This is a draft statement for discussion.

It does not reflect the final views of the Committee and should not be cited.

TOX/2025/30

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)

Second Draft Statement on the Effects of Mercury on Maternal Health

Introduction

1. As part of the current programme of work on the maternal diet initiated by the Scientific Advisory Committee on Nutrition (SACN), the COT agreed to prioritise papers on iodine, vitamin D, dietary supplements, and heavy metals including lead, mercury, cadmium, and arsenic, each to be considered in separate papers.

2. In May 2025, the first draft statement on the on the effects of mercury on maternal health was presented to the Committee (TOX/2025/22). Overall, the Committee was content with the risk characterisation and conclusions of the statement but had some comments on the structure and content of the ADME, toxicity and derivation of health-based guidance value (HBGV) sections.

3. To address these comments in the second draft statement additional primary literature has been provided (paragraphs 16, 22, 27-28, 33-42, 45-46 and 48-50) and the structure has been altered to maintain separate discussions on inorganic mercury and methylmercury and their effects on adults, children or animals to improve flow and clarity of the document. It has also been made clearer which texts in the derivation of HBGV section are opinions of other authorities and what primary evidence their opinions are based upon.

4. Additional changes have been made in the exposure assessment section to clarify pica behaviour as an uncertainty of the risk assessment

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(paragraphs 94 and 108) and to address the National Diet and Nutrition Survey (NDNS) underestimating energy intake (paragraphs 99-101).

5. The second draft statement (Annex A) includes a summary of ADME and toxicity of mercury, the derivation of HBGVs for MeHg and inorganic mercury, an exposure assessment from all major sources including food, drinking water, soil and air, the risk characterisation and conclusions.

Questions for the Committee

6. The Committee are asked to consider the following questions:

a) Are Members now content with the layout and structure of the second draft statement following the changes made?
b) Does the Committee have any further comments on the content of the statement?

Secretariat
September 2025

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TOX/2025/05 Annex A

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)

Second Draft Statement on the Effects of Mercury on Maternal Health

Introduction

1. The Scientific Advisory Committee on Nutrition (SACN) last considered maternal diet and nutrition in relation to offspring health in its reports on ‘The influence of maternal, fetal and child nutrition on the development of chronic disease in later life’ (SACN, 2011) and on ‘Feeding in the first year of life’ (SACN, 2018). The latter report also considered the impact of breastfeeding on maternal health.

2. In 2019, SACN agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet.

3. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete relevant risk assessments e.g., in the area of food safety advice. This subject was initially discussed by COT at its January 2020 meeting and a scoping paper was presented to the Committee in July 2020. This included background information on a provisional list of chemicals proposed by SACN. The list was brought back to the COT with additional information in September 2020. The COT agreed, at its meeting in September 2020, that papers on a number of components should be prioritised. To this end, papers on iodine, vitamin D and dietary supplements have been or will be presented to the Committee. The remaining list of compounds were to be triaged on the basis of toxicity and exposure.

4. Following discussion of the first prioritisation paper on substances to be considered for risk assessment, the Committee decided that each of the heavy metals (lead, mercury, cadmium, and arsenic) should be considered in separate papers. The following statement discusses the risks posed to maternal health by mercury in the diet and the environment.

Background

5. Mercury (Hg) is the only metallic element known to be liquid at standard temperature and pressure. Mercury is a group 12 metal, with atomic number 80 and a relative atomic mass of 200.592; its most abundant isotope is ^{202}Hg with atomic mass 201.970 (Laeter et al., 2003). Mercury occurs naturally in the earth's crust at an abundance of 0.0000085%, chiefly as mercury (II) sulfide, also known as cinnabar, cinnabarite or mercurblende (Haynes, Lide and Bruno., 2016). Mercury has been used in thermometers, barometers, manometers, sphygmomanometers, float valves, mercury switches, mercury relays, fluorescent lamps, and other devices; however, its toxicity has led to phasing out of such mercury-containing instruments. Mercury remains in use for scientific research purposes, fluorescent lighting and in amalgam for dental restoration.

6. The three chemical forms of mercury are (i) elemental or metallic mercury (Hg^0), (ii) inorganic mercury (mercurous (Hg_2^{2+}) and mercuric (Hg^{2+}) cations) and (iii) organic mercury.

7. Inorganic mercury exists as mercurous (Hg_2^{2+}) and mercuric (Hg^{2+}) salts, which are used in several industrial processes and found in batteries, fungicides, antiseptics and disinfectants (EFSA., 2008).

8. Organic mercury compounds have at least one carbon atom covalently bound to the mercury atom (FAO/WHO., 2011). Methylmercury (MeHg) is by far the most common form in the food chain (FAO/WHO., 2011). Other organic mercury compounds such as phenylmercury, thiomersal and

merbromin (also known as Mercurochrome) have been used as fungicides and in pharmaceutical products (EFSA., 2008).

9. Mercury is released into the environment from both natural and anthropogenic sources. After release into the environment, it undergoes complex transformations and cycles between atmosphere, land, and aquatic systems. Mercury ultimately settles in the sediment of lakes, rivers or bays, where it is transformed into MeHg, absorbed by phytoplankton, ingested by zooplankton and fish, and accumulates especially in long-lived predatory. Such species include sharks, swordfish, and tuna in the ocean and trout, pike, walleye, and bass in freshwater systems (WHO/IPCS., 1990). Because many of these species are food sources, populations that predominately depend on foods derived from fish or other aquatic environments are more vulnerable to MeHg exposure.

10. Food sources other than fish and seafood products may contain mercury, but mostly in the form of inorganic mercury. The available data indicates that the contribution to MeHg exposure from non-seafood sources is insignificant (EFSA., 2012).

11. The main adverse effect associated with MeHg exposure is toxicity to the central and peripheral nervous systems (WHO., 2017). Due to its ability to cross the placenta and the blood-brain barrier (BBB), MeHg exposure is of particular concern during embryonic neurodevelopment and in young children (COT., 2004). Pregnant and breastfeeding women are identified as sensitive sub-populations because maternal exposure can lead to exposure of the infant via breast milk or the unborn child via the placenta. The bioaccumulative properties and long half-life of MeHg mean that the blood concentration of MeHg at the time of becoming pregnant depends on the exposure to MeHg during the preceding year.

12. MeHg can also affect the kidneys. Acute neuro- and nephrotoxicity have been reported in cases of human MeHg poisoning, whereas

neurotoxicity is usually associated with lower-level chronic exposures, especially in the developing fetus (COT., 2004).

13. Inorganic mercury in food is considerably less toxic than MeHg (EFSA., 2004). This is attributed to the lower absorption of inorganic mercury. In addition, due to its limited lipophilicity, mercuric mercury does not readily cross the placental, blood-brain or blood-cerebrospinal fluid barriers (EFSA., 2012).

14. Animal studies have shown that the critical target for inorganic mercury toxicity is the kidney (NTP., 1993) but other targets include the liver, nervous system, immune system, reproductive and developmental systems (EFSA., 2012).

Previous evaluations and Toxicity

15. The safety of mercury in food has previously been evaluated by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) (EFSA., 2004; 2012), the Joint Food and Agriculture Organisation of the United Nations (FAO)/ World Health Organisation (WHO) Expert Committee on Food Additives (JECFA) (FAO/WHO., 2004; 2011) and the COT (COT., 2018). The US Agency for Toxic Substances and Disease Registry (ATSDR) has also recently reviewed the toxicological profile for mercury (ATSDR., 2024). These evaluations are considered in detail in the discussion paper for mercury in the maternal diet (TOX/2025/03; COT., 2025).

Absorption, distribution, metabolism, and excretion (ADME)

Inorganic mercury

16. Inorganic mercuric mercury has low bioavailability via the oral route. Rahola et al. (1972; 1973) measured whole-body elimination kinetics and excretion in adult humans following ingestion of a single tracer dose of mercury (6 µg as $^{203}Hg(NO_3)_2$ in drinking water (two women) or mixed with

calf liver paste (three women and five men)). As a percent of administered dose, the mean absorbed dose fraction for all subjects was 7.0% (range 1.4 – 15.6%, n = 10).

