SCIENTIFIC OPINION

Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

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ABSTRACT

EFSA was asked by the European Commission to consider new developments regarding inorganic mercury and methylmercury toxicity and evaluate whether the Joint FAO/WHO Expert Committee on Food Additives (JECFA) provisional tolerable weekly intakes for methylmercury of 1.6 µg/kg body weight (b.w.) and of 4 µg/kg b.w. for inorganic mercury were still appropriate. In line with JECFA, the CONTAM Panel established a tolerable weekly intake (TWI) for inorganic mercury of 4 µg/kg b.w., expressed as mercury. For methylmercury, new developments in epidemiological studies from the Seychelles Child Developmental Study Nutrition Cohort have indicated that n-3 long-chain polyunsaturated fatty acids in fish may counteract negative effects from methylmercury exposure. 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 methylmercury of 1.3 µg/kg b.w., expressed as mercury. The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The 95th percentile dietary exposure is 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. Unborn children constitute the most vulnerable group. Biomonitoring data from blood and hair indicate that methylmercury exposure is generally below the TWI in Europe, but higher levels are also observed. Exposure to methylmercury above the TWI is of concern. If measures to reduce methylmercury exposure are considered, the potential beneficial effects of fish consumption should also be taken into account. 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.

KEY WORDS

total mercury, methylmercury, inorganic mercury, tolerable weekly intake, risk assessment, fish, food

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SUMMARY

Following a request from the European Commission, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) was asked to deliver a scientific opinion on the risks to human health related to the presence of inorganic mercury and methylmercury in food. The Panel was asked to consider new developments regarding the toxicity of inorganic mercury and methylmercury since the last opinion of the European Food Safety Authority (EFSA) of 24 February 2004 and to evaluate whether the provisional tolerable weekly intakes (PTWIs) established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) of 1.6 µg/kg body weight (b.w.) for methylmercury and of 4 µg/kg b.w. for inorganic mercury were considered appropriate. The CONTAM Panel was also asked to assess human dietary exposure, taking into account specific sensitive groups and to consider the non-dietary sources of exposure to mercury species.

Mercury is a metal that is released into the environment from both natural and anthropogenic sources. Once released, mercury undergoes a series of complex transformations and cycles between atmosphere, ocean and land. 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. Methylmercury is by far the most common form of organic mercury in the food chain.

This opinion focuses only on the risks related to dietary inorganic mercury and methylmercury exposure and does not assess the nutritional benefits linked to certain foods (e.g. fish and other seafood).

A call for annual collection of chemical contaminant occurrence data in food and feed, including mercury, was issued by EFSA in December 2010. In response, EFSA received 59 820 results on mercury in food from 20 European countries, mainly covering the period from 2004 to 2011. A total number of 59 650 results were described with sufficient detail to be used in the statistical analysis of the respective food groups; 98.2 % of the samples were for total mercury, 1.8 % for methylmercury and three samples for inorganic mercury.

All the 20 food groups available at the first level of FoodEx were covered in the current data collection. The food groups 'Fish and other seafood' and 'Meat and meat products' dominated the food product coverage with 36.8 % and 17.6 % respectively. These were followed by 'Grain and grain-based products' at 7.8 % and 'Vegetables and vegetable products (including fungi)' at 7.3 %. More than 60 % of the data were below the limit of detection (LOD) or the limit of quantification (LOQ) (left-censored (LC)) in 11 of the food groups. However, 12 % of the results for 'Fish and other seafood', which had the highest values of total mercury in comparison to all other food categories, were LC. The mercury content varied widely among different fish species, and was highest in predatory fish.

Because of the lack of specific information on methylmercury and inorganic mercury data in the database, the exposure assessment (except for human milk) was based on the data submitted for total mercury. The analysed total mercury was converted to methylmercury and inorganic mercury by applying conversion factors based on the methylmercury/total mercury proportion derived from literature data, using a conservative approach. For fish meat, fish products, fish offal and unspecified fish and seafood a conversion factor of 1.0 was used for methylmercury and 0.2 for inorganic mercury. For crustaceans, molluscs and amphibians the conversion factor was 0.8 for methylmercury and 0.5 for inorganic mercury. For all other food categories apart from 'Fish and other seafood', total mercury was regarded as inorganic mercury. Because this approach was chosen, total mercury dietary exposure cannot be derived by adding inorganic and methylmercury dietary exposure together. In order to estimate dietary exposure, the consumption data of each individual within the surveys were multiplied by the mean occurrence data for the relevant food categories, resulting in a distribution of exposure, from which the mean and 95th percentile were identified for each survey and age class. For

human milk, the mean concentrations of methylmercury and inorganic mercury in a limited number of European studies were used for exposure assessment.

The dietary exposure to methylmercury was based only on the food group 'Fish and other seafood' and since there was little difference between the lower bound (LB) and upper bound (UB) exposure estimates, the middle bound (MB) exposures were used. The mean MB methylmercury dietary exposure varied from the lowest minimum of 0.06 µg/kg b.w. per week seen in elderly and very elderly to the highest maximum of 1.57 µg/kg b.w. per week in toddlers. The 95th percentile MB dietary exposure ranged from the lowest minimum of 0.14 µg/kg b.w. per week in very elderly to the highest maximum of 5.05 µg/kg b.w. per week in adolescents. Based on mean concentrations of methylmercury in human milk, the dietary exposure to methylmercury for infants with an average human milk consumption ranged from 0.09 to 0.62 µg/kg b.w. per week and for infants with high milk consumption the dietary exposure ranged from 0.14 to 0.94 µg/kg b.w. per week.

Fish meat was the dominating contributor to methylmercury dietary exposure for all age classes, followed by fish products. In particular tuna, swordfish, cod, whiting and pike were major contributors to methylmercury dietary exposure in the adult age groups, while the same species, with the addition of hake, were the most important contributors in the child age groups. Dietary exposure in women of child-bearing age was especially considered and found not to be different from adults in general. The dietary exposure estimations in high and frequent consumers of fish meat (95th percentile, consumers only) was in general approximately two-fold higher in comparison to the total population and varied from a minimum MB of 0.54 µg/kg b.w. per week in elderly to a maximum MB of 7.48 µg/kg b.w. per week in other children.

The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations. The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers. The 95th percentile dietary exposure was estimated to be from the lowest minimum LB of 0.25 µg/kg b.w. per week in elderly and very elderly to the highest maximum UB of 4.06 µg/kg b.w. per week in toddlers. Based on mean concentrations of inorganic mercury in human milk, the dietary exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week and from 0.25 to 1.94 µg/kg b.w. per week for infants with a high milk consumption.

At FoodEx Level 1, 'Fish and other seafood', 'Non-alcoholic beverages' and 'Composite food' were the most important contributors to inorganic mercury dietary exposure in the European population. Dietary exposure to inorganic mercury was driven by high concentrations in the case of fish and other seafood and composite food (where a high proportion of the data were LC), but was more likely driven by high consumption in the case of non-alcoholic beverages.

Non-dietary exposure to methylmercury is likely to be of minor importance for the general population in Europe, but exposure to elemental mercury via the outgassing of dental amalgam is believed to strongly contribute to the internal inorganic mercury exposure.

After oral intake, methylmercury is much more extensively and rapidly absorbed than mercuric and mercurous mercury. In human blood mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma, whereas methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes. In contrast to mercuric mercury, methylmercury is able to enter the hair follicle, and to cross the placenta as well as the blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in hair, the fetus and the brain. Mercuric mercury in the brain is generally the result of either in situ demethylation of organic mercury species or oxidation of elemental mercury. Excretion of absorbed mercuric mercury occurs mainly via urine, whereas the main pathway of excretion of absorbed methylmercury is via faeces in the form of mercuric mercury. Urinary total mercury might be a suitable biomarker of inorganic (and elemental) mercury, but not for methylmercury exposure. Total mercury in hair and blood are routinely used as biomarkers to assess long term methylmercury

exposure. A frequently cited total mercury blood to hair ratio is 1:250, however large variations exist, especially in people with infrequent fish consumption.

A recent developmental study of methylmercury in mice, applying only one low dose, indicated effects on body weight gain, locomotor function and auditory function. A large study in rats showed developmental immunotoxic effects at low doses, and the lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 0.01 mg/kg b.w. per day, expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day, expressed as mercury) for the specific antibody response in rats was the lowest BMDL. While bearing this in mind, the Panel concluded that experimental animal studies on methylmercury did not provide a better primary basis than the human data for a health-based guidance value.

New data from the Faroe Islands Cohort 1 at children's age 14 years indicated that the association between prenatal exposure and neurological auditory function was still present at 14 years, but with a smaller impact than at seven years. Reassessment of the data from the Faroese Cohort 1 participants at age seven years indicated that beneficial effects of fish consumption together with imprecision in the measurements of fish consumption and determination of mercury in hair might underestimate the effects of methylmercury.

Reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the Seychelles Child Developmental Study have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints. Results from the smaller Nutrition Cohort in the Seychelles Child Developmental Study indicated an association between prenatal mercury exposure and decreased scores on neurodevelopmental indices at 9 and 30 months after adjustment for prenatal blood maternal n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs). An apparent no-observed-effect level (NOEL) at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study. However, a positive association between maternal prenatal n-3 LCPUFAs, in particular docosahexaenoic acid, and preschool language scores was reported from the five years follow up.

The reported associations between methylmercury exposure and cardiovascular disease were addressed by JECFA in their update in 2006 (FAO/WHO, 2007), and additional studies have become available. The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. Although the observations related to myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, they are still not conclusive. Consequently, after carefully considering other endpoints than neurodevelopmental outcomes, and in particular cardiovascular disease, the CONTAM Panel concludes that associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value for methylmercury.

The mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese cohort 1 at age seven years (12 mg/kg in maternal hair), resulting in 11.5 mg/kg maternal hair, was used as the basis for derivation of a health-based guidance value. By application of a maternal hair to maternal blood ratio of 250, the maternal hair mercury concentration with no appreciable adverse effect was converted into a maternal blood mercury concentration of 46 µg/L. Using a one-compartment toxicokinetic model, the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w. A data-derived uncertainty factor of 2 was applied to account for variation in the hair to blood ratio. In addition, a standard factor of 3.2 was applied to account for interindividual variation in toxicokinetics, resulting in a total uncertainty factor of 6.4. A tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w. expressed as mercury, was established. The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response in rats.

The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The medians of 95th percentile dietary exposures across surveys are close to or above the TWI for all age groups. High consumers of fish meat may exceed the TWI by up to approximately six-fold. Unborn children constitute the most vulnerable group for developmental effects of methylmercury exposure, and pregnant women can be present in the group of high and frequent fish consumers. Biomonitoring data on blood and hair concentrations indicate that in the general European population, methylmercury exposure is generally below the TWI. However, higher concentrations in blood and hair are also observed, confirming higher dietary exposure in some population groups. Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered, the potential beneficial effects of fish consumption should also be taken into account.

The critical target for toxicity of inorganic mercury is the kidney. Other targets include the liver, nervous system, immune system, reproductive and developmental systems. Having considered the experimental animal data on inorganic mercury, including some recent studies not reviewed by JECFA in its evaluation of 2010, the Panel agrees with the rationale of JECFA in setting a health-based guidance value using kidney weight changes in male rats as the pivotal effect. Based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury and an uncertainty factor of 100 to account for inter and intra species differences, with conversion to a weekly basis and rounding to one significant figure, the Panel established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

The estimated exposure to inorganic mercury in Europe from the diet alone does not exceed the TWI. Inhaled elemental mercury vapour from dental amalgam, which after absorption is converted to inorganic mercury, is an additional source that is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded.

The CONTAM Panel recommends to develop certified reference materials and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood. Further effort should be made to increase the number of methylmercury and inorganic mercury data in all food groups that contribute significantly to overall exposure. In order to decrease the uncertainty in the point of departure derived from the epidemiological studies, more reliable definition of the dose response taking confounding factors into account is needed. Future studies should elucidate the relevance of additional endpoints, such as immunological and cardiovascular endpoints.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) issued a scientific opinion on mercury and methylmercury in food on 24 February 2004[4]. The scientific opinion focussed mainly on methylmercury. The Panel concluded that in some countries the exposure resulting from average intake of fish and seafood products may be close to the provisional tolerable weekly intake (PTWI) of 1.6 µg/kg b.w. for methylmercury established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Some population groups who frequently consume large predatory fish may have a considerably higher intake of methylmercury and exceed the PTWI. The Panel also concluded that the occurrence data available at that time did not allow reliable estimations of the intakes by high consumers in different populations.

Regulation (EC) No. 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs[5] contains maximum levels for mercury in fish and seafood. In order to decide whether a review of these levels is appropriate, an updated scientific opinion is needed. New occurrence data on mercury as well as more detailed consumption data have become available since the EFSA opinion of 2004 and should be taken into account for more reliable intake estimations.

The updated scientific opinion should cover both forms of mercury: organic mercury (methylmercury) as the most toxic form that is prevalent in fish and seafood, as well as inorganic mercury, prevalent in most other foodstuffs. The evaluation of mercury carried out by JECFA at its 72nd meeting in February 2010[6] should be taken into account.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002 the European Commission asks the European Food Safety Authority for a scientific opinion on the risks to human health related to the presence of mercury and methylmercury in food.

The opinion should address both inorganic mercury and organic forms of mercury (in particular methylmercury).

In particular, the opinion should

- consider any new developments regarding the toxicity of inorganic mercury and methylmercury since the last EFSA opinion of 24 February 2004. This should comprise an evaluation whether the JECFA PTWIs for methylmercury of 1.6 µg/kg b.w. and of 4 µg/kg b.w. for inorganic mercury are considered appropriate,

- contain an updated exposure assessment for inorganic mercury and methylmercury in food (incl. drinking water) and outline those food groups that are main contributors to exposure for inorganic mercury and methylmercury, respectively,

- address the exposure to methylmercury for specific sensitive groups of the population (e.g. the unborn child, children, high consumers of fish and seafood) and give an indication of the age group in which children would be most exposed to the toxic effects of methylmercury,

- highlight the population groups most exposed to inorganic mercury and give an indication of the age group in which children would be most exposed to inorganic mercury,

- give a rough estimation of other non-dietary sources of exposure to mercury.

[4] The EFSA Journal (2004) 34, 1-14.
[5] OJ L 364, 20.12.2006, p. 5.
[6] WHO TRS 959, Seventy-second report of the Joint FAO/WHO Expert Committee on Food Additives, 16-25 February 2010.

ASSESSMENT

1. INTRODUCTION

1.1. General information

Mercury (Hg) is a metal that 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. During this biogeochemical cycle, humans, plants, and animals are exposed to mercury, potentially resulting in a variety of health impacts (EFSA, 2008).

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.

In its elemental form, mercury is a liquid at ambient temperatures and pressures and it volatilises strongly. In general, elemental mercury is the predominant form of mercury in the atmosphere (Selin, 2009).

Inorganic mercury (IHg) compounds are salts of Hg_2^{2+} and Hg^{2+}, which are used in several industrial processes and can be found in batteries, fungicides, antiseptics or disinfectants (US-EPA, 2007; EFSA, 2008).

Organic mercury compounds have at least one carbon atom covalently bound to the mercury atom (WHO, 1991). Methylmercury (MeHg) is by far the most common form in the food chain (EFSA, 2008). Other organic mercury compounds like phenylmercury, thiomersal and merbromin (also known as Mercurochrome) have been used as fungicides and in pharmaceutical products (EFSA, 2008).

The largest source of mercury exposure for most people in developed countries is inhalation of mercury vapour due to the continuous release of elemental mercury from dental amalgam. Exposure to methylmercury mostly occurs via the diet. Methylmercury collects and concentrates especially in the aquatic food chain, making populations with a high intake of fish and seafood particularly vulnerable (European Commission, 2005a; Richardson et al., 2011).

The European Commission asked the European Food Safety Authority (EFSA) to provide an updated scientific opinion on the risks for public health related to the presence of mercury and methylmercury in food. Therefore, this opinion focuses only on the risks related to dietary mercury and methylmercury exposure and does not assess the nutritional benefits linked to certain foods (e.g. fish and other seafood).

1.2. Previous risk assessments

Mercury, particularly methylmercury, has been the subject of many previous risk assessments. The most relevant and recent of these are described below.

In 1999, the United States Environmental Protection Agency (US-EPA) asked the National Research Council (NRC) of the National Academy of Sciences (NAS) to provide recommendations on derivation of an appropriate reference dose (RfD) for methylmercury. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The NRC concluded that the RfD should be based on a benchmark dose (BMD) for a reliable neurobehavioural endpoint from the study conducted in the Faroe Islands. The NRC considered that dose-response data for the Boston Naming Test should be modelled based on mercury concentrations in cord blood as a reasonable point of departure for deriving the RfD. A benchmark response (BMR) of 5 % was selected, which would result in a doubling of the number of children with a response at the 5th percentile of the population, and considered significantly developmentally

compromised. That approach estimated a lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 58 µg/kg of mercury in cord blood (corresponding to a $BMDL_{05}$ of 12 mg/kg of mercury in hair). To calculate the RfD, the BMDL should be divided by uncertainty factors of at least 10 to take into consideration biological variability when estimating dose and methylmercury database insufficiencies. On this basis, the NRC concluded that the value of EPA's previously established RfD for methylmercury, 0.1 µg/kg body weight (b.w.) per day, was a scientifically justifiable level for the protection of public health but that the basis for this value required revision (NRC, 2000).

The US-EPA subsequently revised its risk assessment (US-EPA, 2001a). BMD analyses, in terms of cord-blood mercury, were performed for a number of endpoints from the Faroe Islands study, and also from studies conducted in the Seychelles and New Zealand. The US-EPA based its RfD of 0.1 µg/kg b.w. per day on an integrative analysis of the $BMDL_{05}$s from these three studies, which were expressed as mercury in cord blood, by converting to an ingested dose using a pharmacokinetic model and applying an uncertainty factor of 10. This factor of 10 comprised a factor of 3 to allow for pharmacokinetic variability and uncertainty in estimating an ingested dose from cord-blood mercury and a factor of 3 for pharmacodynamic variability and uncertainty.

In 1972, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) of 5 µg/kg b.w. for total mercury (THg) of which no more than 3.3 µg/kg b.w. should be in the form of methylmercury (FAO/WHO, 1972). This 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. The JECFA maintained the PTWI of 3.3 µg/kg b.w. for methylmercury throughout a number of subsequent evaluations, whilst noting that fetuses and infants might be more sensitive than adults to its toxic effects. In 2003, the JECFA revised the PTWI to 1.6 µg/kg b.w. based on the results of the epidemiological studies in the Faroe Islands and the Seychelles (FAO/WHO, 2004). The JECFA selected the $BMDL_{05}$ of 12 mg/kg mercury in maternal hair from the Faroe Islands and the no-observed-effect level (NOEL) of 15.3 mg/kg mercury in maternal hair from the Seychelles as the basis for its revised PTWI. The average of these two values, 14 mg/kg, was considered to be an estimate of the concentration of mercury in maternal hair reflecting exposure that would have no appreciable adverse effects in these two study populations. The maternal hair concentration was extrapolated to a blood concentration of 56 µg/L by dividing by the average reported ratio of mercury in hair to mercury in blood (250:1). This blood concentration was then converted to a steady-state intake of 1.5 µg/kg b.w. per day using a similar pharmacokinetic model as used by NRC and US-EPA, incorporating values for body weight and blood volume for pregnant women. A composite uncertainty factor of 6.4 was applied, incorporating a data-derived factor of 2 for variation in hair to blood ratio, and a default factor of 3.2 for toxicokinetic variability in the relationship between blood mercury and steady state dietary intake, resulting in the PTWI of 1.6 µg/kg b.w. The JECFA considered that a factor for toxicodynamic variability was not needed because the data were derived from sensitive subgroups representing diverse populations (FAO/WHO, 2004). Hence, the key difference between the US-EPA and JECFA evaluations is that US-EPA took a more conservative view in deciding that a factor was required for toxicodynamic variability.

In 2006, the JECFA was asked to clarify the relevance of the PTWI for different subgroups of the population, taking into account that guidance values based on developmental endpoints may be overly conservative for some parts of the population. The JECFA confirmed that the methylmercury PTWI of 1.6 µg/kg b.w. was based on the most sensitive toxicological endpoint (developmental neurotoxicity) in the most susceptible species (humans). Intakes of up to about twice the PTWI would not pose a risk of neurotoxicity to adults except potentially for women of childbearing age because of the effects on the embryo and fetus. However, whilst infants and children up to about 17 years of age are not more sensitive than the embryo or fetus the data did not allow firm conclusions regarding sensitivity compared with adults (FAO/WHO, 2007).

The FAO and WHO convened a Joint Expert Consultation on the Risks and Benefits of Fish Consumption in 2010, which considered nutrients (n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs)) and specific chemical contaminants (methylmercury and dioxin-like compounds) in

a range of fish species. The consultation concluded that among women of childbearing age, pregnant women and nursing mothers, considering the benefits of docosahexaenoic acid (DHA) versus the risks of methylmercury, fish consumption lowers the risk of suboptimal neurodevelopment in their offspring compared with not eating fish in most circumstances evaluated. Among infants, young children and adolescents, the evidence was insufficient to derive a quantitative framework of health risks and benefits (FAO/WHO, 2011a).

In 2004, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) published an opinion on mercury and methylmercury in food (EFSA, 2004). In view of the terms of reference and timescale of the request from the European Commission, the CONTAM Panel did not conduct a hazard characterisation, and based its risk characterisation on comparison of mercury dietary exposure with both the RfD established by the NRC and US-EPA and the JECFA PTWI. The CONTAM Panel concluded that estimates of dietary exposure to methylmercury of average consumers of fish and seafood products in some countries were close to the PTWI and exceeded the RfD. However, the available data did not allow reliable estimates of the intakes of high consumers in different populations. Therefore, there was a need for reliable intake data from studies focused on women of childbearing age.

In 2010, the JECFA reviewed the PTWI for total mercury. It was assumed that the predominant form of mercury in foods other than fish and shellfish is inorganic mercury, and that the toxicological database for mercuric chloride was relevant for assessing the health risk of foodborne inorganic mercury. An increase in relative kidney weight in male rats was identified as the appropriate basis for establishing a PTWI. The lowest $BMDL_{10}$ for mercuric chloride was equivalent to 0.06 mg/kg b.w. per day of mercury. After application of a 100-fold uncertainty factor and converting to a weekly basis, the JECFA established a PTWI of 4 µg/kg b.w for inorganic mercury. In the absence of evidence to the contrary, this PTWI was considered applicable to dietary exposure to total mercury from foods other than fish and shellfish. The estimates of average dietary exposure were at or below the PTWI (FAO/WHO, 2011b).

1.3. Chemistry

Mercury is a metal that occurs naturally in the earth's crust and in the environment. Mercury belongs to Group IIB of the periodic table and has an atomic number of 80 and molecular mass of 200.59 g/mol. There are seven stable isotopes of mercury, with ^{202}Hg being the most abundant (29.86 %). In pure form, it is known alternatively as 'elemental' or 'metallic' mercury (also expressed as Hg(0) or Hg^0). Elemental mercury is a odourless, shiny, silver-white metal and is the only common metal to be liquid at ordinary temperatures and pressures (density = 13.534 g/cm^3).

The three chemical forms of mercury known to be present in the environment (see Table 1 adapted from Kuban et al. (2007) are (i) elemental mercury (Hg^0), which has high vapour pressure and relatively low solubility in water; (ii) mercurous (Hg_2^{2+} or Hg(I)) and mercuric (Hg^{2+} or Hg(II)) inorganic cations, which can be far more soluble and which have a strong affinity for many inorganic and organic ligands, especially those containing sulphur, and (iii) organometallic compounds with one or two alkyl-/aryl- substituents are bound to the mercury atom, forming (mono-/di-) alkylated and/or arylated RHgX or RHgR' mercury species, where R and R' represent alkyl and/or aryl substituents (CH_3–, C_2H_5–, C_6H_5–) and X is an anion (halide, nitrate or sulphate). Many inorganic and organic compounds of mercury can be formed from Hg^{2+}. Inorganic mercury salts are usually found in the forms of mercuric sulphide (HgS), mercuric oxide (HgO) and mercuric chloride ($HgCl_2$). There are several organic mercury compounds; by far the most common in the environment and in the aquatic food chain is methylmercury (FAO/WHO 2011b). Because methylmercury is strongly bound to muscle, methylmercury does accumulate appreciably with increased muscle mass and increased duration of exposure.

Table 1: Elemental mercury and major mercury ions/species in environmental and biological samples (adapted from Kuban et al. (2007)).

			CAS number
Elemental mercury		Hg^0	92786-62-4
Inorganic mercury ions	Mercurous ion	Hg_2^{2+}	n/a
	Mercuric ion	Hg^{2+}	7439-97-6
Organic mercury ions/species	Methylmercury	CH_3Hg^+	22967-92-6
	Dimethylmercury	$(CH_3)_2Hg$	593-74-8
	Ethylmercury	$CH_3CH_2Hg^+$	627-44-1
	Phenylmercury	$C_6H_5Hg^+$	23172-37-4

n/a: not available.

In summary, mercury exists in the following main states under natural conditions (UNEP, 2002):

- as metallic vapour and liquid/elemental mercury;
- bound in mercury-containing minerals (solid);
- as ions in solution or bound in ionic compounds (inorganic and organic salts);
- as soluble ion complexes;
- as gaseous or dissolved non-ionic organic compounds;
- bound to inorganic or organic particles/matter by ionic, electrophilic or lipophilic adsorption.

1.4. Production, use and environmental fate

1.4.1. Production

The mercury available on the world market is supplied from a number of different sources, of which the main sources are primary production (mercury mining); secondary production (where mercury is a by-product, for example in zinc production); recycling (from fluorescent lamps, etc.); and reuse of surpluses (for example from the chloralkali industry). The total global mercury supply was estimated in 2007 at about 3 100 - 3 900 tonnes per year (Maxson, 2009).

1.4.2. Use

Batteries, gold mining and the chloralkali industry are the most important global uses, accounting for over 75 % of worldwide mercury consumption (European Commission, 2005a).

In order to reduce the mercury levels in the environment and the human exposure, the European Commission launched the European Union (EU) mercury strategy in 2005. It is a comprehensive plan that includes 20 measures to reduce mercury emissions, to reduce the supply and demand of mercury and protect against exposure.[7] In 2010 the European Commission reviewed the mercury strategy and concluded that the implementation of the strategy is in an advanced stage and almost all actions are delivered.[8] The implementation of these policies is expected to reduce the emissions, although data are not yet available.

Mercury is used in the form of thiomersal in vaccines. Thiomersal (synonyms sodium 2-ethylmercurothio-benzoate, thimerosal, merthiolate, mercurothiolate, merfamin, mertorgan, merzonin, $C_9H_9HgNaO_2S$, CAS No 54-64-8) is used to prevent bacterial and fungal growth in vaccines, especially in vaccines formulated in multidose vials.

The following global past and present mercury applications and sources have been identified (based on UNEP, 2002; Fauser et al., 2011):

[7] http://ec.europa.eu/environment/chemicals/mercury/
[8] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52010DC0723:EN:NOT

- chloralkali production (chlorine and caustic soda);
- dental amalgam;
- artisanal gold and silver mining;
- batteries;
- measuring and control equipment (e.g. thermometers, manometers);
- electric and electronic switches (e.g. switches in sports shoes with lights in soles, thermo-switches);
- discharge lamps (e.g. fluorescent lamps);
- laboratory chemicals, electrodes and apparatus for analysis;
- pesticides (seed dressing and/or others);
- biocides for different products and processes (e.g. paints);
- slimicides for paper production;
- pharmaceuticals (e.g. preservatives in vaccines, preservatives in eye drops);
- catalytic mercury compounds;
- cosmetics (creams, soaps);
- lighthouses (marine use; for establishing lenses);
- production of counterfeit money;
- mercury metal use in religious rituals and folklore medicine;
- pigments;
- tanning;
- browning and etching steel;
- colour photograph paper;
- explosives, fireworks;
- airbag activators and anti-lock braking system mechanisms in cars;
- artisanal diamond production;
- recoil softeners for rifles;
- arm and leg bands;
- executive toys;
- surfacing material used in running tracks in sports stadiums;
- ammunition;
- hardeners and resins in plastics, fillers;
- liquid crystal displays (LCDs).

1.4.3. Environmental fate and levels

Mercury is released into the environment by both natural and anthropogenic sources. The most important natural sources of mercury are the degassing of the earth's crust, emissions from volcanoes and evaporation from water. Anthropogenic emissions such as coal burning, mining and other industrial activities add to the overall mercury release. It has been estimated that the amounts of mercury resulting from this may be quite small relative to the global emissions. However, it was stressed that there are considerable uncertainties in the estimated mercury emissions (WHO, 1991). Mercury is continuously mobilised, deposited and re-mobilised in the atmosphere, ocean and land, and a recent review by Selin (2009) describes the current understanding of this biogeochemical cycle.

Atmosphere

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 (Selin, 2009; Sprovieri et al., 2010). The global background concentration of airborne mercury is considered to be in the range 1.5 - 1.7 ng/m^3 in the Northern Hemisphere and 1.1 - 1.3 ng/m^3 in the Southern Hemisphere (Lindberg et al., 2007).

The global anthropogenic emission of mercury was estimated for 2000 to be ca. 2 190 tonnes (Pacyna et al., 2006). A similar estimation was performed for 2005 but included additional sources that had not been included previously, such as emissions from human cremation and artisanal and small-scale gold mining, and showed a total emission of 1 930 tonnes (Pacyna et al., 2010). UNEP is currently updating the estimation of mercury emissions and new data should be available in 2013.[9] Asia is the highest contributor (about 67 %) to the global anthropogenic emission of mercury, followed by North America and Europe. The main source of mercury emission is the combustion of fossil fuels, mainly coal in power plants and industrial and residential boilers (Pacyna et al., 2010). Crematoria are in relative terms not a large source, but the emissions from crematoria are significant in some countries (European Commission, 2005b). It was estimated that crematoria will be the single biggest contributor to national mercury emissions in the United Kingdom (UK) by 2020 (Wood et al., 2008).

Soil

Mercury is present in geologically enriched areas in the earth, but can be deposited from the atmosphere to the soil as mercuric mercury (Morel et al., 1998). A portion of this newly deposited mercury will be reduced to elemental mercury, which will rapidly evaporate again to the atmosphere (Selin, 2009). Newly deposited mercury that is not immediately reduced and evaporated can accumulate in vegetation, and Boening (2000) describes the factors influencing accumulation in terrestrial plants. The remaining mercury will be incorporated into a soil mercury pool, which shows slow transformation and which will be slowly released to the atmosphere, during a process that can take centuries or millennia (Schlüter, 2000; Selin, 2009).

Aquatic systems and sediments

The CONTAM Panel refers to Ullrich et al. (2001) for a comprehensive review on the occurrence of mercury in aquatic systems and sediments and discusses this topic briefly below.

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 methylmercury and dimethylmercury. The occurrence of these chemical forms depends on the pH, redox potential and the concentration of inorganic and organic complexing agents (Ullrich et al., 2001). The contribution of methylmercury to total mercury is typically less than 5 % in estuarine and marine waters, but can be up to 30 % in fresh water (Ullrich et al., 2001).

Total mercury concentrations in marine systems have been reported between 0.2 and 0.5 ng/L (Cossa et al., 1997; Mason et al., 1998; Laurier et al., 2004). However, higher concentrations in the range of 1.0 - 20.1 ng/L are reported in fresh water (Morel et al., 1998).

The levels of mercury in uncontaminated sediments are comparable to levels in uncontaminated soils. The contribution of methylmercury to total mercury in sediments is typically about 1 - 1.5 % and < 0.5 % in estuarine and marine waters (Ullrich et al., 2001).

The methylation of mercury takes place mostly on sediments in fresh and ocean water but also in the water columns (WHO, 1990). The biological methylation is performed by both sulphate-reducing bacteria and iron-reducing bacteria (Kerin et al., 2006; Slowey and Brown, 2007; Yu et al., 2012). Abiotic methylation is a pure chemical process, which is also possible when suitable methyl donors are available (Ullrich et al., 2001). The methylation is influenced by several factors that often interact. It depends in the first place on microbial activity and the concentration of bioavailable mercury. However, these factors are influenced by temperature, pH, redox potential and the presence on inorganic and organic complexing agents (Ullrich et al., 2001). The results of this process are mercury species with higher solubility, bioavailability and toxicity to animals and humans (Stein et al., 1996).

9 http://www.unep.org/hazardoussubstances/Mercury/MercuryPublications/GlobalAtmosphericMercuryAssessmentSourcesEm/tabid/3618/language/en-US/Default.aspx

2. LEGISLATION

In order to protect public health, Article 2 of Council Regulation (EEC) No 315/93[10] stipulates that, where necessary, maximum tolerances for specific contaminants shall be established. The current maximum levels (MLs) for mercury are laid down in the Annex, Section 3, of Commission Regulation (EC) No 1881/2006,[11] amended by Commission Regulation (EC) No 629/2008.[12] The MLs established for mercury reflect the results of a dietary exposure assessment carried out in the SCOOP-task 3.2.11[13] and the outcome of the EFSA opinion on mercury and methylmercury in food (EFSA, 2004).

