ConsumerReports®

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Comments of Consumer Reports to the Food and Drug Administration on Inorganic Arsenic in Rice Cereals for Infants: Action Level; Draft Guidance for Industry; Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants; Arsenic in Rice and Rice Products Risk Assessment Docket No. FDA-2016-D-1099

Consumer Reports appreciates the opportunity to comment on the Arsenic in Rice and Rice Products Risk Assessment as well as on the draft guidance for industry on the action level for inorganic arsenic in rice cereal for infants. This risk assessment and action by the Food and Drug Administration (FDA) is particularly important in light of the multiple toxic endpoints of chronic arsenic exposure and the relatively high levels of this harmful metalloid consumed by all Americans, but especially children, in rice and rice products.

We applaud the FDA for its proposed action level for inorganic arsenic in infant rice cereal, to be used as a factor in possible enforcement action. We also are pleased to see the FDA's advice to parents that rice does not have to be an infant's first or only food. Unfortunately, despite the advice of Consumer Reports, the government, and pediatric societies, many parents still feed their children rice cereal as their first food and feed them rice cereal exclusively. Setting a limit of 100 ppb of inorganic arsenic in these products will help to reduce exposure to this contaminant in our most vulnerable population. Nevertheless, we also would like the agency to set action levels for inorganic arsenic in other foods that are regularly consumed by children, such as ready-to-eat cereals and rice beverages. We discuss this recommendation in detail below.

We are also pleased to see the risk assessment released to the public. We do have concerns about the methodology used in the assessment, and discuss suggested improvements below.

Need for Additional Protective Action Levels

The FDA has taken an important step in proposing an action level for inorganic arsenic in infant rice cereal. In 2012, using the data collected in our tests and data on consumption, Consumer Reports proposed to the FDA limits for inorganic arsenic in rice and rice products. These limits were determined by calculating the number of excess cases of cancer in the population consuming an average number of servings of each product per day and determining the level that would be necessary to reduce population risk among consumers to a reasonable level. We use the word "reasonable" here, because we know that rice is a culturally and nutritionally important food and we did not think it was appropriate to recommend eating no rice, or to recommend limits that would be impossible to meet.

The limits we calculated for rice and rice products are presented in table 1 below.

Table 1

	Rice Product							
	Infant Cereal	Hot Cereal	RTE Cereal	Drinks	Rice	Pasta	Crackers	Cakes
Recommended Limit for inorganic arsenic (ppb)	90	60	37	3	120	30	74	74

As one can see from the table, we originally suggested a limit of 90 ppb for infant rice cereal. 90 ppb would be a more protective limit than the proposed 100 ppb, though 100 ppb is close and acceptable, because according to the FDA's calculations the average level infants would be exposed to would be less than 90 ppb. However, the methods the FDA used to calculate the average levels of exposure and risk after the action level is put into place are potentially problematic. The FDA calculated the average level after the action level by calculating the average of the samples in the current data set that were below the action level. In other words, the FDA has assumed that the products with levels greater than the action level would not enter the market, and that the products on the market would have levels essentially the same as what was found in the FDA's tests.

This assumption may be proven correct, but we consider it very likely that the average after the action level is in place will be much higher than what the FDA calculated. That is because those manufacturers making a product with levels of inorganic arsenic greater than the action level may reformulate the product to be just below the action level, rather than significantly below the action level as many of the products the FDA included in its average are. This might occur because it may be that the most cost-effective action for these manufacturers would be to manufacture a product that is just below the action level rather than well below it. If this is the case, then we will see more products entering the market at just below the action level, which will increase the average level of exposure to an amount above what the FDA has assumed when setting and justifying this level. Therefore, the FDA should do everything it can to encourage manufacturers to strive to make products with the lowest possible levels—and for the protection of public health, to set an action level of no greater than 100 ppb after reviewing submitted comments.

