Food and Agriculture Organization of the United Nations

World Health Organization

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

One-hundred-and-first meeting

Geneva, 15–21 October 2025

SUMMARY AND CONCLUSIONS

Issued on 28 October 2025[1]

The One-hundred-and-first meeting of the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) was held in Geneva from 15 to 21 October 2025. The purpose of the meeting was to evaluate the safety of certain food contaminants, specifically inorganic and organic arsenic species. Arsenic is on the *Priority list of contaminants for evaluation by JECFA*, last amended for this contaminant at the Eighteenth session of the Codex Committee on Contaminants in Foods (CCCF).

Dr Martin van den Berg served as Chairperson and Dr Richard Cantrill as Vice-Chairperson. Dr Vittorio Fattori (FAO) and Mr Kim Petersen (WHO) served as joint secretaries.

Arsenic was last evaluated at the Seventy-second meeting of the Committee, following previous evaluations conducted at earlier sessions. As requested by the CCCF, the tasks before the Committee during the current meeting were to conduct a re-evaluation of arsenic species including updated toxicological, occurrence and dietary exposure data available since the last review. The Committee evaluated the safety of various small and complex organoarsenic as well as inorganic arsenic species.

The report of the meeting will be published as WHO Technical Report Series No. 1061, summarizing the main conclusions of the Committee in terms of values for point of departure (POD) determined from dose–response analyses, and dietary exposure estimates. Toxicological and dietary exposure monographs on the arsenic species considered by the Committee will be published as WHO Food Additives Series No. 92.

The participants are listed in Annex 1. Information of a general nature that the Committee wishes to disseminate quickly is provided in Annex 2. Recommendations made by the Committee at the One-hundred-and-first JECFA meeting are summarized in Annex 3.

More information on the work of JECFA is available at: http://www.fao.org/food-safety/scientific-advice/jecfa/en/ and https://www.who.int/foodsafety/en/.

[1] Reissued on 30 October 2025 after the correction of “glomerular nephropathy” to “urinary bladder hyperplasia” in the second paragraph of the Evaluation for dimethylarsinate (DMA^V).

Toxicological and dietary exposure information and conclusions: inorganic arsenic and small and complex organoarsenic species

Arsenic is a metalloid that occurs in different inorganic and organic forms that are found in the environment both from natural occurrence and from anthropogenic activity. Arsenic was previously evaluated by the Committee at its Tenth, Twenty-seventh, Thirty-third and Seventy-second meetings. At its Seventy-second meeting, because of a lack of data on both toxicity and dietary exposure to organic arsenicals, the Committee only extensively evaluated inorganic arsenic. At the present meeting, the Committee evaluated the safety of various small and complex organoarsenic as well as inorganic arsenic species.

Inorganic arsenic (iAs)

No new human studies were identified by the Committee that would alter the previous assessment that iAs causes cancer (lung, bladder and skin); in fact, the evidence base for cancer has been strengthened. Several new studies have also strengthened the evidence base for the association between arsenic exposure and ischemic heart disease (IHD). The Committee therefore conducted dose–response analyses for both cancer and IHD. The Committee noted that the dose–response modelling of the three key human studies on IHD produced values for the benchmark dose lower confidence interval for a 0.5% increased incidence ($BMDL_{0.5}$) that were similar (range, 0.30–0.34 μg/kg bw per day). The Committee therefore selected a $BMDL_{0.5}$ of 0.3 μg/kg bw per day for IHD as a POD. The Committee noted that the POD for IHD of 0.3 μg/kg bw per day is lower than the lowest benchmark dose lower confidence interval for a 0.1% increased incidence ($BMDL_{0.1}$) for cancer (lung) of 1 μg/kg bw per day; it therefore provides a comparable level of protection for cancer at a benchmark response (BMR) of less than 0.1% and for IHD at a BMR of 0.5%.

In areas where contamination of drinking-water with iAs is expected to be low (< 10 μg/L total arsenic [tAs]), the estimates of mean dietary iAs exposure in children and adults, excluding high seaweed consumers, ranged from less than 0.05 to 0.8 μg/kg bw per day, and P95 estimates ranged from 0.08 to 1.2 μg/kg bw per day. For high seaweed consumers, mean dietary exposures ranged from 0.2 to 3.8 μg/kg bw per day. The Committee noted that the upper end of the ranges for both mean and P95 estimates of dietary exposure exceed the identified POD of 0.3 μg/kg bw per day by at least 2.5-fold.

The mean iAs dietary exposure estimates for populations in areas in which drinking-water is contaminated (> 10 μg/L tAs) ranged from 0.4 to 52.5 μg/kg bw per day. P95 values ranged from 2.8 to 131.3 μg/kg bw per day. The Committee noted that there is high uncertainty in the P95 values. The upper end of the mean exposure value is 175-fold higher than the identified POD.