Currently, MLs are established for mercury in fishery products and muscle meat of fish and in food supplements. An ML of 0.5 mg/kg wet weight (w.w.) applies to fishery products and muscle meat of fish (including crustaceans, excluding the brown meat of crab and excluding head and thorax meat of lobster and similar large crustaceans (*Nephropidae* and *Palinuridae*). An exception is made for muscle meat of some specific fish,[14] and an ML of 1.0 mg/kg w.w. applies. Performance characteristics for the analytical determination of mercury are set in Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011.[16]

Harmonised levels for mercury in drinking water are set by Council Directive 98/83/EC.[17] The Directive stipulates that Member States set limit values of 1 µg/L for mercury in water intended for human consumption. Commission Directive 2003/40/EC[18] also sets a maximum limit for mercury in natural mineral water of 1 µg/L. Performance characteristics for the analytical determination of mercury in water are set both in Council Directive 98/83/EC[17] and in Commission Directive 2003/40/EC.[18]

Commission Directive 2008/84/EC,[19] amended by Commission Directive 2009/10/EC,[20] and Commission Directive 2008/128/EC,[21] amended by Commission Directive 2011/3/EC,[22] all provide MLs between 0.1 and 3 mg/kg for mercury as an impurity in numerous food additives.

[10] Council Regulation (EEC) No 315/93 of 8 February 1993 laying down Community procedures for contaminants in food. OJ L 37, 13.02.1993 p. 1-3.

[11] Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. OJ L 364, 20.12.2006, p. 5-24.

[12] Commission Regulation (EC) No 629/2008 of 2 July 2008 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs. OJ L 173, 3.7.2008, p. 6-9.

[13] Reports on tasks for scientific co-operation, Task 3.2.11 'Assessment of dietary exposure to arsenic, cadmium, lead and mercury of the population of the EU Member States'. http://ec.europa.eu/food/food/chemicalsafety/contaminants/scoop_3-2-11_heavy_metals_report_en.pdf

[14] Anglerfish (*Lophius* species), Atlantic catfish (*Anarhichas lupus*), bonito (*Sarda sarda*), eel (*Anguilla* species), emperor, orange roughy, rosy soldierfish (*Hoplostethus* species), grenadier (*Coryphaenoides rupestris*), halibut (*Hippoglossus hippoglossus*), marlin (*Makaira* species), megrim (*Lepidorhombus* species), mullet (*Mullus* species), pike (*Esox lucius*), plain bonito (*Orcynopsis unicolor*), poor cod (*Tricopterus minutes*), Portuguese dogfish (*Centroscymnus coelolepis*), rays (*Raja* species), redfish (*Sebastes marinus*, *S. mentella*, *S. viviparus*), sail fish (*Istiophorus platypterus*), scabbard fish (*Lepidopus caudatus*, *Aphanopus carbo*), seabream, pandora (*Pagellus* species), shark (all species), snake mackerel or butterfish (*Lepidocybium flavobrunneum*, *Ruvettus pretiosus*, *Gempylus serpens*), sturgeon (*Acipenser* species), swordfish (*Xiphias gladius*) and tuna (*Thunnus* species, *Euthynnus* species, *Katsuwonus pelamis*)

[15] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs OJ L 88, 29.3.2007, p.29-38.

[16] Commission Regulation (EU) No 836/2011 of 19 August 2011 amending Regulation (EC) No 333/2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs. by OJ L 215, 20.8.2011, p. 9-16.

[17] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption OJ L 330, 5.12.1998, p.32-54.

[18] Commission Directive 2003/40/EC of 16 May 2003 establishing the list, concentration limits and labelling requirements for the constituents of natural mineral waters and the conditions for using ozone-enriched air for the treatment of natural mineral waters and spring waters OJ L126, 22.5.2003, p. 34-39.

[19] Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners. OJ L253, 20.9.2008, p.1-175.

[20] Commission Directive 2009/10/EC of 13 February 2009 amending Directive 2008/84/EC laying down specific purity criteria on food additives other than colours and sweeteners.OJ L44, 14.2.2009, p. 62-78.

Mercury compounds have been used in the past as pesticides but are no longer authorised in the EU (Council Directive 79/117/EEC).[23] Commission Regulation 149/2008[24] provides maximum residue levels (MRLs) for mercury compounds in various food types of 0.01 and 0.02 mg/kg (sum of mercury compounds expressed as mercury). These MRLs are default values used for unauthorised substances.

Codex Alimentarius[25] has also set a number of guidelines for mercury (total) and methylmercury, namely for natural mineral waters (total mercury: 0.001 mg/kg), food grade salt (total mercury: 0.1 mg/kg), fish except predatory fish (methylmercury: 0.5 mg/kg) and predatory fish such as shark, swordfish, tuna and pike (methylmercury: 1 mg/kg). The guideline levels for methylmercury are intended for fresh or processed fish and fish products moving in international trade.

Directive 2009/48/EC[26] sets migration limits, from toys or components of toys that shall not be exceeded. For mercury the migration limits range from 1.9 mg/kg in liquid or sticky toy material to 94 mg/kg in scraped-off toy material.

Directive 2002/32/EC[27] amended by Directive 2010/6/EU[28] sets maximum contents for mercury in a number of feed commodities (see Table 2). All levels are based on a product with a moisture content of 12 %.

Table 2: EU legislation on mercury in products intended for animal feed.

Products intended for animal feed	Maximum content in mg/kg relative to a feedingstuff with a moisture content of 12 %
Feed materials	0.1
with the exception of:	
- feedingstuffs produced from fish or by the processing of fish or other aquatic animals,	0.5
- calcium carbonate.	0.3
Compound (complementary and complete) feedingstuffs	0.1
with the exception of:	
- mineral feed,	0.2
- compound feedingstuffs for fish,	0.2
- compound feedingstuffs for dogs, cats and fur animals	0.3

[21] Commission Directive 2008/128/EC of 22 December 2008 laying down specific purity criteria concerning colours for use in foodstuffs OJ L6, 10.1.2009, p. 20-63.
[22] Commission Directive 2011/3/EU of 17 January 2011 amending Directive 2008/128/EC laying down specific purity criteria on colours for use in foodstuffs. OJ L13, 18.1.2011, p. 59-63.
[23] Council Directive of 21 December 1978 prohibiting the placing on the market and use of plant protection products containing certain active substances (79/117/EEC). OJ L33, 8.2.1979, p. 36-40.
[24] Commission Regulation (EC) No 149/2008 of 29 January 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council by establishing Annexes II, III and IV setting maximum residue levels for products covered by Annex I thereto. OJ L58, 1.3.2008, p. 1-398.
[25] Codex general standard for contaminants and toxins in food and feed. CODEX STAN 193-1995, p. 1-41.
[26] Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys. OJ L170, 30.6.2009, p. 1-37.
[27] Directive 2002/32/EC of the European Parliament and of the Council of 7 May 2002 on undesirable substances in animal feed. OJ L140, 30.5.2002, p. 10-21.
[28] Commission Directive 2010/6/EU of 9 February 2010 amending Annex I to Directive 2002/32/EC of the European Parliament and of the Council as regards mercury, free gossypol, nitrites and Mowrah, Bassia, Madhuca. OJ L37, 10.2.2010, p. 29-32.

3. SAMPLING AND METHODS OF ANALYSIS

3.1. Sample collection and storage

Sampling as well as analytical quality play a crucial role in the accuracy and precision of the determination of mercury in food commodities.

The sampling of food for mercury analysis requires specific precautions in order to avoid contamination or losses during handling, storage and transport to the laboratory. Samples must be collected so that the sample integrity and traceability are maintained. Sample handling is generally critical only for water samples. The best materials for water sample storage and processing are polytetrafluoroethylene (PTFE) and fluorinated ethylene-propylene. Fresh samples are usually stored deep-frozen, lyophilised in darkness or sometimes sterilised. It has been reported that methylmercury may be decomposed in some food matrices with repeated freezing and unfreezing (particularly in bivalves). However, relatively little is known about the effect of storage on the stability of methylmercury in food samples (FAO/WHO 2011b).

In the EU, methods of sampling for the official control of levels of mercury in foodstuffs have to fulfil the sampling methods described in Commission Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011.[16]

3.2. Methods of analysis

3.2.1. Sample preparation

The analyst must ensure that samples do not become contaminated during sample preparation. Wherever possible, apparatus and equipment that comes into contact with the sample should not contain those metals to be determined and should be made of inert materials e.g. plastics such as polypropylene or PTFE. In speciation analysis the use of dark Pyrex glass containers is recommended for mercury species. These should be acid cleaned to minimise the risk of contamination. High quality stainless steel or ceramic knives may be used for cutting edges. According to Commission Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011,[16] there are many satisfactory specific sample preparation procedures that can be used for the products under consideration. Those described in the European Committee for Standardisation (CEN, 2002 modified by CEN, 2012) have been found to be satisfactory, but others may be equally valid. According to CEN (2012), samples intended for speciation purposes should be stored at 4 °C or lower in darkness. Dilution shall be done only immediately before the analysis. Some considerations shall be kept in mind when storing samples for speciation purposes. Parameters with a strong influence in speciation analysis are:

a) temperature: storage shall be done at –20 °C to prevent microbial activity resulting in reactions e.g. methylation and biodegradation. Generally storage should be kept as short as possible.

b) pH: the pH of the media may strongly affect the stability of the inorganic species. Samples intended for species analysis shall not be changed in their acidity for preservation purposes.

c) light: light may cause instability of organometallic compounds by photodegrading. When analysing organometallic compounds storage shall be done in the dark or in opaque containers.

3.2.2. Instrumental techniques

3.2.2.1. For total mercury analysis

The methods of analysis of total mercury have been reviewed by Evans et al. (2006), Bolann et al. (2007) and Sardans et al. (2010). The methods that have become the most established ones will be briefly summarised below.

Following acidic digestion of samples (Evans et al. 2006), cold vapour atomic absorption spectrometry (CV-AAS; Torres et al., 2009; Mousavi et al., 2010; Jarzynska and Falandysz, 2011) or cold vapour atomic fluorescence spectrometry (CV-AFS; Cava-Montesinos et al., 2004; da Silva et al., 2010; Xia et al., 2010; Senila et al., 2011) has been widely used for the determination of total mercury in several food matrices. Similar limits of quantification (LOQ) may be obtained by CV-AFS (LOQ of about 2 - 10 µg/kg) and CV-AAS (about 3 ng/L in water and 4 - 30 µg/kg in foods). The main advantages of the cold vapour (CV) technique are the separation of the analyte from the potentially interfering sample matrix and its comparatively low cost. However, to avoid interferences by CV-AFS, special precautions must be taken to completely remove vapours when nitric acid is used for digestion. Elemental mercury analysers, also known as automated or direct mercury analysers, with atomic absorption spectrometry (AAS) or atomic fluorescence spectrometry (AFS) detection are also commonly used with the main advantages that they are designed for the direct mercury determination in solid and liquid samples without the need for sample chemical pre-treatment (no digestion step) and have a high sensitivity (LOQ < 1 µg/kg; Carbonell et al., 2009).

After pressure digestion of the samples, inductively coupled plasma-mass spectrometry (ICP-MS) is increasingly being used even if its cost is slightly higher, due to its multielement capacity, sensitivity (LOQ of about 10 µg/kg) and its greater selectivity (Nardi et al., 2009; Rose et al., 2010; Millour et al., 2011a). To limit the memory effects of mercury in the sample delivery system, which may influence the results of samples analysed after measurement of high concentrations and need prolonged washout times, gold chloride is added to the internal standard solution to stabilise mercury in the solution.

3.2.2.2. For mercury speciation analysis

The methods of analysis of mercury species have been reviewed by several authors and can be classified into two general approaches: chromatographic methods (including gas chromatography (GC), liquid chromatography and capillary electrophoresis) and non-chromatographic methods based on the chemical and physical properties of different mercury species (Pereiro and Diaz, 2002; Evans et al., 2006; Diez and Bayona, 2008; Chen and Belzile, 2010; Leopold et al., 2010; Sanchez-Rodas et al., 2010; Amouroux et al., 2011; Clémens et al., 2012). This section will focus on chromatographic separation techniques. The separation of the mercury species can be achieved either by GC or by high-performance liquid chromatography (HPLC), although GC is preferred. Although capillary electrophoresis has not yet been extensively used for mercury speciation (Evans et al., 2006), there is a growing interest, as evidenced in the reviews of Kuban et al. (2007, 2009). Owing to the greater complexity of these hyphenated techniques, it should be noted that the cost of mercury speciation analysis is higher than that of total mercury. The methods that have become the most established ones are briefly summarised below.

Mercury speciation analysis in food is influenced by the nature of the matrix and by the analytical method used. Consequently, the main difficulty is to preserve the initial distribution of mercury species in the sample because of losses and/or cross-species transformations that may occur. Extraction is one of the most critical steps, because two conflicting issues need to be addressed: obtaining high extraction efficiency and minimising losses. Extraction of the mercury species from its matrix requires an aggressive treatment, such as acid digestion, distillation or alkaline extraction, with the option of applying ultrasonic or microwave energy to assist in the procedure (Abrankó et al., 2007; Hajeb et al., 2009a). Methylmercury appears to be more stable in alkaline media than in acid media, with proteins being easily hydrolysed. Once in solution, methylmercury may decompose when

exposed to light, low pH and high storage temperatures. Other factors, such as the type of storage container, may also affect the stability.

Gas chromatography techniques

Speciation of organomercury compounds is most commonly performed by GC with both packed and capillary columns, coupled to several detectors such as mass spectrometry (MS), AAS, AFS, CV-AFS, ICP-MS, microwave-induced plasma atomic emission spectroscopy or furnace atomisation plasma emission spectrometry, and with excellent sensitivity and selectivity (Pereiro and Diaz, 2002; Landaluze et al., 2004; Evans et al., 2006; Abrankó et al., 2007; Diez and Bayona, 2008; Hippler et al., 2009; Jackson et al., 2009; Sanchez-Rodas et al., 2010; Clémens et al., 2011). Following aqueous ethylation with sodium tetraethylborate ($NaBEt_4$), advantages and disadvantages of three hyphenated techniques for mercury speciation analysis in different sample matrices using GC with mass spectrometry (GC-MS), ICP-MS (GC-ICP-MS) and pyrolysis atomic fluorescence (GC-pyro-AFS) detection were recently evaluated by Nevado et al. (2011). Absolute detection and quantification limits were in the range of 2 - 6 pg for GC-pyro-AFS, 1 - 4 pg for GC-MS, with 0.05 - 0.21 pg for GC-ICP-MS, the latter showing the best limits of detection of the three systems employed. However, all systems are sufficiently sensitive for mercury speciation in food samples, with GC-MS and GC-ICP-MS offering isotope analysis capabilities for the use of species-specific isotope dilution analysis, and GC-pyro-AFS being the most cost-effective alternative.

The recent developments in species-specific isotope dilution procedures (i.e. spiking the samples with isotopically enriched species) with GC-MS and GC-ICP-MS techniques has drastically improved the quality and accuracy of the data on mercury speciation analysis (Jackson et al., 2009; Leopold et al., 2010; Amouroux et al., 2011; Clémens et al., 2012). Indeed, the use of isotopically enriched species (i.e. spikes) as tracers overcame the traditional problems related to non-quantitative recoveries and the formation of mercury artefacts that can occur during the extraction and derivatisation steps. The main extraction method used is microwave-assisted extraction because of its speed, efficiency and low occurrence of methylation and demethylation reactions. For the derivatisation of mercury species, alkylating reagents such as sodium tetrapropylborate ($NaBPr_4$) and $NaBEt_4$ are mainly used because derivation takes place in an aqueous medium, the natural environment of most biological samples. Such derivatisation procedures avoid additional solvent extraction steps needed, for example, when Grignard reagents are used (Clémens et al., 2012).

In the last few years, several methodologies, based on the use of multiple spiking species-specific isotope dilution analysis have been developed to overcome abiotic artificial transformations of mercury species (i.e. methylation and demethylation). In the case of mercury speciation analysis, the addition of two isotopically enriched species to the sample (double spiking) provides the quantification of the extent of both methylation and demethylation processes and, therefore, the correction of the final mercury species concentrations (Amouroux et al., 2011; Clémens et al., 2011, 2012). Advantages and limitations of isotopic dilution analysis have also been discussed recently (Clémens et al., 2012).

High-performance liquid chromatography techniques

HPLC is increasingly being applied instead of GC for the separation of mercury species because the mercury species do not need to be derivatised to volatile compounds before HPLC separation. The main methods of analysis have been reviewed (Evans et al., 2006; Chen and Belzile, 2010; Leopold et al., 2010; Sanchez-Rodas et al., 2010; Amouroux et al., 2011; Clémens et al., 2012).

A mild extraction method may be carried out by acid leaching or enzymatic extraction, with the option of applying ultrasonic (Lopez et al., 2010; Rodrigues et al., 2010a; Batista et al., 2011; Guzman-Mar et al., 2011) or microwave energy (Jagtap et al., 2011) to assist in the procedure. The digest is then analysed for methylmercury and the mercuric cation with reversed-phase HPLC after simple filtration.

Separation with a reversed phase column based on alkyl-silica and a mobile phase containing an organic modifier, together with a chelating or ion pair reagent (and in some cases a pH buffer) is usually used. ICP-MS has the highest sensitivity for the detection of mercury species in the HPLC eluent, which is directly injected to the nebuliser of the ICP-MS without splitting or dilution (Lopez et al., 2010; Rodrigues et al., 2010a; Batista et al., 2011; Jagtap et al., 2011). The use of CV generation after HPLC separation coupled to AFS detection is the most common approach to lower the detection limit (Bramanti et al., 2005; Guzman-Mar et al., 2011). However, an extra step for the conversion of mercury species to inorganic mercuric mercury prior to CV generation is necessary, or else the magnitude of the response would be dependent on the species present. Recently, a novel solution cathode glow discharge induced vapour generation was developed as interface to on-line couple HPLC-AFS (He et al., 2011). Alternatively, pre-concentration on a suitable microcolumn prior to HPLC separation coupled to ICP-MS or CV-AAS detection, or the use of micro-HPLC coupled through a micronebuliser to ICP-MS, achieves detection limits in the low ng/L range. The advantage of MS and ICP-MS is their multielement and multi-isotope capabilities offering isotope dilution analysis capabilities (Amouroux et al., 2011; Clémens et al., 2012), whereas CV-AAS and CV-AFS have the advantage of being comparatively low-cost and simple operations.

3.2.3. Analytical quality assurance: performance criteria, reference materials, validation and proficiency testing

The performance criteria for methods of analysis for official control are also laid down in Commission Regulation (EC) No 333/2007[15] amended by Commission Regulation (EU) No 836/2011.[16] The Regulation follows the 'criteria approach'. This means that no prescribed fixed official methods have to be followed, but laboratories can use any method of analysis, provided it can be demonstrated in a traceable manner that it strictly fulfils the analytical requirements laid down in the relevant legislation. The methods used for the determination should be applicable to those foodstuffs specified in Commission Regulation (EC) No 1881/2006,[11] amended by Commission Regulation (EC) No 629/2008.[12] The limit of detection (LOD) is required to be less than one-tenth of the ML (see Section 2) and the LOQ to be less than one-fifth of the ML. The LOD and LOQ will vary with the analytical technique, the sample mass, the laboratory and the food matrix.

When no extraction step is applied in the analytical method (e.g. in the case of metals), the result may be reported uncorrected for recovery if evidence is provided by ideally making use of suitable certified reference material that the certified concentration allowing for the measurement uncertainty is achieved (i.e. high accuracy of the measurement), and thus that the method is not biased. If the result is reported uncorrected for recovery this shall be mentioned. Concerning precision, it is required that the $HORRAT_r$[29] and $HORRAT_R$[30] values are less than 2. The requirement for specificity is given as 'free from matrix or spectral interferences'.

Finally, Commission Regulation (EC) No 333/2007[15] amended by Commission Regulation (EU) No 836/2011[16] sets requirements for reporting results and for the assessment of compliance of the lot or sublots. For this, the analytical result corrected for recovery, if necessary, should be used for checking compliance. The analytical result shall be reported as $x \pm U$, whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2, which gives a level of confidence of approximately 95 %. The lot or sublot is accepted if the analytical result of the laboratory sample does not exceed the respective ML as laid down in Regulation (EC) No 1881/2006,[11] modified by Regulation (EC) No 629/2008,[12] taking into account the expanded measurement uncertainty and correction of the result for recovery, if an extraction step has been applied in the analytical method used.

[29] $HORRAT_r$: The observed relative standard deviation calculated from results generated under repeatability conditions (RSD_r) divided by the RSD_r value estimated from the (modified) Horwitz equation using the assumption that the repeatability r = 0.66R (reproducibility). The Horwitz equation and the modified Horwitz are generalised precision equations which are independent of analyte and matrix but solely dependent on concentration for most routine methods of analysis.

[30] $HORRAT_R$: The observed relative standard deviation calculated from results generated under reproducibility conditions (RSD_R) divided by the RSD_R value calculated from the (modified) Horwitz equation.

To demonstrate the trueness (i.e. systematic error) and precision (i.e. random error) of trace element data, one of the important criteria is the reporting of correct (and precise) data for the mercury content of certified reference materials that closely match the matrix of the samples under investigation (Jorhem, 2004). Several standard or certified reference materials (SRMs and CRMs) are available for both total mercury and methylmercury (Table 3). However, there is a current need for CRMs in other foodstuffs certified in inorganic mercury. The status of certification of the new reference materials can be found on the web sites of the reference material providers.

Table 3: Some standards or certified reference materials relevant to mercury food analysis (in mg Hg/kg dry mass).

Food type	Descriptor (supplier)[(a)]	Total mercury	Methylmercury
Fish and other seafood			
Fish protein	DORM-3 (NRCC)	0.382 ± 0.060[(b)]	0.355 ± 0.056
Dogfish liver	DOLT-4 (NRCC)	2.58 ± 0.22	1.33 ± 0.12
Tuna fish	BCR 463 (IRMM)	2.85 ± 0.16	3.04 ± 0.16
Fish muscle	IAEA 407 (IAEA)	0.222 ± 0.006	0.200 ± 0.012
Oyster tissue	SRM 1566b (NIST)	0.0371 ± 0.0013	0.0132 ± 0.0007
Mussel tissue	SRM 2976 (NIST)	0.0610 ± 0.0036	0.02809 ± 0.00031
Lobster hepatopancreas	TORT-2 (NRCC)	0.27 ± 0.06	0.152 ± 0.013
Mussel tissue	ERM-CE278 (IRMM)	0.196 ± 0.009	
Crab	LGC 7160 (LGC)	0.096 ± 0.034	
Other foodstuffs			
Cabbage	GBW 10014 (IGGE)	0.0109 ± 0.0016	
Chicken	GBW 10018 (IGGE)	0.0036 ± 0.0015	
Rice flour	SRM 1568a (NIST)	0.0058 ± 0.0005	
Spinach leaves	SRM 1570a (NIST)	0.030 ± 0.003	
Skimmed milk powder	BCR 150 (IRMM)	0.0094 ± 0.0017	
White cabbage	BCR 679 (IRMM)	0.0063 ± 0.0014	

(a): NRCC: National Research Council of Canada (Canada); IRMM: Institute for Reference Materials and Measurements (Belgium); IAEA: International Atomic Energy Agency (Austria); NIST: National Institute of Standards and Technology (USA); LGC: LGC (UK); IGGE: Institute of Geophysical Exploration (China).
(b): The uncertainty is usually given as the 95 % confidence interval.

Most of analytical methods published in the literature are to a certain extent in-house validated for total mercury (Cava-Montesinos et al., 2004; Carbonell et al., 2009; Nardi et al., 2009; Torres et al., 2009; da Silva et al., 2010; Xia et al., 2010; Jarzynska and Falandysz, 2011; Millour et al., 2011a; Senila et al., 2011; Djedjibegovic et al., 2012) and methylmercury (Landaluze et al., 2004; Abrankó et al., 2007; Diez and Bayona 2008; Hippler et al., 2009; Jackson et al., 2009; Clémens et al., 2011; Guzman-Mar et al., 2011; He et al., 2011; Nevado et al., 2011). Two fully validated, European standardised methods for determination of total mercury by CV-AAS and ICP-MS detection are available (CEN, 2003, 2010). No standardised methods are available for determination of methylmercury and inorganic mercury, but the European Commission has mandated the European Committee for Standardization (CEN) to establish a standardised method of analysis by isotopic dilution for the determination of methylmercury in food of marine origin (including seaweed).

Some proficiency testing schemes are regularly organised by several providers for both total mercury and methylmercury to demonstrate and maintain analytical quality assurance. In 2010-2011, a proficiency testing on the determination of total mercury in frozen fish was organised by the European Union Reference Laboratory for Chemical Elements in Food of Animal Origin (EURL-CEFAO, ISS, Rome, Italy). All the results of the 28 European National Reference Laboratories (NRLs) were considered satisfactory (EURL-CEFAO, 2011). In 2010, two proficiency tests on the determination of total mercury and methylmercury in seafood and of total mercury in vegetable food were organised for the European NRLs by the European Union Reference Laboratory for Heavy Metals in Feed and Food (Institute for Reference Materials and Measurements (IRMM), Joint Research Centre, Geel, Belgium). Twenty-one out of the 28 participants performed satisfactorily for total mercury in vegetable food

(IMEP 110).[31] Thirty-four out of 35 participants scored satisfactorily for total mercury in the dogfish liver and four out of five results were considered satisfactory for methylmercury (IMEP 109). A parallel proficiency test (IMEP 30) open to all laboratories willing to take part in the exercise was also organised using the same test material. Of the 57 participants (45 from EU), 90 % of the 52 results for total mercury and 89 % of the nine results for methylmercury were considered satisfactory.

Between March and December 2011, the Food Analysis Performance Assessment Scheme (FAPAS) organised seven different proficiency tests: six on the determination of total mercury in canned fish (FAPAS® reports 07156 and 07164), canned crab meat (FAPAS® report 07160), infant cereal (FAPAS® report 07165), milk powder (FAPAS® report 07154) and soy flour (FAPAS® report 07166) and one on the determination of total mercury and methylmercury in canned fish (FAPAS® report 07153). The results indicate that most of the participating laboratories, although applying different methods, are capable of reliably analysing total mercury (range 82 - 98 % satisfactory results, 45 to 98 participants) and methylmercury (100 % satisfactory results, 17 participants) at the level of interest.

Finally, a world-wide proficiency test was conducted by the International Atomic Energy Agency (IAEA) in 2009 to determine total mercury and methylmercury in marine biota (scallop) (IAEA, 2010). Out of the 80 and 20 participating laboratories, 62 showed satisfactory analytical results for total mercury (assigned value 0.15 mg/kg) and 15 laboratories for methylmercury (assigned value 0.0217 mg Hg/kg), respectively.

3.3. Concluding comments

In summary, several analytical techniques are suitable for the determination of mercury in foods. For total mercury, CV-AAS, CV-AFS and increasingly ICP-MS have been used for a wide variety of foodstuffs and two European standardised methods by CV-AAS and ICP-MS detection are available (CEN, 2003, 2010).

GC coupled to MS or ICP-MS are the most widely used techniques for the separation and detection of mercury species. This is due to their multi-element and multi-isotope capabilities which allow for more accurate and precise results by speciated isotope dilution MS, which can also check for species transformations and extraction recoveries. More recently, HPLC techniques are also increasingly being used but, usually, GC methods have higher sensitivity than liquid chromatography. For the moment, no fully validated or standardised methods are available for the separation and detection of mercury species.

Several SRMs and CRMs are available for both total mercury and methylmercury. Regular proficiency testing schemes are organised by several providers for both total mercury and methylmercury in foodstuffs to demonstrate and maintain analytical quality assurance. However, there is a current need to develop CRMs and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood.

4. OCCURRENCE OF METHYLMERCURY AND INORGANIC MERCURY IN FOOD

4.1. Background

Total mercury concentrations in foods, other than fish and other seafood, are in the range < LOD/LOQ – 50 µg/kg. Higher concentrations are observed in fish and other seafood and concentrations up to 11 400 µg/kg were reported by JECFA in 2011 (FAO/WHO, 2011b). The amount of mercury is related to the age of the fish and the position of the fish species within the food chain; predatory fish and older fish having higher concentrations than others. Unlike some contaminants, mercury content is not related to the fat content of the fish and, as such, mercury is not considered a problem associated especially with oily fish. Some fish species that usually have higher concentrations of mercury include

[31] IMEP reports are available from http://irmm.jrc.ec.europa.eu/interlaboratory_comparisons/imep/Pages/index.aspx

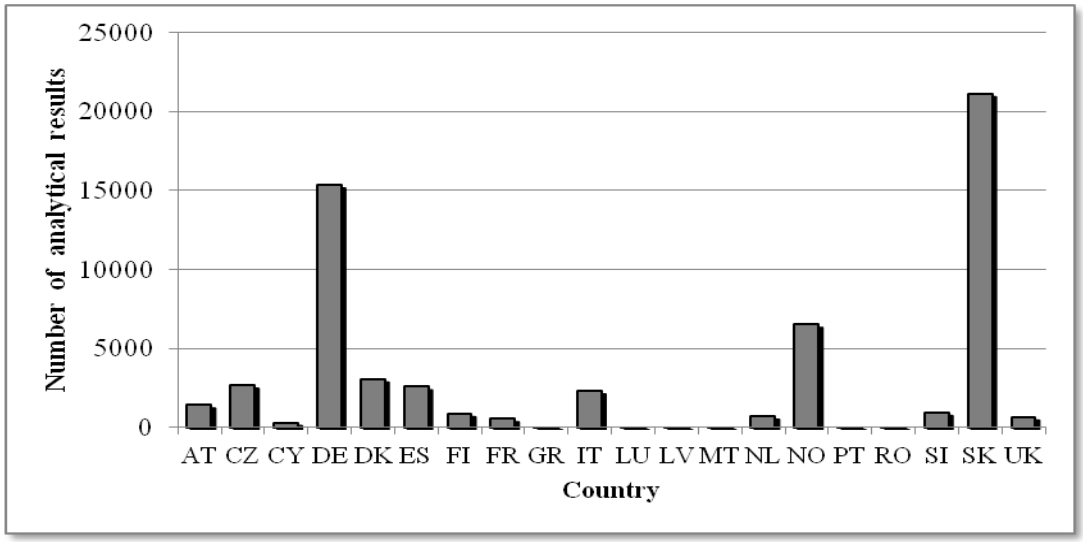
shark, swordfish and marlin. Mercury in these fish species may exceed 1 000 µg/kg. Fresh tuna often contains mercury concentrations between about 100 and 1 500 µg/kg. Predatory freshwater fish are also a source of mercury dietary exposure. Specific ecosystem characteristics contribute to the variability in mercury concentration (Munthe et al., 2007). A table listing mean content of mercury (plus certain nutrients and dioxins) of 103 species of fish is presented as Appendix A of the report of the WHO risk benefit assessment for fish consumption (FAO/WHO, 2011a).

4.2. Occurrence results reported to EFSA

Since the exposure assessment in the previous EFSA opinion on mercury and methylmercury of 2004 (EFSA, 2004) was based on a very limited number of data from a SCOOP exercise,[13] it was decided that there was a need for a new data collection, covering the years from 2006. Following a European Commission mandate to EFSA, a call for annual collection of chemical contaminant occurrence data in food and feed, including mercury, was issued by EFSA in December 2010 with a closing date of 1 October of each year. In response EFSA has received a total of 59 820 results from testing of the presence of mercury in food from 20 European countries. The data reported represent the period from 2002 to 2011, although the call for data was originally limited to the period from 2006 to 2011.

4.2.1. Data collection summary

The source of 59 820 analytical results for mercury submitted by 20 European countries is illustrated in Figure 1. Slovakia reported 35.4 % of the data followed by Germany (25.8 %) and Norway (11 %).



Legend: AT: Austria; CY: Cyprus; CZ: Czech Republic; DE: Germany; DK: Denmark; ES: Spain; FI: Finland; FR: France; GR: Greece; IT: Italy; LV: Latvia; LU: Luxembourg; MT: Malta; NL: the Netherlands; NO: Norway; PT: Portugal; RO: Romania; SI: Slovenia; SK: Slovakia; UK: United Kingdom.

Figure 1: The number of reported analytical results for mercury across European countries.

Overall, 58 730 (98.2 %) of the analytical results were reported for total mercury, 1 087 (1.8 %) for methylmercury and only three samples were reported for inorganic mercury. Data on methylmercury were provided by four countries: Germany (788 results), Spain (206 results), Czech Republic (90 results) and Slovakia (three results).

The data provided were sampled in the period 2002 - 2011, with only 55 results covering the period before 2004. The distribution of the results over the years of sampling is shown in Figure 2.

