Hazard Characterisation

In this guide

146. The derivation of a health-based guidance value (HBGV) for MeHg has been reviewed and summarised in the 2018 COT statement. These are summarised in brief in the following paragraphs.

Derivation of HBGV for MeHg JECFA, 2004

147. The basis for establishing the 2004 JECFA HBGV was the human epidemiology studies from the Faroe Islands and the Seychelles. The assessments were made on the basis of the evaluations of children at 7 years of age in the Faroe Islands and 5.5 years of age in the Seychelles.

148. Concentrations of mercury in maternal hair and/or cord blood were used as biomarkers for exposure to methylmercury *in utero*.

149. A NOAEL for neurobehavioural effects of 15.3 mg/kg mercury in maternal hair was established in the Seychelles study. A mathematical analysis of the concentration to response relationship was used to determine a BMDL05 of 12.0 mg/kg mercury in maternal hair in the Faroe Islands. An average of the NOAEL and BMDL05 from the Seychelles and Faroe Island studies was used (14 mg/kg mercury in maternal hair) as an estimate of the concentration of methylmercury in maternal hair that reflects exposures that would have no appreciable effect on the offspring in these two study populations.

150. The concentration of methylmercury in maternal hair was converted to mercury in maternal blood using an average overall ratio of 250 (paragraph 17). Based on this factor, the methylmercury 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.

151. By use of a one-compartment toxicokinetic model (WHO, 1990), refined to better reflect the situation in pregnant women, the JECFA calculated the daily ingestion of methylmercury (1.5 µg/kg bw/day) corresponding to a maternal BHg concentration that would have no appreciable adverse effects on the offspring in the two study populations.

152. A data derived factor of 2 for variation in hair to blood ratio of mercury was applied by JECFA. Interindividual variation in toxicokinetics when converting the concentration of mercury in blood to an estimated daily intake was taken into account by a standard factor of 3.2 (100.5). This resulted in an overall uncertainty factor of 6.4.

153. Following application of this uncertainty factor, a PTWI of 1.6 µg/kg bw was established.

EFSA, 2012

154. The CONTAM Panel evaluated any available studies since their 2004 evaluation, in which the PTWI established by JECFA was also adopted. The biggest change since the evaluation of 2004 was new information on cofounding by beneficial factors in fish on associations between prenatal methylmercury exposures and neurodevelopmental endpoints.

155. Results from the first Nutrition Cohort (NC1) of the SCDS suggested an effect at age 9 and 30 months but not at 5 years related to prenatal methylmercury exposure, whereby it appeared that the positive effects from intake of n-3 LCPUFAs no longer outweighed detrimental effects from methylmercury exposure. The Nutrition study examined associations between methylmercury, maternal nutrition, and children's scores on the Bayley's scale of infant development-II test.

156. The CONTAM panel found that a methylmercury concentration of 11 mg/kg in maternal hair was an apparent NOAEL for decreased scores on neurodevelopmental indices after adjustment for prenatal blood maternal n-3 LCPUFAs and this formed a better point of departure than the unadjusted figure of 15.3 mg/kg methylmercury in maternal hair derived from the Seychelles main cohort.

157. For the Faroe Islands cohort, the Panel could not identify a more appropriate point of departure than the BMDL05 of 12 mg/kg selected by JECFA.

158. Based on the above, a maternal hair methylmercury concentration of 11.5 mg/kg (the mean of the two values) was used as an estimate of the concentration of methylmercury in maternal hair that reflects exposures that would have no appreciable effect on the offspring in these two study populations.

159. A factor of 250 was used to convert this to an equivalent concentration of mercury in maternal blood of 46 µg/L.

160. Output from the one-compartment toxicokinetic model determined that a maternal daily dietary mercury intake of 1.2 µg/kg bw corresponded to a maternal BHg concentration that was considered to have no appreciable adverse effects on the offspring. By applying a total uncertainty factor of 6.4 to this value, the CONTAM panel established a TWI for methylmercury of 1.3 µg/kg bw expressed as mercury.

Derivation of HBGV for inorganic mercury JECFA, 2011

161. The Committee noted that there was a lack of quantitative data on MeHg in non-fish products and on inorganic mercury in general.

162. The Committee assumed that the predominant form of mercury in foods other than fish and shellfish is inorganic mercury.

163. Human data on the adverse effects to inorganic mercury exposure is limited to case reports or series that do not allow identification of dose- response relationships and hence an HBGV cannot be derived. The adverse effects observed in human cases however still provides evidence that supports findings from experimental species studies.

164. The committee agreed that the toxicological database for mercury(II) chloride was relevant for assessing the health risk of foodborne inorganic mercury.

165. For JECFA’s risk assessment the NTP (1993) rat bioassay study was considered the most important as it used low-dose exposures to mercury(II) chloride administered via the oral route. Mercury(II) chloride was administered by gavage, 5 days/week, for 6 months to rats in the NTP (1993) bioassay. The most sensitive endpoint was found to be relative kidney weight. The BMDLs generated for relative kidney weight were higher than those generated for all other endpoints investigated, such as terminal body weight, serum alkaline phosphatase, serum cholinesterase and incidence of nephropathy. Short term exposure of mercury(II) chloride to weanling rats administered orally also yielded similar results.

166. The lowest BMDL10 for relative kidney weight increase in male rats was calculated to be 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 days/week dosing schedule to an average daily dose and for the percent contribution of inorganic mercury to mercury(II) chloride dose. After application of a 100-fold uncertainty factor, the Committee established a PTWI for inorganic mercury of 4 µg/kg bw (rounded to one significant number).

167. The previous PTWI of 5 µg/kg bw for total mercury, established at the sixteenth meeting, was withdrawn.

168. The new PTWI for inorganic mercury was considered applicable to dietary exposure to total mercury from foods other than fish and shellfish.

EFSA CONTAM Panel, 2012

169. EFSA evaluated the same evidence as JECFA as well as more recent studies and the Panel agreed with the rationale of JECFA in setting a HBGV based on relative kidney weight in rats as the pivotal effect.

170. The more recent studies EFSA evaluated reported other effects at low levels of exposure to mercuric chloride; however, no NOAELs or BMDLs could be identified due to limitations of these studies.

171. The Panel derived the same TWI for inorganic mercury as JECFA, 4 µg/kg bw.

COT, 2018

172. The COT Committee agreed that the TWI of 1.3 µg/kg bw established by EFSA could be used for characterising potential risks from the exposure of infants and young children to MeHg. Therefore, to characterise the potential risks from the exposure of women of maternal age to total mercury in the diet the EFSA TWIs for MeHg and inorganic mercury have been applied in the below exposure assessment.

173. The Committee has not previously evaluated the EFSA TWI for inorganic mercury.