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Guidance for Industry Arsenic in Apple Juice: Action Level

Draft Guidance

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For questions regarding this draft document contact the Center for Food Safety and Applied Nutrition (CFSAN) at 240-402-1700.

**U.S. Department of Health and Human Services
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Guidance for Industry¹

Arsenic in Apple Juice: Action Level

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this guidance.

I. Introduction

This draft guidance document provides information to manufacturers on the action level for inorganic arsenic in apple juice that FDA considers protective of human health and achievable with the use of good manufacturing practices.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

Arsenic is an element that occurs in the environment from both natural and anthropogenic sources including erosion of arsenic-containing rocks, volcanic eruptions, contamination from mining and smelting ores, and previous or current use of arsenic-containing pesticides (Ref. 1).² Arsenic is found in both inorganic and organic forms (together referred to as total arsenic), and inorganic arsenic is generally considered more toxic than organic arsenic (Ref. 2). Consumption of inorganic arsenic has been associated with cancer, skin lesions, developmental effects, cardiovascular disease, neurotoxicity, and diabetes in humans (Ref. 2). In recent assessments, the Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert

¹ This guidance has been prepared by the Division of Plant and Dairy Food Safety, Office of Food Safety, in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration.

² Generally, it is not possible for FDA to identify the source of arsenic in food, including apple juice, when found. Therefore, for purposes of this guidance FDA is not distinguishing the presence of arsenic that may be due to prior pesticide use, such that the residues are pesticide chemical residues subject to a tolerance or tolerance exemption by EPA under section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a)), or other environmental contamination.

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Committee on Food Additives (JECFA) (Ref. 2), which includes participation by U.S. FDA scientists, concluded that food can be a major contributor to inorganic arsenic exposure, and the European Food Safety Authority (EFSA) (Ref. 3) concluded that dietary exposure to inorganic arsenic should be reduced. These findings suggest a need to reduce exposure to inorganic arsenic from food.

Occurrence in Apple Juice

Apple juice is one source of exposure to arsenic from food. Apple juice is a greater potential source of dietary inorganic arsenic exposure for children than for adults, because children's dietary patterns are often less varied than those of adults, and they consume more apple juice relative to their body weight than do adults (Ref. 4). FDA has conducted routine surveillance for arsenic in apple juice for many years through its Total Diet Study (Ref. 5) and Toxic Elements in Food and Foodware, and Radionuclides in Food Program (Ref. 6), and through monitoring of imports and targeted domestic assignments. Total arsenic levels in apple juice samples have routinely been below 10 parts per billion (ppb); for example, more than 95 percent of total arsenic levels in a set of 94 apple juice samples collected at retail as part of a fiscal year 2011 assignment were below 10 ppb (Ref. 7). The remaining four samples in that assignment with total arsenic levels above 10 ppb had inorganic arsenic levels below 10 ppb. However, FDA has identified apple juice samples with inorganic arsenic levels above 10 ppb in previous years (Ref. 8). FDA considers that it is possible to further reduce public exposure to inorganic arsenic from apple juice in general, and specifically from apple juice that currently may contain inorganic arsenic at levels above 10 ppb. Therefore, FDA is issuing draft guidance on an action level for inorganic arsenic in apple juice.

Possible sources of inorganic arsenic in apple juice include processing aids, prior use of arsenic-based pesticides on land currently used for apple orchards, current use of arsenic-based pesticides in other countries, naturally high levels of arsenic in soil or water, and atmospheric deposition from industrial activities. It may be possible in some cases for manufacturers who have found inorganic arsenic in sources of apples or apple juice concentrate to reduce or limit inorganic arsenic in apple juice by choosing sources of apples or apple juice concentrate with lower inorganic arsenic levels or no detectable inorganic arsenic.

Another potential source of inorganic arsenic in apple juice is water used by manufacturers to dilute concentrate to prepare ready-to-drink juice. It may be possible in some cases for manufacturers who have found arsenic in water used to dilute concentrate to reduce or limit levels of inorganic arsenic in ready-to-drink apple juice by examining and controlling arsenic levels in water used for dilution of juice concentrate.

Risk Assessment, Level of Concern, and Achievability

In 2008, FDA established a level of concern (Ref. 9) of 23 ppb for inorganic arsenic in single-strength (ready to drink) apple juice as part of a hazard assessment. This level of concern focused on non-cancer endpoints and average consumption of apple juice with higher levels of arsenic for a limited (not lifetime) period of time.