17. Studies conducted in animals indicate that the predominant site of absorption of inorganic mercury is the small intestine (ATSDR., 2024). Absorption mechanisms for Hg^{2+} in the small intestine include both active and passive processes.

18. In human blood, mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma (EFSA., 2012). In plasma, the main sulfhydryls that form S-conjugates with Hg^{2+} are albumin (Ikegaya et al., 2010) and low molecular weight thiols such as glutathione, cysteine metallothionine and red blood cell haemoglobin (ATSDR., 2024).

19. Mercuric mercury distribution in the body is specific to certain organs and cell types within them. The formation of thiol S-conjugates of Hg^{2+} produces molecules that can act as homologues of endogenous molecules/polypeptides. Hence, possible routes of uptake include interaction with plasma membrane amino acids, peptides, drugs, and ion transporters (Bridges and Zalups., 2010; 2017). The kidney bears the greatest mercuric mercury burden, predominantly in the proximal convoluted renal tubule (EFSA., 2012). The next largest deposition occurs in the liver; the highest concentrations being found in the periportal areas. Additionally, the mucous membranes of the intestinal tract, the epithelium of the skin and the interstitial cells of the testes have been shown to accumulate mercuric mercury (EFSA., 2012). Due to their limited lipophilicity neither mercurous nor mercuric mercury readily cross the placental or BBB.

20. There is no evidence in the literature that methylated mercury species are synthesised in human tissue (EFSA., 2012). The metabolism of mercury species, which appears to be similar between humans and experimental animals, involves oxidation and reduction processes and conjugation to glutathione. Studies in mice have suggested that a small amount of mercuric

mercury can be reduced to elemental mercury and eliminated as elemental mercury vapour.

21. Inorganic mercuric mercury is eliminated through faeces and urine. In a clinical study involving five adult men who received a single intravenous dose of $^{203}Hg(NO_3)_2$ (0.6–2.8 µg Hg), faecal excretion measured over 70 days ranged from 18% to 38% of the administered dose, while urinary excretion was 6% to 35% (Smith et al., 1995). Farris et al. (2008) reanalysed the Smith et al. (1995) data and estimated that, on average, around 30% of the dose was excreted via faeces and 25% via urine. Mercury is also excreted in human sweat and saliva (ATSDR., 2024).

22. Studies have also shown that inorganic mercury is excreted into breast milk from the plasma (Sundberg et al., 1999, Vahter et al., 2000) and correlations have been reported between levels of inorganic mercury in milk and whole blood (Oskarsson et al., 1996). However, as mentioned, inorganic mercury is poorly absorbed via the oral route (Rahola et al., 1972; 1973) and is not expected to be toxicologically significant compared to MeHg in infants nursed with breast milk (Iwai-Shimada et al., 2015).

23. The half-life of absorbed mercuric mercury in the human body is approximately 40 days (EFSA., 2012).

Methylmercury

24. Following oral intake, MeHg is absorbed readily by the gastrointestinal tract and enters the systemic circulation, where mercuric ions can be delivered to target organs (ATSDR., 2004). MeHg has a larger oral absorption fraction than inorganic mercuric mercury, and greater accumulation in the brain and the kidneys (ATSDR., 2024).

25. Studies in humans and experimental animals have demonstrated that gastrointestinal absorption of mercury is almost 100% following ingestion of

MeHg as the chloride salt or when incorporated into fish or other protein (ATSDR., 2024). Following absorption, MeHg is able to cross the placenta, blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in the fetus and brain, respectively (EFSA., 2012). MeHg can also enter the hair follicle following ingestion which is relevant for biomonitoring purposes (EFSA., 2012).

26. In contrast to mercuric mercury, in human blood >90 % MeHg accumulates in the erythrocytes, where it is bound to the cysteinyl residues of haemoglobin. The remaining blood MeHg (up to 10% of the total) is present in the plasma; about 99 % of plasma MeHg is bound to albumin. Plasma protein-bound MeHg is transferred to low molecular weight thiols (e.g., glutathione and cysteine) by ligand exchange mechanisms (EFSA., 2012).

27. Animal studies have shown that MeHg can combine with serum albumin, caseins and thiol-containing proteins on the surface of fat globules, allowing passive transfer of MeHg into breast milk from plasma (Sundberg et al., 1999); however, only up to 10% of whole blood MeHg is located in the plasma and available for lactational transfer (Kershaw et al., 1980). The concentration of MeHg in human milk and its proportion as a percentage of total mercury vary among different populations. Only a limited number of studies have reported concentrations of total mercury (THg) and MeHg in human milk (THg: Björnberg et al., 2005; Ursinyova and Masanova., 2005; Garcia-Esquinas et al., 2011; Miklavčič et al., 2011; Miklavčič et al., 2013. MeHg: Miklavčič et al., 2011; Miklavčič et al., 2013; Valent et al., 2013). Reported mean or median THg values are between 0.2 and 0.9 ng/g (or mL); mean or median percentages of MeHg in THg are 38 to 60% depending on the method of analysis and sample population. The remainder of THg is assumed to be inorganic mercury.

28. Fetal distribution of MeHg is similar to maternal distribution, although fetal brain mercury concentrations are approximately 5-7 times higher than those in maternal blood (COT, 2004). Cord blood concentrations are also

reported at up to twice the maternal blood concentration at parturition (Bocca et al., 2019; FAO/WHO., 2007; Lee et al., 2010; Sakamoto et al., 2002, 2018; Vigeh et al., 2018); however, blood mercury concentrations in infants have been shown to decline significantly over the first weeks of life. Sakamoto et al. (2002) reported that at 3 months of age infants mean red blood cell mercury concentration accounted for 54 % of the measured umbilical cord concentration and lower than the maternal blood concentration, opposite to the situation at parturition. The rapid reduction of infant blood mercury concentration was attributed to low rates of lactational mercury transfer and rapid increase in infants body weight after birth (almost 2-fold at 3 months old) (Sakamoto et al., 2002). The higher concentration of mercury in the umbilical cord is hypothesised to be due to the action of active transport mechanisms via amino acid carriers such as system L, the two isoforms of which (LAT1 and LAT2) have been shown to mediate the transport of MeHg cysteine S-conjugates in astrocytes and endothelial cells of the BBB (Aschner et al. 1990; Kerper et al. 1992; Mokrzan et al. 1995; Simmons-Willis et al. 2002). Straka et al. (2016) also found that LAT1, another amino acid transporter rBAT, and an ATP-binding cassette transporter MRP1, are all involved in mercury toxicokinetics of trophoblast cells. The authors proposed a model involving these transporters that explains the preferential transport of mercury across the placenta towards the fetus. Other transport mechanisms have been identified in the placenta; however, their roles in the transport of MeHg are unknown (Bridges and Zalups., 2017).

29. Partial demethylation of MeHg occurs in mammals in the presence of reactive oxygen species. Demethylation occurs predominantly in the liver, intestinal tract, spleen, and to a lesser extent in phagocytic cells and the brain (Suda et al., 1992). Mercuric mercury in the brain is generally the result of either *in situ* dealkylation of organic mercury species such as MeHg or oxidation of elemental mercury. Demethylation of MeHg by intestinal bacteria also contributes to the excretion of inorganic mercuric mercury in faeces (Li et al., 2019).

30. MeHg has a half-life of approximately 70 - 80 days in the human body and steady state is achieved within a year (COT., 2004). Approximately 90 % is excreted by the faecal route as mercuric mercury (EFSA., 2012). Enterohepatic recycling of MeHg by metabolism of its glutathione S-conjugate (CH_3Hg-S-CysGlyGlu) and reabsorptive transport of its cysteine S-conjugate (CH_3Hg-S-Cys) (Tanaka et al., 1992; Tanaka-Kagawa et al., 1993) limits the urinary excretion of MeHg.

Toxicity

31. In October 2024 the US ATSDR published a toxicological profile for mercury which characterises the toxicologic and adverse health effects of organic and inorganic mercury. Mercury compounds exhibit a wide range of toxic effects, targeting common cellular functions. These include disrupting intracellular calcium balance, the cytoskeleton, mitochondrial function, oxidative stress, neurotransmitter release, and DNA methylation. The array of toxic effects is due to the strong affinity of Hg^{2+} and CH_3Hg^{2+} for the thiolate anion, which leads to the formation of Hg^{2+} and CH_3Hg^{2+} S-conjugates. This allows inorganic and MeHg to bind to and interfere with the structure and function of enzymes, transporters, and proteins that rely on functional thiol groups (ATSDR., 2024).