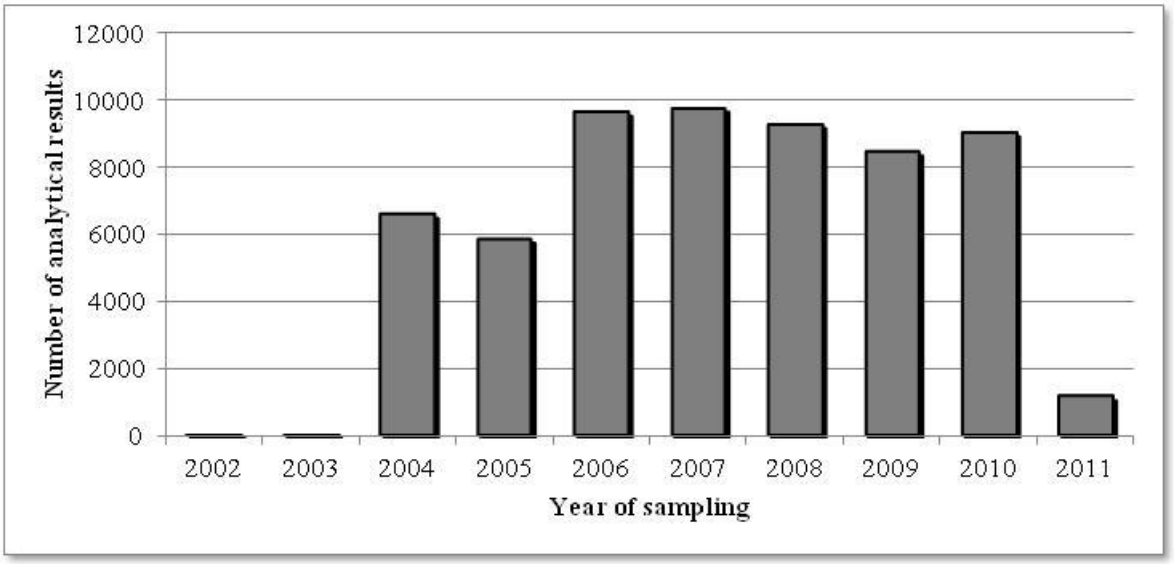


Figure 2: The number of reported analytical results for mercury over years of sampling (note that 2011 was not a complete year of sampling).

A total of 170 samples were excluded from further analysis during the data cleaning steps as they provided incomplete or incorrect description of food type or unit of measure. Some data from fish were excluded because they showed insufficient sensitivity of the analytical method (a LOD of more than 50 µg/kg or a LOQ of more than 100 µg/kg). The cut-off value of left-censored (LC) data was determined according to the criteria defined in Commission Regulation (EC) No 836/2011,[16] amending Commission Regulation (EC) No 333/2007,[15] which defines that the LOD for mercury should be equal to or less than one-tenth of the ML and the LOQ should be equal to or less than one-fifth of the ML. The ML of 0.5 mg/kg w.w. for a range of fishery products and muscle meat of fish set by Commission regulation (EC) No 629/2008,[12] amending Commission Regulation (EC) No 1881/2006,[11] was used.

A total number of 59 650 results were described with sufficient detail to be used in the statistical analysis of the respective food groups; 58 560 samples were analysed for total mercury (98.2 %), 1 087 samples (1.8 %) for methylmercury and three samples for inorganic mercury.

4.2.2. Distribution of samples across food categories

The data providers were asked to codify all food descriptors according to the EFSA FoodEx 1 Classification system (EFSA, 2011a).

FoodEx 1 (hereinafter referred to as 'FoodEx') is a provisional food classification system developed by the EFSA Dietary and Chemical Monitoring Unit (DCM, formerly DATEX) in 2009 with the objective of simplifying the linkage between occurrence and food consumption data when assessing dietary exposure to hazardous substances.[32] It contains 20 main food categories (FoodEx Level 1), which are further divided into subgroups having 140 items at the FoodEx Level 2, 1 260 items at the FoodEx Level 3 and reaching about 1 800 endpoints (food names or generic food names) at the FoodEx Level 4. It is based on a hierarchical coding for an easier cross-checking and it is structured in a child-parent relationship, as illustrated in Figure 3.

The distribution of analytical results across the different food groups for total mercury and methylmercury is illustrated in Figure 4.

[32] Recently, the FoodEx 2 classification system has been developed and is available now for future applications, but for this opinion the previous version (FoodEx 1) was used. Further information on FoodEx 2 is available at http://www.efsa.europa.eu/en/supporting/doc/215e.pdf

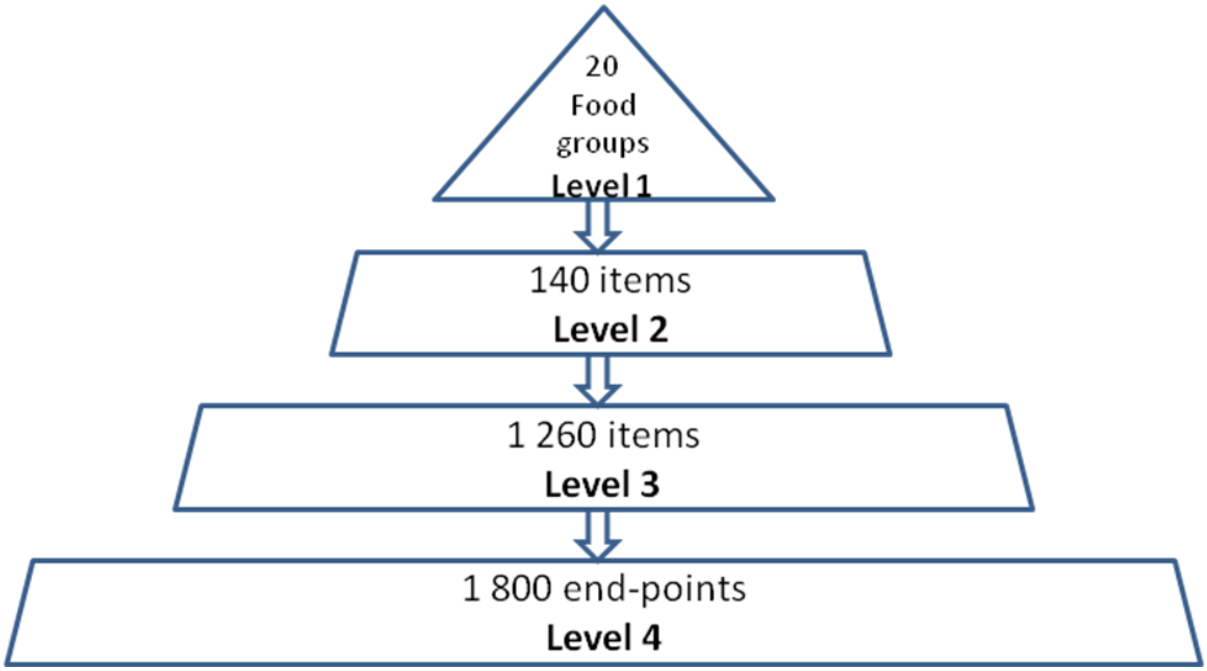


Figure 3: Hierarchy of the FoodEx food classification system.

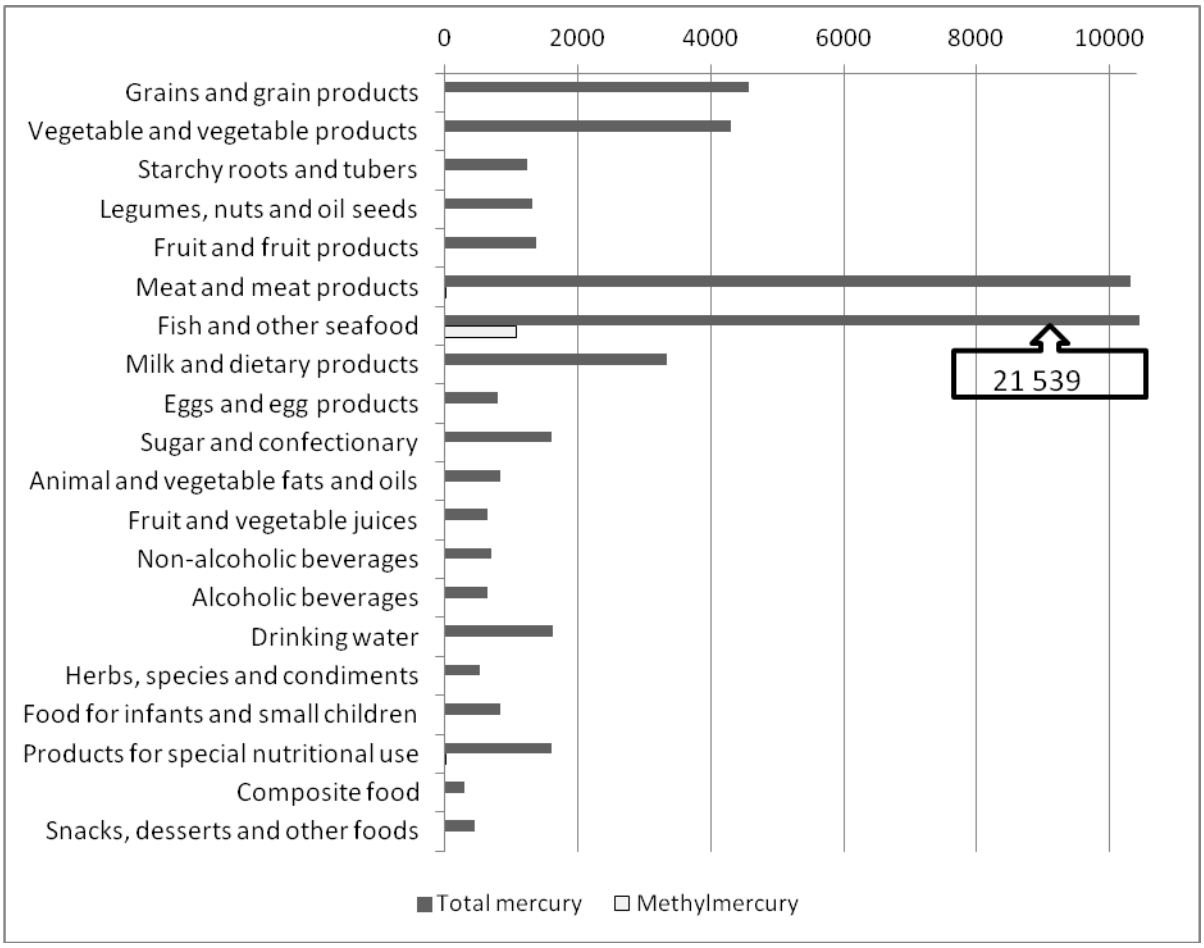


Figure 4: The number of mercury analytical results reported for food groups according to the FoodEx Level 1 (the arrow indicates the number of mercury analytical results for fish and other seafood).

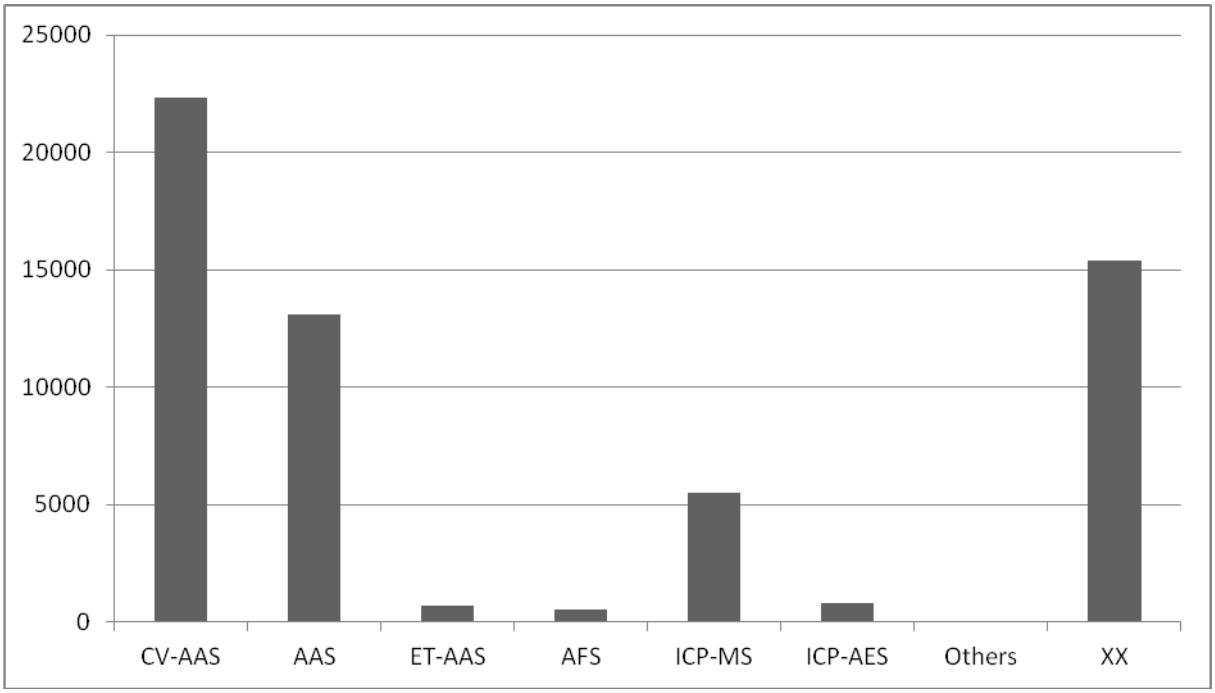
Regarding total mercury analyses, all the 20 food groups available at the first level of FoodEx were covered in the current data collection. The food groups 'Fish and other seafood (including amphibians, reptiles, snails and insects)' (hereinafter referred to as 'Fish and other seafood') and 'Meat and meat products' dominated the food product coverage, with 36.8 % and 17.6 % respectively. These were followed by 'Grain and grain-based products' at 7.8 % and 'Vegetables and vegetable products (including fungi)' at 7.3 %. Regarding more detailed levels of the FoodEx classification for 'Fish and other seafood', the most analysed food category at Level 2 was 'Fish meat' (13 737 results). Salmon and trout[33] (1 741 results) and halibut (1 713 results) were the most reported fish species at FoodEx Level 3.

The lowest number of samples (fewer than 500) of total mercury was reported for the food groups 'Composite food (including frozen products)' and 'Snacks, desserts and other food'.

All analytical results were reported on a wet weight basis.

4.2.3. Analytical methods used

The original results were reported in mg/kg (95 %), in mg/L (3 %), in µg/kg (1.9 %), in µg/L (0.7 %), in ng/g (0.025 %) and one result in mg/100 g. All the measurements were converted to µg/kg. For the measurements expressed as a volume unit, the approximate equivalence of 1 kg = 1 L has been used. As demonstrated in Figure 5, the most commonly used method for total mercury analysis was CV-AAS with 38 %, followed by unspecified AAS technique(s) with 22 %. In 26 % of the cases, no information was provided on the analytical method used. Since so many of the results lacked a description of the analytical method, it was not meaningful to cross-tabulate the food matrix results with the analytical method.



Legend: AAS – atomic absorption spectrometry (unspecified); AFS - atomic fluorescence spectrometry (unspecified); CV-AAS - cold vapour - atomic absorption spectrometry; ET-AAS – electrothermal atomic absorption spectrometry; ICP-AES - inductively coupled plasma atomic emission spectrometry; ICP-MS - inductively coupled plasma mass spectrometry; XX: analytical method not specified.

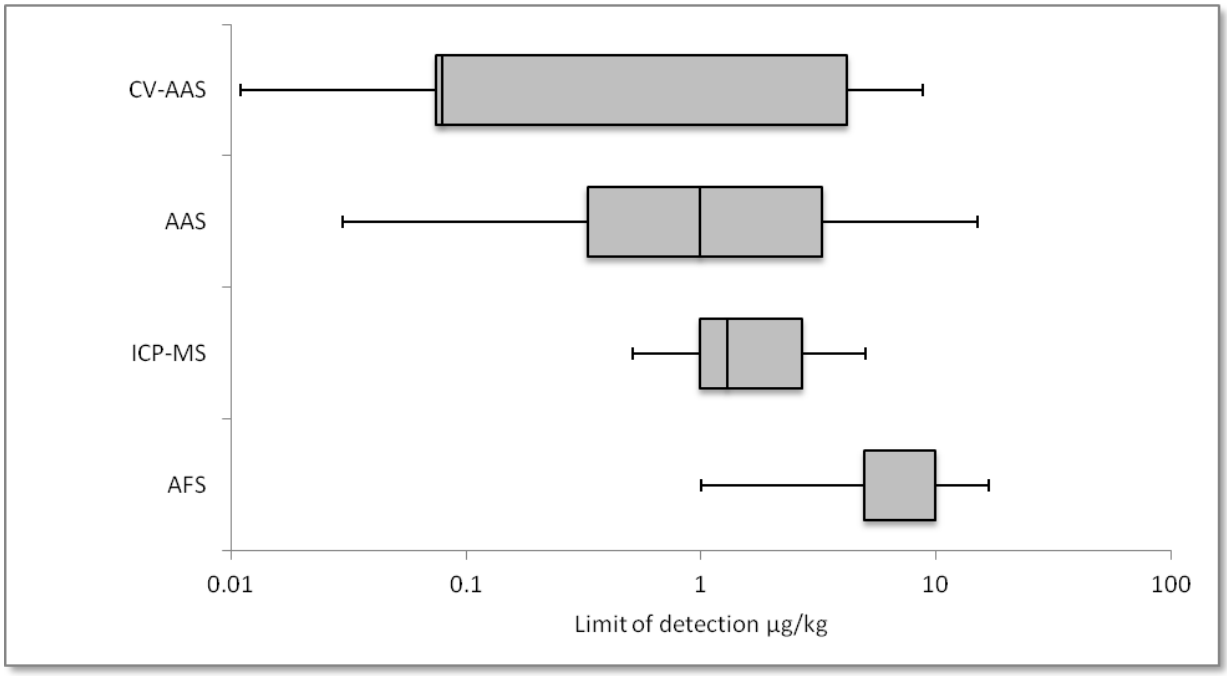
Figure 5: Distribution of analytical methods used for total mercury analysis.

[33] These species are reported as one category at FoodEx Level 3.

Regarding methylmercury, complete information on the separation technique was not always obtained. For 73 % of analytical results the analytical method was not specified, while in 16 % AAS and in 9 % ICP-MS were reported as the detection method used, but the separation technique was not given. For 30 methylmercury results HPLC was indicated as a separation technique hyphenated with an unspecified detector.

Overall, 44 % of the results for total mercury and 14 % of the results for methylmercury were LC, meaning below LOD or LOQ. For 17 % of the LC data, the LOD was not reported; in these cases the LOD was replaced by the reported LOQs divided by a conversion factor of two in accordance with Commission Regulation (EC) No 836/2011[16] amending Regulation (EC) No 333/2007.[15] Since it is not mandatory to report LOD or LOQ when the value is quantified, 7 218 results were not included in the analysis of LODs (Figures 6 and 7).

The LODs varied with the analytical technique (Figure 6), the laboratory (not shown) and the food group (Figure 7). As mentioned above, according to the performance criteria defined in legislation, the LOD for mercury should be equal to or less than one-tenth of specified MLs. However, performance characteristics for the analytical quantification of mercury are set by legislation only for the analysis of fish and some other seafood for human consumption. There is no current legislation defining the performance characteristics for analytical methods applied to any other food group; laboratories are therefore free to modify the analytical methods to be fit for purpose for the particular set of samples tested. This may be a reason for some of the differences observed.



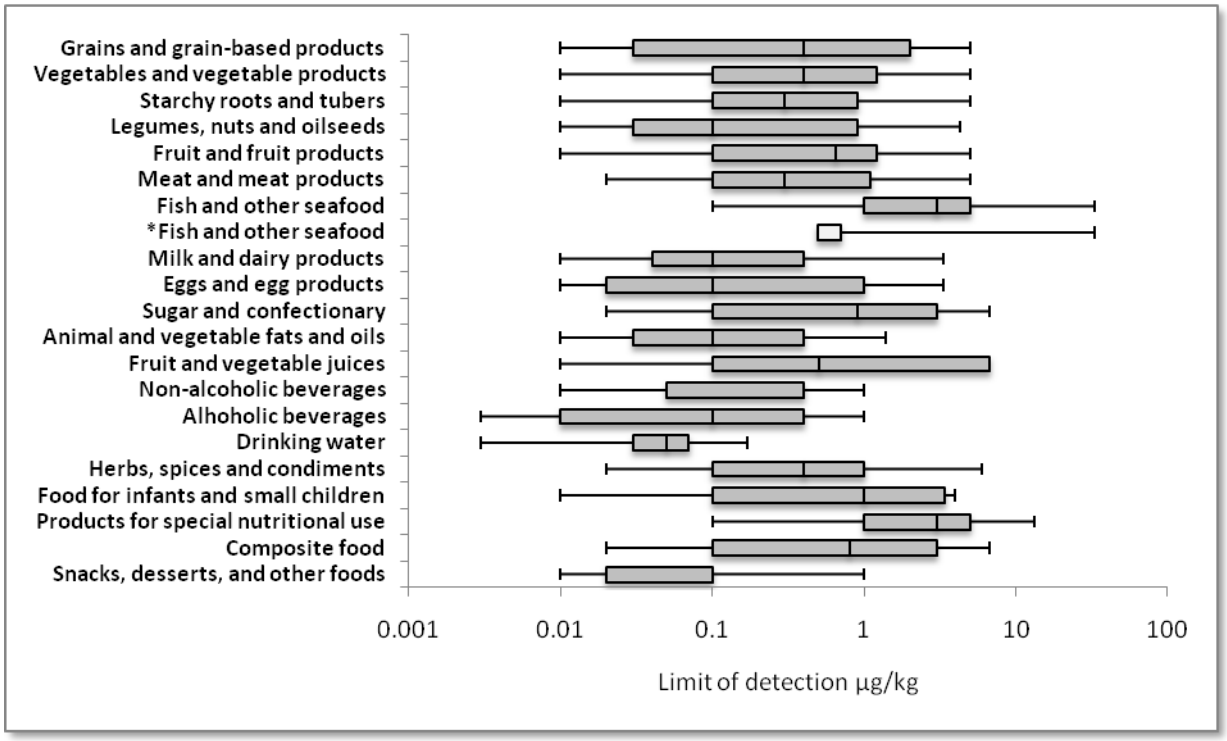
Legend: AAS – atomic absorption spectrometry (unspecified); AFS - atomic fluorescence spectrometry (unspecified); CV-AAS - cold vapour - atomic absorption spectrometry; ICP-MS - inductively coupled plasma mass spectrometry. Number of missing results = 24 878; Box-plot: whiskers at P5 and P95, box at P25 and P75 with line at P50

Figure 6: Distribution of the LOD for total mercury according to the most commonly used analytical methods as reported by laboratories.

Concerning the analytical methods for total mercury, the laboratories using CV-AAS reported the lowest LODs with a median of 0.08 µg/kg (Figure 6). On the other hand, higher LODs were shown in the samples analysed by unspecified AFS (median of 10 µg/kg). A limited number of data on LOD were obtained for electrothermal atomic absorption spectrometry (ET-AAS) and inductively coupled plasma atomic emission spectroscopy (ICP-AES). The LOD range for the ET-AAS was

0.5 - 33.3 µg/kg. The LOD for the ICP-AES was reported for all results at a concentration of 6.6 µg/kg.

Concerning methylmercury analyses, lower LODs were achieved by ICP-MS (median of 0.66 µg/kg) while higher LODs were observed for AAS (median of LOD of 33.3 µg/kg). The sensitivity of the method is often set by the laboratory to fulfil legislative requirements for mercury in fish. The extra cost and time to fine-tune the method to achieve optimally low LODs may not be warranted. This is satisfactory for routine monitoring purposes, but does cause slight problems when results are used also to calculate human dietary exposure since high LODs for LC data might increase the upper bound (UB) exposure estimates.



Legend: *: data on methylmercury; box-plot: whiskers at P5 and P95, box at P25 and P75 with line at P50.

Figure 7: Distribution of the LOD for total mercury and methylmercury according to the FoodEx Level 1.

The lowest LODs were shown for the food group 'Drinking water' with a median of 0.05 µg/kg followed by 'Legumes, nuts and oilseeds', 'Milk and dairy products', 'Eggs and egg products', 'Animal and vegetable fats and oils', 'Alcoholic beverages' and 'Snacks, desserts, and other foods' with a median of 0.1 µg/kg. On the other hand, the highest LOD is observed in 'Fish and other seafood' with a median of 3 µg/kg for total mercury and 0.5 µg/kg for methylmercury.

4.2.4. Occurrence data on total mercury by food category

The proportions of LC and quantified results in the 20 food groups at FoodEx Level 1 are shown in Figure 8.

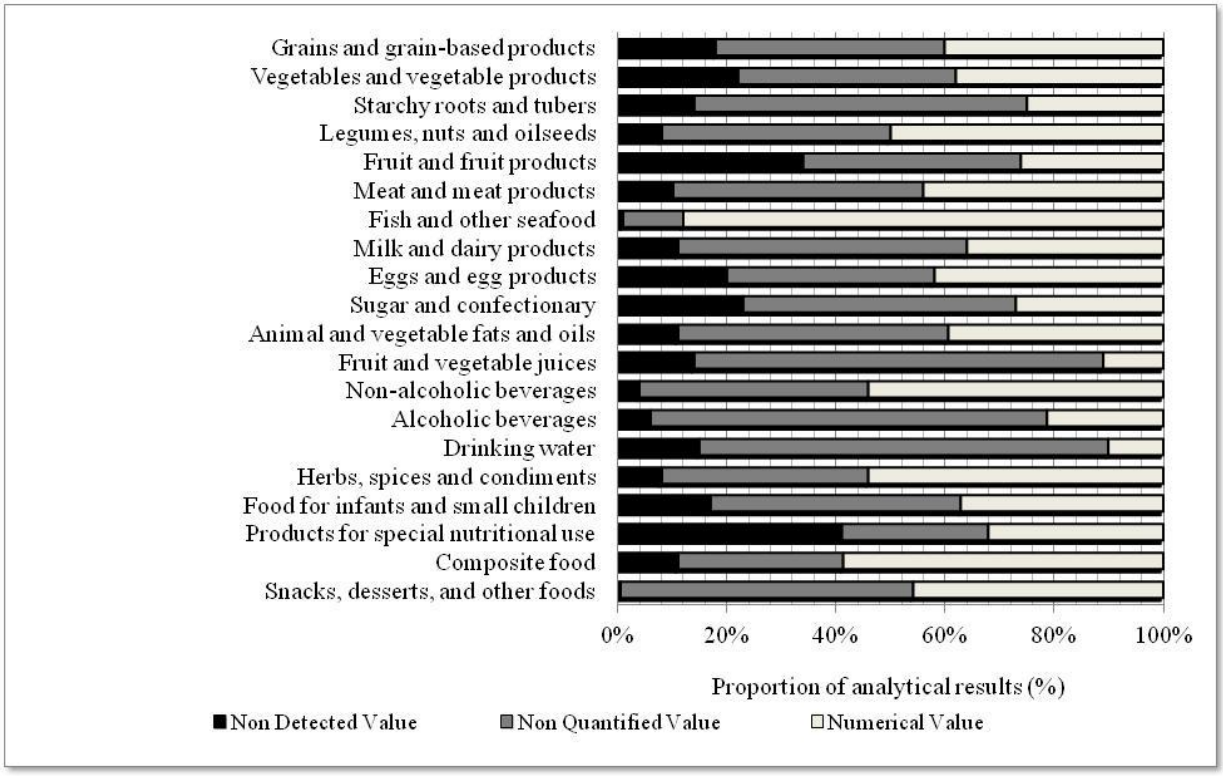


Figure 8: Proportion of quantified results and results below the limits of detection or quantification for total mercury reported for individual food groups according FoodEx Level 1.

Since the proportion of quantified results was below 40 % in 11 food groups (Figure 8), the handling of the LC data was carefully considered. As recommended in the 'Principles and Methods for the Risk Assessment of Chemicals in Food' (WHO, 2009) and in the EFSA scientific report 'Management of LC data in dietary exposure assessment of chemical substances' (EFSA, 2010) the substitution method was applied for the treatment of LC data. The lower bound (LB) was obtained by assigning a value of zero to all the samples reported as less than the LC limit, the middle bound (MB) by assigning half of the LC limit and the UB by assigning the LC limit as the sample result.

Table 4 provides a summary of occurrence data on total mercury including the number of results reported and statistical descriptors of the results (proportion of LC data in %, mean, and 95th percentile for LB, MB and UB results). More details on statistical description are reported in Appendix A, Table A1-A24.

Table 4: Summary of the total mercury occurrence data by food group (µg/kg).

Food category, Level 1	N	% LC	Mean			P95		
			LB	MB	UB	LB	MB	UB
Grains and grain-based products	4 545	60	0.9	2.0	3.1	4.0	5.3	10
Vegetables and vegetable products	4 299	62	6.0	7.0	7.8	8.3	10	11
Starchy roots and tubers	1 234	75	0.2	0.8	1.4	0.8	2.5	5.0
Legumes, nuts and oilseeds	1 311	51	2.3	2.8	3.3	9.6	10	10
Fruit and fruit products	1 368	74	0.3	1.2	2.1	1.0	5.0	9.6
Meat and meat products	10 304	56	1.9	2.7	3.5	9.0	10	11
Fish and other seafood	21 539	12	131	133	136	540	540	540
Milk and dairy products	3 345	64	0.9	1.5	2.1	4.3	8.0	11
Eggs and egg products	798	58	0.6	1.2	1.8	3.2	4.6	6.3
Sugar and confectionery	1 617	73	0.6	2.6	4.7	2.9	10	20
Animal and vegetable fats and oils	835	61	1.1	1.6	2.0	6.0	6.0	6.0
Fruit and vegetable juices	651	89	0.1	3.2	6.2	0.4	10	20
Non-alcoholic beverages	699	46	3.4	4.0	4.5	16	16	20
Alcoholic beverages	652	79	0.1	0.4	0.7	0.3	1.0	2.0
Drinking water	1 637	90	0.0	0.1	0.2	0.1	0.3	0.5
Herbs, spices and condiments	529	47	3.1	4.3	5.5	10	13	20
Food for infants and small children	834	63	0.6	1.6	2.5	3.0	5.0	6.0
Products for special nutritional use[(a)]	1 608	68	96	99	102	35	38	43
Composite food	304	41	16	18	19	59	59	59
Snacks, desserts, and other foods	451	54	1.2	1.5	1.9	3.0	4.7	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Note that mean values are higher than P95 values because of a heavily right-skewed distribution of the data.

Tables 5 and 6 provide summaries of occurrence data for the 'Fish and other seafood' category split into the FoodEx Level 2 and Level 3, respectively, with the number of results reported and statistical descriptors of the results (proportion of LC data in %, mean and 95th percentile for LB, MB and UB results). In cases where the number of results is less than 60, the 95th percentile descriptor should be considered indicative only, owing to the limited number of data (EFSA, 2011b).

Since a few very high values heavily influenced the estimated mean value a specific analysis of such values was carried out. Those very high results did not show a uniform trend and were spread across reporting countries and food groups. When the mercury concentration was ten times higher than the second highest value within the same subcategory and influenced significantly the mean, the result was considered as an outlier and excluded from the calculation. Moreover, several extremely high values were considered as erroneously reported, a view supported by literature data on mercury concentration (WHO, 2008; Spada et al., 2012), and therefore excluded. In total, nine samples have been eliminated following these criteria. Four samples in the food group 'Fish and other seafood' were excluded because of extremely high concentrations: three samples of swordfish reported to contain mercury at 1.5 g/kg, 1.2 g/kg and 1.2 g/kg, and one sample of shark reported to contain mercury at 14 600 µg/kg. It was considered unlikely from a biological point of view to be real data and therefore with a high probability of having been erroneously reported. Another five samples excluded from other food groups because of extremely high concentrations and because of significant influence on the mean were: (i) two samples of products for special nutritional use, with reported mercury content of 2.3 g/kg and 0.52 g/kg, originating from India, (ii) one sample of lettuce reported to contain 10 001 µg/kg, (iii) one sample of confectionery (not-chocolate) reported to contain 1 000 µg/kg, and (iv) one sample of poultry mixed meat reported to contain 498 µg/kg. Since some genuine or occasional causes may lead to high mercury contamination, for example in old large predatory fish, in specific species of wild mushrooms and in herbal dietary supplements some moderately high results were kept in the database.

The 'Fish and other seafood' category comprises a total of 21 539 analytical results on total mercury divided into six subcategories at FoodEx Level 2 (Table 5). Two groups of unspecified fish and seafood samples were identified in the dataset: (i) within the FoodEx Level 1, in a group of 1 968 samples for which the specification at FoodEx Level 2 was missing (these results were for dietary exposure calculation matched to consumption data at FoodEx Level 1, Table 5); (ii) within the FoodEx Level 2 a group of 1 502 samples for which the specification at FoodEx Level 3 was missing and these data were replaced by overall concentration reported in specified fish species, as explained later (Table 6 and Section 6.1).

Table 5: Statistical description of concentrations of total mercury for the six FoodEx Level 2 subgroups of the food group 'Fish and other seafood' in µg/kg.

Food category Level 2	N	% LC	Mean			P95[(b)]		
			LB	MB	UB	LB	MB	UB
Fish and other seafood, unspecified (FoodEx1[(a)])	1 968	3	100	100	101	273	273	273
Fish meat	13 737	7	177	178	180	710	710	710
Fish products	241	8	37	38	38	109	109	109
Fish offal	158	58	12	19	26	67	67	70
Crustaceans	1 478	21	43	47	50	189	189	189
Molluscs	3 926	26	31	36	41	100	100	100
Amphibians, reptiles, snails, insects	31	48	19	20	21	140	140	140

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Data available only on FoodEx Level 1.
(b): The 95th percentile obtained on occurrence data with fewer than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore is considered only indicative.