In areas in which the water supply is highly contaminated with iAs, adverse health effects are well established and have been prevalent.

In areas where the water supply is not highly contaminated, the Committee concluded that there is a potential for human health concerns in both children and adults at mean dietary exposures.

Dimethylarsinate (DMA^V)

There were no relevant human data for establishing a health-based guidance value (HBGV) for exposure to DMA^V.

Following dose–response analysis of the key outcomes identified from the critical study in rats, a POD of 0.74 mg/kg bw per day was selected based on urinary bladder hyperplasia in female rats exposed for 104 weeks to DMA^V.

The Committee determined that a composite uncertainty factor of 125 was suitable to address uncertainties that were identified. This composite uncertainty factor comprises a default factor of 10-fold for intra-species differences in toxicodynamics and toxicokinetics and a 2.5-fold default factor for inter-species differences in toxicodynamics. The Committee determined that an uncertainty factor of

1 for interspecies differences in toxicokinetics is sufficient, as rats are expected to metabolize and retain more DMA^V compared with humans, resulting in a greater sensitivity to the adverse effects of oral exposure to DMA^V. An additional 5-fold factor for database uncertainty (e.g. clinical relevance for non-apical outcomes in the urinary bladder at lower doses compared with histopathological lesions, and additional uncertainty concerning the potential for heightened sensitivity of young animals) was included, which is within the range (2–10) suggested in *Environmental Health Criteria (EHC) 240: Principles and Methods for the Risk Assessment of Chemicals in Food*. Accordingly, the Committee established a non-neoplastic HBGV of 6 µg/kg bw per day (rounded from 5.9 µg/kg bw per day).

Since the Committee expressed some uncertainty concerning the adversity of the sporadic incidence of urinary bladder tumours in treated male rats below the stated no-observed-adverse-effects limit (NOAEL) of the authors of the critical study, and considering the proximity of the neoplastic POD (1.03 mg/kg bw per day) to the non-neoplastic POD (0.74 mg/kg bw per day), the Committee considered an additional approach to risk characterization, that is, calculating margins of exposure (MOE) using the neoplastic POD to evaluate the level of concern associated with carcinogenesis at the estimated dietary exposures. The Committee calculated MOEs ranging from 6400 to more than 100 000 for mean dietary exposures (range, < 0.01 to 0.16 µg/kg bw per day; oxidation state not specified and across different cohorts) and from 2100 to more than 50 000 for P95 dietary exposures (range, 0.02 to 0.48 µg/kg bw per day; oxidation state not specified and across different cohorts). The Committee concluded that these MOEs were adequate to address the uncertainties previously mentioned and, given the likely mode of action (non-DNA-reactive mechanism) and the conservatism in some of the assumptions in estimating high level exposures, concluded that, with respect to cancer, dietary exposure to DMA^V is unlikely to be of concern to human health.

The Committee noted that the dietary exposure estimates for the general population (mean range, < 0.01 to 0.16 µg/kg bw per day; P95 range, 0.02 to 0.48 µg/kg bw per day; oxidation state not specified and across different cohorts) for DMA are below the HBGV. Overall, the Committee concluded that dietary exposure to DMA^V is unlikely to be of concern to human health. However, the Committee also noted that a proportion of the DMA dietary exposure may come from DMA^{III}, which may be more hazardous.

Methylarsonate (MMA^V)

There were no relevant human data for establishing an HBGV for exposure to MMA^V.

Following dose–response analysis of the key outcomes identified from the critical study in mice, a POD of 0.53 mg/kg bw per day was selected based on glomerular nephropathy in male mice exposed for 104 weeks to MMA^V.

The toxicological database was considered sufficiently robust, meaning that the Committee decided that a default uncertainty factor of 100 was appropriate to address uncertainties identified in the evaluation (i.e. 10-fold for intra- and 10-fold for inter-species differences). Accordingly, the Committee established an HBGV of 5 µg/kg bw per day (rounded from 5.3 µg/kg bw per day).

The Committee noted that the mean dietary exposure estimates (range, < 0.01 to 0.03 µg/kg bw per day; oxidation state not specified and across different cohorts) for MMA are below the HBGV. Although a P95 dietary exposure estimate was not available to the Committee for MMA, it was considered reasonable to assume that the P95 for MMA is likely to be approximately 2.5-fold the UB mean (i.e. ~0.08 µg/kg bw per day), which is below the HBGV. Overall, the Committee concluded that dietary exposure to MMA^V is unlikely to be of concern. However, the Committee also noted that a proportion of the MMA dietary exposure may come from MMA^{III}, which may be more hazardous.