Inorganic mercury

32. Information on the health effects of inorganic mercury comes primarily from oral studies in laboratory animals, with supporting data from acute poisoning case reports in humans. No epidemiological studies specific for exposure to inorganic mercury salts have been identified; however, animal studies consistently report dose-related impairments in fertility in male and female rodents following oral exposure (ATSDR., 2024). Animal studies have also shown that the critical target organ for inorganic mercury toxicity is the kidney (NTP., 1993); other targets include the liver, nervous system, immune system, reproductive system (EFSA., 2012).

33. Generational studies in rats and mice have shown that reproductive capacity decreases in a dose- and duration-dependent manner following oral exposure to mercuric chloride (Atkinson et al., 2001; Szász et al., 2002; Khan et al., 2004; Huang et al., 2011; Lukačínová et al., 2011; Heath et al., 2009; 2012; Laaroussi et al., 2025).

34. The effects of mercuric chloride were examined via 2-generation reproductive and fertility study in Sprague Dawley rats (Atkinson et al., 2001). Parental animals (F0, n=20 per group) were exposed daily via oral gavage to mercuric chloride in water from pre-mating through mating, gestation and lactation, before selected offspring (F1, n=25 for control + low dose and n=15 for mid dose) were then mated to produce a 2nd generation (F2). The study design is outlined below (Table 1).

Table 1. Study design for 2-generation reproductive and fertility study in Sprague Dawley rats (Atkinson et al., 2001).

Group	**Dose levels (mg/kg bw/d)**	**Pre-mating (Exposure duration in days)**	**Mating (Exposure duration in days)**	**Gestation (Exposure duration in days)**	**Lactation (Exposure duration in days)**
F0 Males	0, 0.5, 1 or 2.0/1.5	60	21	21	21
F1 Males	0, 0.5, 1.02	60	21	21	21
Fo Females	0, 0.75, 1.5 and 3.0/2.51	16	21	21	21
F1 Females	0, 1.5, 2.52	16	21	21	21

Control was milli-Q water. Pre-mating periods were selected to cover one spermatogenic or oogenic cycle. (1) High dose levels were adjusted during pre-mating in F0 animals due to excess toxicity, after 43 days for males, and 27 days for females. (2) Due to insufficient numbers of offspring in the high dose group, no 2nd generation was possible in this group.

35. Toxicity (including clinical signs and mortality) was present in all dosed parental F0 groups but not repeated in parental F1 groups. Body weight was significantly lower in high dose F0 females vs. control from study week 7, without corresponding effects on food consumption. Impacts on various organ weights were reported in F0 and F1 animals, although only kidney weight remained significantly reduced when adjusted for body weight.

36. Impacts on fertility and development included reductions in fertility indices and number of pregnant animals, live births and 4-day survival indices versus control in all treated F1 and F2 animals. Mean number of live pups per litter and pup body weight was also significantly reduced at days 4, 7, 14, 21 in all mercuric chloride treated groups, and at day 0 in pups of high dose parents. Implant efficiency (number of pups born/number implantation sites in dam) was significantly reduced in all treated F0 and mid-dose F1 females. At weaning, body weight in all F1 males of mercuric chloride dosed groups was significantly lower than control, and did not recover. Reduced body weight gain was also reported in all treated F1 females until week 11. It is not possible based on the study design to determine whether one or both sexes are responsible for the adverse impacts on reproduction. The remaining parameters, including fertility indices and number of pregnant animals in the F1 generation, sex ratio of pups (F1 and F2), pup survival (F1 and F2 at 7, 14 and 21-days), mean number of live F2 pups, and post-partum dam weight (F0 and F1) were unaffected by treatment.

37. A further 2-generation reproductive toxicity study in Swiss albino mice examined the impact of chronic exposure to mercuric chloride via the maternal lineage (Laaroussi et al., 2025). Dams (F0, n=12) were given 40

ppm mercuric chloride in their drinking water (equivalent to approximately 6 mg/kg bw/day) or untreated water (control) from gestation day 0. The F1 offspring remained with their mothers until weaning; only female pups were retained for further analysis. F1 treated mice continued to receive treatment until they reached adulthood. At 10 weeks old, adult F1 females in both control and treatment groups were mated with untreated males to produce a second (F2) generation. The F1 dams were split into two groups: one which continued to receive treatment and another that was no longer exposed to mercuric chloride (n=12 per group). This created a second generation that was directly exposed to mercuric chloride (F2) through gestation, lactation and adulthood and another (F2') that was only indirectly exposed through the maternal gametes of their F1 mothers that were exposed to mercuric chloride during their development and adulthood. Maternal care, sexual maturation, fertility and hypothalamic function were evaluated (an area of the brain for which the BBB remains 'leaky' until later in development, making it more susceptible to toxicity where substances are small enough to pass through the incomplete barrier).

38. Although live birth index was unaffected across groups, reproductive dysfunction was observed in exposed females from development through adulthood (F1 and F2 generations). Litter size and lactation index (indicative of how successful dams are at rearing pups through lactation) were decreased versus control. A decline in maternal care behaviours was observed in all exposed groups, including reduced nursing frequency and grooming/licking behaviours. In all treatment groups, delayed vaginal opening (achieved in 80 % control versus 20 % F1, 10 % F2 and 50 % F2' animals at 33 days), and first oestrus (achieved by 44 days of age in 70 % control versus 30 % F1, 0 % F2 and 60 % F2') were reported. Furthermore, altered oestrous cyclicity and reduced mating interest was recorded in all directly and indirectly exposed animals (F1, F2 and F2'). Such effects in F2′ females, exposed indirectly via the germline, are suggestive of transgenerational effects following mercuric chloride exposure. Finally, changes in key hypothalamic genes associated with control of the hypothalamus-pituitary-gonadal axis,

neuroplasticity and inflammation were identified, indicating potential neuroendocrine disruption following mercuric chloride exposure in both directly and indirectly exposed animals. The COT note that the number of animals per group (n=12) is low in the Laaroussi et al. (2025) study and may be considered underpowered considering there were abortions and mortalities in the dams, and decreased numbers of pups per litter.

39. The impact of lifetime low-dose exposure to mercuric chloride via drinking water was explored in Wistar rats (Lukačínová et al., 2011). Male animals (n=10 per generation) originating from the parental, F1 and F2 generations of a reproductive trial were exposed to 1µM mercuric chloride via drinking water (treatment) or pure water (control) from 52 days of age for 156 weeks (3 years), with toxicity parameters measured every 26th week. Similar longtime average daily doses were calculated as 0.036, 0.036 and 0.035 mg/kg bw for animals from the parental, F1 and F2 generations, respectively. Mercuric chloride exposure led to a significant reduction in survival in all generations (controls 90-100 % versus treated 30-35 %). Leading causes of mortality included tumours and gastrointestinal haemorrhage. Increasingly shortened lifespan was reported in all generations (control >1100 days, F0 823 days, F1 736 days and F2 674 days). A similar pattern of increasing effect by generation from F0 to F2 was observed in all remaining parameters examined. Body weight was statistically significantly reduced, and food and water intake were increased (not statistically significant for food) in all generations. Total serum protein, serum albumin, transferrin (F1 and F2 groups only) and ferritin were significantly increased in mercuric chloride treated animals versus control, again with increasing impact by generation.

40. Data on reproductive hormones are limited to two sub-acute (60 day) oral gavage studies in Sprague-Dawley rats, whereby animals were exposed daily to low or high mercuric chloride (0.5, or 1.0 mg/kg bw/d), or deionised water control (Heath et al., 2009, 2012). Heath et al. (2009) took groups of 20 young female rats (30 days of age) and exposed them for 60 days. 10 females per group were then mated with untreated adult males; pregnant

females were euthanised at approximately gestation day 13. In Heath et al. (2012) young male rats were exposed from 30 days of age for 60 days, before being bred with unexposed adult females (n=10 per group). Male animals were euthanised after 21 days of cohabitation; the females were observed for a further 21 days, with all pregnant animals being allowed to reach term. Selected general, reproductive and hormonal parameters were examined. The COT noted that the number of animals per group (n=10) is low in the Heath et al. (2009) and (2012) studies and may be considered underpowered.