As shown in Table 4 the 'Fish and other seafood' category was the one that recorded the highest values of total mercury in comparison to all other food categories. This is very much driven by high mean values in the fish meat category, as can be seen in Table 5. The LB, MB and UB mean values of total mercury content in 'Fish meat' were all around 180 µg/kg, with the 95th percentile at 710 µg/kg. The maximum value recorded in this category was for a sample of unspecified fish meat with a total mercury concentration of 6 890 µg/kg (Appendix A, Table A8). Further descriptive statistics of concentration of total mercury for the food group 'Fish and other seafood' at FoodEx Level 2 are presented in more detail in Appendix A, Table A8.

The food category 'Fish meat' split at FoodEx Level 3 is described in more detail in Table 6.

Table 6: Statistical description of concentrations of total mercury in the FoodEx Level 3 food categories of 'Fish meat' in µg/kg.

Fish species[(a)], FoodEx Level 3	N	% LC	Mean			P95[(b)]		
			LB	MB	UB	LB	MB	UB
Anchovy	110	33	73	83	92	200	200	200
Angler fish	61	30	186	195	204	551	551	551
Barbel	10	0	211	211	211	n/a	n/a	n/a
Barracuda	1	0	340	340	340	n/a	n/a	n/a
Bass	78	10	199	203	206	698	698	698
Bonito	25	8	580	583	586	1 920	1 920	1 920
Bream	253	11	224	225	226	883	833	883
Capelin	11	82	2.0	5.0	8.0	n/a	n/a	n/a
Carp	338	5	55	55	55	194	194	194
Char	8	0	32	32	32	n/a	n/a	n/a
Cod and whiting	1 308	18	91	94	96	340	340	340

Table 6: Continued.

Fish species[a], FoodEx Level 3	N	% LC	Mean			P95[b]		
			LB	MB	UB	LB	MB	UB
Dentex	3	0	2 019	2 019	2 019	n/a	n/a	n/a
Eel	487	2	177	178	178	461	461	461
Flounder	23	17	85	91	97	185	185	185
Garfish	3	0	1 180	1 180	1 180	n/a	n/a	n/a
Grenadier	3	0	104	104	104	n/a	n/a	n/a
Grey mullet	52	23	152	159	167	566	566	566
Grouper	2	0	195	195	195	n/a	n/a	n/a
Gurnard	4	25	103	109	116	n/a	n/a	n/a
Hake	131	16	130	136	142	420	420	420
Halibut	1 713	0	209	209	209	610	610	610
Herring	1 272	0	36	36	36	78	78	78
Jack mackerel	3	0	127	127	127	n/a	n/a	n/a
John Dory	6	0	302	302	302	n/a	n/a	n/a
Lizardfish	2	0	611	611	611	n/a	n/a	n/a
Luvarus	1	0	590	590	590	n/a	n/a	n/a
Mackerel	1 348	5	106	108	109	520	520	520
Meagre	2	50	145	170	195	n/a	n/a	n/a
Perch	423	0	165	165	165	370	370	370
Pike	267	0	394	394	394	979	979	979
Plaice	194	2	64	64	65	160	160	160
Ray	32	3	229	229	230	1 170	1 170	1 170
Redfish	221	0	189	189	189	676	676	676
Roach	17	0	122	122	122	n/a	n/a	n/a
Salmon and trout	1 741	7	31	33	35	57	57	70
Sardine and pilchard	399	18	32	38	44	116	116	116
Scorpion fish	1	0	422	422	422	n/a	n/a	n/a
Sea bass	10	0	300	300	300	n/a	n/a	n/a
Sea catfish and wolf-fish	67	54	103	109	114	770	770	770
Shad	1	0	173	173	173	n/a	n/a	n/a
Shark	272	11	688	691	695	1 900	1 900	1 900
Smelt	2	0	325	325	325	n/a	n/a	n/a
Sole	49	24	69	77	84	180	180	180
Sprat	107	1	21	21	21	50	50	50
Sturgeon	4	50	40	52	65	n/a	n/a	n/a
Swordfish	264	5	1 210	1 212	1 214	3 300	3 300	3 300
Tuna	849	5	286	290	291	850	850	850
Turbot	4	0	62	62	62	n/a	n/a	n/a
Weever	11	0	763	763	763	n/a	n/a	n/a
Whitefish	37	16	77	85	93	250	250	250
Wrasse	12	0	511	511	511	n/a	n/a	n/a
Fish meat, unspecified[c]	1 502	10	279	280	280	1 194	1 194	1 194
Fish meat, overall[d]	12 235	10	164	166	168	499	500	501

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): Common names and Latin names reported in the Glossary

(b): The 95th percentile obtained on occurrence data with fewer than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore is considered only indicative.

(c): Data reported as fish meat without further specification.

(d): Data calculated on overall concentrations of individual specified fish species.

As shown in Table 6, the mercury content varied widely among different fish species, depending on the size and feeding habits, and as expected, was higher in predatory fish. This is in line with the results from other studies showing a higher mercury concentration in older predatory fish species (WHO, 2008). Considering only fish species with a sufficient number of results reported (N ≥ 25), the highest mean concentrations were found in swordfish (MB mean = 1 212 µg/kg) and in shark (MB mean = 691 µg/kg). Very high mean values were also recorded in dentex, garfish and weever, but because of the very low number of samples analysed for these species, the results may be considered only as indicative. Further descriptive statistics of the concentration of total mercury across the fish species and in unspecified fish meat is presented in more detail in Appendix A, Table A9.

4.2.5. Occurrence data on methylmercury

Methylmercury was analysed in 1 083 samples for 'Fish and other seafood' category in five subcategories of FoodEx Level 2 (Appendix A, Table A10).

Similarly to total mercury, for FoodEx Level 2 the highest methylmercury concentration was reported in 'Fish meat' (MB mean = 135 µg/kg), followed by 'Crustaceans' (MB mean = 102 µg/kg). Owing to the low number of reported results, especially for the most important contributing fish species, it was not possible to clearly identify the fish species with the highest content of methylmercury. The statistical description of reported results is summarised in Appendix A, Table A11.

4.2.6. Relationship between concentrations of total mercury and methylmercury in data reported to EFSA

A total of 377 samples from the dataset submitted to EFSA were analysed both for total mercury and methylmercury. In order to assess whether the contribution of methylmercury to total mercury is in line with the literature data, the mean (± standard deviation (SD)) and the range of the contributions were calculated in 239 samples reported as quantified data. The summary from these calculations covering various fish species, crustaceans, molluscs and fish products are reported in Table 7.

Table 7: Description of the contribution of methylmercury to total mercury for quantified results.

Food category	N	Mean	SD	Range
Angler fish	2	0.89	0.01	0.88-0.89
Anchovy	1	0.85	-	-
Bass	2	0.91	0.37	0.61-1.00
Bream	2	0.90	0.14	0.81-1.00
Carp	26	0.71	0.24	0.28-1.00
Cod and whiting	1	0.67	-	-
Eel	3	1.23	0.30	0.95-1.55
Grey mullet	1	0.81	-	-
Hake	3	0.92	0.13	0.77-1.00
Halibut	9	0.95	0.37	0.58-1.88
Mackerel	29	1.04	0.28	0.50-2.05
Salmon and trout	14	0.87	0.26	0.41-1.33
Sardine and pilchard	2	0.92	0.00	0.91-0.92
Shark	4	0.81	0.04	0.79-0.87
Tuna	45	0.80	0.31	0.27-1.73
Fish meat, unspecified	53	0.89	0.38	0.03-1.92
Crustaceans	10	0.95	0.09	0.74-1.00
Fish products	29	0.78	0.17	0.39-1.17
Molluscs	2	0.85	0.21	0.69-1.00

N: number of results; SD: standard deviation.

Taking into account the individual measurement uncertainties of total mercury and methylmercury results, it is expected that some contributions of methylmercury to total mercury exceeded 100 %, but a contribution above 130 - 140 % is considered inaccurate. This may have influenced the mean

contributions calculated at species level (e.g. for eel) but since a low number of samples were affected overall (n = 15), this was not investigated further.

4.3. Previously reported occurrence results

There is an extensive quantity of data in the literature as regards total mercury in food, although there is less for methylmercury. All the analytical results are reported on a wet weight basis unless otherwise specified.

4.3.1. Occurrence in fish and other seafood

There are many publications giving results for only total mercury in fish and seafood. These papers are in general agreement with each other as regards occurrence, and they are also in agreement with the data reported above in Section 4.2. Selected studies are summarised below to reflect a broad overview of previously reported data from different fish species and from different geographical locations.

In Bosnia and Herzegovina, total mercury concentrations in muscle of six fresh fish species decreased in the following order: mullet > chub > brown trout > common carp > rudd > Prussian carp and were in the range 6 - 611 µg/kg (mean ranges 50 - 401 µg/kg) (Djedjibegovic et al., 2012).

In Italy, total mercury concentrations were measured in edible marine species (18 fish, five cephalopod molluscs, three crustaceans) collected in the Adriatic Sea (Storelli, 2008). Maximum concentrations corresponded to fish (70 - 1 560 µg/kg), followed by cephalopod molluscs (100 - 550 µg/kg) and crustaceans (270 - 330 µg/kg). In 2010, the analysis of total mercury in the flesh and hepatopancreas of 320 cephalopod molluscs sampled in the southern Adriatic Sea indicated that mercury concentrations were equally distributed in the two tissues, hepatopancreas and flesh (Storelli et al., 2010a). Regarding the edible portion (flesh), the highest concentrations were in Octopodidae (440 µg/kg) and Sepiidae (270 µg/kg), while Loliginidae tended to accumulate less mercury (110 µg/kg). Total mercury concentrations in 20 fresh bluefin tuna (*T. thynnus*) and in 45 popular brands of canned tuna were also determined by Storelli et al. (2010b) and ranged from 70 to 1 760 µg/kg (average 610 µg/kg) in fresh tuna and from 40 to 1 790 µg/kg (average 410 µg/kg) in canned tuna. In 32 samples of the most popular brands of salted anchovies (*Engraulis encrasicolus*) from the Mediterranean Sea (n = 20) and Atlantic Ocean (n = 12), total mercury concentrations ranged from 50 to 510 µg/kg (average 240 µg/kg) and from 50 to 350 µg/kg (average 170 µg/kg), respectively (Storelli et al., 2011).

In France, of the 1 319 food samples analysed for the second total diet study (TDS) (Millour et al., 2011b), only 5 % of total mercury values were quantified (LOQ of 10 µg/kg). The highest mean concentration (45 µg/kg) was found in the group 'Fish and fish products'. In fish, the mean content was 65 µg/kg and oven cooked tuna was found to have the highest concentrations on average (476 µg/kg, maximum 702 µg/kg). 'Shellfish' had a mean concentration of 19 µg/kg with highest concentrations found in shrimps (mean 26 µg/kg, maximum 40 µg/kg) and mussels (mean 15 µg/kg and maximum 32 µg/kg). For oysters and scallops, the mean concentrations were close to the LOQ (12 µg/kg and 10 µg/kg, respectively). Total mercury contents were quantified in 97 % of samples (LOQ of 40 µg/kg) in white and brown meat of 108 batches of crustaceans (lobsters, spider crabs, common crabs, swimming crabs and king crabs) from France (Noël et al., 2011a). In white meat, the mean mercury concentrations ranged from 76 µg/kg for king crabs to 151 µg/kg for swimming crabs. The concentration obtained was within the range of typical concentrations found in crustacean muscle (20 - 200 µg/kg) (Francesconi, 2007). The highest concentrations were found in common crabs in both white meat (465 µg/kg) and brown meat (331 µg/kg). Among 118 batches of marine gastropods, echinoderms and tunicates, 94 % were below the LOQ of 40 µg/kg (Noël et al., 2011b). Mercury was quantified only in marine gastropods. Mean mercury concentrations ranged from 40 µg/kg in common winkles and abalone to 71 µg/kg in murex where the highest concentration was found (185 µg/kg). Another French study of total mercury in eight shark species indicated that 5 out of 91 samples exceeded the ML of 1 000 µg/kg, ranging from 2 430 to 4 780 µg/kg (Velge et al., 2010). In 67 fish

(Artic charr) from four lakes located in the French Alps, total mercury muscle concentrations did not exceed 500 µg/kg (Marusczak et al., 2011).

In the UK TDS (Rose et al., 2010), the highest mean total mercury was found in fish (56 µg/kg).

In Alaska, United States of America (USA), mercury concentrations were overall ≤ 1 000 µg/kg in 17 freshwater fish species and 24 anadromous and marine fish species, for a total of 2 692 specimens (Jewett and Duffy, 2007). Northern pike contained the highest muscle mercury values, whereas Pacific salmon had low mercury concentrations (≤ 100 µg/kg) and Pacific halibut contained less than 300 µg/kg. The amount of mercury present in canned tuna purchased in Las Vegas, Nevada, USA indicated that chunk white tuna (619 ± 212 µg/kg) and solid white tuna (576 ± 178 µg/kg) were both statistically significantly ($p < 0.001$) higher in mean mercury than chunk light tuna (137 ± 63 µg/kg) (Gerstenberger et al., 2010).

Most of the methylmercury occurrence data available in the literature concern fish and sometimes other seafood products. Some of the previously reported methylmercury data quantified in fish and other seafood since 2000 and the percentage of methylmercury are summarised in Table 8 and at a fish species level in Appendix B (Tables B1 and B2).

Table 8: Comparison of the range (mean) and percentage of methylmercury quantified in fish and shellfish (µg Hg/kg wet weight).

Group	Origin	Number species	Number samples	MeHg	THg or ∑Hg species	% MeHg	References
Fish							
	Belgium	15[b]	170	43-598	39-613	91-98	Baeyens et al. (2003)
	Czech Republic	1[a]	96	33-362	39-384 (128)	76-90 (82)	Kružíková et al. (2008)
	France	3[b]	28	28-588 (90)	30-642 (97)	84-97 (93)	Clémens et al. (2011)
	France	41[b]	108	10-944 (169)	-	70-100	Sirot et al. (2008)
	Germany	32[b]	536[c]	6-567 (38)	-	14-100 (70)	Kuballa et al. (2011)
	Italy	9[b]	1081	170-16 060	170-18 290	43-100	Storelli et al. (2002a)
	Italy	3[b]	15	400-4 560	670-5 160	51-97	Storelli et al. (2002b)
	Italy	15[b]	2 880	0-1 740 (314)	0-1 870 (356)	52-100 (88)	Storelli et al. (2003)
	Italy	2[b]	n.r.	ND-1 740	ND-1 740	60-100	Storelli et al. (2005)
	Poland	1[a]	4	18-2 630	25-2950	72-98 (87)	Baralkiewicz et al. (2006)
	Portugal	1[a]	45	70-200	63-240	85-97	Mieiro et al. (2009)
	Slovenia	27[b]	52	2-1 120 (127)	3-1 110 (150)	40-110 (80)	Miklavčič et al. (2011a)
	Spain	14[b]	25	54-596	-	-	Sahuquillo et al. (2007)
	Canada	9[b]	112	9-2 346 (342)	20-2 729 (542)	30-94 (64)	Forsyth et al. (2004)
	Caspian sea	1[a]	12	10-107	10-108 (40)	97-100	Agah et al. (2007)
	China	13[b]	148	40-590 (260)	10-660 (180)	59-84 (74)	Cheng et al. (2009)
	China	1[a]	12	24-98 (60)	61-680 (292)	7-93 (28)	Qiu et al. (2009)
	China	4[a]	40	5-499	24-1 199	18-85	Jin et al. (2006)
	Ghana	24[a]	-	9-107	-	-	Voegborlo et al. (2011)
	Hong-Kong	89[a,b]	280	3-1 010 (72)	3-1 370 (91)	-	Tang et al. (2009)
	India	7[b]	-	8.0-16 (13)	8.7-17 (15)	71-95	Mishra et al. (2007)
	Malaysia	3[b]	17	20-100	41-120	50-89	Hajeb et al. (2009b)
	Malaysia	2[b]	69	(378)	(459)	70-82 (77)	Hajeb et al. (2010)
	Papua New Guinea	7[a]	95	26-458	48-500	54-94	Bowles et al. (2001)
	Persian gulf	6[b]	63	11-100	12-87 (37)	63-100	Agah et al. (2007)
	USA	9[b]	-	(13-278)	(16-292)	93-98 (96)	Hight and Cheng (2006)
Shellfish							
	France	4	34	1.9-33 (16)	3.9-34 (20)	28-98 (75)	Clémens et al. (2011)
	France	18	47	3-219 (54)	-	-	Sirot et al. (2008)
	Italy	1	10	66-155 (110)	236-559 (386)	17-49 (32)	Di Leo et al. (2010)
	Italy[d]	1	10	17-116	40-830	33-91	Ipolyi et al. (2004)
	Italy(e)	1	10	15-51	35-115	14-98	Ipolyi et al. (2004)
	Brazil	4	14	3.8-37 (15)	3.8-40 (16)	-	Batista et al. (2011)

Table 8: Continued.

Group	Origin	Number species	Number samples	MeHg	THg or ∑Hg species	% MeHg	References
	China	3	-	11-25	-	-	Xiong and Hu (2007)
	India	3	-	(34)	(48)	-	Mishra et al. (2007)

n.r.: not reported; ND: not detected; MeHg: methylmercury; THg: total mercury; ∑Hg species: some of mercury species.
(a): freshwater fish;
(b): marine fish;
(c): for fish and shellfish;
(d): Sardinian coast campaign 1;
(e): Sardinian coast campaign 2.

Table 8 indicates a range of concentrations of methylmercury or total mercury in freshwater fish (methylmercury: 5 - 2 630 µg/kg; total mercury: 10 - 2 950 µg/kg), in shellfish (methylmercury: 2 - 220 µg/kg; total mercury: 40 - 830 µg/kg) and in marine fish (methylmercury: 0 - 16 000 µg/kg; total mercury: 0 - 18 000 µg/kg). These concentrations of total mercury and methylmercury are similar to those reported to EFSA and are in good agreement with the general conclusions of the JECFA (FAO/WHO, 2011b), which indicated that:

- Total mercury concentrations in 6 114 fish samples ranged from 1 to 11 400 µg/kg, with the maximum concentration found in marlin. About 5 % exceeded 1 000 µg/kg, particularly for lamprey, Portuguese dogfish, swordfish, shark, marlin, splendid alfonsino, picked dogfish, tuna, catshark, scabbardfish, ling, pike and ray.

- Total mercury concentrations in 1 892 shellfish samples (80 % above LOQ) ranged from 2 to 860 µg/kg. No shellfish species contained methylmercury at concentrations greater than 500 µg/kg (range 2 - 451 µg/kg), with the maximum concentration found in edible crab.

4.3.2. Occurrence in other food

Of the 1 319 food samples analysed for the second French TDS (Millour et al., 2011b), only 5 % of total mercury values were quantified (LOQ of 10 µg/kg). The highest mean concentration for foods other than fish and seafood were found in 'sweeteners, honey and confectionery' (12 µg/kg) where the product group 'chocolate' contained on average 17 µg/kg of mercury with a maximum concentration of 50 µg/kg found in a dark chocolate while the mean concentration in sugars and sugar-based products was lower than LOD (5 µg/kg). For the other food groups, the mean content was lower than the LOQ but high concentrations (243 µg/kg) were found in a merguez sausage in the food group 'meat and offal'. In the first French TDS (Leblanc et al., 2005), the food groups apart from fish and seafood containing the highest concentrations of mercury were 'sweeteners, honey and confectionery' (13 µg/kg). The other food groups had contents lower than the LOQ of 10 µg/kg.

The means of mercury content in mushrooms in Poland (LOQ of 5 µg Hg/kg dry weight (d.w.)) varied between 95 and 280 µg/kg d.w. in caps and between 45 and 130 µg/kg d.w. in stipes in 120 composite samples of 383 Slippery Jack, *Suillus luteus*, mushroom (Chudzynski et al., 2011).

In Spain, the concentration of total mercury found in 24 natural rice samples from four different origin ranged between 1.3 and 7.8 µg/kg (LOQ of 0.9 µg/kg) (da Silva et al., 2010). Mercury has also been found in rice from close to a former mining area in China (see Section 4.4 below).

In the UK TDS (Rose et al., 2010), total mercury was detected in the 'Offal' (4 µg/kg), and 'Other vegetables' food groups (0.7 µg/kg); the concentration was below the LODs (0.5 - 3 µg/kg[34] depending on food group in all other categories (apart from fish and seafood).

[34] LOD errorounously reported as 0.005-0.003 in the paper (M.Rose, 2012, personal communication).

Also in the UK, mercury was detected at concentrations at or above the LOD (0.2 – 1.0 µg/kg depending on sample weight taken) in only about one quarter of the samples in a wide range of commercial weaning foods and formulae, usually in those containing fish (FSA, 2006). The mean mercury concentration was 1 µg/kg, slightly lower than the mean value from a previous survey where the mean was 3 µg/kg (FSA, 2003).

The general conclusions of the JECFA (FAO/WHO, 2011b) indicated that total mercury concentrations in foods other than fish products were generally low (range 0.1 - 50 µg/kg), with about 80 % of the 6 183 samples containing concentrations below the LOQs. The highest concentrations were found in fungi. Mean methylmercury concentrations reported by China in non-fish samples ranged from 1 to 23 µg/kg, with a maximum concentration found in poultry. No other information on methylmercury in non-fish samples was received from other countries. In water, total mercury concentrations in 98 % of 90 545 samples analysed in France were below the LOQ of 0.02 µg/L, with a maximum of 4.3 µg/ L.

In summary, the published data since 2000 on total mercury and methylmercury in fish and other seafood and on total mercury in other food are in the same range as those reported to EFSA and support the findings and evaluation reported above in Section 4.2.

4.3.3. Occurrence in human milk

Mercury can be transferred into human milk as inorganic and methylmercury. This section gives an overview of concentrations in human milk in Europe sampled since 2000 or during a period that started earlier but included the year 2000 (Table 9).

Three studies were identified in which both total and methylmercury were measured in the same human milk samples. Valent et al. (2011) studied mother-infant pairs living in the region Friuli Venezia Giulia (Italy). Total mercury was measured in 77 samples of human milk with a mean concentration of 0.70 µg/kg and methylmercury in 79 samples with a mean concentration of 0.20 µg/kg. For the 77 human milk samples in which both methylmercury and total mercury were measured, the mean contribution of methylmercury to total mercury was 0.31 (median: 0.25; P75: 0.42; P100: 1.00). A statistically significant, but weak correlation was observed between methylmercury in human milk and the total fish consumption (Spearman correlation coefficient (r_s) = 0.29, p = 0.085, n = 79) and fresh fish consumption (r_s = 0.31, p = 0.0054, n = 79).

Miklavčič et al. (2011b) analysed in Slovenia total mercury in human milk and found a mean concentration of 0.3 µg/kg. Human milk samples (n = 11) from mothers with a concentration of total mercury in hair of at least 1.0 mg/kg were also analysed for methylmercury and a mean concentration of 0.68 µg/kg was reported. For nine human milk samples, both methylmercury and total mercury concentrations were determined and the mean contribution of methylmercury to total mercury was 0.39 (Miklavčič, personal communication, 2012). No correlation was observed between total mercury concentrations in human milk and the frequency of fish consumption (r_s = 0.08, 95 % confidence interval (CI): -0.04 - 0.20), but a weak correlation was observed between total mercury in human milk and calculated methylmercury concentrations in the most frequently eaten fish species (r_s = 0.14; 95 % CI: 0.02 - 0.25).

The third study analysed total mercury in human milk from Italian, Croatian and Greek women and compared the data on human milk with a subset of the results reported by Miklavčič et al. (2011b). When the total mercury concentration in the mother's hair was at least 1.0 mg/kg, methylmercury was analysed as well. The highest concentrations of total mercury in human milk were reported in Greek women (n = 44) with a median concentration of 0.6 µg/kg (range: < LOD - 12 µg/kg). Statistically significant lower concentrations were reported for Italian (n = 605), Slovenian (n = 284) and Croatian (n = 125) women, all with a median concentration of 0.2 µg/kg (Miklavčič et al., in press). The mean contributions of methylmercury to total mercury were 0.59 in Italian women (n = 224), 0.63 in Croatian women (n = 26) and 0.26 in Greek women (n = 21) (Miklavčič, personal communication,

2012), so the highest median methylmercury concentration (0.17 µg/kg) among women with hair mercury of at least 1 mg/kg was found in Croatian women. The authors reported a statistically significant but weak correlation for total and methylmercury in human milk from Mediterranean women (Italy, Slovenia, Croatia and Greece) and frequency of total fish consumption (total mercury: $r_s = 0.0977$, $p = 0.002$, $n = 1\,005$; methylmercury: $r_s = 0.1377$, $p = 0.027$, $n = 259$)

Garcia-Esquinas et al. (2011) reported a geometric mean total mercury concentration of 0.53 µg/L (n = 100) in human milk in Spain. Total mercury in human milk was not statistically significant correlated with the presence of dental amalgam fillings and fish and shellfish consumption. A mean concentration of 0.94 µg/L was reported by Ursinyova and Masanova (2005) in Slovakia republic (n = 158) and Björnberg et al. (2005) reported a median concentration of 0.29 µg/L, 4 days postpartum and 0.14 µg/L, 6 weeks postpartum in human milk from Sweden.

In contrast to the above-mentioned studies, Aballe et al. (2008) reported mean concentrations of total mercury between 2.63 (n = 13) and 3.53 µg/L (n = 10). However, the concentrations did not appear to be related to the amount of fish and fishery products consumed.

One study was identified that analysed inorganic mercury in 21 human milk samples from Austria and reported a median concentration of 0.2 µg/L (Gundacker et al., 2010a).

A limited number of studies report concentrations of mercury (total, methyl- or inorganic) in human milk. Mean concentrations of total mercury between 0.3 and 3.53 µg/L were reported. The mean contribution of methylmercury to total mercury ranged from 26 to 63 %. Inconsistent results regarding the correlation between total mercury or methylmercury in human milk and fish consumption were observed.

Table 9: Overview of mercury concentrations in the European population in human milk.

Country	Additional information	Human milk (µg Hg/L) N	mean	SD	P50	Variation (specified by footnotes)	Reference
Sweden	Day 4 postpartum	20			T:0.29	T:0.06-2.1[(b)]	Björnberg et al. (2005)
	6 weeks postpartum	20			T:0.14	T:0.07-0.37[(b)]	
Slovak Republic		158	T:0.94[(e)]		T:0.72[(e)]	T:<LOD-4.74[(b,e)]	Ursinyova and Masanova (2005)
Italy	Mothers from Venice with low consumption of local fish and fishery products (region Veneto)	10	T:2.68				Abballe et al. (2008)
	Mothers from Venice with medium consumption of local fish and fishery products (region Veneto)	13	T:2.63				
	Mothers from Venice with high consumption of local fish and fishery products (region Veneto)	6	T:2.99				
	Mothers from Rome (region Lazio)	10	T:3.53				
Austria		21			I:0.2	I:0.1-2.0[(b)] I:0.1-0.3[(d)]	Gundacker et al. (2010a)
Spain		100	T:0.53[(a)]		T:0.61	T:0.22-1.17[(c)]	García-Esquinas et al. (2011)
Slovenia	All mothers	284	T:0.3[(e)]		T:0.2[(e)]	T:0.06-0.6[(c,e)]	Miklavčič et al. (2011)
	Mothers of which the T in hair ≥ 1 mg/kg	11	M:0.68[(e)]	M:1.8[(e)]	M:0.07[(e)]	M:0.03-6.2[(c,e)]	
Italy	Mothers from the region Friuli Venezia Giulia	77	T:0.7[(e)]	T:1.29[(e)]	T:0.4 [(e)]	T:10.29[(e,f)] T:0.66[(e,g)]	Valent et al. (2011)
		79	M:0.2[(e)]	M:0.4[(e)]	M:0.08[(e)]	M:2.43[(e,f)] M:0.15[(e,g)]	
Italy	All mothers	605			T:0.2[(e)]	T:<0.045-28[(b,e)]	Miklavčič et al. (in press); Miklavčič, personal communication (2012)
	Mothers of which the T in hair ≥ 1 mg/kg	224	M:0.17[(e)]	M:0.14[(e)]	M:0.13[(e)]	M:0.01-1.09[(b,e)]	
Croatia	All mothers	125			T:0.2[(e)]	T:<0.045-2.4[(b,e)]	
	Mothers of which the T in hair ≥ 1 mg/kg	26	M:0.18[(e)]	M:0.11[(e)]	M:0.17[(e)]	M:0.04-0.55[(b,e)]	
Greece	All mothers	44			T:0.6[(e)]	T:<0.045-12[(b,e)]	
	Mothers of which the T in hair ≥ 1 mg/kg	21	M:0.1[(e)]	M:0.08[(e)]	M:0.08[(e)]	M:0.01-0.23[(b,e)]	

N: number of samples; SD: standard deviation; PX: Xth percentile; T: total mercury; M: methylmercury; I: inorganic mercury; Hg: mercury.
(a): Geometric mean
(b): Minimum-maximum
(c): P10-P90
(d): P25-P75
(e): µg/kg
(f): Maximum
(g): P75

4.4. Relationship between concentrations of total mercury and methylmercury

In order to assess the relationship between total mercury and methylmercury in foods, the data discussed above (see Section 4.2.6) together with the available scientific literature (Appendix B, Tables B1 and B2) was evaluated and the amounts found are described below.

Fish

It is generally found that about 80 - 100 % of total mercury in fish muscle is methylmercury; details from specific studies are shown in Table 8. However, studies in which methylmercury was also determined in fish lower in the food chain showed that not only was the total mercury content lower, but the percentage of methylmercury may be quite variable and even down to around 50 % of total mercury. This is in agreement with the conclusion of the JECFA, which indicated that in fish, the contribution of methylmercury to total mercury generally ranged between 30 % and 100 %, depending on species of fish, size, age and diet (FAO/WHO, 2011b). Furthermore, in about 80 % of these data, methylmercury accounted for more than 80 % of total mercury. However, a few submitted data showed contributions of methylmercury to total mercury of about 10 % or less.

The CONTAM Panel used a conservative approach to calculate methylmercury dietary exposure by assuming that 100 % of mercury in fish is in the form of methylmercury. However, in order to ensure that dietary exposure to inorganic mercury was not underestimated, 20 % of total mercury in fish was simultaneously assumed to be inorganic mercury when calculating inorganic mercury dietary exposure.

Other seafood

In seafood other than fish, methylmercury typically comprises 50 - 80 % of total mercury. In order to be conservative and to avoid underestimating methylmercury, the Panel assumed 80 % methylmercury for this type of food. Again, in order to ensure that dietary exposure to inorganic mercury was not underestimated, for shellfish a figure of 50 % inorganic mercury was assumed for dietary exposure estimates.

Other foods

There are data in the literature about mercury in rice originating from close to a former mercury mining area in China. In this area, methylmercury was reported to be around 20 - 40 % of the total mercury present in the rice, but this was associated with this particular contamination incident (Qiu et al., 2008). The contribution of methylmercury to total mercury in rice from non-contaminated areas is unknown and therefore not taken into consideration.

In other foods, mercury is presumed to be present as inorganic mercury. Because of this and since the number of data for other foods is low, a contribution of methylmercury to total mercury was not proposed for other foods, and a figure of 100 % inorganic mercury was assumed for dietary exposure estimates.

Human milk

Three European studies were identified in which both methylmercury and total mercury were analysed in human milk and the mean contribution of methylmercury to total mercury reported in these studies ranged from 26 to 63 % (See Section 4.3.3.).

The limited available data on the contribution of methylmercury to total mercury in human milk showed a wide variation, and the mean contribution was not considered sufficiently robust to form a basis for exposure assessment. Therefore, mean concentrations of methylmercury in human milk were used for methylmercury exposure assessment and the difference between total mercury and

methylmercury concentrations in human milk was used to calculate mean inorganic mercury concentrations for use in the exposure assessment.

4.5. Food processing

Mercury when present in food is stable and resistant to the effects generally encountered during processing. WHO (2008) stated that methylmercury in fish is bound to tissue protein rather than with fatty deposits, therefore trimming and skinning of fish does not reduce the mercury content of the fillet portion. Moreover, the mercury concentration in fish is not changed when cooked. However, because some moisture is usually lost during cooking, mercury concentrations are often slightly higher in cooked fish than in raw wet tissue. In addition, some preparation methods, such as deep frying, can actually increase the weight of the fish, potentially resulting in slightly lower concentrations of mercury. However, the total amount of mercury in fish remains relatively unchanged after cooking, and the slight changes in mercury concentrations due to cooking methods are relatively insignificant and generally do not need to be considered when estimating dietary exposures.

There have been a few studies that have specifically looked at the impact of processing and these are summarised below.

Frying and baking were found not to affect the mercury content of blue shark in a study by Chicourel et al. (2001). Deep frying was found to increase concentrations of mercury in fish in a study by Burger et al. (2003), but the increase was probably accounted for by weight loss combined with breading and absorption of oil. A small increase in mercury concentrations in fish after cooking was also found by Perelló et al. (2008), probably also accounted for by changes in weight. Fish cooked in rice was found to have an increased mercury content in a study by Musaiger and D'Souza (2008) and this was attributed to spices used with the rice, which are reported to be an additional source of heavy metals.

Farias et al. (2010) looked at the impact of different cooking processes on mercury consumed in a community in the Amazon region and concluded that up to 30 % of mercury may be lost during cooking. It was suggested that the volatility of methylmercury could be a contributory factor.

