U.S. FOOD & DRUG ADMINISTRATION

Memorandum

Date: December 15, 2021

Subject: Health and Chemicals Coalition Meeting

On Wednesday, December 15, 2021, FDA participated in a meeting of the "Health and Chemicals Coalition" that included representatives from the following stakeholder groups: Breast Cancer Prevention Partners, Center for Food Safety, Center for Science in the Public Interest, Consumer Reports, Defend Our Health, Environmental Working Group, Environmental Defense Fund, Healthy Babies Bright Futures, and Natural Resource Defense Fund.

During this meeting, petitioners raised the status of a citizen petition filed with FDA on September 23, 2020 requesting that we revise our regulations and associated guidance and forms to ensure that cumulative effect of chemically- or pharmacologically related substances in the diet are taken into account when assessing the safety of a food additive, a food contact substance, a generally recognized as safe substance, or a color additive. FDA highlighted several complex issues raised by the petition and invited interested parties to submit information to the docket for this petition (FDA-2020-P-2003) that may help inform consideration of these issues.

Summary of Issues Raised by FDA

The petition suggested definitions to demonstrate "relatedness" of substances for use in the evaluation of safety. Petitioners identified several elements, any of which, would satisfy this definition. FDA is currently considering how we and petitioners should consider conflicting data and information.

As examples, FDA is aware of instances where:

- chemicals that could be considered "chemically related" are metabolized differently or have different toxicological effects.
- substances may bind specific receptors, but differing downstream biological mechanisms mediate that effect, resulting in a lack of toxicity.

In such cases, the element as defined in this petition, such as chemically related, or similar action at a receptor, may not be the most relevant effect for evaluation of the safety of such substances.

FDA is also considering how one could establish the most relevant element for use in the safety assessment when conflicting data are available. In light of this knowledge, how FDA establishes that the elements suggested in the petition, in the absence of other confirmatory information, is the most suitable for evaluation of relatedness relevant to the safety evaluation. FDA would like to ensure that definitions described in our regulations do not constrain our ability to use all the data and information relevant for the safety evaluation or, conversely, do not result in a need to evaluate "similar" substances whose pharmacological or toxicological effects are different.