FLAVOR AND EXTRACT MANUFACTURERS ASSOCIATION OF THE UNITED STATES
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October 4, 2019

Via Electronic Transmission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Food and Drug Administration Docket No. FDA-2012-N-0143: Harmful and Potentially Harmful Constituents in Tobacco Products; Established List; Proposed Additions; Request for Comments (84 *Fed. Reg*. 38032 (August 5, 2019)).

Dear Sir or Madam:

On behalf of the Flavor and Extract Manufacturers Association of the United States (FEMA), we appreciate the opportunity to submit comments in response to the U.S. Food and Drug Administration's (FDA) Harmful and Potentially Harmful Constituents in Tobacco Products; Established List; Proposed Additional; Request for Comments (84 *Fed. Reg.* 38032 (August 5, 2019)).

I. Introduction

FEMA, founded in 1909, is the Washington, D.C.-based national association of the U.S. flavor industry. FEMA's members include flavor manufacturers, flavor users, flavor ingredient suppliers and others interested in assuring the supply of safe flavoring materials. FEMA members manufacture or market more than 95% of all flavors sold in the United States and create flavors for use in a wide variety of food and beverage products. FEMA is in its 110th year of existence and has a long history of working collaboratively with regulatory authorities, including the FDA.

II. Background

Section 101(b) of the 2009 Family Smoking Prevention and Tobacco Control Act (Pub. L. 111-31) amended the Federal Food Drug and Cosmetic Act (FD&C Act) by providing FDA with the authority to regulate tobacco products. Section 904(e) of the FD&C Act as amended (21 U.S.C. §387d(e)) requires FDA to establish, and periodically revise as appropriate, "a list of harmful constituents, including smoke constituents, to health in each tobacco product by brand and by quantity in each brand and sub-brand."

In final guidance published in 2010, the agency defined a harmful and potentially harmful constituent (HPHC) as "any chemical or chemical compound in a tobacco product or in tobacco smoke: (a) that is or potentially is inhaled, ingested, or absorbed into the body; and (b) that causes or has the potential to cause direct or indirect harm to users or non-users of tobacco products." (*see* 76 *Fed. Reg.* 5387 (January 31, 2011)). The FDA first established the list of HPHCs used in tobacco products on April 3, 2012 (77 *Fed. Reg*. 20034). The current list contains 93 substances that are identified as HPHCs as used in tobacco products. Now, in this proposed rule, the agency

is proposing to add 19 additional substances to the list as HPHCs as used in tobacco products. (84 *Fed. Reg.* 38032 (August 5, 2019)).

III. The FEMA GRAS Program Does Not Evaluate Flavor Ingredients for Use in Products Other than in Food

In the U.S., the vast majority of flavor ingredients are added to food consistent with the "generally recognized as safe" (GRAS) provision of the FD&C Act. The GRAS provision of Section 201(s) of the FD&C Act applies, however, only to food as defined in Section 201(f) of the Act. For the purposes of the GRAS provision, food is defined as "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article."[1] More than fifty years ago, FEMA began a program to assess the safety and GRAS status of flavor ingredients under the authority of the 1958 Food Additives Amendment to the FD&C Act.[2] In accordance with the statute, the FEMA GRAS program provides the primary route to achieve regulatory authority to use flavor ingredients in food in the U.S. It is important to note that a FEMA GRAS determination for a flavor ingredient does not constitute "approval" of that substance by FDA.

The FEMA Expert Panel evaluates the safety of flavor ingredients only under their conditions of intended use in food, including beverages and chewing gum. Therefore, the Expert Panel only evaluates flavor ingredients for exposure through ingestion. The Expert Panel does not evaluate flavor ingredients for use in tobacco products including e-cigarettes or other ENDS devices, other products that are not food, or products that result in exposures other than by ingestion. Therefore, FEMA GRAS status for the use of a flavor ingredient in food does not provide regulatory authority to use the flavor ingredient in e-cigarettes, ENDS devices or other tobacco products in the U.S.

In addition, there are a variety of programs in various countries and geographic regions that evaluate the safety of flavor ingredients, and like the FEMA GRAS program, all of these programs evaluate the safety of flavor ingredients under their conditions of use in food. In Europe, flavor ingredients are evaluated by the European Food Safety Authority (EFSA) solely for their use in food. Also consistent with this principle is the global food safety evaluation program conducted by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) that also evaluates the safety of flavor ingredients solely for their use in food. None of these primary global safety assessment programs for flavor ingredients, including the FEMA GRAS program, evaluate flavor ingredients for use in products other than in food and as such evaluate flavor ingredients only for safety upon ingestion.

FEMA generally supports the FDA's activities related to constituents as used in tobacco products. We would like to make the agency aware that FEMA has made publicly available on its website a long-standing statement that flavor ingredients are not evaluated by the FEMA Expert Panel for safety and GRAS status for any uses other than use in food (https://www.femaflavor.org/safety-assessment-and-regulatory-authority-use-flavors-focus-electronic-nicotine-delivery-systems). Therefore, use in ENDS and other tobacco products must have separate safety assessments to assure safety and establish regulatory authority to use

[1] 21 U.S.C. §321(f) (2012).

[2] John B. Hallagan and Richard L. Hall, *FEMA GRAS – A GRAS Assessment Program for Flavor Ingredients*, 21 REGULATORY TOXICOLOGY AND PHARMACOLOGY 422, 422 – 430 (1995); John B. Hallagan and Richard L. Hall, *Under the Conditions of Intended Use – New Developments in the FEMA GRAS Program and the Safety Assessment of Flavor Ingredients*, 47 FOOD AND CHEMICAL TOXICOLOGY 267, 268 (2009).

flavors in such products. FEMA has periodically updated this statement to reflect new regulatory activity related to flavored tobacco products, and to include citations to recent publications known to FEMA regarding flavors and ENDS devices.

IV. Information Relevant to the FDA's Evaluation of the Use of Flavors in Tobacco Products – the Opportunity to Cooperate and Collaborate

Because the FEMA Expert Panel's GRAS evaluations apply only to the conditions of intended use of flavor ingredients in food, FEMA does not focus on scientific information within the FEMA GRAS program related to inhalation exposure to flavors or their use in tobacco products. However, FEMA has collected voluminous scientific information on flavor ingredients over the years and would be pleased to discuss with FDA how FEMA and the agency may cooperate and collaborate on sharing relevant information. A FEMA resource that will be of value to the agency is the FEMA Flavor Ingredient Library on the public portion of the FEMA website (www.femaflavor.org). The Library contains an inventory of all FEMA GRAS flavor ingredients plus supporting information.

V. Conclusion

FEMA appreciates the opportunity to comment on FDA's Proposed Additions to the HPHC in Tobacco Products Established List and would be pleased to address additional concerns directly with the FDA Office of Tobacco Products.

Sincerely,

Joanna Drake

Joanna R. Drake
General Counsel