Some studies used *in vitro* gastrointestinal digestion techniques to make preliminary assessments with respect to mercury bioavailability and these are discussed below. Torres-Escribano et al. (2011) found that mercury bioaccessibility decreases after cooking by up to around half of the original concentration. It was proposed that the change in bioaccessibility after cooking might be attributable to alterations in the structural conformation of the fish muscle proteins produced by temperature, which could cause the loss of the native protein structure. These changes might impede the access of the enzymes used in *in vitro* gastrointestinal digestion to the structures to which mercury is bound in the muscle low-molecular-weight thiols, i.e. sulphydryl groups containing molecules such as cysteine. Maulvault et al. (2011) also found reductions of up to 40 % in the bioaccessible fraction of mercury in fish after it was cooked. Ouédraogo and Amyot (2011) found that mercury concentrations (dry weight) were slightly higher in boiled fish but that boiling or frying reduced bioaccessibility by 40 - 50 % and that the reduction was greater, 50 - 60 %, in the presence of tea or coffee.

In general, there is a consensus from both the *in vitro* studies discussed above and the studies conducted on cooking and processing described earlier that there is little impact of cooking or processing on the content of mercury in foods and so data for mercury in raw foods are suitable to use for dietary exposure estimates.

5. FOOD CONSUMPTION

5.1. EFSA's Comprehensive European Food Consumption Database

During 2010, the EFSA Comprehensive European Food Consumption Database (hereinafter Comprehensive Database) was built from existing national information on food consumption at a detailed level. Competent organisations in the EU Member States provided EFSA with data from the

most recent national dietary survey in their country at the level of consumption by the individual consumer. Survey results for children were mainly obtained through the EFSA Article 36 project 'Individual food consumption data and exposure assessment studies for children' through the EXPOCHI consortium (EFSA, 2011b). Results from a total of 32 different dietary surveys carried out in 22 different Member States covering more than 67 000 individuals are included in the Comprehensive Database version 1 as published (EFSA, 2011b; Merten et al., 2011).

Individuals were categorised into seven age groups covering infants (< 1 year), toddlers (1-< 3 years), other children (3-< 10 years), adolescents (10-< 18 years), adults (18-< 65 years), elderly (65 - < 75 years) and the very elderly (≥ 75 years) (EFSA, 2011b). There are two surveys available for infants, nine surveys available for toddlers, 17 surveys available for other children, 12 surveys available for adolescents, 15 surveys available for adults, seven surveys available for elderly and six surveys available for very elderly.

For each survey, food consumption data are presented according to the FoodEx classification system at FoodEx Level 1 (including 20 categories) and Level 2 (including around 160 categories). The FoodEx Level 1 food category 'Fish and other seafood ' is split in six subcategories at FoodEx Level 2, including 'Fish meat', 'Fish products', 'Fish offal', 'Crustaceans', 'Molluscs' and 'Amphibians, reptiles, snails, insects'. The 'Fish meat' category contains 32 fish species to be merged with occurrence data for calculating dietary exposure.

Although the food consumption data in the Comprehensive Database are the most complete and detailed currently available in the EU, it should be pointed out that different methodologies were used between surveys to collect the data and thus direct country-to-country comparisons can be misleading (Merten et al., 2011). Only surveys covering more than one day as described in Table 10, and thus appropriate for calculating chronic dietary exposure, were selected.

Table 10: Surveys included from the Comprehensive Database version 1 for calculating dietary exposure.

Country	Survey	N	Method	Days	Age	Year
Belgium	Regional Flanders	661	Dietary record	3	2-6	2003
Belgium	Diet National 2004	3 245	24-h dietary recall	2	15-105	2004
Bulgaria	NUTRICHILD	1 723	24-h dietary recall	2	0.1-5	2007
Cyprus	Childhealth	303	Dietary record	3	11-18	2003
Czech Republic	SISP04	1 751	24-h dietary recall	2	4-64	2004
Germany	DONALD 2006	303	Dietary record	3	1-10	2006
Germany	DONALD 2007	311	Dietary record	3	1-10	2007
Germany	DONALD 2008	307	Dietary record	3	1-10	2008
Germany	National Nutrition Survey II	13 926	24-h dietary recall	2	14-80	2006
Denmark	Danish Dietary Survey	4 118	Food record	7	4-75	2001
Spain	enKid	382	24-h dietary recall	2	1-14	2000
Spain	NUT INK05	760	24-h dietary recall	2	4-18	2005
Spain	AESAN	418	24-h dietary recall	2	18-60	2009
Spain	AESAN FIAB	1 068	Dietary record	3	17-60	2001
Finland	DIPP	1 448	Dietary record	3	1-6	2005
Finland	STRIP	250	Dietary record	4	7-8	2000
Finland	FINDIET 2007	2 038	48-h dietary recall	2	25-74	2007
France	INCA2	4 079	Dietary record	7	3-79	2006
United Kingdom	NDNS	1 724	Dietary record	7	19-64	2001
Greece	Regional Crete	874	Dietary record	3	4-6	2005
Hungary	National Representative Survey	1 360	Dietary record	3	18-96	2003
Ireland	NSIFCS	958	Dietary record	7	18-64	1998
Italy	INRAN SCAI 2005/06	3 323	Dietary record	3	0.1-98	2006
Latvia	EFSA TEST	2 070	24-h dietary recall	2	7-66	2008
the Netherlands	VCP kids	1 279	Dietary record	3	2-6	2006

Table 10: Continued.

Country	Survey	N	Method	Days	Age	Year
the Netherlands	DNFCS 2003	750	24-h dietary recall	2	19-30	2003
Sweden	NFA	2 495	24-h dietary recall	4	3-18	2003
Sweden	Riksmaten 1997/98	1 210	Dietary record	7	18-74	1997

N: number of participants.

5.2. Food consumption data for different age and consumer groups

5.2.1. Specific consumption patterns of 'Fish and other seafood' in the total population and in consumers only in European countries

Consumption data for 'Fish and other seafood' were analysed in all dietary studies specified in Table 10 for both the total population (meaning all participants in the surveys) and the consumers only.

The median of the mean consumption levels for this food group in the total population across all countries and dietary surveys was highest in the group elderly followed by adults and very elderly and lowest in child age groups (Appendix C, Table C1). A similar pattern was seen for 95th percentile fish and other seafood consumption.

The elderly and adults age groups also had the highest consumption among consumers only of fish and other seafood both for the median of mean and 95th percentile consumption (Appendix C, Table C2).

5.2.2. Specific consumption patterns of 'Fish meat' in the total population and in consumers only in European countries

Consumption data for fish meat were analysed in all dietary studies specified in Table 10 for both the total population (meaning all participants in the surveys) and the consumers only.

The highest consumption level for fish meat in the total population across all countries and dietary surveys was seen in the group elderly and very elderly (Appendix C Table C3). On the other hand, lower consumption levels of fish meat were found in other children, toddlers and in infants.

The highest median values of the 95th percentile fish meat consumption in the total population were observed in elderly followed by adults. The highest maximum consumption across the dietary surveys was reported in adults, adolescents and elderly.

The highest consumption level for fish meat in consumers only across all countries and dietary surveys was seen in the group elderly followed by adults and very elderly (Appendix C Table C4). Lower consumption levels were seen in other children, infants and in toddlers.

The 95th percentile fish meat consumption in the consumers only followed a similar pattern to the mean consumption. The highest values were observed in adults followed by elderly. The highest maximum consumption across the dietary surveys was reported in elderly, adults and adolescents.

6. EXPOSURE ASSESSMENT IN HUMANS

6.1. Occurrence data used for exposure assessment

In order to ensure quality and representativeness of the data, specific adjustments to 'Fish and other seafood' results were carried out as described in this section.

Most of the data reported to EFSA were for total mercury, and since the low number of results reported for methylmercury was difficult to combine with data for total mercury, the methylmercury data were excluded from further analyses.

It was assumed that the group of unspecified fish meat probably reflected fish species that are not covered by the FoodEx classification and, because of the high mercury mean concentration, the CONTAM Panel believed that large predatory fish might be overrepresented in this group. For this reason, the unspecified fish meat entry was replaced by the mean of all individually specified fish species to be matched with consumption of unspecified fish meat for the dietary exposure calculation (Table 6).

Fish species with insufficient numbers of samples (n < 25) were merged into three groups for calculating dietary exposure: (i) freshwater fish (containing sturgeon, barbel, char, meagre, roach and smelt); (ii) lower concentration marine fish (containing capelin, Jack mackerel, flounder, grouper, gurnard, shad and turbot); and (iii) higher concentration marine fish (containing barracuda, dentex, garfish, lizardfish, luvarus, scorpion fish, sea bass, weever, wrasse and John Dory).

Because of the lack of specific information on methylmercury and inorganic mercury data in the database, with the exception of human milk, the exposure assessment was based on the data submitted for total mercury. The analysed total mercury was converted to methylmercury and inorganic mercury by applying conversion factors based on the contribution of methylmercury to total mercury derived from literature data (Section 4.3 and Section 4.4). The following conversion factors for different food categories were proposed and used for dietary exposure calculation:

- fish meat, fish products, fish offal and unspecified fish and seafood: 1.0 for methylmercury and 0.2 for inorganic mercury;
- crustaceans, molluscs and amphibians, reptiles, snails, insects: 0.8 for methylmercury and 0.5 for inorganic mercury;
- all other food categories apart from 'Fish and other seafood': 1.0 for inorganic mercury and 0 for methylmercury;

Because this approach was chosen, total mercury dietary exposure cannot be derived by adding inorganic and methylmercury dietary exposure together for these foods.

For human milk, the dietary exposures were calculated using measured data for methylmercury. The concentration of inorganic mercury in human milk was estimated from the difference between the total mercury and methylmercury concentration.

6.2. Exposure assessment to methylmercury based on data reported to EFSA

Mean occurrence results are used by EFSA to calculate chronic dietary exposure. This is also the most common input used internationally for contaminant data since, in the case of datasets in which LC data constitute more than half of the results, the median will not be influenced at all by the magnitude of the positive results. Thus, dietary exposure was calculated by multiplying the mean mercury concentration for each food or food group by the corresponding consumption amount per kg b.w. separately for each individual in the database, calculating the sum of exposure for each survey day for the individual and then deriving the daily mean for the survey period. The mean and 95th percentile

dietary exposures were calculated for the total survey population separately for each survey and age class.

The CONTAM Panel focused the calculation of dietary exposure to methylmercury only on the food group 'Fish and other seafood' since it was assumed that in foods other than fish and other seafood mercury is present in inorganic form.

For this opinion, exposure estimates were calculated for 28 different dietary surveys carried out in 17 European countries (denoted the total population). The estimation of the dietary exposure to methylmercury in the text below is based on MB data since there was virtually no difference between LB and UB. The MB mean methylmercury concentration data of the food group 'Fish and other seafood' described in Section 4.2.4. were combined with the consumption and body weight data at the individual level to express methylmercury dietary exposure in µg/kg b.w. per week.

The minimum, median and maximum of the mean and the 95th percentile dietary exposure to methylmercury for all age groups across the surveys are summarised in Table 11. The MB mean methylmercury dietary exposure varied between 0.06 µg/kg b.w. per week seen in the elderly and very elderly groups to 1.57 µg/kg b.w. per week in toddlers. The MB 95th percentile dietary exposure ranged from 0.14 µg/kg b.w. per week in very elderly to 5.05 µg/kg b.w. per week in adolescents. The detailed results of the exposure calculation are presented in Appendix D, Table D1-D6 for the different surveys and age groups.

Table 11: Summary statistics of the chronic dietary exposure to methylmercury (µg Hg/kg b.w. per week) by age class. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown (further details are shown in Appendix D, Tables D1-D6).

	Minimum			Median			Maximum		
	LB	**MB**	**UB**	**LB**	**MB**	**UB**	**LB**	**MB**	**UB**
Mean dietary exposure in total population									
Toddlers	0.09	0.09	0.09	0.26	0.27	0.28	1.49	1.57	1.65
Other children	0.13	0.14	0.14	0.31	0.32	0.32	1.45	1.49	1.54
Adolescents	0.07	0.08	0.08	0.31	0.31	0.32	1.06	1.09	1.12
Adults	0.07	0.07	0.07	0.24	0.24	0.25	1.04	1.08	1.12
Elderly	0.06	0.06	0.07	0.25	0.26	0.26	0.61	0.63	0.65
Very elderly	0.05	0.06	0.06	0.24	0.25	0.25	0.37	0.38	0.39
P95 dietary exposure in total population									
Toddlers	0.66	0.68	0.70	1.57	1.59	1.62	2.70	2.72	2.74
Other children	0.73	0.75	0.76	1.59	1.60	1.62	4.60	4.96	5.04
Adolescents	0.41	0.42	0.42	1.32	1.38	1.48	5.04	5.05	5.06
Adults	0.50	0.51	0.53	1.11	1.13	1.14	3.00	3.04	3.08
Elderly	0.34	0.34	0.35	1.23	1.24	1.26	2.49	2.49	2.49
Very elderly	0.13	0.14	0.16	1.15	1.17	1.19	1.40	1.42	1.42

b.w.: body weight; Hg: mercury; LB: lower bound; MB: middle bound; P95: 95th percentile; UB; upper bound.

6.2.1. Infants (less than one year old)

Breast-fed infants

For the exposure assessment of infants below six months of age, a value of three months was selected, assuming a body weight of 6.1 kg, with an estimated average daily consumption of 800 mL and a high consumption of 1 200 mL of human milk (Table 12). For the occurrence data, mean occurrence levels of methylmercury reported in the literature were used (see Section 4.3.3.). The CONTAM Panel noted that in two of these studies, methylmercury was not analysed in milk from mothers with total mercury

concentrations in hair below 1 mg/kg, but concluded that this was unlikely to have a major impact on the data.

Based on the reported mean concentrations of methylmercury in human milk, the mean dietary exposure to methylmercury for infants with an average milk consumption ranged from 0.09 to 0.62 µg/kg b.w. per week (Table 12). For infants with a high milk consumption the dietary exposure ranged from 0.14 to 0.94 µg/kg b.w. per week.

Table 12: Exposure scenario to methylmercury based on average and high human milk consumption for infants below 6 months based on the mean occurrence data reported in literature (see Section 4.3.3.).

Country	Dietary exposure to methylmercury (µg Hg/kg b.w. per week)		Reference
	Average human milk consumption	High human milk consumption	
Slovenia[(a)]	0.62	0.94	Miklavčič et al. (2011b)
Italy	0.18	0.28	Valent et al. (2011)
Italy[(a)]	0.16	0.23	Miklavčič et al. (in press) and Miklavčič, personal communication, 2012
Croatia[(a)]	0.17	0.25	
Greece[(a)]	0.09	0.14	

b.w.: body weight; Hg: mercury.
(a): methylmercury was only analysed in human milk from mothers with total mercury concentrations in hair above 1 mg/kg.

This exposure assessment was based on a low number of studies reporting concentrations of methylmercury in human milk. The contribution of methylmercury to total mercury in human milk shows high variation. A study reporting only total mercury in human milk has shown higher concentrations than the studies that also provided speciation analyses (Table 9). Therefore, the possibility of higher dietary exposures to methylmercury from human milk in Europe cannot be excluded.

Total dietary intake for infants

Only two dietary surveys reported consumption data for infants, therefore the dietary exposure calculation should not be considered as representative of the European infant population. Moreover, only 16 participants were included in one of these surveys. Therefore, these data were not included in Table 11. Taking into account these limitations, the mean methylmercury dietary exposure was for the MB 0.02 and 0.08 µg/kg b.w. per week.

6.2.2. Children and adolescents (≥ 1 to < 18 years old)

There were nine surveys available reporting food consumption for toddlers, covering a total of 1 597 survey participants (Appendix D, Table D1). The MB methylmercury dietary exposure varied for the mean between 0.09 and 1.57 µg/kg b.w. per week with a median of 0.27 µg/kg b.w. per week and for the 95th percentile between 0.68 and 2.72 µg/kg b.w. per week with a median of 1.59 µg/kg b.w. per week (Table 11).

There were 17 surveys available reporting food consumption for other children covering a total of 8 468 survey participants (Appendix D, Table D2). The MB methylmercury dietary exposure varied for the mean between 0.14 and 1.49 µg/kg b.w. per week, with a median of 0.32 µg/kg b.w. per week, and for the 95th percentile between 0.75 and 4.96 µg/kg b.w. per week, with a median of 1.60 µg/kg b.w. per week (Table 11).

There were 12 surveys available reporting food consumption for adolescents, covering a total of 6 329 survey participants (Appendix D, Table D3). The MB methylmercury dietary exposure varied for the mean between 0.08 and 1.09 µg/kg b.w. per week, with a median of 0.31 µg/kg b.w. per week, and for the 95th percentile between 0.42 and 5.05 µg/kg b.w. per week, with a median of 1.38 µg/kg b.w. per week (Table 11).

Of the reported age groups, other children and adolescents were those with the highest median of mean methylmercury dietary exposure (0.32 and 0.31 µg/kg b.w. per week for MB, respectively). toddlers and other children were those with the highest median of 95th percentile dietary exposure (1.59 and 1.60 µg/kg b.w. per week for MB, respectively). This outcome may be influenced by the higher consumption of fish relative to body weight. This was observed in most surveys included in the Comprehensive Database when children and adolescents versus adults were compared.

6.2.3. Adults (≥ 18 to < 65 years old)

There were 15 surveys available reporting food consumption for adults covering a total of 30 788 survey participants (Appendix D, Table D4). The MB methylmercury dietary exposure varied for the mean between 0.07 and 1.08 µg/kg b.w. per week, with a median of 0.24 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.51 and 3.04 µg/kg b.w. per week, with a median of 1.13 µg/kg b.w. per week (Table 11).

6.2.4. Elderly (≥ 65 to < 75 years old) and very elderly (≥ 75 years old)

There were seven surveys available reporting food consumption for the elderly covering a total of 4 056 survey participants (Appendix D, Table D5). The MB methylmercury dietary exposure varied for the mean between 0.06 and 0.63 µg/kg b.w. per week, with a median of 0.26 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.34 and 2.49 µg/kg b.w. per week, with a median of 1.24 µg/kg b.w. per week (Table 11).

There were six surveys available reporting food consumption for the very elderly covering a total of 1 614 survey participants (Appendix D, Table D6). The MB methylmercury dietary exposure varied for the mean between 0.06 and 0.38 µg/kg b.w. per week, with a median of 0.25 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.14 and 1.42 µg/kg b.w. per week, with a median of 1.17 µg/kg b.w. per week (Table 11).

The highest dietary exposure was seen in surveys carried out in Mediterranean countries (Italy, Spain and France). The higher exposure seems to be more related to type of fish consumed rather than amounts consumed. In fact, the consumption of bass and mullet, which contain a considerable amount of methylmercury, is reported in Italy, France, Spain and Greece and not in northern Europe, where the more preferred fish species are cod, herring and salmon. Moreover, consumption of other fish species with typically high methylmercury concentrations reported by southern European countries only are swordfish (Italy, Spain and Greece) and shark (Italy, France and Spain), but this could be survey related (Welch et al., 2002).

6.2.5. Contributions of different food groups to methylmercury exposure

The contribution to methylmercury dietary exposure for each of the six subcategories at FoodEx Level 2 in the food category 'Fish and other seafood' was assessed separately for each survey and age group with a summary presented in Table 13. Dietary exposure was calculated based on MB mean methylmercury concentration combined with individual consumption in the total population and presented as the range of mean contribution as calculated for different surveys.

Table 13: Contribution (%) of 'Fish and other seafood' at FoodEx Level 2 to chronic dietary exposure of methylmercury using middle bound concentrations. Range of the mean contribution for each age class and food category is shown.

Food category	Lowest mean contribution – highest mean contribution (%)					
	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Fish meat	59-100	69-100	74-97	81-100	92-100	90-100
Fish products	0-40	0-29	0-22	0-13	0-2.2	0-1.5
Molluscs	0-5.3	0-8.2	0-9.7	0-7.2	0-6.3	0-6.9
Crustaceans	0-5.1	0-3.2	0-12	0.0-6.4	0-3.5	0-2.8
Fish offal	0	0-1.9	0-0.9	0-1.0	0-0.6	0-0.7
Amphibians, reptiles, snails, insects	0	0-0.1	0-0.1	0-0.1	0-0.1	0-0.1

Fish meat is the dominating contributor to methylmercury dietary exposure for all age classes followed by fish products, the latter particularly in the younger but not the older age groups. Fish offal as well as amphibians, reptiles, snails and insects each contribute to less than 1 % of methylmercury exposure except in the other children age group with slightly higher fish offal consumption.

'Fish meat' was further split into individual fish species at FoodEx Level 3. The results are reported as a number of surveys for the following contribution ranges: 0 - 5 %, 5 - 10 %, 10 - 25 %, 25 - 50 %, 50 - 75 %, 75 - 90 %, higher than 90 % (Table 14). The number of surveys reported for the same contribution ranges at FoodEx Level 2 is shown in Appendix D, Table D7.

Contributions of individual fish species to methylmercury dietary exposure varied considerably between the surveys and age groups, reflecting different food consumption habits across European countries. In particular tuna, swordfish, cod and whiting and pike were major contributors to methylmercury dietary exposure in the adult age groups, while the same species and hake were the most important contributors in the child age groups. Unfortunately, in some surveys a large part of the fish consumption was not broken down into individual fish species and thus the 'Fish meat, unspecified' category has a high mean contribution.

Table 14: Number of surveys split according to their percentage contribution to chronic dietary exposure of methylmercury using middle bound concentrations across age groups and fish species at FoodEx Level 3.

	Toddlers							Other children							Adolescents						
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %
Fish meat (unspecified)	3	-	2	4	-	-	-	4	-	3	6	3	-	1	4	-	2	5	-	1	-
Tuna	5	3	1	-	-	-	-	4	4	8	-	1	-	-	2	1	4	3	2	-	-
Swordfish	9	-	-	-	-	-	-	15	-	1	1	-	-	-	10	-	1	1	-	-	-
Cod and whiting	5	1	1	2	-	-	-	9	2	4	2	-	-	-	4	6	2	-	-	-	-
Pike	7	-	1	1	-	-	-	14	-	3	-	-	-	-	11	-	1	-	-	-	-
Hake	7	-	1	1	-	-	-	14	-	-	3	-	-	-	9	-	1	2	-	-	-
Carp	9	-	-	-	-	-	-	16	-	1	-	-	-	-	12	-	-	-	-	-	-
Salmon and trout	5	2	2	-	-	-	-	11	5	1	-	-	-	-	11	1	-	-	-	-	-
Plaice	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Perch	8	-	1	-	-	-	-	14	3	-	-	-	-	-	12	-	-	-	-	-	-
Bream	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Herring	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Bass	8	1	-	-	-	-	-	15	2	-	-	-	-	-	11	1	-	-	-	-	-
Fish meat, marine, high	9	-	-	-	-	-	-	16	-	-	1	-	-	-	12	-	-	-	-	-	-
Angler fish	8	-	-	1	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Mackerel	8	-	1	-	-	-	-	15	1	1	-	-	-	-	11	1	-	-	-	-	-
Sole	7	-	-	2	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Anchovy	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Whitefish	8	-	1	-	-	-	-	16	-	-	1	-	-	-	12	-	-	-	-	-	-
Sardine and pilchard	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Eel	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Ray	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Halibut	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Fish meat, freshwater	9	-	-	-	-	-	-	15	1	1	-	-	-	-	12	-	-	-	-	-	-
Fish meat, marine, low	9	-	-	-	-	-	-	16	1	-	-	-	-	-	12	-	-	-	-	-	-
Sea catfish, wolf-fish	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Grey mullet	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Shark	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Sprat	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Redfish	6	1	2	-	-	-	-	14	-	3	-	-	-	-	12	-	-	-	-	-	-

Table 14: Continued.

	Adults							Elderly							Very elderly						
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %
Fish meat (unspecified)	3	2	4	3	1	2	-	2	1	1	3	-	-	-	3	-	-	3	-	-	-
Tuna	2	1	4	7	1	-	-	2	1	3	-	1	-	-	1	-	2	3	-	-	-
Swordfish	11	2	1	1	-	-	-	4	1	1	1	-	-	-	4	2	-	-	-	-	-
Cod and whiting	5	4	5	1	-	-	-	1	-	6	-	-	-	-	-	3	2	1	-	-	-
Pike	13	1	-	1	-	-	-	6	-	-	-	1	-	-	6	-	-	-	-	-	-
Hake	13	-	2	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Carp	14	-	1	-	-	-	-	6	-	1	-	-	-	-	6	-	-	-	-	-	-
Salmon and trout	9	6	-	-	-	-	-	4	3	-	-	-	-	-	5	1	-	-	-	-	-
Plaice	14	1	-	-	-	-	-	6	-	1	-	-	-	-	5	-	1	-	-	-	-
Perch	14	1	-	-	-	-	-	5	1	1	-	-	-	-	5	1	-	-	-	-	-
Bream	14	1	-	-	-	-	-	6	1	-	-	-	-	-	5	1	-	-	-	-	-
Herring	14	1	-	-	-	-	-	5	1	1	-	-	-	-	4	1	1	-	-	-	-
Bass	14	1	-	-	-	-	-	6	1	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, marine, high	14	1	-	-	-	-	-	6	-	1	-	-	-	-	6	-	-	-	-	-	-
Angler fish	14	1	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Mackerel	14	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sole	15	-	-	-	-	-	-	5	2	-	-	-	-	-	5	-	1	-	-	-	-
Anchovy	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Whitefish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sardine and pilchard	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Eel	15	-	-	-	-	-	-	6	1	-	-	-	-	-	5	1	-	-	-	-	-
Ray	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Halibut	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, freshwater	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, marine, low	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sea catfish, wolf-fish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Grey mullet	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Shark	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sprat	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Redfish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-

6.2.6. Dietary exposure to methylmercury for specific groups

6.2.6.1. Women in child-bearing age

Since the prenatal period is the most sensitive stage of the life cycle for the neurodevelopmental effects of methylmercury, dietary exposure was calculated separately for women of child-bearing age. Consumption data for women aged 18 - 45 years available in 15 surveys in the Comprehensive Database were combined with methylmercury concentration levels. No appreciable differences were detected in this subpopulation compared with adults in general.

6.2.6.2. High and frequent fish consumers

There is a concern that high and frequent consumers of fish meat might have elevated levels of methylmercury dietary exposure. To test such a hypothesis, the 95th percentile dietary exposure from the daily consumption of fish meat among consumers only was retrieved from the Comprehensive Database for surveys in which the number of selected participants exceeded 60.

Results calculated for the 25 surveys that included the minimum, median and maximum of 95th percentile methylmercury dietary exposure are shown in Table 15. The dietary exposure estimations in high and frequent consumers varied from a minimum MB of 0.54 µg/kg b.w. per week in elderly to a maximum MB of 7.48 µg/kg b.w. per week in other children.

The methylmercury dietary exposure in high and frequent consumers of fish meat was higher in the child age groups than in adult population groups. This is explained by the higher food consumption of children in relation to their body weight.

The dietary exposure to methylmercury in high and frequent consumers is approximately two-fold higher than in the total population, but the increase ranged from one-fold to seven-fold. For further details see Appendix D, Table D8.

Table 15: Minimum, median and maximum of the 95th percentile dietary exposure to methylmercury among fish meat consumers only by age class (µg Hg/kg b.w. per week) (further details are shown in Appendix D, Table D8).

Age group	P95 dietary exposure in the fish meat consumers only								
	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Toddlers	4.60	4.66	4.72	4.73	4.88	5.02	4.87	5.10	5.32
Other children	1.39	1.41	1.43	3.51	3.88	4.09	7.47	7.48	7.49
Adolescents	0.80	0.80	0.81	2.53	2.56	2.58	7.22	7.25	7.29
Adults	0.56	0.57	0.58	2.05	2.08	2.10	6.15	6.16	6.17
Elderly	0.54	0.54	0.55	2.03	2.05	2.06	4.52	4.52	4.52
Very elderly	1.07	1.10	1.12	1.63	1.64	1.65	2.29	2.31	2.33

b.w.: body weight; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound; Hg: mercury.

6.3. Exposure assessment to inorganic mercury based on data reported to EFSA

Similarly to methylmercury exposure estimation, the mean and the 95th percentile inorganic dietary exposures were calculated separately for each country and age class for all participants in the surveys (the total population) using consumption data at individual level from the Comprehensive Database. The LB and UB mean total mercury results for each food group described in Section 4.2 and Appendix A, transformed into inorganic mercury by applying the conversion factors as described in Section 6.1, were used as occurrence values and combined with consumption data for the exposure assessment.

The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations.

Table 16 provides an overview of the results of the surveys that included the minimum, median and maximum of mean and 95th percentile dietary exposure to inorganic mercury for different age groups. The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers. The 95th percentile dietary exposure was estimated to range from 0.25 µg/kg b.w. per week in elderly and very elderly to 4.06 µg/kg b.w. per week in toddlers. The detailed results of the dietary exposure calculation are presented in Appendix D, Tables D9-D14 for the different surveys and age group.

Table 16: Summary statistics of the chronic dietary exposure to inorganic mercury (µg Hg/kg b.w. per week) by age class. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown (further details are shown in Appendix D, Tables D9-D14).

Age group	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Mean dietary exposure in total population									
Toddlers	0.27	0.79	1.31	0.37	1.13	1.71	0.59	1.36	2.16
Other children	0.24	0.59	0.89	0.38	0.84	1.24	0.76	1.13	1.75
Adolescents	0.16	0.39	0.59	0.25	0.44	0.68	0.51	0.73	0.94
Adults	0.14	0.26	0.38	0.23	0.41	0.55	0.40	0.53	0.70
Elderly	0.13	0.23	0.33	0.22	0.35	0.48	0.30	0.42	0.55
Very elderly	0.14	0.25	0.35	0.19	0.33	0.47	0.24	0.38	0.52
P95 dietary exposure in total population									
Toddlers	0.67	1.35	2.18	0.84	1.77	2.83	1.07	2.30	4.06
Other children	0.50	1.12	1.66	0.86	1.62	2.20	1.85	2.27	3.37
Adolescents	0.31	0.71	1.00	0.62	0.88	1.26	1.70	1.85	2.33
Adults	0.36	0.53	0.72	0.59	0.78	1.02	1.52	1.66	1.83
Elderly	0.25	0.40	0.55	0.54	0.72	0.92	0.77	0.94	1.12
Very elderly	0.25	0.40	0.54	0.47	0.62	0.82	0.64	0.81	1.01

b.w.: body weight; Hg: mercury; LB: lower bound; MB: middle bound; P95: 95th percentile; UB: upper bound.

There is considerable uncertainty associated with the calculation of dietary exposure to inorganic mercury. The number of sample results reported is low for some of the FoodEx Level 1 food groups. The proportion of LC data is 60 % or more in 11 of the food groups. Finally the assumptions made in relation to the contribution of inorganic mercury to total mercury in the fish and other seafood categories are conservative. The results should be interpreted with these caveats in mind.

6.3.1. Infants (less than one year old)

Breast-fed infants

The dietary exposure of infants below six months of age to inorganic mercury was calculated as described in Section 6.2.1. For the occurrence data, inorganic mercury concentrations were calculated as the difference between total mercury and methylmercury (see Section 4.3.3.). The CONTAM Panel noted that in two of these studies, methylmercury was not analysed in milk of mothers with total mercury concentrations in hair below 1 mg/kg, but concluded that this was unlikely to have a major impact on the data.

Based on mean concentrations of inorganic mercury in human milk, the mean weekly exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week (Table 17). For infants with a high milk consumption the dietary exposure ranges from 0.25 to 1.94 µg/kg b.w. per week.

Table 17: Exposure scenario to inorganic mercury based on average and high human milk consumption for infants below 6 months based on the mean occurrence data reported in literature (see Section 4.3.3).

Country	Dietary exposure to inorganic mercury (µg Hg/kg b.w. per week)		Reference
	Average human milk consumption	High human milk consumption	
Slovenia[(a)]	0.39	0.59	Miklavčič et al. (2011b)
Italy	0.44	0.67	Valent et al. (2011)
Italy[(a)]	0.28	0.41	Miklavčič et al. (in press); Miklavčič, personal communication (2012)
Croatia[(a)]	0.17	0.25	
Greece[(a)]	1.29	1.94	

b.w.: body weight; Hg: mercury.
(a): methylmercury was only analysed in human milk from mothers with total mercury concentrations in hair above 1 mg/kg.

This exposure assessment was based on a low number of studies reporting concentrations of methylmercury and total mercury in human milk. The concentrations of inorganic mercury were calculated as the difference between total and methylmercury. The contribution of inorganic mercury to total mercury in human milk shows a high variation. A study reporting only total mercury in human milk has shown higher concentrations of total mercury in human milk than the studies that provided speciation analyses (Table 9). Therefore, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

Total dietary intake for infants

Only two dietary surveys reported consumption data for infants, therefore the exposure calculation should not be considered as representative of the European infant population. Moreover, only 16 participants were included in one of these surveys. Therefore, these data were not included in Table 16. Taking into account these limitations, mean MB dietary exposure to inorganic mercury was estimated to be 0.74 and 0.80 µg/kg b.w. per week in these two survey populations.

6.3.2. Children and adolescents (≥ 1 to < 18 years old)

There were nine surveys available reporting food consumption for toddlers, covering a total of 1 597 survey participants (Appendix D, Table D9). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.27 µg/kg b.w. per week to the highest maximum UB of 2.16 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.67 µg/kg b.w. per week to 4.06 µg/kg b.w. per week (Table 16).

There were 17 surveys available reporting food consumption for other children covering a total of 8 468 survey participants (Appendix D, Table D10). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.24 µg/kg b.w. per week to the highest maximum UB of 1.75 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.50 µg/kg b.w. per week to 3.37 µg/kg b.w. per week (Table 16).