41. Heath et al. (2009) reported a significant impact of mercuric chloride exposure on body weight gain, and on implantation number, but no impact on number of corpora lutea (a measure of ovulation rate). No impact on follicle stimulating hormone was identified following mercuric chloride treatment. However, significantly lower serum progesterone and significantly higher pituitary luteinizing hormone levels were identified in the high dose group, compared to control. The authors suggested these results indicated mercuric chloride may have a disruptive effect on progesterone production by the corpora lutea (leading to impacts on viable implantations given progesterone's role in maintaining pregnancy), but the mechanisms are not understood.

42. Heath et al. (2012) reported mercuric chloride exposure had a significant impact on body weight of high dose but not low dose males vs. control at necropsy. High dose males had a significantly poorer impregnation rate than low-dose or control groups, and there was a loss of correlation between testosterone levels and time to impregnate. Epididymal sperm counts were statistically significantly reduced in all exposed groups vs. control, and all exposed groups had significantly lower testicular testosterone vs. control (a similar effect was identified in plasma testosterone, although this did not reach statistical significance). The authors concluded that at doses lower than those producing clinical toxicity, mercuric chloride was able to significantly impact male reproductive hormones and performance.

Methylmercury

43. Studies in humans and animals provide some evidence that oral exposure to organic mercury has renal, cardiovascular, immune, reproductive, and developmental effects; however, neurological and neurodevelopmental effects are established as the most sensitive effects of oral organic mercury exposure (ATSDR., 2024).

44. JECFA and EFSA have repeatedly evaluated the safety of mercury (EFSA, 2004; 2012; FAO/WHO, 1966; 1970; 1972; 1978; 1988; 2004; 2007; 2011) and agreed that the most sensitive endpoint is neurotoxicity and that life *in utero* is the critical period for the occurrence of neurodevelopmental toxicity (FAO/WHO., 2004; EFSA., 2012). This makes pregnant women a susceptible population. The bioaccumulative properties and long half-life of MeHg mean that the blood concentration of MeHg at the time of becoming pregnant depends on the exposure to MeHg during the preceding year (COT., 2004).

45. Following the Japanese Minamata MeHg poisoning incident, adults exposed to high levels of MeHg exhibited symptoms including sensory disturbances in the distal parts of the extremities followed by ataxia, concentric contraction of the visual field, impairment of gait and/or speech, muscle weakness, tremors, abnormal eye movement, and hearing impairments (Sakamoto et al., 2018). Similar symptoms were reported for Iraqi adults affected after a large-scale epidemic of MeHg poisoning from wheat seeds disinfected with MeHg in 1972-73.A total of 6000 people were affected resulting in 400 deaths (Bakir et al., 1973). A study on the Iraq population estimated mercury body burden thresholds (mg) at diagnosis for various symptoms: abnormal sensory perception, ~25 mg (equivalent to a mercury blood concentration of 250 µg/L); ataxia, ~50 mg; articulation disorders, ~90 mg; hearing loss, ~180 mg; death, >200 mg (Bakir et al., 1973).

46. The symptoms observed in fetal-type Minamata disease patients (22 typical severe cases) were mental retardation, inability to walk unaided, disturbances of coordination, speech, chewing and swallowing, and increased muscle tone (Sakamoto et al., 2018). Developmental effects such as polydactyly, syndactyly, craniofacial malformations, microcornea, undescended testicles, enlarged colon, and coccyx protrusion were also observed in fetal-type Minamata disease patients. Histopathological examination of samples from Japanese fetal-type Minamata disease patients revealed widespread and severe neuronal degeneration in the central nervous system (Akagi et al., 1998). In Iraq, the children most severely affected by MeHg poisoning manifested with severe sensory impairments, general paralysis, hyperactive reflexes and/or impaired mental development (Bakir et al., 1973).

47. EFSA and the COT have both highlighted dietary factors that can reduce or prevent MeHg toxicity, including n-3 long chain polyunsaturated fatty acids (LCPUFAs), selenium, iodine, choline and vitamin E (EFSA, 2012; COT, 2018). The dietary substance most extensively studied as a confounding factor in studies of mercury is selenium.

48. MeHg and inorganic mercury binding affinities for selenium (10^{45}) are up to a million times higher than its affinity for sulphur (10^{39}) in analogous forms (Dyrssen and Wedborg., 1991). The high affinity means that in the presence of mercury the availability of selenium is reduced and its biological functions compromised. The ability of MeHg to cross the placenta and BBB means that MeHg can specifically sequester selenium at the active sites of essential selenium-dependent enzymes (selenoenzymes) in fetal neuroendocrine tissues that lack adequate reserves of selenium because of their rapid growth. As intracellular concentrations of MeHg approach – and especially as they exceed – 1:1 molar stoichiometries with selenium in these vulnerable tissues, vital selenoenzyme activities. In addition, formation of insoluble mercury selenides depletes availability of selenium for subsequent cycles of selenoprotein synthesis. Selenoenzymes are vital for redox control

as well as preventing and reversing oxidative damage in the brain and neuroendocrine tissues (among other important biological functions) and their loss can have severe adverse effects (Ralston and Raymond., 2010).

49. Animal studies have demonstrated that high maternal MeHg exposures diminish fetal brain selenium and brain selenoenzyme activities to around 30% of normal (Watanabe et al., 1999a,b). The consequences of MeHg exposure in these studies and those of Ralston et al. (2007; Ralston, 2008) were directly proportional to dietary mercury:selenium molar ratios, which need to be significantly lower than 1:1 to prevent impaired maternal export of selenium to the fetus and adverse neurodevelopmental outcomes in the offspring (Newland et al., 2006; Reed et al., 2006, 2008).

50. Studies that have found associations between MeHg exposure from seafood consumption and neurodevelopmental impairments have uniformly involved consumption of foods containing mercury in molar excess of selenium e.g., pilot whale (5:1 reported by Julshamn et al., 1987) or varieties of shark (>2:1, reported by Kaneko and Ralston, 2007). In contrast, studies examining the effects of maternal exposure to MeHg from typical varieties of ocean fish (Davidson et al., 1998; Myers and Davidson, 1998; Hibbeln et al., 2007; Oken et al., 2008; Lederman et al., 2008) have not found adverse effects, but have instead found beneficial effects from increasing seafood consumption (Hibbeln et al., 2007; Oken et al., 2008; Lederman et al., 2008). In the UK, multiple examinations of the Avon Longitudinal Study of Parents and Children cohort – as of 2023 14,833 unique mothers and 15,447 associated pregnancies enrolled (Major-Smith et al., 2023) – have all reported either no significant associations or beneficial associations between prenatal mercury exposure and child outcomes, especially in mothers that had eaten fish during pregnancy (Golding et al., 2022; Dack et al., 2023).

51. The International Agency for Research on Cancer (IARC) concluded that elemental mercury and inorganic mercury compounds are not classifiable as to their carcinogenicity to humans (Group 3), but that MeHg compounds

are possibly carcinogenic to humans (Group 2B). These conclusions were based on inadequate evidence in humans for mercury and mercury compounds, inadequate evidence in experimental animals for elemental mercury, limited evidence for carcinogenicity of mercuric chloride in experimental animals (forestomach tumours in rats), and sufficient evidence for carcinogenicity of methylmercuric chloride in experimental animals (kidney tumours in male mice) (IARC, 1993). The U.S. Department of Health and Human Services has not classified the potential for elemental mercury, inorganic mercury compounds, or MeHg compounds to cause cancer in humans (NTP, 2016).

52. The neurological effects of MeHg in animals include sensorimotor dysfunction, vision and hearing deficits, impaired learning, and memory, along with clear signs of neurotoxicity such as clumsiness, motor incoordination, lethargy, hindlimb crossing, tremors, ataxia, and partial paralysis. Both developing humans and animals are more vulnerable to MeHg-induced neurotoxic effects compared to adults (ATSDR., 2024). Animal studies also consistently show that exposure to MeHg leads to dose- and duration-dependent decreases in offspring survival, increased fetal malformations and variations (including cleft palate, skeletal malformations, and hydronephrosis), and reduced fetal weight (ATSDR., 2024).