Other small and complex organoarsenic species

The Committee considered that the toxicological and exposure data for other small and complex organoarsenic species were too limited to conduct a risk characterization.

Annex 1. List of participants

Members

Dr A. Agudo, Unit of Nutrition and Cancer, Catalan Institute of Oncology, Barcelona, Spain *(invited by WHO)*

Dr S. Barlow, Brighton, East Sussex, United Kingdom of Great Britain and Northern Ireland *(Joint Rapporteur) (invited by WHO)*

Dr A. R. Boobis, National Heart and Lung Institute, Imperial College London, London, United Kingdom *(invited by WHO)*

Dr R. Cantrill, Bedford, Nova Scotia, Canada *(Vice-Chairperson) (invited by FAO)*

Mr P. Cressey, New Zealand Institute for Public Health and Forensic Science, Christchurch, New Zealand *(invited by FAO)*

Ms K. Laurvick, United States Pharmacopeia, Rockville (MD), USA *(invited by FAO)*

Dr M. van den Berg, Department of Population Health Sciences, Institute for Risk Assessment Sciences, University of Utrecht, Utrecht, the Netherlands *(Chairperson) (invited by WHO)*

Additional experts invited by FAO and WHO

Mr A. Afghan, Food and Nutrition Directorate, Health Canada, Ottawa, Canada *(invited by WHO)*

Dr N. Arnich, Risk Assessment Department, French Agency for Food, Environmental and Occupational Health and Safety, Maisons-Alfort, France *(invited by WHO)*

Professor P. Berka Njobeh, Department of Biotechnology and Food Technology, University of Johannesburg, Johannesburg, South Africa *(invited by FAO)*

Dr L. Edler, Dudenhofen, Germany *(invited by WHO)*

Professor T. Halldorsson, Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland *(invited by WHO)*

Dr K.K. Jinadasa, Ministry of Fisheries, Aquatic and Ocean Resources, Colombo, Sri Lanka *(invited by FAO)*

Dr L. le Hegerat, Unit of Toxicology and Contaminants, French Agency for Food, Environmental and Occupational Health and Safety, Fougeres, France *(invited by WHO)*

Dr H. Louro, Department of Human Genetics, National Institute of Health Doutor Ricardo Jorge, Lisbon, Portugal *(invited by WHO)*

Ms C. Mulholland, Food Standards Agency, London, United Kingdom *(Joint Rapporteur) (invited by FAO)*

Dr V. Sirot, Risk Assessment Department, French Agency for Food, Environmental and Occupational Health and Safety, Maisons-Alfort, France *(invited by WHO)*

Dr A. Turnbull, Institute for Marine and Antarctic Studies, College of Sciences and Engineering, University of Tasmania, Taroona, Australia *(invited by FAO)*

Dr S.G. Walch, Chemisches und Veterinäruntersuchungsamt, Karlsruhe, Germany *(invited by FAO)*

Secretariat

Dr M. Anastassiadou, Risk Assessment Production Department, European Food Safety Authority, Parma, Italy *(WHO Secretariat)*

Mr A. Coursier, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland *(WHO Secretariat)*

Dr J. de Oliveira Mota, Department of Nutrition and Food Safety, World Health Organization, Geneva *(WHO Secretariat)*

Dr V. Fattori, Agrifood Systems and Food Safety Division, Food and Agriculture Organization of the United Nations, Rome, Italy *(FAO Joint Secretary)*

Ms N.Y. Ho, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland *(WHO Consultant)*

Dr S. Moraes Raszl, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland *(WHO Secretariat)*

Dr M. Niegowska Conforti, Agrifood Systems and Food Safety Division, Food and Agriculture Organization of the United Nations, Rome, Italy *(FAO Secretariat)*

Mr K. Petersen, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland *(WHO Joint Secretary)*

Ms A. Vlachou, Agrifood Systems and Food Safety Division, Food and Agriculture Organization of the United Nations, Rome, Italy *(FAO Secretariat)*

Annex 2. General considerations

New approach methodologies (NAMs)

Advances in science are rapidly expanding the application of NAMs, including in vitro, in silico and other non-animal testing methods. However, a clear definition of NAMs is still needed, and their use in food chemical safety evaluation is not yet extensive.

This topic was the focus of a workshop jointly organized by WHO and Nanyang Technological University, Singapore, in June 2025. The conclusions and recommendations from the workshop were subsequently placed on the agenda of the WHO Core Assessment Group Meeting on Pesticide Residues, held in Bangkok, Thailand in September 2025.