We also strongly urge the FDA continue to set action levels for other rice products. As shown in Table 1, Consumer Reports recommended to the FDA in 2012 that a limit for inorganic arsenic in ready-to-eat cereals (RTE cereals, commonly known as breakfast cereals) be set at 37 ppb. This was calculated by conducting a quantitative cancer risk assessment utilizing the levels of consumption estimated in the 2011 EPA Exposure Factors Handbook for ready-to-eat cereals. The average level of inorganic arsenic in ready-to-eat cereals (not including hot cereals) from the FDA data set is about 100 ppb, which is approximately 3 micrograms per serving. Assuming average daily consumption over 50 years and using an underestimated, but previously approved slope factor of 1.5 per mg/kg-day, the population risk is approximately 110 excess cases of cancer per million over 78.6 years. We estimated that our proposed limit would reduce that total by approximately 63% to about 40 excess cases per million. This is still a very large number, however, and ideally it would be even lower, or people would consume less rice-based cereal.

If we focus just on our most vulnerable population, young children, and look at the risk of childhood-only consumption from age one to six, with the average level of exposure—using exposure data from the EPA Exposure Factors Handbook[1]—the risk is 15 excess cases per million. This is about three excess cases of cancer per million per year of exposure (over five years), and so this is similar to the per-life year risk of infant rice cereal, but it ultimately represents a much greater population risk. Setting a limit for RTE cereal at 37 ppb would reduce this risk to about 5.5 in a million. While very few samples tested by the FDA would already meet a standard like this (less than 4%), there were samples with levels at or below 37 ppb, which shows that it is possible to meet this limit. The FDA should determine best practices that would enable the industry to do so.

For any product, if manufacturers state that they simply are not able to make a product that can meet an inorganic arsenic protective standard, then the agency should give consumption advice to consumers about limiting intake to reduce exposure. This is what Consumer Reports has done to date.

Because of the relatively high levels of inorganic arsenic found in ready-to-eat breakfast cereals, Consumer Reports has recommended that children not eat more than 1.5 servings of these products per week. Based on the Consumer Reports point system for arsenic in rice and rice products, if the levels of inorganic arsenic in ready-to-eat cereals were 37 ppb, children could consume one serving per day without exceeding the maximum arsenic exposure over a week or month for a population cancer risk of roughly one excess case per 100,000.

Even if the FDA does not agree with the limit for RTE cereal proposed by Consumer Reports, in proposing the action level for rice cereal for infants, the agency has set a precedent, and therefore *the FDA should at the very least apply the same logic it used to determine the action level for infant rice cereal to other rice products. The FDA*

[1] U.S. Environmental Protection Agency (EPA). (2011) Exposure Factors Handbook: 2011 Edition. National Center for Environmental Assessment, Washington, D.C.; EPA/600/R-09/052F. Table 12-26.

should protect young children (age one to six)—who are vulnerable to the effects of arsenic and who eat more relative to body weight than adults—by setting limits on rice products on ready-to-eat cereals, as well as on other rice products such as hot cereals, rice pastas, crackers, cakes, and drinks.

According to the supporting document,[2] the FDA has made its current action level proposal because rice and rice products are a significant source of inorganic arsenic exposure for infants and children, which in turn is because they eat a less varied diet than adults, and because they consume more food relative to their body weight than adults. The agency also noted that infants and children might be especially vulnerable to the neurodevelopmental effects of arsenic.

Also according to the supporting document,[2] the FDA arrived at the 100 ppb action level for infant rice cereal because it would mean that there would be an approximately 18.8% reduction in cancer risk in the population of infants who eat white rice infant cereal and a 37% reduction in a population consuming brown infant rice cereal. In addition, the agency determined that it was feasible for manufacturers to make products that would meet this limit. Feasibility was mainly based on the fact that 36% to 47% of the samples tested by the FDA already met these limits.

At this time, the FDA has not proposed action levels for rice or other rice products despite the fact that essentially the same scenario applies to all of these products—relatively high levels of exposure to inorganic arsenic and risk from this exposure as well as feasibility of reducing exposure and risk.

As noted above, the risk to the population from eating ready-to-eat cereal is actually greater than that of infant rice cereal. This is because exposure duration is longer, average concentration of inorganic arsenic is higher, and these products may be consumed in large quantities.