Recently published literature

53. The previous discussion paper (TOX/2025/03) on mercury in the maternal diet included a comprehensive literature review on the toxicological effects of inorganic and organic mercury exposure including summaries of recent reviews and toxicologic/epidemiologic studies identified therein. The literature review predominantly covered reproductive toxicology – i.e., pregnancy outcomes and effects on maternal health – in addition to blood pressure, biomarkers and epigenetic effects of mercury exposure.

54. An additional literature search was performed to specifically identify recent publications on the Faroe Islands (Oulhote et al., 2019) and Republic of Seychelles birth cohorts (Wahlberg et al., 2018; Xu et al., 2019; Zareba et al., 2019; McSorley et al., 2020; Yeates et al., 2020; Cediel Ulloa et al., 2021; Strain et al., 2021; Love et al., 2022; De Paula et al., 2023; Wesolowska et al., 2024). The first of the numerous observation cohort studies established in the Faroe Islands and Republic of Seychelles began over three decades ago (Weihe and Grandjean., 2012; Shamlaye et al., 2020). The goal of these studies has been to understand potential adverse health effects in children raised by mothers with high seafood diets and thus high exposures to marine contaminants such as MeHg. The results of these studies have been crucial to deriving health-based guidance values (HBGVs) for MeHg and inorganic mercury by leading authorities JECFA and EFSA (search terms in Annex B).

55. The previous COT statement on MeHg in the infant and child diet (COT., 2018) included a similar literature search for the 2012-2018 period (year of last EFSA evaluation to year of COT discussion); hence the most recent literature searches specified years 2018-2025.

56. Upon review of the recent literature, the COT concluded that the data confirmed the current knowledge on the toxicity of inorganic and MeHg and did not constitute a basis for revising the current HBGVs. The section below, therefore, describes the JECFA and EFSA evaluations and derivations of HBGVs for MeHg and inorganic mercury.

Derivation of health-based guidance value (HBGV)

Derivation of HBGV for MeHg

57. The original provisional tolerable weekly intake (PTWI) for MeHg (3.3 µg/kg bw) was revised at the sixty-first JECFA meeting to protect the developing fetus from neurotoxic effects (FAO/WHO, 2004). This change was based on findings from two major epidemiology studies from the Faroe Islands and the Seychelles (FAO/WHO, 2004). The assessments were made

on the basis of the evaluations of children at 7 years of age in the Faroe Islands (Grandjean et al., 1997) and 5.5 years of age in the Seychelles (Davidson et al., 1998).

58. A no observed adverse effect level (NOAEL) for neurobehavioural effects of 15.3 mg/kg mercury in maternal hair was established from the Seychelles main cohort study (Davidson et al., 1998). JECFA performed a mathematical analysis of the concentration to response relationship to determine a benchmark dose lower confidence limit ($BMDL_{05}$) of 12.0 mg/kg mercury in maternal hair in the Faroe Islands (Grandjean et al., 1997; Budtz-Jørgensen et al., 1999; 2000; 2001; National Research Council., 2000; Rice et al., 2003). An average of the NOAEL and $BMDL_{05}$ from the Seychelles and Faroe Island studies was used (14 mg/kg mercury in maternal hair) as an estimate of the concentration of MeHg in maternal hair that reflects exposures that would have no appreciable effect on the offspring in these two study populations.

59. The concentration of MeHg in maternal hair was converted to mercury in maternal blood using an average overall ratio of 250. Based on this factor, 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 (FAO/WHO, 2004).

60. 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 MeHg (1.5 µg/kg bw/day) corresponding to a maternal blood mercury concentration that would have no appreciable adverse effects on the offspring in the two study populations (FAO/WHO, 2004).

61. 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 ($10^{0.5}$). This resulted in an overall uncertainty factor (UF) of 6.4 (FAO/WHO, 2004).

62. Following application of this UF, a PTWI of 1.6 µg/kg bw was established by JECFA (FAO/WHO, 2004).

63. In 2012 the EFSA CONTAM Panel assessed new literature published since the 2004 JECFA evaluation (EFSA, 2012). The CONTAM Panel identified new information on confounding by beneficial factors in fish on associations between prenatal MeHg exposures and neurodevelopmental endpoints.

64. New developments from the first nutrition cohort of the Seychelles Child Development Study (SCDS) indicated a negative association between prenatal mercury exposure and neurodevelopmental endpoints in children at age 9 and 30 months (Stokes-Riner et al., 2011), but not at 5 years (Strain et al., 2012), whereby it appeared that the positive effects from intake of n-3 LCPUFAs no longer outweighed detrimental effects from MeHg exposure. The studies examined associations between MeHg, maternal nutrition, and children's scores on the Bayley Scales of Infant Development-II test.

65. The CONTAM panel found that, based on results from the newer SCDS nutrition cohort studies, a MeHg 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 (Lynch et al., 2011). They considered this a better point of departure than the unadjusted figure of 15.3 mg/kg MeHg in maternal hair previously derived from the SCDS main cohort (EFSA., 2012).

66. For the Faroe Islands cohort, the CONTAM Panel could not identify a more appropriate point of departure than the $BMDL_{05}$ of 12 mg/kg selected by JECFA (EFSA., 2012).

67. Based on the above, a maternal hair MeHg concentration of 11.5 mg/kg (the mean of the Faroese and Seychelles cohorts) was used as an estimate of the concentration of MeHg in maternal hair reflecting exposures that would have no appreciable effect on the offspring in these two study populations (EFSA., 2012).

68. A factor of 250 was used to convert this to an equivalent concentration of mercury in maternal blood of 46 µg/L (EFSA., 2012).

69. Output from a one-compartment toxicokinetic model determined that a maternal daily dietary mercury intake of 1.2 µg/kg bw corresponded to a maternal blood mercury concentration that was considered to have no appreciable adverse effects on the offspring. By applying a total UF of 6.4 to this value, the CONTAM Panel established a TWI for MeHg of 1.3 µg/kg bw expressed as mercury (EFSA, 2012).

Derivation of HBGV for inorganic mercury

70. The first HBGV for inorganic mercury was derived by JECFA in 2011 based on animal studies as 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 (FAO/WHO, 2011).

71. JECFA agreed that the toxicological database for mercuric chloride was relevant for assessing the health risk of foodborne inorganic mercury.

72. For JECFA's risk assessment the National Toxicology Program (NTP) 1993 rat bioassay study was considered the most informative because it used low-dose exposures to mercuric chloride administered via the oral route. Groups of 10 male and 10 female F344 rats received 0, 0.312, 0.625, 1.25, 2.5, or 5 mg mercuric chloride/kg bw in deionized water (5 mL/kg dose volume) by gavage 5 days/week for 26 weeks. The most sensitive endpoint

was found to be relative kidney weight. The BMDLs generated for relative kidney weight were lower than those generated for all other endpoints investigated (FAO/WHO, 2011).

73. The lowest $BMDL_{10}$ for relative kidney weight increase in male F344 rats was calculated to be 0.11 mg/kg bw per day as mercuric chloride, corresponding 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 mercuric chloride dose (FAO/WHO, 2011). After application of a 100-fold UF, JECFA established a PTWI for inorganic mercury of 4 µg/kg bw (rounded to one significant number) (FAO/WHO, 2011).

74. The previous PTWI of 5 µg/kg bw for total mercury, established at the sixteenth JECFA meeting (FAO/WHO., 1972), was withdrawn. 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).

75. In 2012 the EFSA CONTAM Panel evaluated the same evidence as JECFA as well as more recent studies and the Panel agreed with the rationale of JECFA, i.e., setting a HBGV based on relative kidney weight in rats from the NTP 1993 study as the pivotal effect. The CONTAM Panel derived the same TWI for inorganic mercury as JECFA, 4 µg/kg bw (EFSA, 2012).