There were 12 surveys available reporting food consumption for adolescents covering a total of 6 329 survey participants (Appendix D, Table D11). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.16 µg/kg b.w. per week to the highest maximum UB of 0.94 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.31 µg/kg b.w. per week to 2.33 µg/kg b.w. per week (Table 16).

6.3.3. *Adults (≥ 18 to < 65 years old)*

There were 15 surveys available reporting food consumption for adults covering a total of 30 788 survey participants (Appendix D, Table D12). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.14 µg/kg b.w. per week to the highest maximum UB of 0.70 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.36 µg/kg b.w. per week to 1.83 µg/kg b.w. per week (Table 16).

6.3.4. *Elderly (≥ 65 to < 75 years old) and very elderly (≥ 75 years old)*

There were seven surveys available reporting food consumption for the elderly covering a total of 4 056 survey participants (Appendix D, Table D13). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week to the highest maximum UB of 0.55 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.25 µg/kg b.w. per week to 1.12 µg/kg b.w. per week (Table 16).

There were six surveys available reporting food consumption for very elderly, covering a total of 1 614 survey participants (Appendix D, Table D14). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.14 µg/kg b.w. per week to the highest maximum UB of 0.52 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.25 µg/kg b.w. per week to 1.01 µg/kg b.w. per week (Table 16).

6.3.5. *Contributions of different food groups to inorganic mercury exposure*

The contribution to inorganic mercury dietary exposure for each of the 20 main food groups of the FoodEx classification system, FoodEx Level 1, was assessed separately for each survey and age group. Dietary exposure was calculated based on mean inorganic mercury concentration combined with individual consumption and is presented in Appendix D, Table D15 as the range of mean contributions as calculated for the different surveys. An overview of the results reported as the number of surveys for the contribution ranges: 0 - 5 %, 5 - 10 %, 10 - 25 %, 25 - 50 % and 50 - 75 % is presented in Table 18.

The main contributors to inorganic mercury dietary exposure varied between age groups reflecting different consumption patterns at different ages. The food group ‘Fish and other seafood’ contributed more than 25 % of inorganic mercury dietary exposure in 15 surveys. In nine surveys, mainly covering other children, ‘Composite food’, and in eight surveys, mainly covering adults, ‘Non-alcoholic beverages’ contributed more than 25 %. Dietary exposure seemed to be driven by high mercury concentration for ‘Fish and other seafood’ and ‘Composite food’ that might include fish as an ingredient, while it seemed to be consumption driven for ‘Non-alcoholic beverages’. In the case of ‘Composite food’, a high percentage of LC data in some food categories also influenced the dietary exposure estimation outcome.

Other food groups that were important for inorganic mercury dietary exposure included ‘Vegetable and vegetable products’, ‘Fruit and vegetable juices’, ‘Grains and grain products’ and ‘Milk and dairy products’, ‘Meat and meat products’ in all cases driven by a high percentage of LC data (≥ 60 % of LC data within the main food group or within the food categories at lower FoodEx levels).

Table 18: Number of surveys split according to their percentage contribution to chronic dietary exposure of inorganic mercury using middle bound concentrations across age groups for the main food groups at FoodEx Level 1.

	Toddlers					Other children					Adolescents				
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %
Fish and other seafood	4	2	1	2	-	2	8	4	3	-	2	1	5	4	-
Non-alcoholic beverages	7	2	-	-	-	7	9	1	-	-	5	3	4	-	-
Composite food	5	3	1	-	-	7	3	3	4	-	5	4	-	3	-
Vegetables and vegetable products	3	4	2	-	-	7	8	2	-	-	7	4	1	-	-
Fruit and vegetable juices	-	1	7	1	-	1	4	9	3	-	1	6	4	1	-
Grains and grain-based products	-	4	5	-	-	-	3	14	-	-	-	3	9	-	-
Milk and dairy products	-	-	7	2	-	-	2	15	-	-	-	5	7	-	-
Meat and meat products	6	3	-	-	-	10	7	-	-	-	5	5	2	-	-
Starchy roots and tubers	8	1	-	-	-	17	-	-	-	-	12	-	-	-	-
Alcoholic beverages	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Fruit and fruit products	5	4	-	-	-	12	5	-	-	-	11	1	-	-	-
Drinking water	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Products for special nutritional use	9	-	-	-	-	17	-	-	-	-	11	1	-	-	-
Animal and vegetable fats and oils	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Legumes, nuts and oilseeds	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Herbs, spices and condiments	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Sugar and confectionery	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Eggs and egg products	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Snacks, desserts, and other foods	8	1	-	-	-	16	1	-	-	-	12	-	-	-	-
Food for infants and small children	4	2	3	-	-	17	-	-	-	-	12	-	-	-	-

Table 18: Continued.

	Adults					Elderly					Very elderly				
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %
Fish and other seafood	1	4	7	2	1	-	1	4	2	-	1	-	4	1	-
Non-alcoholic beverages	4	-	7	4	-	1	-	5	1	-	-	2	1	3	-
Composite food	9	4	-	2	-	6	1	-	-	-	4	2	-	-	-
Vegetables and vegetable products	5	8	1	1	-	1	4	2	-	-	2	2	2	-	-
Fruit and vegetable juices	6	4	5	-	-	3	3	1	-	-	4	2	-	-	-
Grains and grain-based products	-	9	6	-	-	-	1	6	-	-	-	2	4	-	-
Milk and dairy products	1	11	3	-	-	-	4	3	-	-	-	5	1	-	-
Meat and meat products	3	10	2	-	-	2	4	1	-	-	1	4	1	-	-
Starchy roots and tubers	14	1	-	-	-	7	-	-	-	-	4	2	-	-	-
Alcoholic beverages	14	1	-	-	-	7	-	-	-	-	6	-	-	-	-
Fruit and fruit products	14	1	-	-	-	1	6	-	-	-	-	6	-	-	-
Drinking water	14	1	-	-	-	7	-	-	-	-	6	-	-	-	-
Products for special nutritional use	15	-	-	-	-	7	-	-	-	-	5	1	-	-	-
Animal and vegetable fats and oils	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Legumes, nuts and oilseeds	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Herbs, spices and condiments	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Sugar and confectionery	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Eggs and egg products	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Snacks, desserts, and other foods	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Food for infants and small children	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-

The major contributors, defined as the food groups contributing to 5 % or more of inorganic mercury exposure at FoodEx Level 2, reported for individual age groups are listed in Table 19. The number of surveys and the highest recorded contribution (%) is reported.

Table 19: Major contributors to mean middle bound chronic dietary inorganic mercury exposure for the food groups at FoodEx Level 2 contributing to 5 % or more of total exposure. Number of surveys and the highest mean contribution are shown.

Food category	Toddlers		Other children		Adolescents		Adults		Elderly		Very elderly	
	N	%	N	%	N	%	N	%	N	%	N	%
Non alcoholic beverages												
Tea (infusion)[35]	2	6	3	19	3	19	11	40	6	28	6	30
Soft drinks	-	-	5	7	4	10	2	7	-	-	-	-
Fish and other seafood												
Fish meat	6	26	15	28	10	34	14	39	7	27	5	23
Molluscs	-	-	1	7	3	8	3	7	1	6	-	-
Crustaceans	-	-	-	-	1	10	2	7	-	-	-	-
Composite food												
Cereal-based dishes	-	-	5	20	3	25	2	11	-	-	-	-
Prepared salads	-	-	2	17	2	18	1	22	-	-	-	-
Ready to eat soups	-	-	3	9	1	9	2	11	1	7	1	8
Fish and seafood based meals	-	-	1	10	-	-	-	-	-	-	-	-
Meat-based meals	-	-	4	7	1	7	1	7	-	-	-	-
Mushroom-based meals	-	-	-	-	-	-	1	6	-	-	-	-
Vegetables and vegetable products												
Fungi, wild, edible	-	-	1	15	1	11	1	15	2	10	1	9
Fungi, cultivated	1	11	-	-	1	6	1	6	1	7	1	5
Vegetable products	1	5	1	5	-	-	-	-	-	-	-	-
Fruit and vegetable juices												
Fruit juice	8	16	15	20	9	20	4	13	3	9	2	8
Concentrated fruit juice	1	15	3	15	2	16	2	7	-	-	-	-
Mixed fruit juice	3	7	4	21	1	11	1	6	-	-	-	-
Fruit nectar	-	-	-	-	-	-	1	6	-	-	-	-
Grains and grain based products												
Bread and rolls	6	7	10	9	9	8	9	10	6	10	6	10
Pasta (raw)	1	5	-	-	-	-	-	-	-	-	-	-
Grain milling products	1	5	-	-	-	-	1	5	1	5	-	-
Breakfast cereals	-	-	1	5	-	-	-	-	-	-	-	-
Fine bakery wares	-	-	1	5	2	5	-	-	-	-	-	-
Milk and dairy products												
Fermented milk products	7	17	13	13	2	6	2	6	1	6	-	-
Liquid milk	8	15	12	11	6	8	2	5	2	5	1	5
Milk and dairy products	1	7	-	-	-	-	-	-	-	-	-	-
Milk and milk products imitates	1	6	-	-	-	-	-	-	-	-	-	-
Concentrated milk	-	-	1	5	-	-	-	-	-	-	-	-

N: number of surveys; %: highest mean contribution.

'Tea (infusion)' and 'Soft drinks' contributed to inorganic mercury dietary exposure in the food group 'Non-alcoholic beverages' at levels of up to 40 % and 10 %, respectively, mainly driven by high consumption amounts of black tea in particular in the first case.

[35] Includes black tea and others prepared as for consumption

The food category 'Fish meat' was also an important contributor (up to 39 % in adults) to inorganic mercury dietary exposure in all age groups at FoodEx Level 2, mainly through consumption of 'Fish meat, unspecified' (up to 18 %), 'Tuna' (up to 15 %), 'Swordfish' (up to 13 %) and 'Cod and whiting' (up to 11 %) at FoodEx Level 3 (data not shown).

The dietary exposure to inorganic mercury from the 'Composite food' category was mainly due to high occurrence levels in 'Cereal–based dishes' and in 'Prepared salads', with contributions of up to 25 % and 22 %, respectively, but was true for only a few surveys. Within the food group 'Cereal-based dishes' the major contributors were 'Pasta cooked' (up to 18 %) and 'Pizza and pizza-like pies' (up to 8 %) at FoodEx Level 3. Within the food group 'Prepared salads' the major contributor was 'Prepared mixed vegetable salads' (up to 14 %) in FoodEx Level 3 (data not shown).

Other important individual food categories at FoodEx Level 3 contributing to inorganic mercury dietary exposure in one or more age groups include mixed fruit juice (up to 21 %), cow's milk yoghurt (up to 16 %), boletus and unspecified concentrated fruit juice (each up to 15 %), apple juice and cow milk (each up to 14 %), orange juice and orange juice concentrate (each up to 13 %), unspecified fermented milk products (up to 9 %), multi-fruit juice and wheat bread and rolls (each up to 8 %) and mixed wheat and rye bread and rolls (up to 6 %).

The contribution to inorganic mercury dietary exposure from rice was considered negligible at a maximum of 2 %.

6.3.6. Dietary exposure to inorganic mercury for specific groups

6.3.6.1. Dietary supplements consumers

There is a concern that the consumers of dietary supplements might have elevated levels of inorganic mercury dietary exposure. Particularly, traditional herbal preparations used in Asian traditional medicine usually purchased at the European market, may contain significant amounts of mercury (Martena et al., 2010). Since the consumption of dietary supplements in total population is rare, for this opinion the exposure assessment to inorganic mercury from dietary supplements was carried out separately for consumers only. Two groups of dietary supplements with significantly different inorganic mercury concentration levels were identified: (i) a group with high levels (LB mean = 504 µg/kg, UB mean = 513 µg/kg), including unspecified dietary supplements and plant extract formula, and (ii) a group of other dietary supplements with lower levels (LB mean = 5.58 µg/kg, UB mean = 11.7 µg/kg). The exposure to inorganic mercury from dietary supplements was calculated separately with respect to these two groups for every individual using his/her own consumption data.

Results calculated for the eight European surveys included with the minimum, median and maximum of the mean and the 95th percentile inorganic mercury dietary exposure are shown in Table 20. The mean dietary exposure estimations in dietary supplements consumers varied from a minimum LB of 0.00 µg/kg b.w. per week seen almost in all age groups to a maximum UB of 0.19 µg/kg b.w. per week in very elderly. The 95th percentile dietary exposure estimations in dietary supplements consumers varied from a minimum LB of 0.00 µg/kg b.w. per week to a maximum UB of 0.24 µg/kg b.w. per week in adults, but this results could not be obtained for all age groups due to a low number of participants.

The inorganic mercury dietary exposure in consumers of dietary supplements seems to be highest in very elderly. However, only one survey for this age group was available and therefore this outcome needs to take into account a considerable limitation when interpreted.

Table 20: Summary statistics of the chronic dietary exposure to inorganic mercury (µg Hg/kg b.w. per week) from dietary supplements in consumers only by age class. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

	N	Minimum			Median			Maximum		
		LB	MB	UB	LB	MB	UB	LB	MB	UB
		Mean dietary exposure in the dietary supplements consumers only								
Infants[a]	4	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Toddlers	446	0.00	0.00	0.00	0.01	0.01	0.01	0.02	0.03	0.04
Other children	742	0.00	0.00	0.00	0.01	0.02	0.02	0.06	0.06	0.07
Adolescents	182	0.00	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01
Adults	1 426	0.00	0.00	0.00	0.03	0.03	0.04	0.06	0.06	0.06
Elderly	227	0.00	0.00	0.00	0.02	0.02	0.02	0.03	0.03	0.03
Very elderly[a]	17	0.18	0.18	0.19	0.18	0.18	0.19	0.18	0.18	0.19
		P95 dietary exposure in the dietary supplements consumers only								
Infants[a]	4	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]
Toddlers	446	0.00	0.00	0.00	0.02	0.02	0.03	0.02	0.03	0.05
Other children	742	0.00	0.00	0.00	0.01	0.02	0.02	0.09	0.09	0.09
Adolescents	182	0.00	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01
Adults	1 426	0.01	0.01	0.01	0.10	0.11	0.11	0.23	0.24	0.24
Elderly	227	0.01	0.01	0.02	0.07	0.07	0.07	0.13	0.13	0.13
Very elderly[a]	17	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]

b.w. body weight; Hg: mercury; LB: lower bound; MB: middle bound; N: number of participants; P95: 95th percentile; UB: upper bound.
(a): Minimum, median and maximum calculation not possible since only one survey was available.
(b): Calculation of P95 not possible due to a low number of participants.

6.4. Previously reported human exposure assessments

Recently reported exposure assessments were summarised by Arnich et al. (2012). The data in Table 21 are based on Arnich et al. (2012), updated with more recent data, and exposure is expressed on a weekly basis in order to allow comparison.

Table 21: Summary of dietary exposure assessments to mercury in various countries.

Country	Mean adult exposure µg/kg b.w. per week	Mean children's exposure[a] µg/kg b.w. per week	Reference
Total mercury			
Australia	0.07-0.63 [b]	0.07-1.4 [b]	FSANZ (2003)
Australia	0.21-0.35 [b]	0.42-0.56 [b]	FSANZ (2011)
Chile	0.49 [b]		Muñoz et al. (2005)
China	0.63 [b]		Sun et al., 2011
France	0.16-1.39 [b]	0.26-1.94 [b]	Arnich et al. (2012)
Korea	0.21* [b]		Lee et al. (2006)
Lebanon	0.28 [b]		Nasreddine et al., (2006)
Norway	0.35		Jenssen et al., (2012)
Spain	2.1** [b] in men		Falcó et al. (2005)
	1.96** [b] in women		Rubio et al. (2008)
	0.63* [b]		Domingo et al. (2012)
	4.69* [b]		
UK	0.14-0.55 [b]	0.21-0.56 [b]	Rose et al. (2010)
USA	0.28-0.56 [b]		Dougherty et al. (2000)

Table 21: Continued.

Country	Mean adult exposure µg/kg b.w. per week	Mean children's exposure[(a)] µg/kg b.w. per week	Reference
Methylmercury			
Australia	0.43	0.43	FSANZ (2011)
France	0.12-0.13	0.15	Arnich et al. (2012)
Japan	0.71* in pregnant women		Yaginuma-Sakurai et al. (2009)
Spain	0.88 in pregnant women 0.98 in women of child-bearing age		Ortega-Garcia et al. (2009)
Sweden	0.42 in women in child-bearing age [(b)]		Ström et al. (2011)
Germany	0.13*		Kuballa et al. (2011)

b.w.: body weight
(a): children generally from 3 to < 10 years,
(b): reported by the authors as µg/kg b.w. per day.
* Assuming a 60 kg b.w.
** Assuming a 60 kg b.w. for women and 70 kg b.w. for men.

Most previously reported dietary exposure estimates are for total mercury, and results from France, UK, USA and Australia were all in broad agreement with each other on a LB and MB basis. The French population's mean dietary exposure to total mercury was estimated at 0.16 µg/kg b.w. per week in adults for the LB and 1.39 µg/kg b.w. per week for the UB assumption and mean dietary exposure for children was estimated at 0.26 (LB) and 1.94 (UB) µg/kg b.w. per week (Arnich et al 2012). The last UK TDS reported a mean total mercury intake between 0.14 and 0.35 µg/kg b.w. per week for adults and 0.21 and 0.56 µg/kg b.w. per week for children (LB and UB, Rose et al., 2010). Dougherty et al. (2000), reported a mean US dietary exposure of between 0.28 and 0.56 µg/kg b.w. per week (LB and UB). In Australia, mean dietary exposure ranged from 0.07 to 0.63 µg/kg b.w. per day for adults and from 0.07 to 1.4 µg/kg b.w. per week for children in 2003 (FSANZ, 2003) and in 2011 from 0.21 to 0.35 µg/kg b.w. per week for adults and from 0.42 to 0.56 µg/kg b.w. per week for children (FSANZ, 2011). Mean adult intake estimates are also available for Chile (0.49 µg/kg b.w. per week, Muñoz et al., 2005), China (0.63 µg/kg b.w. per week, Sun et al., 2011), Lebanon (0.28 µg/kg b.w. per week, Nasreddine et al., 2006) and Norway (0.35 µg/kg b.w. per week; Jenssen et al., 2012). In Korea, Lee et al. (2006) estimated the mean adult intake at 11.3 µg per day (ca. 0.21 µg/kg b.w. per week assuming a 60 kg default body weight). The highest levels have been reported by Domingo et al. (2012) in Spanish adults, with a mean at 282.8 µg per week (ca. 4.69 µg/kg b.w. per week). In a previous study from Spain (Falcó et al., 2005), mean adult exposure was estimated at 151.9 and 116.9 µg per week for men and women, respectively (ca. 2.10 and 1.96 µg/kg b.w. per week assuming a 70 kg default b.w. for men and 60 kg for women). The authors noted that fish and cereals were the major contributors to total mercury intake in their study. The mean mercury concentration was 97 µg/kg in fish and seafood and 30 µg/kg in cereals. Lower levels have also been reported by Rubio et al. (2008) for Canary Islands (Spain) with a mean estimated total mercury intake at 39.9 µg per week. However, these lower levels can be explained by the differences in assumptions regarding levels below the LOD. Rubio et al. (2008) used a LB assumption where measurements were below the LOD whereas Falcó et al. (2005) and Domingo et al. (2012) used a MB approach, i.e. non-detected values were assumed to be LOD/2.

For methylmercury dietary exposure calculations, it has been assumed that 100 % of mercury in fish and other seafood products is present as methylmercury. The French population's mean dietary exposure to methylmercury through the consumption of fish and seafood products was estimated to be 0.12 µg/kg b.w. per week for adults and 0.15 µg/kg b.w. per week for children (Arnich et al., 2012). In Australia, results from a TDS reported a mean dietary exposure of 0.43 µg/kg b.w. per week both for adults and children aged between 6 and 12 years (FSANZ, 2011). A mean dietary exposure level for

women in Spain is reported at 0.98 µg/kg b.w. per week for women of child-bearing age and 0.88 µg/kg b.w. per week for pregnant women (Ortega-Garcia et al., 2009), a mean and 95th percentile methylmercury exposure for women in child-bearing age in Sweden is reported at 0.42 and 1.05 µg/kg b.w. per week respectively (Ström et al., 2011) and a mean value of 0.70 µg/kg b.w. per week is reported for pregnant Japanese women (Yaginuma-Sakurai et al., 2009). In Germany, methylmercury exposure from fish and other seafood was estimated for adults and showed a mean exposure of 8 µg per week, which corresponds to 0.13 µg/kg b.w per week for a 60 kg adult (Kuballa et al., 2011).

The French population mean dietary exposure to inorganic mercury through the consumption of foods other than seafood products was estimated at 0.04 µg/kg b.w. per week in adults (LB) and 1.26 µg/kg b.w. per week (UB). For children, mean dietary exposure was estimated to be 0.10 µg/kg b.w. per week (LB) and 1.82 µg/kg b.w. per week (UB) (Arnich et al., 2012). It was assumed in this study that 100 % of mercury in foods other than seafood products is present as inorganic mercury. The Australian TDS estimated mean exposure for adults to be between 0.21 and 0.35 µg/kg b.w. per week for adults and between 0.42 and 0.56 µg/kg b.w. per week for children.

Comparison between previously reported data and estimates of dietary exposure made in this opinion

Several factors make a direct comparison between data reported in the literature and that presented in this opinion difficult. This is mostly because it is not always clear which method is used for dietary exposure calculations, it is not always clear in which way the data was handled (e.g. treatment of LC data) and different categories are used for age groups. There are also different approaches used to estimate total mercury and methylmercury. The approach used by EFSA for exposure assessments is conservative and may result in some higher values. A qualitative inspection of the data above supports the detailed exposure assessment presented in Section 6.2.

6.5. Non-dietary exposure

In addition to food, inorganic mercury exposure occurs through medicinal products and the use of alternative medicine and some religious practices (summarised in FAO/WHO, 2011b). Although medicinal uses of mercurous and mercuric species have virtually disappeared in industrial countries, and inorganic mercury is banned as an active ingredient in cosmetics in the EU, it is still used in skin-lightening creams predominantly in less developed countries (Chan, 2011). A recent population-based inorganic mercury biomonitoring in New York identified skin care products as a possible source of high exposure even in industrial countries (McKelvey et al., 2011).

Exposure to elemental mercury (with a special focus on children) has recently been summarised by the Agency for Toxic Substances and Disease Registry (ATSDR) and includes breakage of mercury-containing instruments (e.g. thermometers) and fluorescent light bulbs, off-gassing from flooring materials containing a mercury catalyst and outgassing of mercury vapour from dental amalgams (ATSDR, 2009). Mercury vapour is readily taken up by the lungs, with up to 80 % of the inhaled elemental mercury being retained in human tissues (ATSDR, 1999) and rapidly being oxidised to mercuric mercury. Assessment of exposure from dental amalgam amounts to 0.2 to 0.4 µg/day per amalgam-filled tooth surface or 0.5 to 1 µg/day per amalgam filled tooth (e.g. Health Canada 1995; Richardson et al., 2011); each amalgam-filled surface results in an increase of mercury in urine of 0.1 µg Hg/L or 0.06 to 0.07 µg Hg/g creatinine (summarised in Richardson et al., 2011). Based on an estimated daily absorption of total mercury from diet, water and air of 2.6 µg (WHO 1990, 1991), and the estimated daily absorption of elemental mercury from dental amalgam of 3 – 17 µg (WHO 1990, 1991), in case of individuals with a large number of amalgam fillings, amalgam fillings may account for 87 % (17 µg out of 19) of the absorbed total mercury. In individuals with only a few amalgam fillings, this source may account for about 50 % (3 µg out of 5.6 µg) of the absorbed total mercury (summarised in ATSDR, 1999). It is known that in the human body elemental mercury is oxidised to mercuric mercury. However to date no reliable factor exists for the extent to which elemental mercury contributes to the internal mercuric mercury exposure.

In general, mercury vapour in the ambient atmosphere is low and thus human exposure is negligible; typical outdoor-air mercury concentrations are within the 1 - 4 ng/m^3 range (e.g., Pacyna et al., 2009; Watras et al., 2009; Cairns et al., 2011). However, elemental mercury still has many industrial applications, including for example, the manufacturing of fluorescent lamps and the production of caustic soda and chlorine, which might result in the escape of mercury vapour in the working atmosphere (Berlin et al., 2007). Owing to breakage of mercury-containing thermometers or compact fluorescent light lamps indoor mercury concentrations in the high ng to µg/m³ range can transiently occur (e.g. Smart 1986; Fromme et al., 2011; Salthammer et al., 2012). After breakage of a fluorescent lamp, rapid reduction in mercury concentration in air can be obtained by ventilation (Salthammer et al., 2012). Several institutions, including the WHO, the Californian OEHHA, the US-EPA and the German Federal Ministry for Environment, Nature Conservation and Nuclear Safety (Umweltbundesamt, UBA), have published inhalation-based guideline values for indoor and ambient air not related to the workplace[36,37] (Link, 1999; WHO, 2000, 2003).

Thiomersal is used as a preservative in multidose vials of some vaccines (thiomersal concentrations between 0.001 – 0.01 % (US-FDA, 2009)) as well as in several cosmetic products and cleaning solutions for contact lenses (Aschner et al., 2010). A vaccine containing 0.01 % Thiomersal contains 50 µg thiomersal per 0.5 mL dose, which equates to approximately 25 µg mercury per dose.

7. HAZARD IDENTIFICATION AND CHARACTERISATION

7.1. Toxicokinetics

Toxicokinetics of mercuric, mercurous and methylmercury species are discussed based on the reports of ATSDR (ATSDR 1999), EFSA (EFSA 2008a) and JECFA (FAO/WHO, 2007, 2011b), a number of reviews (Clarkson and Magos, 2006; Berlin et al., 2007; Mutter et al., 2007; Bridges and Zalups, 2010; Ceccatelli et al., 2010; Hirner and Rettenmeier, 2010; Bernhoft, 2012; Syversen and Kaur, 2012) and recent original papers.

7.1.1. Absorption

Absorption of mercuric and mercurous salts in the gastrointestinal tract is in general low, with mercuric species being more readily absorbed than mercurous species because of higher water solubility. In experimental animals absorption of mercuric mercury salts ranges from 2 – 38 %, depending upon the form and the test conditions. Old experimental human data indicate that approximately 2 % of ingested mercuric chloride is absorbed. In case of high intake, the corrosive action of mercuric chloride might disturb permeability of the gastrointestinal tract, thereby increasing the absorption rate. Absorption of mercuric salts is higher in experimental animals, including mice, rats and goats, and is strongly influenced by nutritional factors (e.g. selenium, sulphydryl-containing molecules, organic ligands such as phytate). It has been suggested that the means by which mercuric mercury is absorbed via the intestine strongly depend on the existence of ligands in the intestinal lumen to which mercuric mercury can bind and form specific mercuric species. Thus, mercuric thio S-conjugates formed within the gastrointestinal tract have been discussed to act as structural and/or functional homologues of endogenous molecules such as amino acids and peptides that are absorbed by specific enterocytic transporters along the small intestine.

Methylmercury species are much more extensively and rapidly absorbed after oral intake than inorganic mercuric and mercurous salts. Absorption rates are higher than 80 % and do not greatly vary between humans and experimental animals. Whether the acidic, high chlorine conditions in the human stomach convert methylmercury cysteine or other S-conjugates of methylmercury present in seafood to methylmercuric chloride is still to be elucidated. Similarly to elemental mercury, methylmercury most likely crosses cell membranes by passive diffusion. The methylmercury L-cysteine complex (MeHgCys) is believed to be transported via the respective amino acid transporters by mimicking L-

[36] http://www.oehha.ca.gov/air/allrels.html
[37] http://www.epa.gov/iris/subst/0370.htm#inhalrfc

methionine. Methylmercury L-cysteine and glutathione complexes might also be transported by organic anion transporters. In humans methylmercury is recycled through the enterohepatic system and nutritional factors seem to influence methylmercury reabsorption rate rather than its primary absorption (Chapman and Chan, 2000). During reabsorption methylmercury comes in contact with the intestinal microflora, which is able to convert methylmercury to mercuric mercury. Additionally, the contribution of genetic background to individual differences in methylmercury absorption has been recently discussed (Gundacker et al., 2010b).

7.1.2. Distribution

In blood mercuric mercury is divided between plasma and erythrocytes, with somewhat more mercuric mercury being present in plasma. In erythrocytes, mercuric mercury is bound to sulphydrylgroups of hemoglobin, probably to metallothionein and to glutathione; in plasma it is distributed in different plasma protein fractions. Based on limited lipophilicity, neither mercurous nor mercuric mercury readily crosses the placental or the blood-brain barrier. Mercuric mercury distribution in the body is strongly differentiated to specific organs and within the respective organs to specific cells. The highest proportion of the body burden is located in the kidney, where mercuric mercury is located in the proximal convoluted renal tubule. Mercuric mercury accumulation in the kidney has been related to induction of binding to metallothionein and the formation of mercuric glutathione conjugates. The next largest deposition occurs in the liver, with highest concentrations to be found in the periportal areas. Additionally, the mucous membranes of the intestinal tract, the epithelium of the skin, the interstitial cells of the testes as well as the choroid plexus in the brain are likely to accumulate mercuric mercury.

In contrast to mercuric mercury, in human blood methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes, where it is bound to the cysteinyl residues of hemoglobin. Interestingly, the fraction of methylmercury bound to red blood cells strongly depends on the species; in humans, the erythrocytes to plasma ratio is about 20, in mice and monkeys about 10 and in rats about 300. The accumulation of methylmercury in rat erythrocytes might also result from the fact that, in comparison with human hemoglobin, rat hemoglobin exhibits almost twice as many free thiol groups. Thus, hemoglobin of rats has recently been shown to bind significantly more ethylmercury units than human hemoglobin, which is most likely the similar case for methylmercury (Janzen et al., 2011). In plasma, most methylmercury (about 99 %) is bound to albumin, which has a free sulphydryl group in a terminal cysteinyl residue. By complex ligand exchange mechanisms, methylmercury is transferred from plasma proteins to the low molecular weight thiols glutathione and cysteine.

The amphiphilic methylmercury crosses the mammary gland, is excreted in milk and thus can reach the child during breastfeeding. In human milk, a mean of 26 - 63 % of total mercury was found to be methylmercury, however the proportion can rise with increased methylmercury intake (Miklavčič et al., 2011b), see also Section 4.4. Moreover, methylmercury is able to cross the hair follicle, the placenta and the blood-brain barrier, allowing accumulation in hair, the fetus and the brain. Fetal distribution is similar to maternal distribution, although fetal methylmercury levels in erythrocytes (Sakamoto et al., 2004, 2008, 2010) and total mercury levels in brain may be higher. The exact mechanisms, by which methylmercury crosses barriers are not fully understood. Due to structural similarities to methionine, methylmercury L-cysteine has been proposed to cross membranes via specific amino acid transporters. Probably because the binding of methylmercury to the erythrocytes retards its entry into the brain, the erythrocytes to plasma ratios correlate with the blood to brain ratios. Thus rats have a much higher blood to brain ratio than humans, which has to be taken into account when using rats to study methylmercury neurotoxicity.

In humans, after absorption into the blood, equilibrium between the blood and body is reached within 30 hours to three days, with about 5 and 10 % ending up in blood and brain, respectively (Kershaw et al., 1980; Clarkson, 2002). Since methylmercury is able to penetrate all membranes and to cross barriers, its tissue distribution is generally uniform and tissue concentrations tend to be constant relative to blood levels. Transport across cell membranes into cells is believed to occur by a

methylmercury complex with cysteine or homocysteine and, exit from cells by a glutathione complex via endogenous glutathione carriers. The highest total mercury concentrations are found in the kidneys.

7.1.3. Metabolism

The metabolism of mercury species involves an oxidation/reduction cycle and the conjugation with glutathione, and seems to be similar in humans and experimental animals. From mice studies some limited evidence exists suggesting that a small amount of mercuric mercury can be reduced to elemental mercury and eliminated as elemental mercury vapour. In contrast, elemental mercury can be readily oxidised by hydrogen peroxide and catalase to mercuric mercury. There is no evidence in literature for the synthesis of methylated mercury species in human tissue. In mammals, methylmercury is partly demethylated to mercuric mercury in the presence of reactive oxygen species (e.g. the hydroxyl radical), which in liver may be formed through the involvement of nicotinamide adenine dinucleotide phosphate (NADPH) cytochrome P450 reductase (Suda and Hirayama, 1992). Besides the liver, demethylation occurs predominantly in the intestinal tract, the spleen, and to a lesser extent in phagocytic cells and slowly in the brain. Thus, mercuric mercury in the brain is generally the result of either in situ dealkylation of organic mercury species, including methylmercury and thiomersal (Rodrigues et al., 2010b), or oxidation of elemental mercury. Demethylation also can not be excluded in other tissues, including the kidney and the gallbladder.

7.1.4. Excretion

The main pathway of excretion of absorbed mercuric mercury is via the urine and, to a lesser extent, via faeces. Excretion via faeces most likely involves formation of glutathione complexes prior to secretion into bile. The half-life of absorbed mercuric mercury in the human body is approximately 40 days.