Even if the FDA does not agree with Consumer Reports' proposed action level (37 ppb), based on the logic of the action level for infant rice cereal, the FDA should at least begin by setting an interim preliminary limit of no more than 90 ppb for ready-to-eat cereals. This would reduce the average level of inorganic arsenic to approximately 60 ppb (using the FDA's method of calculation) and reduce the risk by about 40%, which is similar to the reduction in risk the FDA calculated for the population consuming brown rice infant cereal if the 100 ppb action level were in place. 50% of the samples tested by the FDA would have already met this 90 ppb standard, meaning that this level is even more feasible than that proposed level for infant rice cereal. Since 90 ppb is higher than the 37 ppb Consumer Reports recommends, if the FDA were to set a level at 90 ppb we would also urge the agency to advise that children eat no more than five servings per week.

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[2] FDA (2016). Supporting Document for Action Level for Inorganic Arsenic in Rice Cereals for Infants. Available at www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM493580.pdf.

The FDA should set a limit for breakfast cereals at 37 ppb. However, even if it does not, the FDA should apply the same logic to these products that it has applied to infant rice cereals. The agency should determine the typical consumption of these products and calculate an appropriate action level to protect vulnerable children who consume these products.

Also, the FDA should ungroup hot cereals and ready-to-eat cereals (cold) in its analysis , because hot rice cereals on average contain over twice as much inorganic arsenic as ready-to-eat cereals.

The FDA has grouped ready-to-eat cereals and hot cereals into one group. The agency should ungroup these and set separate limits for each. These products have very different levels of inorganic arsenic, with hot cereals having more than twice as much on average.

The FDA should conduct additional analysis on vulnerable populations.

In addition to children, individuals in ethnic groups that eat rice as a traditional food, as well as individuals on a gluten-free diet, are even more vulnerable to the chronic effects of arsenic because of the large quantities of rice and rice products they consume. The FDA should include analysis of population risk among those in these groups in its risk assessment of rice and rice products. They are at elevated risk for arsenic exposure, and the FDA should offer special guidance to these consumers.

Risk Assessment Methodological Concerns

We are pleased to see that the FDA has released its risk assessment for arsenic in rice and rice products. It is clear from the document that this assessment was initially completed May 13, 2014, and then revised in March 2016, just prior to its release. We understand the significant amount of work that the FDA has put into this assessment and applaud the FDA for taking on this difficult task. We are glad that the results of this work have finally been made available to the public. This document is significant, because it acknowledges the concerns that Consumer Reports, as well as many others, have expressed about the potential cancer and non-cancer adverse health effects of arsenic in the food supply. The risk assessment is also important, because it points out that the actions being taken by Codex Alimentarius to limit arsenic in the food supply by setting a limit for arsenic in white rice of 200 ppb will have no meaningful impact on public health.[3] We hope the agency will use its analysis to push for limits on arsenic in rice at the international level that are truly protective of public health, such as limits below 150 ppb.

[3] Codex Alimentarius Commission (2014). Report of the Eighth Session of the Codex Committee on Contaminants in Food; The Hague, The Netherlands; 31 March–4 April 2014. Rep14/CF.

However, we have a number of specific concerns with methodology used for the risk assessment, which we believe leads to an underestimate of the potential risks of arsenic exposure from rice.

First, we are pleased to see that the FDA has conducted a quantitative cancer risk assessment to analyze the potential excess cases of cancer that may result from consumption of rice and rice products. *As the agency knows, this approach is important and useful, though limited, because cancer is only one of negative health endpoints associated with inorganic arsenic and there are potentially many others.*

This limitation serves as strong justification for the FDA to set action levels for arsenic in rice and rice products, as the magnitude of the health problem associated with this exposure is likely much greater than that estimated by the quantitative cancer risk assessment. For example, developmental effects resulting from exposure to inorganic arsenic in utero and infancy are currently being studied and characterized by the New Hampshire Birth Cohort Study.

The current methodology to assess risk from arsenic in food was first introduced by the agency in the Assessment of Inorganic Arsenic in Apple Juice, and was a major improvement over the previous analysis that the FDA had conducted to determine action levels for arsenic. However, we think that *at this time the FDA should also conduct a quantitate risk assessment based on the risk of cardiovascular disease and diabetes.*

Both the first and second external peer reviewer of the risk assessment suggested this analysis. We believe there is sufficient data to conduct this analysis and it could add significantly to our understanding of the magnitude of the population affected. While this would not be a substitute for the quantitative cancer risk assessment, it would provide additional information to better characterize the potential risks.