Exposure Assessment

Exposure from food

76. The FSA Exposure Assessment Team provided dietary exposure data on mercury for women of childbearing age (16-49 yrs of age) as a proxy for the maternal diet (Table 1). Exposure to mercury was determined using data from the National Diet and Nutrition Survey (NDNS) (Bates et al., 2014, 2016, 2020; Roberts et al., 2018), and 2014 total diet survey (TDS) (FERA, 2015).

77. Exposure estimates are presented as lower- and upper-bound mean and 97.5th percentile. Lower bound: concentration values below the limit of quantification (LOQ) are treated as zero. Upper bound: concentration values below the LOQ are treated as at the LOQ. The food commodities that result in the highest exposures to mercury are fish and seafoods, and non-alcoholic beverages with mean exposure values of 0.13 and 0.07 µg/kg bw/week, and 97.5th percentile values of 0.62 and 0.17 µg/kg bw/week, respectively.

78. Mean total exposure (combined exposure from all food groups) to mercury for women of child-bearing age ranges from 0.13-0.29 µg/kg bw/week, whilst exposure in high consumers (97.5th percentile) ranges from 0.62-0.84 µg/kg bw/week.

Table 1. Estimated exposure (in µg/kg bw/day and µg/kg bw/week) to mercury from foods consumed by women of childbearing age (16-49 years)

Food Groups	**Mean - Daily exposure to mercury LB to UB (µg/kg bw/day) ***	**97.5th Percentile - Daily exposure to mercury LB to UB (µg/kg bw/day) ***	**Mean - Weekly exposure to mercury LB to UB (µg/kg bw/week) ***	**97.5th Percentile - Weekly exposure to mercury LB to UB (µg/kg bw/week) ***
Bread	0-0.00099	0-0.0026	0-0.0069	0-0.018
Misc Cereals	0-0.0010	0-0.0029	0-0.007	0-0.020
Carcass meat	0-0.00034	0-0.0016	0-0.0024	0-0.011
Offal	0.000045	0.00075	0.00032	0.0053
Meat products	0-0.00027	0-0.0011	0-0.0019	0-0.0077
Poultry	0-0.00039	0-0.0014	0-0.0027	0-0.0098
Fish and seafood	0.018	0.089	0.13	0.62
Fats and oils	0-0.000086	0-0.00027	0-0.00060	0-0.0019
Eggs	0-0.00014	0-0.00067	0-0.00098	0-0.0047

Sugars and confectionary	0.00033	0.0013	0.0023	0.0091
Green vegetables	0-0.00028	0-0.0011	0-0.0020	0-0.0077
Potatoes	0-0.0011	0-0.0032	0-0.0077	0-0.022
Other vegetables	0-0.0013	0-0.0043	0-0.0091	0-0.030
Canned vegetables	0-0.00026	0-0.0012	0-0.0018	0-0.0084
Fresh fruit	0-0.0012	0-0.0045	0-0.0084	0-0.032
Fruit products	0-0.00038	0-0.0021	0-0.0027	0-0.015
Non-alcoholic beverages	0-0.010	0-0.024	0-0.07	0-0.17
Milk	0-0.00090	0-0.0033	0-0.0063	0-0.023
Dairy products	0-0.0004	0-0.0015	0-0.0028	0-0.011
Nuts and seeds	0-0.000043	0-0.00037	0-0.00030	0-0.0026
Alcoholic beverages	0-0.00083	0-0.0055	0-0.0058	0-0.039
Meat alternatives	0-0.000024	0-0.00029	0-0.00017	0-0.0020
Snacks	0.000055	0.00025	0.00039	0.0018
Desserts	0-0.000039	0-0.00025	0-0.00027	0-0.0018
Condiments	0-0.00010	0-0.00038	0-0.0007	0-0.0027
Tap water only	0-0.0014	0-0.0061	0-0.0098	0-0.043
Bottled water still or carbonated	0-0.00034	0-0.0028	0-0.0024	0-0.020
Total	0.019-0.041	0.089-0.12	0.13-0.29	0.62-0.84

LB= Lower-bound; UB = Upper-bound.

Exposure from drinking water

79. The main chemical forms in which mercury occurs in water are elemental mercury, complexes of mercuric mercury with various inorganic and organic ligands, and organic mercury forms, mainly MeHg and dimethylmercury. The chemical form in which mercury occurs depends on pH, redox potential and concentration of inorganic and organic complexing agents. The contribution of MeHg to total mercury is typically less than 5 % in estuarine and marine waters but can be up to 30 % in fresh water (EFSA, 2012).

80. Concentrations of mercury in water were provided by the Drinking Water Inspectorate for England and Wales, the Drinking Water Quality Regulator for Scotland and Northern Ireland (NI) Water. 2023 median and 97.5th percentile concentrations were provided for England and Wales. 2023 data for NI and Scotland was requested; however, NI had no results greater than the LOQ (0.041 µg/L) and Scotland had no results greater than the limit of detection (LOD) (0.02 µg/L). The LOD and LOQ were therefore used as proxies for 97.5th percentiles for Scotland and NI. For median concentrations, 2016 data from a previous COT paper were used for Scotland and NI (COT, 2018).

81. The FSA Exposure Assessment Team provided values for water consumption for women of child-bearing age in grams (ml) of water per kg bodyweight per day. These were 8 g/kg bw/day (mean) and 32 g/kg bw/day (97.5th percentile) using data from the 2014 TDS (FERA, 2015). Using median mercury concentration values in drinking water of 0.04, 0.03 and 0.01 µg/L for England/Wales, Scotland and NI respectively, a 97.5th percentile concentration of 0.12 for England/Wales and LOQ and LOD concentrations of 0.041 and 0.02 µg/L for NI and Scotland, respectively, the calculated exposures to mercury from drinking water are shown in Table 2.

82. The estimated exposures from drinking water in England and Wales are higher than those in NI and Scotland, probably due to a denser population and a longer history of industrial activity particularly in sectors including coal burning, chlor-alkali production, metal refining and waste incineration (Environment Agency., 2021). These activities historically released into the environment mercury which can persist in soils and sediments and leach into water bodies over time. England and Wales also has more extensive environmental monitoring networks which may detect more instances of elevated mercury levels.

Table 2. Calculated mean and 97.5th percentile exposures (in µg/kg bw/day and µg/kg bw/week) for women of childbearing age to Mercury from drinking water

Region	**N (number of samples)**	**Median (µg/kg bw/day)***	**Median (µg/kg bw/week)***	**97.5th percentile (µg/kg bw/day)***	**97.5th percentile (µg/kg bw/week)***
England and Wales	7944	0.00032	0.00224	0.0038	0.027
Scotland	Median 16424; LOD 585	0.00016	0.00112	0.0013[L]	0.0091[L]
Northern Ireland	Median 395; LOQ 1782	0.000080	0.00056	0.00064[L]	0.0045[L]

* Average body weight for women of childbearing age = 70.3 kg, value provided by the FSA Exposure Assessment Team from years 1 – 11 of the rolling National Diet and Nutrition Survey, NDNS (Bates et al., 2014, Bates et al., 2016, Roberts et al., 2018). L = calculated using 2023 LOD/LOQ.

Exposure from the air

83. Mercury is naturally emitted from land and ocean surfaces as elemental mercury. Anthropogenic sources result in the emission of elemental mercury, mercuric mercury, and particle-bound mercury. In general, elemental mercury is the predominant form of mercury in the atmosphere (EFSA, 2012).

84. The WHO estimates that the average inhalation rate for a 70 kg adult is 20 m^3/day (WHO, 2000). The Department for Environment, Food and Rural Affairs (DEFRA) UK-Air Data Selector tool was used to retrieve total mercury air concentrations and the most recent data available were from 2018 at two sites. The average air mercury concentration in London Westminster (urban background) was 2.68 ng/m^3 and 15.34 ng/m^3 from Runcorn Weston Point (urban industrial site).

85. As a worst-case scenario, constant exposure of an adult female to an air mercury concentration of 15.34 ng/m^3 would result in a daily exposure to 306.8 ng of mercury from the air. For women with an average body weight of 70.3 kg (value provided by the FSA Exposure Assessment Team from years 1 – 11 of the rolling National Diet and Nutrition Survey, NDNS (Bates et al., 2014, Bates et al., 2016, Roberts et al., 2018)), this gives an exposure of 4.36 ng/kg bw/day equivalent to 0.031 µg/kg bw/week.