The WHO Core Assessment Group Meeting on Pesticide Residues discussed the potential and feasibility of expanding the use of NAMs in the safety evaluation of pesticide residues in food. It was acknowledged that although some NAMs are already being used in the work of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and JECFA, there were a number of areas that would benefit from clearer guidance for harmonized approaches. The Meeting Group recognized that an update of *Environmental Health Criteria (EHC) 240: Principles and Methods for the Risk Assessment of Chemicals in Food* (EHC 240), to include guidance on the use of fit-for-purpose NAMs and how they should be reported and evaluated, would be very helpful.

The Committee also recognized the value of NAMs in enhancing the safety evaluation of chemicals, particularly in addressing existing data gaps. Although the reliability and reproducibility of NAMs is an essential pre-requisite for considering their use as alternatives to traditional approaches, full validation can be time-consuming, and methods may be overtaken by new approaches by the time the process is complete. The Committee concluded that the use of suitably robust NAMs in the specific context of food safety evaluation would be valuable.

The Committee acknowledged that NAMs contribute to the reduction, refinement and replacement of animal testing; however, the primary goal of JECFA is the safety assessment of chemicals in food. For that purpose, the Committee uses the best available science. In some cases, NAMs may provide this; however, in other cases the most likely use of NAMs will be in the enhancement and refinement of existing risk assessment approaches, adding to the weight of evidence.

Building trust and confidence among stakeholders (e.g. policy-makers, food business operators, data sponsors) regarding the use of NAMs in chemical safety evaluations is essential for broader acceptance. Providing guidance and feedback from JECFA and JMPR to sponsors, and encouraging the submission of NAMs data and NAMs-based case studies, will facilitate the appropriate use of these methods. Transparent and clear communication about the use of NAMs between the FAO/WHO Expert Bodies and the Codex committees, such as the Codex Committee on Food Additives, the Codex Committee on Residues of Veterinary Drugs in Foods and the Codex Committee on Contaminants in Food, is essential.

In conclusion, the Committee agreed with the WHO Core Assessment Group Meeting on Pesticide Residues on the opportunity to update EHC 240 to provide guidance on general principles for the use of NAMs in the safety assessment of chemicals in food. This update should also be designed such that it can accommodate future scientific and technological developments. The Committee supported the recommendation to establish a dedicated joint working group to undertake this revision.

Mixture toxicity

Given that humans are exposed to a wide variety of arsenic species, the question arises whether the implications of mixture toxicity can currently be included in the evaluation of the food safety risk of arsenic. The mechanism of action for most arsenic species identified in food indicates that the

conversion from pentavalent to the more reactive trivalent arsenic is at least one critical factor in the toxicity of these substances. However, it is important to note that there is a lack of further information on a mode of action for most arsenic species and that other mechanisms of action cannot be dismissed at this time.

The scarcity of comparative chronic and subchronic toxicological, mechanistic and dietary exposure data for the various arsenic forms that may be ingested presents another challenge. The Committee therefore concluded that, at this time, it is not possible to assess mixture toxicity for all arsenic species found in food and water.

Annex 3. Recommendations

In view of the fact that mean dietary exposures to iAs in many areas exceed the POD, national/regional authorities should consider appropriate risk management action.

With regards to DMA^{III} and MMA^{III}, the Committee recommends the generation of additional biochemical and toxicological data as well as exposure information to enable risk characterization. This would need to be supported by analytical methods that can distinguish DMA and MMA oxidation states.

With regards to MMA, the Committee recommends the generation of additional occurrence and dietary exposure data from the whole diet and not just from seafood, even if MMA is not detected.

With regards to small and complex organoarsenic species, the Committee recommends the generation of:

- information on biochemical aspects, particularly in relation to inter-individual variation in humans, and additional information on the interconversion of different arsenic species (e.g. AsSug and AsLip to DMA);
- information on oral long-term toxicity, genotoxicity and mode of action;
- analytical methods that can extract and distinguish complex organoarsenic species; and
- occurrence data in food (more speciation data is needed in seafood, particularly for AsSug and AsLip).

With regards to combined dietary exposure to multiple arsenical species, to inform a mixture-based risk assessment approach the Committee recommends the development of a mixture toxicity model supported by mode of action data.

Further data focusing on the transformation and formation of the different As species in food and biological matrices during analysis are needed.

Because sample preparation and treatment may influence the formation and transformation of As species (and oxidation state), the Committee recommends the use of isotopically labelled standards during method development, validation and verification.

The Committee recommends that the implications of new food production technologies, such as precision fermentation, and of changing dietary patterns, such as increased consumption of seaweed and plant-based foods, on arsenic dietary exposure should also be considered.