Inorganic Arsenic in Rice Cereals for Infants: Action Level Guidance for Industry

Draft Guidance

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

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition

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Guidance for Industry

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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This draft guidance document provides information to manufacturers on the action level[2] for inorganic arsenic in rice cereals for infants (hereafter referred to as infant rice cereals) that will help protect public health by reducing infants' dietary exposure to inorganic arsenic and is achievable with the use of current good manufacturing practices.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe our 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 FDA 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 manmade sources

[1] This guidance has been prepared by the Division of Plant Products and Beverages, Office of Food Safety, in the Center for Food Safety and Applied Nutrition at the Food and Drug Administration.

[2] Under 21 CFR 109.4, when certain conditions are met, FDA may establish an action level for an added poisonous or deleterious substance to define a level of contamination at which a food may be regarded as adulterated. These levels serve as guidance to FDA field staff. FDA will establish an action level, as opposed to a tolerance or regulatory limit (which must be established by rulemaking), when technological or other changes that might affect the appropriateness of the tolerance are foreseeable in the near future (21 CFR 109.6(d)). Consistent with 21 CFR 109.6, FDA will consider action levels, in addition to other factors, when considering whether to bring enforcement action in a particular case.

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).[3] 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).[4] Consumption of inorganic arsenic has been associated with cancer, skin lesions, cardiovascular disease and diabetes in humans (Refs. 2-3). A report by the National Research Council (NRC) (Ref. 3) also listed adverse pregnancy outcomes and neurodevelopmental toxicity as adverse health effects of concern for inorganic arsenic. The Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA) (Ref. 2), which includes participation by FDA scientists, concluded that food can be a major contributor to inorganic arsenic exposure, and the European Food Safety Authority (EFSA) (Ref. 4) concluded that dietary exposure to inorganic arsenic should be reduced.

These findings support FDA initiatives to assess and reduce exposure to inorganic arsenic in food. For example, in July 2013, FDA issued a draft quantitative assessment of lifetime risk of certain cancers associated with exposure to inorganic arsenic in apple juice (Ref. 5) and draft guidance for industry with an action level for inorganic arsenic in apple juice of 10 micrograms/kilogram (µg/kg), or 10 parts per billion (ppb) (Refs. 6-7). FDA also has conducted surveys of arsenic in other foods (Refs. 8-9), focusing primarily on rice and rice products. In April 2016, FDA released a risk assessment on arsenic in rice and rice products (Ref. 10). FDA has also released consumer advice on consumption of rice and rice products, available online at http://www.fda.gov/food/foodborneillnesscontaminants/metals/ucm319870.htm.

Exposure to Inorganic Arsenic in Rice and Rice Products

Because it is in the environment, inorganic arsenic is found in some foods. Rice and rice-based food products have higher levels of inorganic arsenic than do other foods tested by FDA, and given their widespread consumption, are a major food source of inorganic arsenic. Rice tends to have higher arsenic concentrations than other cereal crops (such as wheat and barley), because of its ability to take up arsenic from soil and water and because it is typically grown under flooded conditions, which increase the potential for arsenic uptake (Ref. 10). Evidence from FDA's Total Diet Study (Ref. 11) – an ongoing survey and analysis of the average American diet – revealed that total arsenic levels, although varying, tend to be higher in rice and rice products than in other foods. Follow-up sampling by FDA has also revealed significant levels of inorganic arsenic in rice and rice products, including rice cereals for infants (Refs. 8-9).

[3] Generally, it is not possible for FDA to identify the specific source of any arsenic that may be found in a particular type of food, including infant rice cereal. 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 the Environmental Protection Agency (EPA) under section 408 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 346a)), or other environmental contamination. Our understanding from EPA information is that currently, arsenical pesticide use in the United States is limited to the organic arsenical monosodium methanearsenate (MSMA) for use on sod farms, golf courses, highway rights-of-way, and to control weeds in cotton fields, and to chromated copper arsenate (CCA) for use by certified pesticide applicators using specialized high-pressure equipment in wood treatment facilities.

[4] Organic in this sentence refers to arsenic molecules that contain carbon. Inorganic arsenic molecules do not contain carbon. This usage does not refer to organically grown food.

Rice is commonly served to infants, primarily in the form of infant rice cereal (Ref. 10), which is the most commonly consumed infant instant cereal in the U.S.[5] Rice and rice products are a greater potential source of dietary inorganic arsenic exposure for infants and children than for adults, because the dietary patterns of infants and children are often less varied than those of adults, and because infants and children consume more food relative to their body weight than do adults (Ref. 13). Therefore, elevated levels of inorganic arsenic in foods that infants eat, such as rice cereals, may represent a significant source of exposure for infants (Ref. 10). In addition, infants and children may be particularly susceptible to adverse neurodevelopmental effects of exposure to inorganic arsenic (Refs. 3, 10). FDA thinks that it is possible to reduce dietary exposure to inorganic arsenic from infant rice cereals through the industry's use of current good manufacturing practices, in particular the selection of sources of rice or rice-derived ingredients with lower inorganic arsenic levels. Therefore, FDA is issuing draft guidance on an action level for inorganic arsenic in rice cereal for infants.

