

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

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**U.S. Department of Health and Human Services
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Inorganic Arsenic in Rice Cereals for Infants: Action Level¹ Guidance for Industry

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I. Introduction

This guidance provides information to manufacturers on the action level² for inorganic arsenic in rice cereals for infants (hereafter referred to as infant rice cereals) that is intended to help protect public health by reducing infants' dietary exposure to inorganic arsenic and is achievable by industry with the use of current good manufacturing practices. This guidance applies to all types of infant rice cereals.

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.

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, within the meaning of section 402(a)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). In this context, "added" does not mean added by the manufacturer, but rather resulting from the hand of man; for example, from previous pesticide use (*see United States vs. Anderson Seafood, Inc.* 622 F.2d 157 (5th Cir. 1980)). These action levels serve as guidance to FDA field staff and industry. We will establish an action level, as opposed to a tolerance or regulatory limit (which must be established by rulemaking (21 CFR 109.4)), 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, we will consider action levels, in addition to other factors, when considering whether to bring enforcement action in a particular case.

II. Background

Arsenic is an element that occurs in the environment from both natural and manmade 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).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. 5).⁴ Consumption of inorganic arsenic has been associated with cancer, skin lesions, cardiovascular disease and diabetes in humans (Refs. 5-6). A report by the National Research Council (NRC) (Ref. 6) also listed adverse pregnancy outcomes and neurodevelopmental toxicity as adverse health effects of concern for exposure to inorganic arsenic. The Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA) (Ref. 5), 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. 7) concluded that dietary exposure to inorganic arsenic should be reduced.

These findings support our initiatives to assess and reduce exposure to inorganic arsenic in food. For example, in July 2013, we announced the availability of a draft quantitative assessment of lifetime risk of certain cancers associated with exposure to inorganic arsenic in apple juice (Ref. 8) and a draft guidance for industry with an action level for inorganic arsenic in apple juice (78 FR 42086). We also conducted surveys in 2013, 2016, and 2018 of arsenic in other foods (Refs. 9-11), focusing primarily on rice and rice products, and released consumer advice on consumption of rice and rice products, available online at <https://www.fda.gov/consumers/consumer-updates/consumers-seven-things-pregnant-women-and-parents-need-know-about-arsenic-rice-and-rice-cereal>. On April 6, 2016, FDA published in the *Federal Register* (81 FR 19976) a notice of availability for a draft guidance for industry entitled “Inorganic Arsenic in Rice Cereals for Infants: Action Level,” a supporting document entitled “Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants,” and a risk assessment report entitled “Arsenic in Rice and Rice Products Risk Assessment: Report.” This guidance finalizes the approach presented in the April 2016 draft guidance.

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 arsenicals monosodium methanearsonate (MSMA) for use on sod farms, golf courses, highway rights-of-way, and to control weeds in cotton fields (Ref. 2) and 10,10'-Oxybisphenoxarsine (OBPA) to prevent microorganism growth in plastics and as a material preservative in adhesives and coatings (Ref. 3), and to chromated arsenicals for use by certified pesticide applicators using specialized high-pressure equipment in wood treatment facilities (Ref. 4).

⁴ Organic in this sentence refers to arsenic molecules that contain carbon. Inorganic arsenic molecules do not contain carbon. Use of the term “organic” here does not refer to organically grown food.

III. Discussion

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 (Ref. 12). Rice also 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 increases the potential for arsenic uptake (Ref. 12). Evidence from FDA's Total Diet Study (Ref. 13) – 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. Our follow-up sampling also revealed significant levels of inorganic arsenic in rice and rice products, including rice cereals for infants (Refs. 9-11). Rice is commonly served to infants, primarily in the form of infant rice cereal (Ref. 12), 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. 15). 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. 12). In addition, infants and children may be particularly susceptible to adverse neurodevelopmental effects of exposure to inorganic arsenic (Refs. 6, 12). We think that it is possible to reduce dietary exposure to inorganic arsenic from infant rice cereals through industry's use of current good manufacturing practices, in particular selection of sources of rice or rice-derived ingredients with lower inorganic arsenic levels and testing these incoming rice and rice-derived ingredients. Using rice with lower levels of inorganic arsenic will result in lower levels of inorganic arsenic in the infant rice cereal because the main ingredient (rice) will have lower levels of inorganic arsenic. Therefore, we are issuing this 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, we conducted a risk assessment on arsenic in rice and rice products (Ref. 12). The risk assessment includes a qualitative component that addresses the risk of certain non-cancer adverse health effects to infants, to 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.

⁵ Based on data from the U.S. National Health and Nutrition Examination Survey (NHANES), What We Eat In America (WWEIA), for the years 2003-2010 (Ref. 14), 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.

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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 (Ref. 16). More information can be found in the Arsenic in Rice and Rice Products Risk Assessment Report (Ref. 12) and the Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants (Ref. 16).

To assess achievability, or manufacturers' ability to achieve hypothetical maximum limits on inorganic arsenic in infant rice cereals, we used results of surveys from three data sets 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 Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants (Ref. 16). FDA used the information in the supporting document and risk assessment document to identify an action level for inorganic arsenic in infant rice cereals.

IV. 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, in particular selective sourcing of rice or rice-derived ingredients with lower levels of inorganic arsenic and testing these incoming rice and rice-derived ingredients. The action level for inorganic arsenic in infant rice cereals that FDA considers achievable with the use of such practices is 100 microgram per kilogram ($\mu\text{g}/\text{kg}$), or 100 parts per billion (ppb) (see Ref. 16). FDA has made the determination that this level is achievable based on sampling and testing results. Based upon our risk assessment and achievability assessment, we consider that this reduction in inorganic arsenic in rice cereal will lead to a predicted 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. This guidance applies to all types of infant rice cereals (e.g., white-rice, brown-rice, organically grown, and conventionally grown). Though not binding, the action level for inorganic arsenic in infant rice cereals is intended to encourage manufacturers to reduce levels of inorganic arsenic in their products, thus reducing the possible risk for infants fed rice cereal.

V. Conclusion

For the reasons discussed above, we have concluded that a level of 100 $\mu\text{g}/\text{kg}$ or 100 ppb inorganic arsenic in infant rice cereals is achievable under current good manufacturing practices, based on evaluation of recent FDA data on inorganic arsenic levels in infant rice cereals. We intend to analyze samples of infant rice cereals for total arsenic, and to speciate samples

⁶ The method used by FDA for analyzing inorganic arsenic in rice is posted on the FDA website at <https://www.fda.gov/media/95197/download>.

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containing more than 100 µg/kg or 100 ppb total arsenic to determine inorganic arsenic levels. We intend to consider the action level of 100 µg/kg or 100 ppb inorganic arsenic as an important source of information for determining whether infant rice cereal is adulterated within the meaning of section 402(a)(1) of the FD&C Act (21 U.S.C. 342(a)(1)). FDA considers on a case-by-case basis whether a food that contains a contaminant is adulterated. When considering whether to bring an enforcement action in a particular case, we will consider whether the inorganic arsenic causes a particular infant rice cereal to be adulterated under section 402(a)(1) of the FD&C Act.

VI. References

We have placed the following references on display in the Dockets Management Staff, 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. These are also available at <https://www.regulations.gov>. As of August 2020, 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 August 2020.

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16. U.S. FDA, 2020b, Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants, accessed online at <https://www.fda.gov/media/97121/download>.