Exposure from the soil

86. Mercury is most commonly found in the environment in elemental form, as inorganic mercuric compounds or as monomethylmercury compounds with the general formula, CH_3HgX. Monomethylated mercury compounds are most likely to be found in soil as a result of natural microbial transformation of inorganic mercury (Environmental Agency, 2009). In surface soils, about 1–3 % of total mercury is in the methylated form with the rest predominantly as Hg^{2+} compounds (Environment Agency., 2009).

87. Mercury was measured in topsoil from England from a depth of 0-15 cm as part of a DEFRA-commissioned project (Ander et al, 2013).

88. Table 3 shows the mercury exposures from soil for women of child-bearing age. Mean and 75th percentile mercury concentrations from soil in regions classified as principal (non-urban) and urban were used to assess potential exposures of adults through soil ingestion (Ander et al, 2013).

89. An ingestion rate of 50 mg soil/day was assumed based on the rate used by the Environment Agency in their Contaminated Land Exposure Assessment (CLEA) model (Environment Agency., 2009) and was based on a consensus value from studies by the U.S. EPA (1997) and Otte et al. (2001). It is a combined value for soil and dust as most of the evidence used to determine the ingestion rate does not differentiate between soil and household dust. Furthermore, the evidence base for selecting a representative soil ingestion rate for adults is much smaller than that for children; the U.S. EPA (1997) has cautioned that the value is highly uncertain and based on a low level of confidence.

Table 3. Median and 75th percentile exposure values (in µg/kg bw/day and µg/kg bw/week) for women of childbearing age to mercury from soil.

Region Type	**Percentile**	**Exposure (µg/kg bw/week)**	**% Inorganic Mercury TWI (4 µg/kg bw)**	**% Methylmercury TWI (1.3 µg/kg bw)**
Non-urban	Median	0.00060	0.015	0.046
Urban	Median	0.0017	0.042	0.13
Non-urban	75th Percentile	0.0011	0.028	0.086
Urban	75th Percentile	0.0032	0.081	0.25

* Average body weight for women of childbearing age = 70.3 kg, value provided by the FSA Exposure Assessment Team from years 1 – 11 of the rolling National Diet and Nutrition Survey, NDNS (Bates *et al*., 2014, Bates *et al*., 2016, Roberts *et al*., 2018).

90. The data presented are representative of mercury concentrations in the soil in England only.

Pica behaviour

91. Pica behaviour is described as the craving for and intentional ingestion of substances that are not described as food. The most frequently reported pica behaviours globally are: geophagia, the consumption of earth, soil or clay; amylophagia, the consumption of starch; and pagophagia, the consumption of ice (Miao et al., 2015). Globally, Pica behaviour is thought to affect up to 28 % of pregnant women, though with a high degree of geographic variability (Fawcett et al., 2016). The majority of pica in pregnant women in the UK is geophagia; any risks posed to women of maternal age, therefore, are likely to be from contaminants present in earth, soil or clay .

92. Geophagia primarily occurs in migrant populations from Africa and South Asia where the practice is commonplace. The soils, chalks and clays consumed by these populations are usually not of UK origin; soils are imported from regions where the practice is prevalent following rudimentary processing such as being oven-baked into blocks (Dean et al., 2004).

93. The toxicological risk of pica to pregnant women is subject to several uncertainties. These include: the highly variable mineralogical and contaminant profile of the soil and clays consumed; the fact that soils and clays are often imported from a variety of countries, resulting in variation in composition and quality; and the reliance of studies on self-reporting of pica behaviour through questionnaires, which could lead to bias in the data and underreporting of pica potentially due to stigma associated with consuming non-food substances.

94. In summary, pica presents a potential route of exposure to mercury from soils/clays and is a source of uncertainty in this risk assessment. Exposure to mercury through pica behaviour is not included in the exposure assessment due to the lack of data available on pica behaviour.

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Exposure from food supplements

95. The FSA has no analytical data on the presence of mercury in supplements, but the levels are regulated in the UK under Assimilated Regulation (EC) 629/2008 at a maximum level of 0.1 mg/kg.

96. The EFSA evaluation of mercury and MeHg in food (EFSA, 2012) conducted a consumer-only exposure assessment and found that the 95th percentile dietary exposure estimations in dietary supplements consumers varied from a minimum LB of 0.00 µg/kg bw per week to a maximum UB of 0.24 µg/kg bw per week in adults. EFSA did not consider dietary supplements a major source of mercury exposure.

Aggregate exposure

97. Aggregate exposure to mercury from food, drinking water, soil and dust, and air were derived by considering a number of scenarios based on the available data. Table 4 shows scenarios of aggregate exposure from the sources listed above and includes estimate of average and high exposure from these sources as indicated below.

98. Average and high exposure for food and drinking water represents the mean and 97.5th percentile exposure. Data for exposure from drinking water in England and Wales were used because this represented the highest exposure compared to Scotland and Northern Ireland. The contribution from air in all scenarios is based on average inhalation rates and the average concentration from an urban industrial site in England. For exposure from soil, the average and high exposure represents the mean and 75th percentile exposure respectively for the region with the highest exposure (i.e., urban region as shown in Table 3).

Table 4. Aggregate exposure to Mercury (in µg/kg bw/day and µg/kg bw/week) from food, drinking water, soil and air*.

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Scenarios	**Aggregate exposure (µg/kg bw/day)**	**Aggregate exposure (µg/kg bw/week)**
Average exposure from all sources[a]	0.045	0.315
High exposure from all sources[b]	0.13	0.91
High exposure from food and mean exposure from all other sources[c]	0.12	0.84
High exposure from drinking water and mean from other sources[d]	0.049	0.34
High exposure from soil and mean from other sources[e]	0.046	0.32

a This scenario represents a summation of average exposure from food, water and soil and a value for air*.
b Exposure is based on summation of 97.5th percentile estimates for food and water, 75th percentile for urban soil and a value for air*.
c Exposure is based on summation of 97.5th percentile estimates for food and the averages for water, urban soil and a value for air*
d Exposure is based on summation of 97.5th percentile estimates for drinking water and the averages for food, urban soil and a value for air*
e Exposure is based on summation of 75th percentile estimate for urban soil and averages for food, water and a value for air*.
*The contribution from air in all scenarios is based on average inhalation rates and the maximum concentration identified for England and Wales.

NDNS uncertainty

99. Doubly labelled water (DLW) studies are used to measure total energy expenditure of individuals. These are carried out alongside the NDNS, and the results are compared with the reported energy intakes in the survey. This comparison shows that on average reported energy intakes are around 30% lower than the total energy expenditure. This could arise due to both individual misreporting and survey design.

100. The NDNS is designed to be as representative as possible, but issues including days of the week sampled in the survey compared to the DLW study may have had an impact, as energy intake has been shown to be higher on weekend days. Misreporting can arise from many factors, such as memory recall bias, social desirability bias (where people consciously or sub-consciously over- or under- report some foods - for example those perceived as healthy or unhealthy) and portion size estimates.

101. Therefore, exposure estimates are not corrected for underreporting of energy intake, as these figures are averages across population groups, and as there is no information on the degree of misreporting of specific foods. However, exposure assessments at the 97.5th percentile are undertaken to ensure that high consumers are accounted for in the assessment, including those who may have mis-reported their energy intake.

Risk characterisation

Food

102. Mean total exposure to mercury from food for women of child-bearing age ranges from 0.13-0.29 µg/kg bw/week, whilst exposure in high consumers (97.5th percentile) ranges from 0.62-0.84 µg/kg bw/week. Without considering exposure from non-dietary sources and assuming all mercury is in the form of MeHg, these estimates are below the EFSA TWI of 1.3 µg/kg bw for MeHg (EFSA, 2012).

Drinking water

103. The 97.5th percentile mercury exposures from drinking water for a woman of childbearing age in England & Wales, Scotland and NI are 0.027, 0.0091 and 0.0045 µg/kg bw/week, respectively. Assuming all the drinking water mercury is in the form of MeHg, these exposures represent 2.1 %, 0.70 % and 0.35 % of the EFSA TWI (1.3 µg/kg bw).

