Previous evaluations

In this guide

In this guide

- 1. The effects of mercury on maternal health Introduction and Background
- 2. The effects of mercury on maternal health Previous evaluations
- 3. The effects of mercury on maternal health Hazard Identification
- 4. The effects of mercury on maternal health Toxicity
- 5. The effects of mercury on maternal health Reproductive toxicology
- 6. The effects of mercury on maternal health Pregnancy outcomes
- 7. The effects of mercury on maternal health Effects on maternal health
- 8. The effects of mercury on maternal health Biomarkers of mercury exposure
- 9. <u>The effects of mercury on maternal health Epigenetic alterations via</u> <u>mercury exposure</u>
- 10. <u>Studies published on the Seychelles and Faroe Islands cohorts since the</u> 2018 COT statement
- 11. The effects of mercury on maternal health Hazard Characterisation
- 12. The effects of mercury on maternal health Exposure assessment
- 13. The effects of mercury on maternal health Aggregate exposure
- 14. The effects of mercury on maternal health Conclusions
- 15. The effects of mercury on maternal health Questions for the Committee
- 16. <u>The effects of mercury on maternal health List of Abbreviations and</u> <u>Technical terms</u>
- 17. The effects of mercury on maternal health Search terms
- 18. The effects of mercury on maternal health References

Joint Food and Agriculture Organisation of the United Nations (FAO)/ World Health Organisation (WHO) Expert Committee on Food Additives (JECFA)

14. Mercury was previously evaluated by JECFA at its tenth, fourteenth, sixteenth and twenty-second meetings (FAO/WHO, 1967; 1971; 1972; 1978). At its sixteenth meeting (FAO/WHO, 1972), the Committee allocated a provisional tolerable weekly intake (PTWI) of 0.3 mg of total mercury (5 μ g/kg body weight (bw)), of which no more than 0.2 mg (3.3 μ g/kg bw) should be in the form of MeHg. This value was based primarily on the relationship between the intake of mercury from fish and mercury levels in blood and hair associated with the onset of clinical disease.

15. At the sixteenth JECFA meeting the Committee noted that almost all dietary exposure to MeHg is from fish and seafood and that MeHg is probably by far the most toxic form of mercury in food; therefore, other forms of mercury could be given less weight when establishing a tolerable intake for mercury (FAO/WHO, 1972).

16. At the thirty-third JECFA meeting, the Committee noted that pregnant women and nursing mothers may be at greater risk than the general population from the adverse effects of MeHg but the available data were insufficient to recommend a specific MeHg intake for this sub-population (FAO/WHO, 1989).

17. The original PTWI for MeHg (3.3 μ g/kg bw) was revised at the sixty-first JECFA meeting to protect the developing fetus from neurotoxic effects. This change was based on findings from two major epidemiological studies of foetal neurotoxicity, conducted in the Faroe Islands, and the Seychelles, involving fisheating populations (FAO/WHO, 2004). The average maternal hair-mercury concentration from the two studies was estimated at the no observed adverse effect level (NOAEL) and benchmark-dose lower confidence limit (BMDL) for neurotoxicity associated with exposure to methylmercury in utero. The average maternal hair-mercury concentration of the two studies, 14 mg/kg, was utilised to estimate the concentration of MeHg in maternal blood that reflects exposures that would have no appreciable adverse effect on the offspring in these two study populations. Based on the average ratio of hair:blood MeHg concentration (250), the MeHg concentration in maternal blood that would be expected to have no appreciable adverse effects on the offspring was calculated to be 0.056 mg/l. The blood MeHg concentration was used to calculate the average steady- state dietary intake of 1.5 µg/kg bw per day, that would result in a maternal bloodmercury concentration that would have no appreciable adverse effects on offspring in these two study populations. The committee then applied a combined uncertainty factor of 6.4 (2 x 3.2) to account for the total human interindividual variation for converting maternal blood concentration to a steady-state dietary

intake. This derived the new PTWI of 1.6 mg/kg bw which is considered sufficient to protect developing foetuses, the most sensitive subgroup of the population.

18. In 2006, JECFA clarified that life stages other than the embryo and fetus may be less sensitive to the adverse effects of MeHg (FAO/WHO, 2007). For adults, up to about twice the PTWI would not pose any risk of neurotoxicity. However, available data did not allow firm conclusions to be drawn for infant and children (aged up to about 17 years), as they may be more sensitive than adults. Hence the tolerable intake established in 2003 applies also to infants and children.

19. At the seventy-second JECFA meeting the total mercury PTWI (5 μ g/kg bw) was reviewed and withdrawn (FAO/WHO, 2011). The committee noted a lack of quantitative data on MeHg in non-fish products and on inorganic mercury in foods in general. The committee assumed that the predominant form of mercury in foods other than fish and shellfish is inorganic mercury.

20. A revised PTWI for inorganic mercury was established based on the lowest BMDL10 for relative kidney weight increase in male rats of 0.11 mg/kg bw per day as mercury (II) chloride. This corresponds to 0.06 mg/kg bw per day as mercury, adjusted from a 5 day per week dosing schedule to an average daily dose and for the percent contribution of inorganic mercury to dose. After application of a 100-fold uncertainty factor, the Committee established a PTWI for inorganic mercury of 4 μ g/kg bw. The new PTWI for inorganic mercury was considered applicable to dietary exposure to total mercury from foods other than fish and shellfish (FAO/WHO, 2011). The upper limits of estimates of average dietary exposure to total mercury from foods other than fish and shellfish for adults (1 μ g/kg bw per week) and for children (4 μ g/kg bw per week) were at or below the PTWI (FAO/WHO, 2011).