Risk Assessment and Achievability

To facilitate development of an action level for inorganic arsenic in rice cereal for infants, FDA conducted a risk assessment (Ref. 10) on arsenic in rice and rice products. The risk assessment includes a qualitative component that addresses the risk of certain non-cancer adverse health effects to infants, young children, and during pregnancy from dietary exposure to inorganic arsenic in rice and rice products. The risk assessment also includes a quantitative component that provides estimates of exposure to inorganic arsenic from rice and rice products and estimates of lifetime cancer risk from this exposure. Finally, the risk assessment estimates potential reductions in inorganic arsenic exposure and cancer risk from possible mitigation actions, including limiting the maximum level of inorganic arsenic in infant rice cereals.

The qualitative component of the risk assessment concluded that exposure to inorganic arsenic during pregnancy, infancy, and early childhood may increase the risk of neurodevelopmental toxicity and/or adverse pregnancy outcomes. The quantitative component of the risk assessment found that exposure to inorganic arsenic in rice and rice products may increase lung and bladder cancer cases in later life, whether exposure occurs only during infancy (through infant rice cereals) or throughout life. The quantitative assessment also showed that establishing an action level will reduce inorganic arsenic exposure and risk. More information can be found in the risk assessment document (Ref. 10) and the Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants (Ref. 14).

To assess achievability, or manufacturers' ability to achieve hypothetical maximum limits on inorganic arsenic in infant rice cereals, FDA used results of surveys of rice cereals to determine the percentage of samples of infant rice cereals that would fall below each of the hypothetical maximum limits.[6] More information on achievability and arsenic data can be found in the

[5] Based on data from the U.S. National Health and Nutrition Examination Survey (NHANES), What We Eat In America (WWEIA), 2003-2010 (Ref. 12), the mean per capita daily intake of dry instant infant cereals (not containing fruit) for the first year of life is as follows: rice, 4.8 g/d; oatmeal 2.8 g/d; barley, 0.1 g/d; and mixed grains, 0.8 g/d.

[6] The method used by FDA for analyzing inorganic arsenic in rice is posted on the FDA website at http://www.fda.gov/downloads/food/foodscienceresearch/laboratorymethods/ucm479987.pdf.

supporting document (Ref. 14). FDA used the information in the supporting document and risk assessment document to identify a draft action level for inorganic arsenic in infant rice cereals.

III. Action Level

Because of the potential for human health risks associated with exposure to inorganic arsenic, human exposure to inorganic arsenic in rice cereal for infants should not exceed levels achievable with the use of current good manufacturing practices. The action level for inorganic arsenic in infant rice cereals that FDA considers achievable with the use of such practices is 100 µg/kg or 100 ppb (see Ref. 14). We request comments on the feasibility of achieving this level and on how the level might affect the availability of infant rice cereals in the marketplace. This guidance applies to all types of infant rice cereals (e.g., white-rice, brown-rice, organically grown, and conventionally grown). The proposed action level for inorganic arsenic in infant rice cereals is intended to reduce the possible risk for infants fed rice cereal by reducing exposure to inorganic arsenic that may be found in rice cereal for infants. FDA considers this reduction in exposure to infants fed rice cereal will lead to a quantifiable reduction in the lifetime risk of certain cancers associated with exposure to inorganic arsenic, as well as an unquantifiable reduction in the risk of certain non-cancer adverse health outcomes reviewed in the risk assessment, including neurodevelopmental effects in infants.

FDA intends to take the following sampling and enforcement approach to inorganic arsenic in infant rice cereals. FDA intends to initially analyze samples of infant rice cereals for total arsenic. FDA intends to speciate samples containing more than 100 µg/kg or 100 ppb total arsenic to determine inorganic arsenic levels. Consistent with 21 CFR 109.6, FDA intends to consider the action level of 100 µg/kg or 100 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 April 1, 2016, 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 April 1, 2016.

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.

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3. National Research Council of the National Academies (NRC), 2013, Critical aspects of EPA's IRIS assessment of inorganic arsenic: interim report. Retrieved from http://www.nap.edu.

4. 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.

5. Food and Drug Administration (FDA), 2013a, A Quantitative Assessment of Inorganic Arsenic in Apple Juice, accessed online at http://www.fda.gov/downloads/Food/FoodScienceResearch/RiskSafetyAssessment/UCM360016.pdf.

6. FDA, 2013b, Draft Guidance for Industry: Arsenic in Apple Juice - Action Level, accessed online at http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ChemicalContaminantsMetalsNaturalToxinsPesticides/ucm360020.htm.

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8. FDA, 2013d, Analytical Results from Inorganic Arsenic in Rice and Rice Products Sampling, accessed online at http://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/Metals/UCM352467.pdf.

9. FDA, 2016a, Analytical Results from Inorganic Arsenic in Rice Cereals for Infants, Non-rice Infant Cereal and Other Foods Commonly Eaten by Infants and Toddlers, accessed online at http://www.fda.gov/Food/FoodScienceResearch/RiskSafetyAssessment/ucm485278.htm.

10. FDA, 2016b, Arsenic in Rice and Rice Products Risk Assessment Report, accessed online at http://www.fda.gov/Food/FoodScienceResearch/RiskSafetyAssessment/ucm485278.htm .

11. FDA, 2016c, Total Diet Study, accessed online at http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/default.htm.

12. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2013, downloaded from http://www.cdc.gov/nchs/nhanes.htm.

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

14. FDA, 2016d, Supporting Document for Action Level for Arsenic in Rice Cereals for Infants, accessed online at http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm486390.htm.