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104. This exposure estimate is conservative, being based on 97.5% percentile water consumption in women of childbearing age; nevertheless, exposures from drinking water alone are far below the TWI.

Air

105. An average adult female is, at worst, expected to be exposed to 0.031 µg/kg bw/week of mercury if resident near an urban industrial site. This exposure is equivalent to 0.78% of the inorganic mercury TWI (4 µg/kg bw) and 2.38% of the MeHg TWI (1.3 µg/kg bw). The industrial site air mercury concentration is 5.7 times higher than the urban background concentration; for the general population; therefore, this value is conservative.

Soil

106. Soil mercury values from England were used to estimate the UK's exposure to mercury from soil because no values were available for Scotland, Wales or NI. Exposure to mercury from soil in both urban and non-urban regions is presented in Table 5 and shown as a percentage proportion of the EFSA TWI's for MeHg and inorganic mercury.

Table 5. Median and 75th percentile exposure to soil mercury in urban and non-urban regions as a proportion of the inorganic mercury and MeHg EFSA TWI's.

Mercury Exposure and Tolerable Weekly Intake (TWI) Contribution by Region

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Region Type	Percentile	Exposure (µg/kg bw/week)*	% inorganic mercury TWI (4 µg/kg bw)	% Methylmercury TWI (1.3 µg/kg bw)
Non-urban	Median	0.00060	0.015	0.046
Urban	Median	0.0017	0.042	0.13
Non-urban	75th percentile	0.0011	0.028	0.086
Urban	75th percentile	0.0032	0.081	0.25

107. The 75th percentile exposure to mercury through soil ingestion is far below the TWIs and therefore of low concern for the general population.

108. There is uncertainty regarding sub-populations that exhibit pica behaviour that may regularly consume soils/clays containing mercury; however, this is unlikely to make a significant contribution to overall mercury exposure in women of maternal age. Exposure via pica behaviour will be kept under review and updated should additional data become available.

Aggregate characterisation

109. A combined exposure assessment considered exposure to mercury from all sources at average and high levels. In a scenario where there are high exposures to mercury from all sources (food, drinking water, soil and air) the estimated aggregate exposure is 0.13 µg/kg bw/day (Table 3), equivalent to 0.91 µg/kg bw/week. This is below the EFSA TWIs for inorganic mercury (4 µg/kg bw) and MeHg (1.3 µg/kg bw). Aggregate exposure estimates under all scenarios are below the EFSA TWI's for inorganic mercury and MeHg, providing reassurance that the risk of toxicity from mercury is low.

Conclusions

110. Mercury is a metal that is released into the environment from both natural and anthropogenic sources. Mercury bioaccumulates in fish as MeHg, especially in long-lived predatory species such as swordfish and tuna. Populations that consume large quantities of foods derived from fish are more vulnerable to mercury exposure. Food sources other than fish and seafood products may contain mercury, but mostly in the form of inorganic mercury.

111. After oral intake in humans, MeHg is more extensively and rapidly absorbed than inorganic mercury. Following ingestion MeHg can enter the hair follicle, cross the placental, blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in hair, the fetus and the brain, respectively. Inorganic mercury does not readily cross the same barriers and is therefore considerably less toxic than MeHg.

112. The main adverse effect associated with MeHg exposure is toxicity to the central and peripheral nervous systems. Due to MeHg's ability to cross barriers, exposure during embryonic neurodevelopment and in young children is of high concern. Thus, pregnant and breastfeeding women are sensitive sub-populations.

113. The most recent HBGVs derived for mercury were calculated by EFSA in 2012 to determine whether the earlier JECFA-derived values were still appropriate. EFSA derived a lower TWI for MeHg of 1.3 µg/kg bw (the JECFA TWI was 1.6 µg/kg bw) and a TWI for inorganic mercury of 4 µg/kg bw (identical to the JECFA TWI).

114. Inorganic mercury could not be separated from MeHg in the exposure data. This was considered irrelevant for the risk assessment, however, because previous evaluations have highlighted the fact that most mercury exposure from the diet is MeHg. Furthermore, MeHg is considered more toxic than inorganic mercury. Regardless, the high individual and aggregate exposure assessments to mercury from food, water, soil and air all estimated exposures were below the EFSA TWIs for both MeHg and inorganic mercury.

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For the UK population, therefore, the risk to women of maternal age and their fetuses is low.

115. The current Government advice on foods to avoid in pregnancy should be maintained. Women of childbearing age should avoid eating more than more than 2 portions of oily fish a week and no more than 2 tuna steaks (about 140g cooked or 170g raw) (tuna is no longer classed as oily fish). Shark, swordfish, marlin, raw shellfish and uncooked, cold-smoked or cured fish should also be avoided by pregnant women and women trying to get pregnant. If pregnant women and women trying to get pregnant are following Government advice the exposure assessment is highly conservative as fish and seafood is the major source of MeHg exposure in the diet.

Secretariat
September 2025

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List of Abbreviations and Technical terms

Acronym	Definition
ADME	Absorption, distribution, metabolism, and excretion
ATSDR	Agency for Toxic Substances and Disease Registry
BBB	Blood brain barrier
BMDL	Benchmark-dose lower confidence limit
Bw	Bodyweight
CONTAM	Panel on Contaminants in the Food Chain
CLEA	Contaminated Land Exposure Assessment
COT	Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment
DEFRA	Department for Environment, Food and Rural Affairs
DHA	Docosahexaenoic acid
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organisation of the United Nations
HBGV	Health-based guidance value
Hg	Mercury
JECFA	Joint Food and Agriculture Organisation of the United Nations / World Health Organisation Expert Committee on Food Additives
LCPUFA	Long chain polyunsaturated fatty acid
MeHg	Methylmercury
MOCEH	Mothers and Children's Environmental Health
NOAEL	No observed adverse effect level
OWO	Overweight or obesity
PTWI	Provisional tolerable weekly intake
SACN	Scientific Advisory Committee on Nutrition
SCDS	Seychelles child development study
SCOOP	Scientific cooperation
TDS	Total diet survey

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TWI	Tolerable weekly intake
WHO	World health organisation

Definitions

Benchmark-dose lower confidence limit (BMDL). The BMDL is the lower boundary of the confidence interval on the benchmark dose. The BMDL accounts for the uncertainty in the estimate of the dose response that is due to characteristics of the experimental design, such as sample size. The BMDL can be used as the point of departure for derivation of a health-based guidance value or a margin of exposure. Numbers in subscript after the BMDL such as $BMDL_{05}$ or $BMDL_{10}$ specify the lower confidence limit of the dose that causes a 5% or 10% change in the response rate.

No observed adverse effect level (NOAEL). The NOAEL is the greatest concentration or amount of a substance, found by experiment or observation, that causes no adverse alteration of morphology, functional capacity, growth, development or lifespan of the target organism distinguishable from those observed in normal (control) organisms of the same species and strain under the same defined conditions of exposure.

Health-based guidance value (HBGV). A numerical value derived by dividing a point of departure (a no observed adverse-effect level, benchmark dose or benchmark dose lower confidence limit) by a composite uncertainty factor to determine a level that can be ingested over a defined time period (e.g. lifetime or 24 h) without appreciable health risk.

Tolerable weekly intake (TWI). Estimated maximum amount of an agent, expressed on a body mass basis, to which each individual in a (sub)population may be exposed over a specified period without appreciable risk.

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Provisional tolerable weekly intake (PTWI). The endpoint used by the Joint FAO/WHO Expert Committee on Food Additives for food contaminants such as heavy metals with cumulative properties. Its value represents permissible human weekly exposure to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods.

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TOX/2025/30 Annex B

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)

Second Draft Statement on the Effects of Mercury on Maternal Health

Search terms

The references cited in this draft statement are of publications found in PubMed or LitFetch searches and references therein, using the following search terms:

Hg AND Maternal,
Maternal health,
Pre-conception,
Conception,
Post-partum,
Toxicity,
Reproductive,
Mechanism,
ADME,
Toxicokinetics,
Absorption,
Distribution,
Metabolism,
Excretion,
Biomarker,
Exposure,
Preeclampsia,
Abortion,
United Kingdom,
Republic of Seychelles,
Seychelles Child Development Study,
Faroe Islands.