The FDA should assume a bioavailability of between 80% and 98% in its modeling, rather than between 70% and 90%.

In the agency's discussion of bioavailability of arsenic after ingestion of rice, two studies are discussed. Based on the first study, looking at bioavailability in pigs, the agency concluded that the relative bioavailability of inorganic arsenic in rice in this study was 89% ±9%. The second study discussed was conducted on only two human volunteers. From this study, the agency concluded that the absorption of inorganic arsenic for one participant was 66% and for the other 80%. The methodology used in this second study suggests that these estimates are underestimates, and the small sample size makes this study very unreliable. The agency should err on the side of caution and use a bioavailability estimate of between 80 and 98%, based on the first study, to better estimate the risk of cancer in the population from consuming inorganic arsenic in rice.

The FDA should better explain why its current estimate of bladder cancer risk is about one-third the risk previously calculated by both Carrington 2013 and Morales.

In the current analysis, while the FDA used a non-linear model and did not calculate a cancer slope factor, one can estimate a slope factor based on the data points presented in tables 3.5 and 3.6 (risk assessment) and in the current analysis a cancer slope factor of approximately 1.5 to 1.6 per mg/kg-day was used to calculate risk. The risk data presented in table 5.2 (risk assessment) appears to correspond with a slope factor of approximately 1.88 per mg/kg-day—though this number is more difficult to ascertain. All of these are lower than the approximate cancer slope factor used in the arsenic in apple juice assessment (between 2.15 and 2.75 per mg/kg-day), and much lower than the 3.67 per mg/kg-day used in the 2001 drinking water rule.[4] In section 3.3 of the risk assessment, the agency points out that the risk of bladder cancer calculated in the current assessment is one-third the risk previously calculated by both Carrington 2013 and Morales 2000. This is also apparent in table 3.5. The agency does an insufficient job of explaining the reason for the difference. Section 3.3 refers to section 3.1.3 for further discussion, but this section is also insufficient. A risk one-third lower than previously calculated and used by both the EPA and the FDA warrants significant discussion and explanation.

Furthermore, previous analyses by Morales (2000) and others (EPA 2010 Draft) have demonstrated a difference in sensitivity between males and females and the incidence of bladder and lung cancer after exposure to inorganic arsenic. Females were determined to be a more vulnerable population. The current analysis does not acknowledge this finding and should address this issue as well.

The FDA should calculate the risk by examining rice consumers only, rather than including all people, whether they ever eat rice or not.

We appreciate the extensive effort from the FDA in assessing exposure to inorganic arsenic in rice and rice products. The agency has done a remarkable job in calculating per capita exposure in the U.S. population. However, this type of analysis does not provide the more accurately focused data that will adequately protect the most vulnerable populations, because it likely underestimates the potential risk from consumption of rice and rice products. By including all persons in the analysis when determining average rice consumption per person per day, the agency has included people in the average who do not eat rice, and therefore likely underestimates the risk of cancer in the population that actually consumes rice.

In addition to the analysis it has already conducted, the FDA should calculate the average rice intake per day for consumers of rice only, and should exclude those who never eat rice. The agency should also exclude people who eat rice very rarely (one to six times per year). These two groups represent about 20% of the population and therefore have a significant effect on the average consumption level. Using consumption estimates for those who eat rice more regularly should give a more accurate picture for the population at risk.

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[4] EPA (2006). Revised Reregistration Eligibility Decision for MSMA, DSMA, CAMA, and Cacodylic Acid. Available at archive.epa.gov/pesticides/reregistration/web/pdf/organic_arsenicals_red.pdf.

The FDA should use the "per eating occasion" analysis for calculating risk rather than per capita analysis. The FDA should also calculate risk for populations that eat more rice and rice products, such as Asians and Pacific Islanders, as well as those on a gluten-free diet.