Methylmercury has a half-life of approximately 70 - 80 days in the human body, with approximately 90 % being excreted by the faecal route as mercuric mercury. The half-life strongly varies in different animal species, e.g. being only 8 and 16 days in mice and rats, respectively. Methylmercury elimination in humans mainly occurs via the biliary route after conjugation with liver glutathione S-transferases (GSTs), which produce a stable glutathione–metal conjugate which is then, eliminated mainly via feces (Ballatori and Clarkson, 1985). GSTs are highly polymorphic in humans and an association between certain GST genotypes (e.g. GSTM1∗0/GSTT1∗0) and the retention of the metal has been established (Mazzaron Barcelos et al., 2012). Methylmercury undergoes enterohepatic cycling, and is thereby partly converted by the intestinal microflora to mercuric mercury, which is less effectively absorbed in the gut and therefore excreted via faeces.

7.1.5. Biomarkers of exposure

In numerous studies fish consumption is positively correlated with total mercury in blood (e.g. Schober et al., 2003; Mahaffey et al., 2004), red blood cells (e.g. Sanzo et al., 2001) and hair, and thus these parameters have often been used as a proxy for methylmercury exposure in individuals. Total blood mercury is closely correlated with ingested methylmercury and generally reflects short-term exposure (giving an estimate of exposure over the most recent two to five months). However, in populations with frequent regular patterns of fish consumption, total blood mercury might reflect a steady-state concentration and could be an accurate measure of average intake over time (NRC, 2000; Roman et al., 2011).

Although total blood mercury is well correlated with methylmercury exposure among populations with regular fish consumption, it is generally known that total blood mercury also comprises inorganic mercury, arising from elemental mercury in dental amalgams and demethylation of methylmercury as well as from other sources of inorganic mercury exposure. Thus depending on the degree of inorganic mercury exposure, total mercury in whole blood is known to give rise to an overestimation of the methylmercury exposure. For these reasons, mercury speciation can be helpful.

Since more than 90 % of methylmercury in the blood is located in the red blood cells and inorganic mercury is more evenly distributed between red blood cells and plasma, total mercury in red blood cells and plasma is sometimes used as a biomarker for methylmercury exposure and inorganic mercury exposure respectively (in the case of low methylmercury exposure in populations with no or low fish consumption) (NRC, 2000). Total mercury in red blood cells seems to be a suitable and even more precise biomarker (compared with total blood mercury) for methylmercury exposure, but has been less commonly reported (Berglund et al., 2005; Roman et al., 2011). In the general population consuming fish, total mercury in plasma is not a reliable biomarker of inorganic mercury exposure, since total mercury in plasma has been shown to be associated with both inorganic and organic mercury (Berglund et al., 2005).

Urinary total mercury (adjusted to specific gravity or creatinine) might be a suitable biomarker of inorganic (and elemental) mercury exposure (also at very low exposure levels), as nearly all mercury in urine is inorganic. Inorganic mercury in urine has been reported not to be strongly associated with fish consumption whereas it is strongly associated with dental amalgam fillings (Berglund et al., 2005) and occupational inorganic/elemental mercury exposure (Morton et al., 2004). In case of frequent tuna consumption (1 - 7 meals per week) (Carta et al., 2003) or high fish consumption (> 4 carnivorous fish meals per week) (Passos et al., 2007) and the absence of occupational inorganic mercury exposure and dental amalgams, urinary total mercury has been related to carnivorous fish consumption. This might result from both absorption of inorganic mercury from fish and demethylation of methylmercury (Passos et al., 2007).

Total mercury in hair is believed to reflect methylmercury exposure at all exposure levels (e.g. Cernichiari et al., 1995; Lindberg et al., 2004; Berglund et al., 2005; Hsiao et al., 2011) and seems to provide the best measure of long term average methylmercury exposure. Measuring total mercury in 1-cm segments of mothers' hair can be used to assess the monthly maternal methylmercury exposure throughout pregnancy (e.g. Boischio and Cernichiari, 1998; Sakamoto et al., 2012). Methylmercury in hair is quite stable over time, indicating that demethylation within the hair is minimal (al-Shahristani and Shihab, 1974; Phelps et al., 1980; Berglund et al., 2005). However, it has to be taken into account that hair treatment as well as inter-individual variability in the toxicokinetics of mercury uptake from blood to hair shaft and hair growth rate may affect mercury hair content. A frequently cited total mercury blood to hair ratio of 1:250 was also used by JECFA (FAO/WHO, 2004). It is well known, that large inter-study and inter-individual variations exist, especially in populations with infrequent fish consumption (WHO, 1990; FAO/WHO, 2004; Berglund et al., 2005; Mergler et al., 2007) and there are some indications that the total mercury blood to hair ratio is lower (e.g. Sakamoto et al., 2007; Yaginuma-Sakurai et al., 2012); however, the Panel considered the evidence insufficient to identify a more appropriate ratio; Appendix E, Table E1 gives an overview of reported blood to hair ratios.

Similarly to hair mercury, total toenail and fingernail mercury are used as indicators of average methylmercury exposure over time, serving as a biomarker for long term methylmercury and most likely not inorganic mercury exposure (Wickre et al., 2004; Björkman et al., 2007; Ohno et al., 2007; Rees et al., 2007; Mozaffarian et al., 2011). Reported hair to toenail ratios for total mercury are in the range 2.38 - 3 (Appendix E, Table E4); reported blood to toenail ratios are summarised in Appendix E, Table E3.

Cord tissue and cord blood are extensively discussed and summarised in a previous evaluation (FAO/WHO, 2007). In summary, total mercury and methylmercury are in general higher (by a factor of 1.7 – 2.2) in cord blood than in maternal blood at parturition (e.g. Björnberg et al., 2005; Kim et al., 2011; Sakamoto et al., 2012). Total mercury in cord tissue correlates with methylmercury in cord tissue, and total mercury and methylmercury in cord tissue correlate with total mercury in cord blood. A significant relationship was reported between fish consumption during pregnancy and total mercury in cord blood (FAO/WHO, 2007). Recently, total mercury in cord blood has been shown to correlate with maternal hair total mercury; the strongest correlation was observed with maternal hair in the first

1 cm-segment from the scalp at parturition (Sakomoto et al., 2012). Appendix E, Table E2 gives an overview of reported ratios for cord blood to maternal biomarkers.

7.1.6. Toxicokinetic models for conversion between chronic dietary exposure and concentration in blood

The concentration of mercury in blood can be related to steady state dietary exposure by a one-compartment toxicokinetic model expressed by the following equation (WHO, 1990; US-EPA 2001b):

$$d = C*b*V/(A*f*b.w.)$$

where

d = dietary exposure (µg/kg b.w. per day)
C = concentration in blood (µg/L)
b = elimination constant (ln 2 / half-life in blood = 0.014 per day)
V = blood volume (L)
A = gastrointestinal absorption factor (0.95)
f = fraction of absorbed dose distributed to blood
b.w. = body weight (kg)

Slightly different values for two of the parameters in this model have been used in different risk assessments of mercury. A blood volume of 5 L (corresponding to 7.1 % of the b.w.) was used both for a 70 kg b.w. by WHO (WHO, 1990) and for a 60 kg b.w. (corresponding to 8.3 % of the b.w.) by US-EPA (US-EPA 2001b). WHO used a fraction of absorbed dose distributed to blood of 0.05, whereas EPA used 0.059. JECFA later refined the model in order to take into account pregnant women, and used a blood volume of 9 % of the b.w. (which corresponds to 6.3 L for a 70 kg pregnant woman), and a fraction of absorbed dose distributed to blood of 0.05 (FAO/WHO, 2004). A thorough discussion of the variabilities and uncertainties associated with the parameters in a similar toxicokinetic model was provided by Stern (Stern, 2005). No new information about the parameters has been indentified by the Panel, except for a longer half-life of mercury in blood reported recently from an intervention study where participants consumed mercury in fish at 3.4 µg/kg b.w. per day for 14 weeks, followed by a 15-weeks washout period (Yaginuma-Sakurai et al., 2012). However, after correcting for background exposure, the half-life was in the same range as the 50 days previously used by WHO and EPA.

Section 7.5.1 gives an overview of the values for the parameters that were used in the current risk assessment.

7.2. Toxicity of mercury in experimental animals

The toxicity of inorganic and organic mercury in experimental animals is discussed below. The toxicity of elemental mercury and thiomersal is not discussed in this opinion since mercury is not present in that form in food in toxicologically significant amounts, unless there is accidental or deliberate contamination with elemental mercury. There are considerable differences in the toxicokinetics between elemental and mercuric mercury. Elemental mercury vapour is readily taken up through the lungs and subsequently easily penetrates membranes and physiological barriers due to its lipophilicity (ATSDR, 1999). On the other hand, lifetime of elemental mercury in the body is rather short, because of the rapid oxidation of elemental mercury to mercuric mercury. Effects on the nervous system seem to be the most sensitive toxicological endpoint following elemental mercury exposure (WHO, 2008), and there is some evidence that the ultimate neurotoxic mercury species after elemental mercury vapour exposure is mercuric mercury (Warfvinge, 2000).

7.2.1. Methylmercury

In all experiments described below, the test substance was given as methylmercuric chloride.

There are extensive toxicological data on the effects of organic mercury, particularly methylmercury, in laboratory animal species. These have been reviewed elsewhere (US-EPA, 1997; ATSDR, 1999; NRC, 2000; WHO, 2000, FAO/WHO, 2004, 2007). A report of an EFSA contractor (Hassauer et al., 2012) was used as a starting point and further details of animal toxicity studies on organic mercury, published since 2002 in addition to those summarised below, can be found in that report. Since the critical toxicological information for establishing a health-based guidance value for methylmercury is derived from the human epidemiological data, the animal data are only briefly discussed here.

As summarised in the CONTAM Panel's earlier opinion (EFSA, 2008), oral exposure of laboratory animals to methylmercuric chloride at doses of > 0.5 mg /kg b.w. per day, expressed as mercury, has resulted in damage to the kidneys, stomach and large intestine, changes in blood pressure and heart rate, as well as adverse effects on sperm and male reproductive organs. In addition, several studies have reported an increase in embryonic lethality, decrease in fetal body weight and teratogenicity in rats (cleft palate, vertebral defects, histological abnormalities in the cerebellum, effects on lachrymal glands and ribs) (ATSDR, 1999).

7.2.1.1. Cardiovascular toxicity

There is evidence in experimental animals that the cardiovascular system might be adversely affected by organic mercury. Grotto et al. (2009b) reported statistically significant increases in systolic blood pressure in adult male rats given methylmercuric chloride by oral gavage for 100 days at 0.1 mg/kg b.w. per day, equivalent to 0.08 mg/kg b.w. per day expressed as mercury. Jin et al. (2012) also found that treatment of adult rats with methylmercury for 14 days by oral gavage at 3 mg/kg b.w. per day (dose said to be expressed as methylmercury) caused changes in several biomarkers that indicate it may increase the risk of cardiovascular disease; methylmercury increased urinary F2-isoprostanes, decreased circulating paraoxonase-1 activity, and increased serum oxidised low-density lipoprotein (LDL) levels and associated systemic inflammation and endothelial dysfunction.

7.2.1.2. Adult and developmental neurotoxicity

The main focus of studies on the effects of methylmercury in experimental animals has been the brain. Both adult and fetal brains are susceptible to methylmercury toxicity. In adult rodents, the major clinical effects include motor disturbances, such as ataxia, tremors and paralysis, as well as signs of sensory dysfunction, such as impaired vision. The predominant neuropathological feature is degenerative changes in the cerebellum, which is likely to be the mechanism involved in many of the motor dysfunctions (US-EPA, 1997). The developing nervous system appears to be more sensitive than that of the adult. Animal studies provide evidence of damage to the nervous system from exposure to methylmercury during development, and these effects remain/continue to develop during aging, even after the exposure stops. Considering the earlier literature (reviewed in NRC, 2000), developmental neurotoxicity has been observed in offspring of monkeys, rats, mice and guinea pigs treated at oral doses of < 1 mg/kg b.w. per day, expressed as methylmercury, during gestation, lactation and/or during the post-weaning period. In monkeys, for example, deficits in social behaviour, and in visual, auditory and somato-sensory function, have been reported. The lowest reported dose of methylmercury causing adverse effects in either rodents or primates was 0.01 mg/kg b.w. per day, expressed as methylmercury.

As with some of the earlier studies, some more recent studies on developmental neurotoxicity of low-dose exposure to methylmercury have indicated adverse effects at or below 0.5 mg/kg b.w. per day, expressed as methylmercury hydroxide, equivalent to 0.47 mg/kg b.w. per day expressed as mercury. Sensory and motor disturbances, cognitive deficits, and depression-like behaviour are among the main alterations observed in rodent offspring following prenatal/perinatal exposure, with males being the most sensitive to the developmental neurotoxic effects of methylmercury (studies reviewed in Onishchenko et al., 2012). For example, the alteration in motivation-driven behaviour (i.e. depression, as measured by inactivity in a forced swim test) has been shown in the offspring of mice exposed to a dose of 0.5 mg/kg b.w. per day, expressed as methylmercury hydroxide, equivalent to 0.47 mg/kg b.w. per day expressed as mercury in the drinking water from gestational day seven until lactational day

seven. The effect is long-lasting and is associated with epigenetic modifications of the brain-derived neurotrophic factor gene in the hippocampus (Onishchenko et al., 2008).

Bourdineaud et al. (2011) have compared the effects of feeding male mice, for one or two months from three weeks of age, a diet containing methylmercury-contaminated fish, with a diet to which methylmercury was directly added, or a control diet. The amount of mercury ingested was equivalent to 0.05 mg/kg b.w. per day, expressed as total mercury, for both treated groups. Those consuming the diet containing methylmercury-contaminated fish showed statistically significant changes in behaviour in a Y-maze (reduction in spontaneous alternations) and in an open field test (decreased grooming and increased time spent in the centre), together with increased dopamine turnover in the hippocampus after 2 months of treatment. There were no statistically significant changes in behaviour after 1 month of treatment. There were no such changes in those given diet to which methylmercury had been directly added.

Paletz et al. (2006) investigated spatial and visual (non-spatial) discrimination reversal in the offspring of rats exposed to methylmercury in the drinking water from 2 weeks before breeding until lactation day 16. The concentrations corresponded to maternal exposures of approximately 0.04 or 0.4 mg/kg b.w. per day, expressed as mercury. Increased errors in both types of discrimination reversal test were observed at both doses in the offspring when adult, aged 15-20 months, particularly in the first reversal trials. There were no effects of treatment when tested later at 24-27 months.

Two of the more recent studies have indicated adverse effects at doses of 0.01 or 0.02 mg/kg b.w. per day. They are described below.

An investigation in 2-month-old mice exposed prenatally to methylmercuric chloride in the diet on gestation days 8 - 18 reported effects on locomotor activity at 0.01 mg/kg b.w. per day, expressed as methylmercury (equivalent to 0.009 mg/kg b.w. per day expressed as mercury), as measured by statistically significantly reduced times on a rotating rod and statistically significantly reduced activity in an open field (Montgomery et al., 2008). However, only one control and one dose group were tested, the number of offspring tested ranged from 4 to 15 per sex, and statistical analyses of the test outcomes did not appear to take account of possible litter effects.

Huang et al. (2011) investigated developmental parameters, locomotor and auditory function in mice following exposure to methylmercury chloride at a dose of 0.02 mg/kg b.w. per day by oral gavage, equivalent to 0.019 mg/kg b.w. per day expressed as mercury (See also Section 7.2.2.3 for more details on this study). Only this one dose was tested. The treatment regime comprised dosing of both male and female parents for four weeks before mating, dosing of the pregnant and lactating dams, and dosing of some of the offspring for a further seven weeks from weaning on postnatal day 21. Some offspring were not exposed prenatally or preweaning but were exposed postnatally for seven weeks from weaning. Motor, behavioural and auditory tests were conducted at the end of the seven-week postweaning dosing period in 12-15 male offspring per treatment group. Statistically significant adverse effects were observed on litter size, male offspring body weight gain to 10 weeks of age, locomotor activity and auditory function. Rats seem to be less sensitive than mice with respect to locomotor activity; in studies in which methylmercuric chloride was given in the drinking water, a no-observed-adverse-effect level (NOAEL) of 0.04 mg/kg b.w. per day, expressed as methylmercury (equivalent to 0.037 mg/kg b.w. per day expressed as mercury), has been reported for effects on locomotor activity following chronic exposure of adult rats, and a NOAEL of 0.4 mg/kg b.w. per day (the highest dose tested), expressed as methylmercury (equivalent to 0.37 mg/kg b.w. per day expressed as mercury), in offspring following prenatal and pre-weaning exposure to methylmercury (Day et al., 2005).

7.2.1.3. Developmental immunotoxicity

The effects of methylmercury on developmental and immune parameters were studied in the offspring of rats given methylmercuric chloride by oral gavage at doses of 0, 0.1, 0.4, 0.7, 1.0, 1.5, or 2.0 mg/kg

b.w. per day, expressed as methylmercuric chloride (equivalent to 0, 0.08, 0.32, 0.56, 0.8, 1.2, or 1.6 mg/kg b.w. per day expressed as mercury) from gestation day 6 to lactation day ten (Tonk et al., 2010). Standard developmental and reproductive parameters were studied together with a wide range of structural and functional immune parameters, covering spleen, thymus and bone marrow development and responses in tests covering the function of the innate, humoral and cellular arms of the immune system. Immune parameters were assessed in male offspring on postnatal day (PND) 21, 42 and 70. Dose-response data were compared using the BMD approach. Methylmercury treatment caused some complete litter losses, reductions in pup growth and increased pup mortality on PND 1-21; the most sensitive developmental parameter was complete litter loss with a BMD of 0.91 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.73 mg/kg b.w. per day expressed as mercury) and a BMDL of 0.18 mg/kg b.w. per day expressed as methylmercuric chloride on a BMR of 10 % loss (equivalent to 0.14 mg/kg b.w. per day expressed as mercury). Effects were observed on a number of immune parameters at one or more of the three postnatal time points and some of these effects were observed at doses lower than those causing effects on litter loss, pup growth and pup mortality. The most sensitive immune parameter was the T-cell dependent antibody response on PND 35, as measured in the primary anti-KLH (Keyhole Limpet Hemocyanin) immunoglobulin (Ig) G response. It showed a dose-related decrease in response for which the BMD was 0.039 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.03 mg/kg b.w. per day expressed as mercury) and the BMDL was 0.010 mg/kg b.w. per day expressed as methylmercuric chloride on a BMR of 5 % (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). Other immune parameters affected at low doses were some red blood cell parameters, and there were dose-dependent decreases in absolute and relative spleen weight, absolute thymus weight, and absolute number and percentage of several splenic lymphocyte subsets. Of the functional parameters, there were dose-dependent decreases in NK cell activity and lymphoproliferative response, and dose-dependent increases in the production of several cytokines. Overall, this study demonstrated that certain immune parameters in developing animals are more sensitive to the effects of methylmercury than are standard developmental parameters, with the lowest BMDL being 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). The Panel noted that the BMD is below the lowest dose tested.

7.2.1.4. Carcinogenicity

Carcinogenicity studies on methylmercury, summarised elsewhere (US-EPA, 1997; NRC, 2000; WHO, 2000, FAO/WHO, 2004, 2007), show some evidence of carcinogenicity in two strains of mice, but studies in rats are negative. In ICR and B6C3F1 mice exposed orally to methylmercuric chloride, only males were observed to have an increased incidence of renal adenomas, adenocarcinomas and carcinomas. Renal epithelial cell hyperplasia and tumours were observed only in the presence of profound nephrotoxicity, suggesting that the tumours may be a consequence of reparative changes to the damaged kidneys. No increase in tumour incidence was observed in studies conducted in rat and cat. In summary, tumours were observed at a single site, in a single animal species and sex. Therefore, they were considered to provide limited evidence of carcinogenicity (US-EPA, 1997; NRC, 2000).

7.2.1.5. Conclusions on methylmercury

Recent studies in experimental animals have indicated effects at low doses. One study has shown adverse effects on litter size and male offspring body weight gain, and changes in locomotor activity and auditory function in mice at a dose of 0.02 mg/kg b.w. per day expressed as mercury (the only dose tested). In a developmental immunotoxicity study the lowest reported-BMDL for methylmercury in animal studies was 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). The Panel noted that the BMD is below the lowest dose tested.

7.2.2. Inorganic mercury

The toxicity of inorganic mercury was reviewed by JECFA at its meeting in February 2010 (FAO/WHO, 2011b) and it was concluded that the kidney is the critical target organ. The Panel has

also briefly reviewed the toxicity of inorganic mercury in an earlier opinion on 'Mercury as an undesirable substance in animal feed' (EFSA, 2008). The key information from those reviews is summarised below, updated with information from studies published since the beginning of 2010 that report adverse effects at doses around or below the previously reported lowest-observed-adverse-effect levels (LOAEL) and NOAELs for effects on the kidney. A report of an EFSA contractor (Hassauer et al., 2012) was used as a starting point and details of other animal toxicity studies on inorganic mercury, published since 2002, can be found in that report. These confirm previous findings on inorganic mercury with respect to known targets and modes of action (i.e. kidney, liver, nervous system, immune system, reproductive system, embryo-fetal development and oxidative stress). The critical new studies were evaluated by the Panel from the original publications. Studies with mercuric chloride, also known as mercury(II) chloride, are the most relevant, since studies carried out using mercuric sulphide, also known as cinnabar, have utilised high oral doses.

7.2.2.1. Acute toxicity

The kidney appears to be the critical target organ for the effects of acute ingestion of inorganic mercury compounds, although there are several animal studies in which neurotoxicity induced by inorganic mercury has been reported. Acute oral exposure of rats and mice to inorganic mercury, given as mercuric chloride, at 2 - 5 mg/kg b.w. per day, expressed as mercury, given by oral gavage five days per week over 14 days, resulted in increases in kidney weight; higher doses given using the same dosing regimen or given as single oral gavage doses induced tubular necrosis (ATSDR, 1999). Male rats show higher sensitivity than females, resulting in more severe histological changes (NTP, 1993). At higher doses of inorganic mercury, haematological and hepatic effects were observed and severe gastrointestinal damage was also seen following very high doses, especially with mercuric compounds, which are more corrosive than mercurous compounds (WHO/IPCS, 2003; FAO/WHO, 2011b).

7.2.2.2. Sub-acute and sub-chronic toxicity

The kidney is also the key target organ in repeated-dose, sub-acute and sub-chronic studies in rodents, causing damage to renal tubular epithelium and immunological glomerular disease (US-EPA, 1997; ATSDR, 1999; FAO/WHO, 2011b). Autoimmune glomerular nephritis has been induced by mercuric chloride in genetically susceptible strains of rats and mice and there is evidence that human exposure to inorganic mercury can also trigger an autoimmune response in glomeruli (NRC, 2000).

Prior to the 2011 JECFA review, reviews by other agencies had identified several studies in rodents from the available toxicology databases and used them to derive health-based guidance values, all based on manifestations of kidney damage (WHO/IPCS, 1991, 2003; US-EPA, 1995; ATSDR, 1999). These included proteinuria in the rat (Druet et al., 1978), IgG deposition in the glomeruli and renal arteries in the rat (Bernaudin et al., 1981; Andres, 1984), and changes in kidney weight and cytoplasmic vacuolation of the renal tubular epithelium in mice (NTP, 1993). The JECFA monograph describes the relevant studies in detail (FAO/WHO, 2011b).

The key studies considered by the JECFA (FAO/WHO, 2011b) for derivation of a PTWI for inorganic mercury were the 6-month rat and mouse studies conducted by the NTP (1993). Fischer 344 rats, 10 animals per sex per group, were given mercuric chloride by oral gavage, at 0, 0.312, 0.625, 1.25, 2.5 or 5 mg/kg b.w. per day, 5 days per week, for 6 months (equivalent to 0, 0.23, 0.46, 0.92, 1.9 or 3.7 mg/kg b.w. per day, expressed as mercury). B6C3F1 mice, 10 animals per sex per group, were given mercuric chloride by oral gavage at 0, 1.25, 2.5, 5, 10 or 20 mg/kg b.w. per day, 5 days per week, for 6 months (equivalent to 0, 0.92, 1.9, 3.7, 7.4 or 14.8 mg/kg b.w. per day, expressed as mercury). In the rats, body weight gains were decreased in males at the highest dose and in females at or above 0.46 mg/kg b.w. per day, expressed as mercury. Absolute and relative kidney weights were statistically significantly increased in both sexes at doses of 0.46 mg/kg b.w. per day expressed as mercury or greater, with no effect on kidney weight observed at 0.23 mg/kg b.w., expressed as mercury. Nephropathy was present in the majority of control and test rats; its severity was increased in males given doses of 0.92 mg/kg b.w. per day expressed as mercury or greater and in females at the

highest dose of 3.7 mg/kg b.w. per day, expressed as mercury. In mice, males in the highest dose group showed a decrease in body weight gain. Statistically significant increases in absolute kidney weight were observed at doses of 3.7 mg/kg b.w. per day expressed as mercury, or greater, and statistically significant increases in relative kidney weight at 7.4 and 14.8 mg/kg b.w. per day, expressed as mercury in male mice. The kidney weight changes were accompanied by an increased incidence of cytoplasmic vacuolation of renal tubular epithelium in males exposed to 3.7 mg/kg b.w. per day expressed as mercury or greater. Female mice showed no kidney changes.

7.2.2.3. Adult and developmental neurotoxicity

Compared with the number of studies on methylmercury, there have been relatively few studies on the possible neurotoxicity of mercuric and mercurous salts at low doses in experimental animals.

In a recent, low-dose study (Huang et al., 2011), mice were exposed to mercuric chloride by oral gavage, as part of a larger study (see Section 7.2.1.2. for a description of the rest of study). The treatment regime comprised dosing of both male and female parents for 4 weeks before mating, dosing of the pregnant and lactating dams, and dosing of some of the offspring for a further seven weeks from weaning on postnatal day 21, while others were not dosed postweaning. A further group of offspring were not exposed prenatally or preweaning but were exposed postnatally for seven weeks from weaning. Controls were given vehicle (distilled water) and treated animals were given 0.5 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.37 mg/kg b.w. per day, expressed as mercury). Only this one dose was tested. There was a statistically significant reduction in litter size in those exposed pre-mating and during gestation. Male offspring body weight gain by 10 weeks of age was statistically significantly reduced in the groups exposed prenatally and preweaning, but not in those exposed only after weaning. Motor, behavioural and auditory tests were conducted at the end of the seven-week postweaning dosing period in 12 - 15 male offspring per treatment group. In open field tests, treated males, in comparison with controls, showed statistically significant increases in spontaneous locomotor activity, irrespective of the time period(s) at which they had been exposed to mercuric chloride. There was a statistically significant reduction in stereotype-1 activity in those exposed only from weaning and a statistically significant increase in stereotype-1 activity in those exposed continuously during the prenatal, preweaning and postweaning periods. The nature of stereotype-1 behaviour was not further explained by the authors. Males exposed continuously during the prenatal, preweaning and postweaning periods and those exposed only postweaning also showed a statistically significant reduction in retention time on an accelerating rotating rod. Hearing thresholds were measured in anaesthetised animals by auditory brainstem responses (or auditory evoked potentials) in response to clicks of varying sound pressure levels, ranging from 110 dB to -5 dB. Hearing thresholds were statistically significantly raised by 20 to 30 dB compared with controls in all groups exposed to mercuric chloride, irrespective of the time period(s) of treatment. Absolute and interwave latencies of the auditory brainstem response waveform recorded at a fixed sound pressure level of 105 dB were also statistically significantly increased in all treated males. Lipid peroxidation levels in cerebral cortex, cerebellar cortex and brainstem were statistically significantly increased in all treated males. Na^+/K^+-ATPase activity was statistically significantly elevated in the cerebral cortex and brainstem of all treated males and statistically significantly reduced in the cerebellar cortex of male offspring treated only in the postweaning period and statistically significantly increased in those treated in the prenatal and preweaning periods or treated continuously in the prenatal, preweaning and postweaning periods. The concentration of nitric oxide was statistically significantly reduced in whole blood of male offspring treated only in the postweaning period and statistically significantly increased in those treated in the prenatal and preweaning periods or treated continuously in the prenatal, preweaning and postweaning periods. In brain tissue (cerebral cortex, cerebellar cortex and brainstem), nitric oxide was statistically significantly decreased in all treated male offspring, irrespective of the time period(s) of treatment. Measurement of the mercury content of whole blood and brain tissue confirmed that exposure of treated animals was statistically significantly increased by up to 50-fold in whole blood, by up to 20-fold in cerebral cortex and by more than 10-fold in the cerebellar cortex and brainstem, compared with controls. The authors of this study proposed that

mercury-induced ototoxicity may be mediated by oxidative stress, altered Na^+/K^+-ATPase and nitric oxide activities, and the signalling between these three systems.

In an earlier study, exposure to a high dose of mercuric sulphide (1 000 mg/kg b.w. per day, expressed as mercuric sulphide, equivalent to 862 mg/kg b.w. per day, expressed as mercury) by oral gavage also caused adverse effects on the auditory system in mice (Chuu et al., 2001). A lower dose of 100 mg/kg b.w. per day, expressed as mercuric sulphide (equivalent to 86 mg/kg b.w. per day, expressed as mercury) was a NOAEL. The higher dose of mercuric sulphide needed to elicit effects on the auditory system compared with mercuric chloride likely reflects the considerably lower solubility and gastrointestinal absorption of mercuric sulphide compared with mercuric chloride (ATSDR, 1999; Liu et al., 2008).

The study of Huang et al. (2011) indicates ototoxicity in mice after prenatal, perinatal and/or post-weaning exposure to inorganic mercury, at a dose equivalent to 0.37 mg/kg b.w. per day, expressed as mercury (the only dose tested). This effect level is slightly higher than the dose of 0.23 mg/kg b.w. per day expressed as mercury in the NTP (1993) studies, which was without effects on kidney weight and was used by the JECFA to establish a PTWI, but a NOAEL for ototoxicity has not been established, nor have the findings yet been replicated by others. However, it should be noted that the JECFA used the lowest $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury for effects on kidney weight as the reference point for deriving the PTWI. The $BMDL_{10}$ is six times lower than the effect level for ototoxicity.

7.2.2.4. Developmental and reproductive toxicity

Oral exposure to inorganic mercury has been reported to cause developmental toxicity, such as increases in resorptions and fetal abnormalities, and reproductive toxicity, such as changes in the oestrous cycle and ovulation (for details see US-EPA, 1997; FAO/WHO, 2011b). These effects occur at doses higher than the lowest $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury for kidney weight changes.

In a recent, low-dose, two-generation study on lead, cadmium and mercury (Lukačínová et al., 2011, 2012), Wistar rats were given 1 µM mercuric chloride in the drinking water, starting with the parental generation from 52 days of age and continuing through the F1 and F2 generations, terminating at the 156^{th} week in each generation. Ten males and females per group were used to breed each generation and all animals were allowed to breed repeatedly between 13 and 78 weeks of age. The concentration of mercuric chloride in the drinking water corresponds to 270 µg/L. From the averages given by the authors for body weight and drinking water intake over the entire duration of the experiment, it can be calculated that the average exposure to mercuric chloride across the parental, F1 and F2 generations was 0.03 – 0.04 mg/kg b.w. per day expressed as mercuric chloride, equivalent to 0.022 – 0.029 mg/kg b.w. per day expressed as mercury. At 78 weeks of age, there were statistically significant reductions in body weight of 26 %, 27 % and 40 % in parental, F1 and F2 mercuric chloride-treated generations compared with controls. Exposure to mercuric chloride was reported to cause a statistically significant reduction in percentage survival to three years of age (controls 90 - 100 % versus treated 30 - 35 %), and consequently in lifespan, in all three generations. In those exposed to mercuric chloride, the number of litters from the parental generation was higher than in controls, comparable to controls in the F1 and statistically significantly lower than controls in the F2. The number of pups per litter at birth was reduced in the F2 generation in those exposed to mercuric chloride compared with controls. The proportion of weanlings surviving from birth was also lower in the breedings from all three generations of those exposed to mercuric chloride (56 - 64 % compared with 90 - 91 % in controls). Serum total protein, albumin, transferrin and ferritin levels, considered to be biomarkers for exposure to heavy metals, were statistically significantly increased following mercuric chloride treatment.

The multigeneration study of Lukačínová et al. (2011, 2012) reported adverse effects on survival, lifespan and reproductive parameters at a lower level of mercury exposure than hitherto reported for kidney effects. In the NTP study (NTP, 1993), it is not known to what extent those exposures might

have influenced survival as the study was not a multigeneration study, but rather only six months in duration. It is noted that only one dose and 10 animals per group were used. It is also noted that these findings are unusual in that survival at three years of age in the three generations of untreated control rats was reported to be 90 - 100 %, compared to 30 - 35 % in the corresponding generations of mercury treated animals. Such a high survival rate in control Wistar rats would not be expected at three years of age. For these various reasons, the Panel considers that these results cannot be used for risk assessment. It is, however, noted that adverse effects on fertility/litter size, postnatal survival and offspring body weight in rats and on fertility in mice were also reported by another research group in two earlier multigeneration studies in which mercuric chloride was administered continuously by oral gavage to Sprague-Dawley rats of the parental, F1 and F2 generations and to C57BL/6 mice of the parental and F1 generations (Atkinson et al., 2001; Khan et al., 2004). Doses ranged from 0.5 – 2.5 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.37 – 1.85 mg/kg b.w. per day, expressed as mercury) in the rat study and from 0.25 – 1.0 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.18 – 0.74 mg/kg b.w. per day, expressed as mercury) in the mouse study. Adverse effects on one or more reproductive parameters were noted in both studies at all dose levels, but it should be noted that in rats the effects were more severe in the parental generation than in the F1 and F2 generations, and in mice the effects on fertility were not dose-related and fertility in controls was low. Although NOAELs were not established in these two studies, the lowest reported levels for reproductive effects are three times higher than the lowest $BMDL_{10}$ for kidney effects of 0.06 mg/kg b.w. per day (expressed as mercury) used as the reference point for establishing the JECFA PTWI.