Opinion of the EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM) on a request from the Commission related to mercury and methylmercury in food, 2004.

21. The Member States gathered data on levels of mercury in foods and made limited estimates on dietary exposure as part of the Scientific Co-Operation (SCOOP) task 3.2.11 (Decision 2001/773/EC5). The results indicated that some consumers may exceed the JECFA PTWI (EFSA, 2004). 22. The maximum levels set for total mercury in Commission Regulation 466/2001 were under review. A maximum level of 0.5 mg/kg applied to fishery products, except for certain listed fish species for which 1 mg/kg was applied. Data from some Member States indicated that elevated levels of mercury could be found in other foods.

23. The data from the SCOOP report indicated that the average intake of fish and seafood products in some countries may be close to or exceed the JECFA MeHg PTWI of 1.6 μ g/kg bw.

24. The EFSA CONTAM panel concluded 'The data available in the SCOOP report do not allow reliable estimations of the intakes by high consumers in different populations. Because in some cases the estimated intakes based on the SCOOP report are close to or exceed the PTWI, specific intake studies, especially for women and children, should be performed on methylmercury'.

Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Panel on CONTAM, 2012

25. EFSA was asked by the European Commission to consider new developments regarding inorganic mercury and MeHg toxicity and evaluate whether the JECFA PTWI for MeHg of 1.6 μ g/kg bw and of 4 μ g/kg bw for inorganic mercury were still appropriate.

26. In line with JECFA, the CONTAM Panel established a tolerable weekly intake (TWI) for inorganic mercury of 4 μg/kg bw, expressed as mercury.

27. For MeHg, new developments in epidemiological studies from the Seychelles Child Developmental Study (SCDS) Nutrition Cohort indicated that n-3 long-chain polyunsaturated fatty acids (LCPUFAs) in fish may counteract negative effects from MeHg exposure. The CONTAM panel concluded "Together with the information that beneficial nutrients in fish may have confounded previous adverse outcomes in child cohort studies from the Faroe Islands, the Panel established a TWI for MeHg of 1.3 μ g/kg bw, expressed as mercury" (EFSA, 2012).

28. The 95th percentile dietary exposure was close to or above the TWI for all age groups. High fish consumers, which might include pregnant women, may

exceed the TWI by up to approximately six-fold. The most vulnerable group are unborn children. Biomonitoring data from blood and hair indicate that MeHg exposure is generally below the TWI in Europe.

29. The CONTAM panel stated, "Dietary inorganic mercury exposure in Europe does not exceed the TWI, but inhalation exposure of elemental mercury from dental amalgam is likely to increase the internal inorganic mercury exposure; thus, the TWI might be exceeded."

COT Statement on potential risks from methylmercury in the diet of infants aged 0 to 12 months and children aged 1 to 5 years, 2018

30. The COT last evaluated the risks from methylmercury in the infant diet in 2018 (COT, 2018). The conclusions of relevance to this current discussion paper on the maternal diet were as follows:

- The general population is exposed to mercury and MeHg through food, drinking water, soil and in trace amounts from the air. The diet, and especially fish consumption, is the main source of exposure to MeHg.
- MeHg is readily absorbed following oral exposure. Following absorption, it can accumulate in the hair and can cross the blood brain barrier, the placenta and is excreted in breastmilk. Thus, it can reach the developing fetus, where it tends to accumulate in the brain and can also be transferred to infants via breastfeeding. It has a long half-life and is eliminated less efficiently in newborns than in later life.
- The main adverse effect associated with exposure to MeHg is toxicity to the developing nervous system. Exposure of the fetus to MeHg depends on the maternal exposure up to a year prior to conception.
- The prenatal MeHg exposure in the high fish-consuming Faroese and Seychelles study populations focused on by EFSA and JECFA are much higher than in typical western populations.
- Exclusively breastfed infants are a vulnerable group to consider in the case of MeHg exposure, as MeHg can be transferred to the newborn via milk. The concentration in human milk will depend on maternal exposure to MeHg. Data for MeHg in the literature suggest that the concentrations in breast milk are generally low.
- For infants of 0-6 months of age that are exclusively or non-exclusively breastfed, or that are fed exclusively with infant formula, dietary exposures

to total mercury are below the TWI for MeHg.

- Fish is one of the most significant contributors to total dietary mercury exposures both in the Infant Metals Survey and the Total Diet Survey (TDS). Based on data from the TDS and a conservative assumption that 100% of the mercury in fish will be MeHg, the TWI would be marginally exceeded for the age groups of 12 to <15, 15 to <18 and 18 to <24 months of age for the high-level consumers.
- The Committee agreed that when taking into consideration the conservatism in the exposure assumptions, the risk to health from the potential minor exceedance of the TWI in infants and children is low but that it would be prudent to maintain existing advice regarding consumption of large predator fish.
- The Government currently advises breastfeeding mothers should avoid eating more than one portion of shark, swordfish or marlin per week and that pregnant women, women trying to get pregnant, and children should avoid eating these species.
- Other dietary factors, such as selenium, can reduce or even prevent MeHg effects.