We reiterate that the FDA has done a commendable job in trying to estimate population risk exposure to inorganic arsenic in rice and rice products. As a result of acknowledged limitations, the FDA also calculated risk for those who eat rice on a regular basis (one eating occasion per day), and calculated the typical amount of rice actually consumed per eating occasion rather than simply use the recommended serving size. We think the use of this more realistic serving size was an excellent decision. These calculations better estimate the risk to the population of those who actually consume rice, unlike the per capita consumption calculation. The FDA should use this information to estimate the risk to the population. It also should go one step further and present data on the consumption of rice and rice products for different populations, including Asians and Pacific Islanders, Latinos, and individuals on gluten-free diets. These populations consume significantly more rice and rice products than the average American, and calculations on the risk to these populations from their higher exposure to inorganic arsenic should be calculated, presented, and utilized to determine appropriate policy interventions.

The FDA should make more data available about exposure from rice products

The FDA has added to our understanding of consumption of rice and exposure to inorganic arsenic in rice by calculating from NHANES how much rice Americans consume on an average eating occasion. The agency should also calculate, or publish if it already has calculated it, the average amount eaten in an eating occasion of rice products, such as ready-to-eat cereals, by age group. This would enable the agency and outside groups to better calculate the risk of these rice products.

The FDA should calculate the risk for consumers of hot cereals, ready-to-eat cereals, rice beverages, rice cakes and pastas.

As discussed above, the FDA should determine the risk of rice products to the population. Many of these products have relatively high levels of inorganic arsenic and may be consumed in large quantities by certain populations. The FDA should apply the same logic it has applied to rice cereal for infants to other rice products for both children and adults.

The FDA should analyze additional data from Consumer Reports on arsenic levels in basmati, jasmine, and sushi rice, which was collected in 2014 from retail markets across the country.

We are pleased to see that the FDA continues to suggest to adults that they diversify their diet as a way to reduce exposure to arsenic contained in any one-food item.

We believe the FDA should give even stronger advice to consumers, and be specific about which grains have the least amount of arsenic. Consumer Reports testing has shown that a wide variety of non-rice grains are available that contain little inorganic arsenic. In addition, we believe that the agency should recommend that when people consume rice, they should consider those types with the lowest amount of inorganic arsenic. In 2014, Consumer Reports purchased and tested 114 samples of basmati, jasmine, and sushi rice from supermarkets around the country. The rice samples were both domestic and imported. Combining this data with our previous data and the FDA data, we were able to conduct an analysis that found a statistically significant difference in inorganic arsenic levels in basmati rice from India, Pakistan, and California, as well as sushi rice from anywhere in the U.S. These rice types were lower in arsenic than other types of rice. If the FDA were to add this data to its data set, the agency should be able to replicate these findings, and as a result, be able to provide more specific consumption advice to consumers regarding the types of rice with the generally lowest levels of arsenic.

Conclusion

Consumer Reports applauds the FDA for releasing its risk assessment on arsenic in rice and proposing an action level for infant rice cereal. We know that the agency has worked hard on this analysis for a long period of time, and we are pleased to see the agency's commitment to this important public health issue.

Overall we think the FDA has begun to take an appropriate approach to this problem; however, we believe that the analysis ultimately underestimates the potential risks, because of the methodological issues outlined above. One of the most important issues is that the FDA has not adequately addressed the true risk to the segments of the population that consume the most rice.

Based on the FDA analysis presented in the risk assessment, we believe that the 100 ppb action level for inorganic arsenic in rice cereal for infants should help reduce exposure to this toxic element. We strongly suggest that at the conclusion of this process, the FDA set the action level no higher than 100 ppb, and do everything in its power to encourage even lower levels in these products. In addition, the message that rice cereal does not have to be an infant's first or only food should be better disseminated to the public and clinicians.

While we applaud the FDA's action on rice cereal for infants, we believe that the agency should also address the potential risk of rice and other rice products. Especially of concern are products consumed in large quantities by vulnerable populations, such as ready-to-eat cereals consumed by children. These products have a greater population risk than infant rice cereal, and the FDA should address this fact. The action level for infant rice cereal has set a precedent for limiting arsenic in food, and the FDA should apply this same logic to other rice products, like ready-to-eat cereal.

We thank you for the opportunity to comment on this important issue. Please feel free to contact us regarding any questions about our comments or to have access to our additional data.

Respectfully submitted,

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