In 2011, FDA initiated a new quantitative risk assessment for inorganic arsenic in apple juice for cancer endpoints and based on chronic and lifetime exposure. The new risk assessment models

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health effects based on average inorganic arsenic levels in apple juice when several hypothetical maximum limits for inorganic arsenic are in place. More information can be found in the risk assessment document, “A Quantitative Assessment of Inorganic Arsenic in Apple Juice” (Ref. 10).

To assess achievability, or manufacturers’ ability to achieve the proposed limits on inorganic arsenic, FDA used survey results to determine the percentage of apple juice samples in the market that would fall at or below each of the hypothetical maximum limits. More information on achievability and arsenic data can be found in the “Supporting Document for Action Level for Arsenic in Apple Juice” (Ref. 11). FDA has used the information in the supporting document and risk assessment document to identify a new action level for inorganic arsenic in apple juice.

III. Action Level

Because of the potential for human health risks associated with exposure to inorganic arsenic, human exposure to inorganic arsenic should not exceed levels achievable with the use of good manufacturing practices. The action level for inorganic arsenic in single-strength (ready to drink) apple juice that FDA considers achievable with the use of good manufacturing practices is 10 micrograms/kilogram ($\mu\text{g}/\text{kg}$) or 10 ppb. FDA considers the action level for inorganic arsenic in apple juice to be protective of public health. The action level can reduce human exposure to inorganic arsenic that may be found in apple juice.

FDA intends to take the following sampling and enforcement approach to arsenic in apple juice. FDA intends to initially analyze apple juice samples for total arsenic. FDA intends to speciate samples containing more than 10 $\mu\text{g}/\text{kg}$ or 10 ppb total arsenic to determine inorganic arsenic levels. Consistent with 21 CFR 109.6, FDA intends to consider the action level of 10 $\mu\text{g}/\text{kg}$ or 10 ppb inorganic arsenic, in addition to other factors, when considering whether to bring enforcement action in a particular case.

IV. References

We have placed the following references on display in the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You may see them at that location between 9 a.m. and 4 p.m., Monday through Friday. As of July 12, 2013, FDA had verified the Web site address for the references it makes available as hyperlinks from the Internet copy of this guidance, but FDA is not responsible for any subsequent changes to Non-FDA Web site references after July 12, 2013.

1. Agency for Toxic Substances and Disease Registry (ATSDR), 2007, Toxicological Profile for Arsenic, U.S. Department of Health and Human Services, Public Health Service, accessed online at <http://www.atsdr.cdc.gov/toxprofiles/tp2.pdf>.

2. WHO/FAO Joint Expert Committee on Food Additives (JECFA), 2010, Evaluation of Certain Contaminants in Food, 72nd Report of the World Health Organization/Food and Agriculture

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Organization of the United Nations Joint Expert Committee on Food Additives, accessed online at http://whqlibdoc.who.int/trs/WHO_TRS_959_eng.pdf.

3. European Food Safety Authority (EFSA), 2010, Scientific Opinion on Arsenic in Food, EFSA Journal 2009, 7(10): 1351, accessed online at <http://www.efsa.europa.eu/en/efsajournal/doc/1351.pdf>.

4. National Research Council (NRC), 1993, Pesticides in the Diets of Infants and Children, National Academy Press, Washington, D.C.

5. U.S. Food and Drug Administration (FDA) Total Diet Study, accessed online at <http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/default.htm>.

6. U.S. FDA Toxic Elements in Food and Foodware, and Radionuclides in Food Program, accessed online at <http://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm2006907.htm>.

7. U.S. FDA, 2011a, Results of Arsenic Analysis in Single-Strength Apple Juice, 2011 (ORA Sampling Assignment 2011102701), December 16, 2011 update, accessed online at <http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm283725.htm>.

8. U.S. FDA, 2011b, Arsenic in Apple Juice Analytical Results, 2005-2011 Toxic Elements Food and Foodware Program, December 16, 2011 update, accessed online at <http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm273328.htm>.

9. U.S. FDA, 2008, FDA Hazard Assessment and Level of Concern--Apple Juice, accessed online at <http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm277681.htm>.

10. U.S. FDA, 2013, A Quantitative Assessment of Inorganic Arsenic in Apple Juice. <http://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM360016.pdf>

11. U.S. FDA, 2013, Supporting Document for Action Level for Arsenic in Apple Juice. <http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ChemicalContaminantsMetalsNaturalToxinsPesticides/ucm360023.htm>