

is in response to a food additive petition filed by Nutrinova, Inc. It will simplify the existing regulations by replacing all of the currently listed uses of ACK with a single-use category for food.

**DATES:** This rule is effective December 31, 2003. Submit written or electronic objections and requests for a hearing by January 30, 2004.

**ADDRESSES:** Submit written objections and requests for a hearing to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic objections at <http://www.fda.gov/dockets/ecomments>.

**FOR FURTHER INFORMATION CONTACT:** Blondell Anderson, Center for Food Safety and Applied Nutrition (HFS-265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835, 202-418-3106.

#### **SUPPLEMENTARY INFORMATION:**

#### **I. Background**

In a notice published in the **Federal Register** on May 20, 2002 (67 FR 35552), FDA announced that Nutrinova, Inc., 285 Davidson Ave., suite 102, Somerset, NJ 08873, had filed a food additive petition (FAP 2A4735). The petition proposed to amend § 172.800 *Acesulfame potassium* (21 CFR 172.800) to provide for the safe use of ACK as a general-purpose sweetener and flavor enhancer.

ACK is currently approved under § 172.800 for use in 12 food categories at levels determined by current good manufacturing practice. The existing regulation has resulted from the approval of seven food additive petitions (FAPs). The practical effect of the amendment requested in the current petition would be to broaden the regulation to include any additional food category not allowed by the current regulation, with the exception, as discussed in the following paragraphs, of meat and poultry, and to replace the 12 currently listed uses of ACK with a single-use category for food.

The acceptable daily intake (ADI) of 15 milligrams per kilogram body weight per day (mg/kg bw/d) or 900 mg per person per day (mg/p/d) was established for ACK as a result of FDA's review of FAP 2A3659 (53 FR 28379, July 28, 1988), which resulted in the agency's initial approval of ACK in several food categories. The ADI is the level of consumption that has been determined to be safe for human consumption every day over an entire lifetime. The present petition does not contain any new information that would cause FDA to

alter this previously determined ADI for ACK.

FDA's review of the petitions submitted subsequent to FAP 2A3659 involved primarily the following factors: (1) An assessment of the estimated exposure from each additional use; and (2) a determination of whether the cumulative estimated exposure, including the newly requested use, would cause the ADI for ACK to be exceeded over a lifetime by individuals who consume ACK at high levels. In its evaluation of ACK for use in nonalcoholic beverages, including beverage bases, FDA also assessed the safety from exposure to acetoacetamide-N-sulfonic acid (AAS) and acetoacetamide (AAA), the two principal hydrolysis products of ACK (63 FR 36344 at 36346 to 36355, July 6, 1998).

Although the functionality of ACK was addressed in earlier FAPs, in the current petition, Nutrinova, Inc., provided the results from taste panel studies demonstrating the sweetness profile of ACK as a function of concentration in a variety of foods. These data demonstrate that ACK can be used alone or in blends with other intense sweeteners or bulk sweeteners (e.g., sucrose) at self-limiting levels depending on the food application (Ref. 1).

#### **II. Determination of Safety**

Under the general safety standard provisions of section 409(c)(3)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A)), a food additive cannot be approved for a particular use unless a fair evaluation of the data available to FDA establishes that the additive is safe for that use. FDA's food additive regulations (21 CFR 170.3(i)) define safe as a "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use."

The food additives anticancer, or Delaney, clause (section 409(c)(3)(A) of the act) further provides that no food additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal. Importantly, however, the Delaney clause applies to the additive itself and not to constituents of the additive. Thus, where an additive has not been shown to cause cancer, even though it contains a carcinogenic impurity, the additive is not subject to the legal effect of the Delaney clause. Rather, the additive is properly evaluated under the general safety standard using risk assessment procedures to determine whether there is a reasonable certainty that no harm

will result from the proposed use of the additive (*Scott v. FDA*, 728 F.2d 322 (6th Cir. 1984)).

#### **III. Evaluation of Safety for the Petitioned Uses of the Food Additive**

To determine whether ACK can be safely used as a general-purpose sweetener and flavor enhancer, FDA focused its evaluation on whether human exposure to ACK from these uses would exceed the ADI of 15 mg/kg bw/d, and on the potential health risk from exposure to the primary hydrolysis products, AAS and AAA, and the impurity, methylene chloride.

##### **A. Exposure to ACK, AAS, and AAA**

FDA has determined the cumulative estimated daily intake (CEDI) for ACK from its use as a general-purpose sweetener and flavor enhancer in food for eaters-only at the 90th percentile intake to be 313 mg/p/d (Refs. 2 and 3). This CEDI is based on the following factors: (1) The amount of ACK that may be used in the currently regulated food categories and (2) the maximum use level of ACK in other representative food categories in which the sweetener may be used. FDA concludes that the updated CEDI for ACK is well below the ADI (900 mg/p/d). FDA has determined that the updated CEDIs for AAS and AAA are 250 micrograms per person per day (µg/p/day) and 0.36 µg/p/day, respectively (Refs. 1 and 3). These hydrolysis products are formed only under extreme conditions of temperature and/or pH. The agency has determined that the increase in exposure to AAS and AAA, due to the additional uses, is negligible and does not pose any safety concerns (Refs. 3, 4, and 5).

##### **B. Methylene Chloride**

Methylene chloride, a carcinogenic chemical, is a potential impurity in ACK resulting from its use as a solvent in the initial manufacturing step of the sweetener. Data previously submitted in FAP 0A4212 show that methylene chloride could not be detected in the final product at a limit of detection (LOD) of 40 parts per billion (ppb) as discussed in the July 6, 1998, final rule (63 FR 36344 at 36346). In the past, FDA has assumed that methylene chloride is present in ACK at the LOD of 40 ppb (worst-case scenario) and has evaluated its safety by performing a risk assessment for methylene chloride based on this level. No new information has been received to change FDA's previous risk assessment for methylene chloride. Moreover, FDA does not expect that methylene chloride will be present in ACK due to the following