20% of the daily value per portion — would capture a much smaller fraction of UPFs for intervention.

Similarly to nutritional composition, **hyperpalatability and energy density are some of the nutrient-related mechanisms underlying the link between UPFs and ill health, but not the only ones. Centering Nova-based ingredient criteria would be the best way to ensure that interventions target products in a manner consistent with the scientific evidence linking UPFs to ill health.**

- Randomized controlled trials suggest that hyperpalatability and energy density likely play an important mediating role in the effects of UPFs on weight gain.[16,17] Even UPFs considered "healthy" based on their macronutrient content and food group have been found to be more energy-dense and lead to higher caloric intake compared to comparable minimally processed options.[18] However, energy-dense UPFs are not the only ones linked to ill-health, as evidenced by a recent large study in which artificially-sweetened beverages (which have zero or few calories) were among the primary UPF sub-categories associated with increased cardiovascular disease risk.[73]
- While UPFs are often energy-dense, they can be reformulated to lower their energy density without altering their UPF status. For example, at the time of

implementation of mandatory warning labels for calories, added sugars, sodium, and saturated fats in Chile, the "high in calories" label (i.e., signaling highly energy-dense products) was the one most commonly applied to products.[74] However, after implementation of such warning labels, Chile saw a large increase in the use of non-nutritive sweeteners,[70–72] which decrease the energy density of products compared to sugar but still characterize products as UPF and are still inked to health harms.[73]

Therefore, similarly to nutritional composition, concepts like hyperpalatability and energy density are distinct from the concept of ultra-processing. **These concepts could serve as a supplemental criterion in approaches for targeting UPFs, provided that the presence of key UPF-marker ingredients remains central to the UPF definition.** However, an important caveat is that, unlike nutritional composition, these concepts are not objectively measured in most studies linking UPFs to ill health and are supported by fewer regulatory precedents. Thus, **establishing palatability and energy density thresholds for regulatory purposes may be more challenging and burdensome when compared to nutritional composition criteria.**

In addition to our aforementioned points, we recognize the FDA's concerns about an overly- inclusive definition of UPFs that would include products for which there is evidence of health benefits (e.g., some whole grain products or yogurts). Importantly, **limited concessions may be possible but should be approached with caution and supported by strong scientific evidence. Even including concessions, an operational UPF definition should still aim to capture most UPFs to maximize population health benefits. Preventing widespread product reformulations that could allow a large portion on UPFs to evade regulation is critical.** We present some suggestions below.

- One approach could be to exempt products that meet the **FDA's "healthy" definition**. Our research group is currently working on assessing how reliable a definition that includes such an exemption would be at approximating Nova's full criteria in the US food supply.
- Another approach could be to include or exempt **food groups** based on evidence of harms or benefits linked to each group. While the vast majority of evidence links UPFs to health harms as a whole category, some recent evidence offers more detailed information about food group- specific associations within the UPF category. For example, a large cohort study recently found sweetened beverages (with both sugar and non-nutritive sweeteners) and processed meats to be the two food groups within the UPF category most strongly associated with higher risks of cardiovascular disease and stroke, while yogurts and savory snacks were associated with lower risk.[73]

Thank you for considering these recommendations and for your commitment to developing a uniform definition of ultra-processed foods (UPFs) for policy and regulation purposes in the US.

Sincerely,

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