7.2.2.5. Carcinogenicity

As summarised in a previous opinion (EFSA, 2008), there is equivocal evidence of carcinogenicity of mercuric chloride in animals. In two-year, oral gavage studies conducted by the NTP (1993), groups of 60 B6C3F1 mice were given mercuric chloride at 0, 5 and 10 mg/kg b.w. per day (equivalent to 3.7 and 7.4 mg/kg b.w. per day, expressed as mercury), for five days per week. Groups of 60 Fischer 344 rats were given 0, 2.5 or 5 mg/kg b.w. per day, expressed as mercuric chloride (equivalent to 1.9 and 3.7 mg/kg b.w. per day, expressed as mercury), for five days per week. Focal papillary hyperplasia and squamous cell papillomas of the forestomach, together with thyroid follicular adenomas and carcinomas, were observed in male rats given 3.7 mg/kg b.w., expressed as mercury. An increased incidence of squamous cell forestomach papillomas in female rats at 3.7 mg/kg b.w. (expressed as mercury) and renal adenomas and carcinomas in male mice at 7.4 mg/kg b.w. (expressed as mercury) were also observed. However, as has been noted by the NTP and others, the forestomach tumours did not progress to malignancy (NTP, 1993; US-EPA, 1997). The relevance of the thyroid carcinomas has also been questioned, because these neoplasms are usually seen in conjunction with increased incidences of hyperplasia and adenomas, which were not observed in this study (NTP, 1993; US-EPA, 1997). The kidney tumours observed in mice occurred at doses that were also nephrotoxic, and would be expected to arise by a non-genotoxic mechanism (ATSDR, 1999). In the JECFA review (FAO/WHO, 2011b) the data from the carcinogenicity studies were not considered to be the critical data for dose-response modelling for establishing the PTWI. The CONTAM Panel agrees with this view, particularly in view of the fact that the PTWI is based on kidney effects at a much lower dose than those resulting in tumours.

7.2.2.6. Conclusions on inorganic mercury toxicity

The critical target organ for toxicity of inorganic mercury is the kidney. Other targets include the liver, nervous system, immune system, reproductive system and the developing organism. Having considered the more recent data on experimental animals exposed to inorganic mercury, the CONTAM Panel has not identified any studies in experimental animals exposed to inorganic mercury indicating effects on the kidney at doses lower than the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, identified for effects on kidney weight from the NTP (1993) study. Table 22 summarises low-dose animal toxicity studies on mercuric chloride. The Panel noted that some recent studies (Huang et al., 2011; Lukačínová et al., 2011, 2012) have reported ototoxicity and reproductive

toxicity at relatively low doses. These studies had limitations, which have been discussed in Sections 7.2.2.3 and 7.2.2.4.

Table 22: Summary of low-dose animal toxicity studies on mercuric chloride.

Species, route, dose, duration	Toxic effects	NOAEL/LOAEL/BMDL expressed as mercury	Comment	Reference
Rat, s.c. 0, 0.05 0.1, 0.25, 0.50, 1.0, 2.0 mg $HgCl_2$/kg b.w., 3 times per week for 8 or 12 weeks	Immune type glomerulonephritis, proteinuria	LOAEL 0.226 mg Hg/kg b.w. per day	Brown Norway rat, regarded as good surrogate for effects of mercury in sensitive humans	Druet et al. (1978)
Rat, oral gavage 3.0 mg $HgCl_2$/kg b.w. once per week for up to 60 days	Immune type glomerulonephritis, proteinuria	LOAEL 0.317 mg Hg/kg b.w. per day	Brown Norway rat	Bernaudin et al. (1981)
Rat, oral gavage 0, 3.0 mg $HgCl_2$/kg b.w., 2 times per week for 60 days	Immune type glomerulonephritis	LOAEL 0.633 mg Hg/kg b.w. per day	Brown Norway rat	Andres (1984)
Rat, oral gavage 0, 0.312, 0.625, 1.25, 2.5, 5 mg $HgCl_2$/kg b.w. per day, 5 days per week, for 6 months	Absolute and relative kidney weights	NOAEL 0.23 mg Hg/kg b.w. per day LOAEL 0.46 mg Hg/kg b.w. per day $BMDL_{10}$ 0.06 mg Hg/kg b.w. per day	Fisher 344 rat $BMDL_{10}$ of 0.06 mg Hg/kg b.w. per day used by JECFA to establish a PTWI of 4 µg/kg b.w.	NTP (1993)
Rat, oral gavage 0, 0.5 – 2.5 mg $HgCl_2$/kg b.w. per day, two-generation study	Dose-related reductions in fertility live pups per litter, postnatal survival and offspring body weight	LOAEL 0.36 mg Hg/kg b.w. per day	NOAEL not established. At lowest dose tested, substantial effects on F_0 fertility and live pups per litter in F_1. In F_2, effects only on live pups per litter and postnatal survival at highest dose tested.	Atkinson et al. (2001)
Mouse, oral gavage 0, 0.25 – 1.0 mg $HgCl_2$/kg b.w. per day, two-generation study	Reduced fertility	LOAEL 0.18 mg Hg/kg b.w. per day	NOAEL not established. At lowest dose tested, substantial effect on fertility, but low in controls (44 %) and no dose-response (16 % in all three dose groups)	Khan et al. (2004)
Mouse, oral gavage 0, 0.5 mg $HgCl_2$/kg b.w. per day, one-generation study	Reduced litter size; offspring had reduced weight gain, changes in motor, behavioural and auditory function	Effects at only dose tested: 0.37 mg Hg/kg b.w. per day	NOAEL not established, only one dose tested	Huang et al. (2011)
Rat, oral in drinking water 0, 0.03 - 0.04 mg $HgCl_2$/kg b.w. per day, two-generation study	Reduced body weight in parents and offspring; reduced litter size, reduced offspring survival to 3 years	Effects at only dose tested: 0.022-0.029 mg Hg/kg b.w. per day	NOAEL not established only one dose tested; very high survival rate to 3 years in controls (see 7.2.2.4.)	Lukačínová et al. (2011, 2012)

b.w.: body weight; BMDL: 95 % benchmark dose lower confidence limit; Hg: mercury; $HgCl_2$: mercuric chloride; LOAEL: lowest-observed-adverse-effect level; NOAEL: no-observed-adverse-effect level; s.c.: subcutaneous.

7.3. Modes of action

Mechanistically cellular toxicity of methylmercury and mercuric mercury is largely dependent upon their electrophilic properties, which allows for their interaction with soft nucleophilic groups, mainly thiols and selenols (especially methylmercury (e.g. Wagner et al., 2010)) from low- and high-molecular-weight biomolecules. These interactions with biomolecules are at the cellular level most likely responsible for oxidative stress, disturbances in calcium homeostasis and, cytoskeletal alterations and contribute to and/or cause toxicity in the target organs.

Based on recent reports of ATSDR (ATSDR 1999), JECFA (FAO/WHO 2007, 2011b), numerous recent reviews and recent original papers, this chapter especially focuses on neurotoxic modes of actions, genotoxic effects and mechanism of vascular/cardiovascular toxicity of mercuric mercury and methylmercury.

Regarding the toxic modes of action of methylmercury it is important to note that the majority of *in vitro* and *in vivo* toxicological studies have used the chloride salt, methylmercuric chloride. However, methylmercury in fish is complexed to cysteine, with cysteine likely to be part of a peptide or protein (Harris et al., 2003), and initial studies indicate that MeHgCys differs from methylmercuric chloride in terms of bioavailability, tissue distribution and toxicity. Therefore, differences between the methylmercury species might depend also on the animal species investigated. Thus, in male Wistar rats fed with fish meal diets containing methylmercury contaminated fish and uncontaminated fish supplemented with methylmercuric chloride at similar levels, Berntssen et al. observed a higher faecal excretion, lower tissue accumulation and metallothionein induction in rats following exposure to methylmercury naturally incorporated in fish compared to methylmercuric chloride supplemented fish (Berntssen et al., 2004). In mice, uptake by liver and brain after intraperitoneal exposure to methylmercuric chloride or MeHgCys was higher in the case of MeHgCys, whereas mercury kidney levels were higher after exposure to methylmercuric chloride (Roos et al., 2010). Glover et al. (2009) determined the impact of methylmercury speciation in the maternal diet on developing offspring of mice and concluded that there are important differences between the mercury species in terms of their toxic impact, although this was not manifested by changes in tissue accumulation. Thus, methylmercuric chloride, but not MeHgCys, disturbed pup behaviour and microarray analyses from pup brains revealed strong differences between the mercury species. There is only one *in vitro* study available that applies shortly before the experiment prepared MeHgCys. This study showed strong differences in cellular toxicity between methylmercuric chloride and the naturally occurring and therefore likely more relevant MeHgCys (Oyama et al., 2000).

7.3.1. Mechanisms of neurotoxicity and neurodevelopmental toxicity

The neurotoxic and neurodevelopmental effects of methylmercury most likely arise from multiple modes of actions, which have been recently summarised in numerous reviews (Castoldi et al., 2008; Aschner et al., 2010; Ceccatelli et al., 2010; Farina et al., 2011a, b; Kaur et al., 2011; Syversen and Kaur, 2012). In the brain methylmercury is converted partly and to unknown extent into mercuric mercury (Clarkson and Magos, 2006). Although there are several studies claiming that mercuric mercury might be the ultimate toxic compound in the brain after methylmercury exposure, many reports provide evidence that mercuric mercury cannot play such a role. Thus, mercuric mercury derived from demethylation of methylmercury in brain cells is most likely not the mercury species responsible for the neurological effects induced by methylmercury intake (summarised in Syversen and Kaur, 2012).

Regarding the search for sensitive brain target cells, Takeuchi et al. (1989) demonstrated a deposition of mercury in the epithelial cells of the choroid plexus of a Minamata disease patient. Additionally, mercury granules have been shown in the choroid plexus of methylmercury-treated rats, and recently high methylmercuric chloride administration to rats has shown to impair blood-cerebrospinal fluid barrier (CSF) function, followed by leakage of albumin-bound methylmercury into CSF (Nakamura et al., 2011). In addition, astrocytes and microglia have been implicated as major targets for methylmercury. By directly comparing effects on primary rat astrocytes and microglia, a recent study

provides evidence that microglia are more sensitive to methylmercuric chloride than astrocytes in terms of the endpoints cell viability and oxidative stress. This finding is consistent with their lower basal glutathione level and higher cellular mercury uptake (Ni et al., 2011). However, although glia cells seem to be the preferential site of methylmercury accumulation in the brain, neurons seem to be more susceptible to methylmercury-induced toxicity, especially in the developing brain.

The mechanisms underlying the high sensitivity of the developing brain to methylmercury exposure can be attributed to the disturbance of the highly regulated processes during brain development, including the very fast and strongly coordinated cell proliferation, differentiation and migration. Very low, sub-cytotoxic methylmercuric chloride concentrations (2.5 - 50 nM, 48 h) have been shown to cause a G1/S cell cycle arrest in primary cultures of progenitor cells from rat embryonic cerebral cortex, most likely via regulating cyclin E expression and perturbing a pathway that involves the extracellular signal regulated kinase, which is one of the key molecules in growth factor signalling (Xu et al., 2010). In rat neuronal stem cells, methylmercuric chloride (2.5 - 5 nM) inhibited neuronal differentiation (Tamm et al., 2006) via activation of Notch signalling (Tamm et al., 2008). In addition, in neural stem cells exposed to nanomolar concentrations of methylmercury long term inherited effects associated with a decrease in global DNA methylation have been recently reported (Bose et al., 2012). The occurrence of gene-specific epigenetic modifications induced by developmental exposure to methylmercury has also been reported in adult mice (Onishchenko et al., 2008). Proliferation of human amniotic fluid stem cells has recently been reported to be inhibited by 300 - 3 000 nM methylmercuric chloride (Gundacker et al., 2012).

In numerous *in vitro* and *in vivo* studies, disruption of cellular redox homeostasis by an increased level of reactive oxygen and nitrogen species (RONS), leading to cumulative oxidative stress, have been shown to play a key role in methylmercury- and mercuric mercury-induced toxicity. The underlying mechanism involved seems to be related to alterations in mitochondrial functions (Garrecht and Austin, 2011), resulting in increased cellular superoxide anion and subsequently hydrogenperoxide and hydroxylradical levels, and a disturbance of the cellular oxidative defence capacity, as shown by decreased glutathione levels and impaired superoxide dismutase, glutathione reductase and glutathione peroxidase activities. Oxidative stress might be accompanied by altered Na^+/K^+-ATPase activities (Huang et al., 2008). Increased RONS levels might result in lipid peroxidation, protein oxidation and oxidative DNA damage (Farina et al., 2011b).

Recent studies in *Caenorhabditis elegans* demonstrate that methylmercuric chloride and mercuric mercury induce oxidative stress, with the organic mercury species inducing oxidative stress at lower concentrations than the inorganic mercury species. Additionally, methylmercuric chloride was more toxic than mercuric chloride regarding endpoints requiring proper neuromuscular activity including feeding, movement and reproduction; effects in terms of *C. elegans* growth were similar (McElwee and Freedman, 2011). In rats, oral administration of methylmercuric chloride 10 mg/kg b.w. per day (equivalent to 8 mg/kg b.w. per day, expressed as mercury) for 5 days caused an inhibition of the electron transport chain activity and induced cytochrome c release in cerebellum mitochondria (Mori et al., 2011). In the brain of developing offspring mice low-dose, oral methylmercuric chloride (0.02 mg/kg b.w. per day, equivalent to 0.016 mg/kg b.w. per day, expressed as mercury) and mercuric chloride (0.5 mg/kg b.w. per day, equivalent to 0.37 mg/kg b.w. per day, expressed as mercury) administration increased lipid peroxidation, nitric oxide levels and changed Na^+/K^+-ATPase activities, which were discussed to contribute to the observed neurobehavioural dysfunction and hearing impairment (Huang et al., 2011).

The impact of mercury species on the cytoskeleton is known since the 1970s. Mechanistically the mercury species target especially microtubules because of the thiol-groups present in tubulin. Depolymerisation of microtubules by mercury species has been shown to disturb numerous cellular processes, including cell survival, proliferation, migration and differentiation (Johansson et al., 2007; Crespo-Lopez et al., 2009).

Methylmercury and mercuric chloride can disrupt glutaminergic, cholinergic and dopaminergic neurotransmitter systems (summarised in Aschner et al. (2010) and intracellular Ca^{2+} homeostasis (Denny and Atchison 1996; Limke et al., 2004). Mercury exposure has been shown in many cell types, including neuronal cells, to increase cellular Ca^{2+} levels, which in turn leads to activation of degradative enzymes, disruption of mitochondrial function and an increase in RONS-induced damage with subsequent cell death. Moreover, cell cycle, cell migration and differentiation might be disturbed (summarised in Aschner et al., 2010; Farina et al., 2011a, b).

7.3.2. Genotoxicity

Several studies have shown that mercuric and methylmercuric chloride induce genotoxicity in various cultured mammalian cells including human lymphocytes (summarised in Crespo-Lopez et al., 2009, 2011; FAO/WHO 2011b). As underlying mechanisms oxidative stress, disruption of microtubules as well as interactions with DNA damage response and DNA repair pathways are discussed (Christie et al., 1986; Cebulska-Wasilewska et al., 2005). Using isolated DNA, mercuric and especially methylmercuric chloride have been shown to bind covalently to endocyclic and exocyclic nitrogen sites of DNA bases (Li et al., 2006). However, to date, formation of such mercury species DNA adducts has not been investigated under physiological conditions.

Data from experimental animals on the genotoxic effects of mercuric chloride are controversial (FAO/WHO, 2011b). Very recently, male rats exposed for 90 days to 50 or 100 mg/L mercuric chloride in drinking water showed a statistically significant increase in the frequency of total chromosomal aberrations and the percentage of aberrant bone marrow metaphases (Boujbiha et al., 2012). Regarding methylmercuric chloride a recent study provide evidence for a genotoxic potential after oral exposure in rats. After 100 days of exposure to 100 µg methylmercuric chloride per day (by gavage), rat white blood cells showed statistically significantly more DNA damage (as measured by the Comet assay) than white blood cells in control animals; co-administration of selenium reduced DNA damage, probably by re-establishment of glutathione peroxidase activity (Grotto et al., 2009a). The same group demonstrated that in direct comparison with rats receiving commercial food or a diet rich in uncontaminated fish, a 12-week diet with methylmercury contaminated fish resulted in an increase of DNA damage in peripheral blood of the respective rats. Oxidative stress biomarkers were not (e.g. reduced glutathione, glutathione peroxidase activity, catalase activity, superoxide dismutase activity, total NO) or only slightly (malondialdehyde) affected (Grotto et al., 2011).

There are no reliable studies investigating genotoxic effects after dietary inorganic mercury intake in humans. Since after inhalation of elemental mercury vapour in the blood elemental mercury is oxidised to mercuric mercury (ATSDR, 1999) the following section summarises genotoxicity in human lymphocytes after exposure towards elemental mercury. In human lymphocytes genetic damage (in terms of chromosome aberrations) has been observed after occupational exposure to elemental and organic mercury (Verschaeve et al., 1976; Popescu et al., 1979; Cebulska-Wasilewska et al., 2005); sister chromatid exchanges (Popescu et al., 1979; Cebulska-Wasilewska et al., 2005) and DNA damage as measured by the alkaline version of the Comet assay (Cebulska-Wasilewska et al., 2005) were not statistically significantly increased in these studies. Repair efficiencies in lymphocytes of 25 workers exposed to elemental mercury vapour were reduced compared with 50 individuals non-occupationally exposed, as measured by the X-rays challenge assay (Cebulska-Wasilewska et al., 2005). In another study increased urinary 8-hydroxy-2-deoxyguanosine levels were observed in occupationally mercury-exposed persons (35 workers, 13 non-occupationally exposed individuals); urinary 8-hydroxy-2-deoxyguanosine levels correlated with both serum and urinary mercury concentration (Chen et al., 2005). On the other hand, studies exist showing no genetic damage after occupational mercury exposure (Verschaeve et al., 1979; Mabille et al., 1984; Barregard et al., 1991; Hansteen et al., 1993).

In a group of 51 fishermen exposed to methylmercury through eating contaminated seafood (6.97 ± 3.49 seafood based meals per week) a statistical correlation was found between micronuclei frequency and total mercury concentration in blood (Franchi et al., 1994); blood mercury levels ranged

from 10.08 to 252.25 µg/L with a mean of 81.97 ± 49.96 µg/L. In lymphocytes of 147 Greenlandic Eskimos, whose main diet consists of seal meat, sister chromatid exchange was found to correlate linearly with blood mercury concentrations (Wulf et al., 1986); thus an increase in the blood mercury concentration of 10 µg/L corresponded to an increase of 0.3 sister chromatid exchanges per cell.

In summary, mercury and methylmercury exert genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent. The most likely mechanism appears to be via oxidative stress, which would be expected to be thresholded. Inorganic and organic mercury species have been shown to bind covalently to isolated DNA, but the formation of such DNA adducts has not been investigated in cell systems or *in vivo* and therefore the consequences of this interaction for genotoxicity have not been elucidated.

7.3.3. Mechanisms of vascular/cardiovascular toxicity

Mechanisms of mercury-induced vascular/cardiovascular toxicity have recently been summarised and comprise the well known modes of action oxidative stress, inflammation, lipid peroxidation and mitochondrial dysfunction as well as thrombosis, vascular smooth muscle and endothelial dysfunction and dyslipidaemia (Houston, 2011; Roman et al., 2011; Azevedo et al., 2012). Methylmercury exposure-related decreased heart rate variability (HRV) might result from methylmercury toxicity to the neurological system, although specific evidence of this mechanism is still lacking.

In mammalian pulmonary artery endothelial cells, methylmercuric chloride generates oxidative stress and has recently been shown to induce phospholipase D activation and generation of phosphatidic acid, through the upstream activation of phospholipase A2 and formation of cyclooxygenase- and lipoxygenase-catalysed eicosanoids, resulting in pulmonary artery endothelial cell cytotoxicity (Sherwani et al., 2011). Chronic mercuric chloride treatment (intramuscular administration, first dose 4.6 µg/kg b.w., subsequent doses 0.07 µg/kg b.w. per day, 30 days (equivalent to 3.4 µg/kg b.w. and 0.05 µg/kg b.w. per day, expressed as mercury, respectively)) of Wistar rats promoted endothelial dysfunction of coronary arteries, as demonstrated by decreased nitric oxide bioavailability induced by oxidative stress (Furieri et al., 2011a). Moreover, this treatment promoted contractility dysfunction as a result of reduced Na^+/K^+-ATPase activity, decreased sarco/endoplasmic reticulum Ca^{2+}-ATPase and sodium/calcium exchanger and increased phospholamban protein expression in isolated (Langendorff-perfused) hearts of the exposed rats. In the chronically treated animals blood pressure, heart rate and left ventricular systolic pressure were not affected, whereas left ventricular and diastolic pressure was slightly but statistically significantly increased (Furieri et al., 2011b).

7.3.4. Nutrients potentially protective against methylmercury toxicity

Dietary factors that are discussed to reduce or prevent methylmercury toxicity include n-3 LCPUFAs, selenium, iodine, choline and vitamin E. Numerous *in vitro* and *in vivo* studies exist, which have recently been reviewed (e.g. Ralston and Raymond., 2010; Kaur et al., 2011) and are not discussed in detail here.

The most extensively studied substance in food, regarding mechanisms of confounding, seems to be selenium. Mercury binding affinity for selenium is a million times higher than its binding affinity for sulphur in analogous forms and attempts have been made to identify detoxification products, which contain selenium and mercury (e.g. mercury-selenide). Whether those compounds really detoxify the mercury species has never been demonstrated. Besides a sequestration of mercury, potential protective modes of action of selenium against methylmercury toxicity include antioxidant effects, increased glutathione peroxidase activity, glutathione synthesis, high selenoprotein levels and increased demethylation of methylmercury (recently summarised in Syversen and Kaur, 2012).

Mechanistically, DHA seems to protect against methylmercury-induced oxidative stress in neuronal cells. Additionally, in neuronal cell lines and primary cells a pre-treatment with DHA was associated with decreased cellular methylmercury bioavailability (summarised in Kaur et al., 2011).

7.4. Observations in humans

7.4.1. Concentrations in biological samples from the European population

A detailed summary of data on mercury concentrations in biological samples, including blood, cord blood, hair, nails and urine, of the European population since 2000 is given in Appendix F. Only studies that comprise all relevant information, including e.g. the number of samples and the mathematical/statistical indications, are listed. Table 23 summarises the studies given in Appendix F and gives the ranges of the means for total mercury levels measured in cord blood as well as in blood and hair of adults and children. The levels in the Faroe Islands population are presented in Table 24 and were not included in Table 23 because of their particular high exposure from whale meat consumption.

Table 23: Range of mean concentrations of total mercury in biological samples from the European population[(a)] (further details are available in Appendix F).

Matrix (unit)	Adults and elderly	Children
Cord blood (µg/L)		0.86 – 13.9
Blood (µg/L)	0.2 – 4.85	0.12[(b)] – 0.94[(b)]
Hair (mg/kg)	0.17 – 1.45	0.14[(b)] – 1.99

(a): Faroe Islands not included.
(b): Geometric mean.

As indicated from the data presented in these tables, considerable differences exist between European countries. The study by Hrubá et al. (2012) is the only study that directly compared total mercury blood levels in children (7 - 14 years of age) in six European countries.

The respective data indicate that total mercury blood concentrations can differ considerably between European countries and that these differences seem to be related to amalgam fillings and fish intake (Hrubá et al., 2012). The study by Miklavčič et al. (in press) compared total mercury levels in human milk and cord blood in four Mediterranean European countries and observed statistically significant differences between countries. In general children and adolescents have lower urinary and blood mercury levels than adults.

Data on temporal trends based on biomonitoring data from the general population are available from Germany (Karch et al., 2011; Link et al., 2012) and the Czech Republic (Puklová et al., 2010). Whereas in the German studies urinary mercury and blood mercury concentrations decreased over the up to 13 years study period between 1997 - 2010, no clear time trends were observed for adults in the Czech Republic between 1996 - 2008. However, a decrease of both urinary and blood mercury levels were determined in children.

7.4.2. New epidemiological reports on methylmercury

As a starting point for the summary of new developments and epidemiological studies on association between mercury exposure and different endpoints, the report of an EFSA contractor (Hassauer et al., 2012) was used. The JECFA PTWI (FAO/WHO, 2004, 2007) was based on data from cohorts from the Seychelles and Faroe Islands, and a total mercury concentration in maternal hair of 14 mg/kg was used as a point of departure. In order to form a basis for a revision of the health-based guidance value, adverse effects should be associated with an exposure lower than 14 mg total mercury/kg hair. However, different biomarkers of exposure have been used in different epidemiological studies. To have a guidance for evaluating whether new epidemiological studies have high or low exposure relative to the point of departure of the existing PTWI, a blood to hair ratio of 250 was used to calculate a corresponding maternal blood concentration of 56 µg/L. The discussion below builds on the earlier literature, but only discusses in detail studies published since 2004. Publications addressing associations between neurodevelopmental outcomes and mercury exposure from thiomersal-

containing vaccines in combination with methylmercury from fish consumption and/or human milk consumption have not been considered relevant for this opinion since thiomersal releases ethylmercury cation, which is not occurring in food. Publications investigating a mixed exposure from both elemental mercury from mining activities and mercury in food have not been addressed since elemental mercury is not present in food and therefore these studies could not be used for derivation of a health-based guidance value.

7.4.2.1. Neurodevelopmental and neurotoxic endpoints

The scientific discoveries relating to health risks associated with methylmercury exposure began in 1865, with reports describing ataxia, dysarthria, constriction of visual fields, impaired hearing, and sensory disturbance as symptoms of fatal methylmercury poisoning in exposed laboratory workers, see Grandjean et al. (2010a) for an overview. Neurodevelopmental toxicity of methylmercury in a population highly exposed from environmental sources was first recognised in the 1950s in Minamata, Japan, in association with consumption of highly contaminated fish during pregnancy. This resulted in at least 30 cases of cerebral palsy and severe developmental retardation in prenatally exposed children (Harada et al., 1968), as well as in several neurotoxic effects in highly exposed adults. Exposure in affected adults and during pregnancies in Minamata was very high, as reflected in maternal hair mercury concentrations that ranged from above 50 mg/kg up to a maximum of 705 mg/kg (Harada, 1995). In 1972 the consumption of seed treated with methylmercury fungicide in Iraq resulted in the poisoning of several thousand inhabitants, again with newborns and infants seen as the most vulnerable group for neurotoxic effects.

The high incidence of structural brain damage and functional impairment in children in both incidents might be due to (a) the lipophilic characteristics of methylmercury, (b) the ability of methylmercury to cross the placental and blood-brain barriers, (c) the resulting higher concentration in fetal and neonatal blood, and (d) the ability to affect the neurological system and its development directly and irreversibly. The highest vulnerability of the embryo and fetus, as well as the high sensitivity of infants and children was emphasised in the 2006 JECFA evaluation (FAO/WHO, 2007).

7.4.2.1.1. Prenatal exposure

A. Faroe Islands

Five birth cohorts have been established in the Faroe Islands in the period 1986 - 2009, all providing information on mercury exposure.[38] Neurodevelopmental endpoints have been studied in the two first of these cohorts, in Cohort 1 (n = 1022), established in 1986 - 1987 and Cohort 2 (n = 182) established in 1994 - 95. Participants in Cohort 1 performed a variety of neurobehavioural tests at age 7 and 14 years, and the investigation included clinical examinations with a focus on nervous system function. Neurological Optimality Score was examined in Cohort 2 participants at the age of two weeks, 7, 18, 30, 42 months and 4.5 and 5.5 years (an extended medical examination was performed at 42 months) as well as detailed neurobehavioural tests at 7 years and 10 years.

Neurotoxicity in seven year-old children in the Faroese Cohort 1 (together with the data from the Seychelles) was used by the JECFA in establishing the PTWI of 1.6 µg/kg b.w. for methylmercury (FAO/WHO, 2004). The associations between prenatal methylmercury exposure and newborn neurological status in the Faroese Cohort 2 were also taken into consideration. In the later update (FAO/WHO, 2007) two 14-year follow up studies from the Faroese Cohort 1 had become available (Murata et al., 2004b; Debes et al., 2006). Re-analysis and new results of the Faroese cohorts that have become available since the 2004 JECFA evaluation are summarised below and in Table 24.

At the age of 14 years, the children in the Faroese Cohort 1 participated in a clinical investigation assessing brainstem auditory evoked potentials (BAEPs) (Murata et al., 2004b). These are very small electrical voltage potentials, which are recorded in response to an auditory stimulus from electrodes

[38] http://www.chef-project.dk/

placed on the scalp and reflect neuronal activity in the auditory nerve, cochlear nucleus, superior olive and inferior colliculus of the brainstem. The physiological basis of measurement of possible neurological effects is a strength of this approach since the measurement is not influenced by the level of education and social mediated stimulation. Hair samples were collected at age 14 years and the concentration was increased with a factor of about 1.5 compared to the hair measurement data at age seven years (Budtz-Jørgensen et al., 2004), but the geometric mean was less than approximately 25 % of that in maternal hair at the end of pregnancy. The correlation to cord blood mercury concentration (after logarithmic transformations) was moderate ($r_{age=7}$ = 0.33 and $r_{age=14}$ = 0.35, $p < 0.01$), pointing to a systematic influence of similarity in exposure conditions over time (nutritional habits in the environment and family). The same laboratory technique was applied as at seven years and the same physiological outcomes were measured with blinded examinations. Auditory stimuli click signals with intensity of 65 dB (0.1 ms impulses) were presented to the right ear (20 Hz and 40 Hz) while the other ear was masked with white noise (45 dB HL). Audiometry was performed in a standardised manner to control for possible influence of hearing impairment. The resulting data set was analysed by multiple regression taking age, sex and the exposure indicators as independent variables and the set of variables that was previously included in neuropsychological test analysis as confounders. Additional analyses included polychlorinated biphenyls (PCB) and postnatal methylmercury exposure. The measured BAEP latencies were similar to the results obtained at age seven years. Total mercury in maternal hair and/or cord blood was statistically significantly associated with latencies within the I–III interval ($p < 0.05$). The associations with the full peak III latency was the most robust finding and statistically significant at both frequencies, and in accordance with the findings at age seven. According to the authors, the inclusion of the set of confounders as well as the inclusion of PCB co-exposure for the subset for which this information was available did not affect the regression coefficients. The regression coefficients at age seven were about twice the magnitude observed at age 14 years. This suggests a persistent neurotoxic effect of intrauterine mercury exposure, while the lower values of the resulting regression coefficients at age 14 might indicate some compensation. Prenatal $BMDL_{05}$ results for peak III at the two frequency conditions corresponded at age 14 again to an average of approximately 10 mg/kg hair based on either cord blood or maternal hair. Recent exposure, measured by hair mercury concentration at 14 years, was associated with prolonged III-V interpeak interval ($p < 0.05$ at 40 Hz). Prolonged III-V interpeak interval showed non-significant regression coefficients with prenatal exposure at both frequencies. Adjustment for recent postnatal exposure, did not affect the regression coefficients for the prenatal exposures.

In the re-examination of the Faroese Cohort 1 at age 14 years, 860 of the 1 010 living participants underwent detailed neurobehavioural examination (Debes et al., 2006). The topics of the neuropsychological test battery were selected on the same criteria as applied at the examination at age seven years. The mercury concentrations in maternal hair and cord blood showed, in confounder adjusted regression analysis, statistically significant associations with deficits on finger tapping and measures of reaction time on a continued performance task. Cued naming was statistically significantly negatively associated with mercury in cord blood. The cord tissue mercury concentrations showed no clear association with these outcomes, but were associated with lower test scores for the naming and for the verbal-learning tasks. In contrast to the prenatal exposure variables, markers of postnatal exposure were generally only weakly related to cognitive test scores at 14 years. Co-exposure by PCB showed only weak, non-significant associations with the outcomes. The comparison of the results at age 7 and 14 years suggests that children with a lower performance level at age 7 show a persistent tendency to lower test scores at age 14. An extended analysis of the data by structural equation models found the strongest mercury associations in regard to the group of the motor and attention test results ($p < 0.05$), with associations for the verbal tasks close to statistical significance ($p = 0.051$) after adjustment for fish intake. For a methodological review of the structural equation modelling approach and how to standardise the scores of the selected set of target variables for nervous system functions, see Budtz-Jørgensen et al. (2002). Memory and spatial tasks appeared not to be associated with prenatal methylmercury exposure. Maternal fish consumption during pregnancy appeared to show a weak, but not statistically significant beneficial association.

In another re-evaluation of the 7 and 14 years data from the Faroese Cohort 1 Budtz-Jørgensen et al. (2007b) tried to separate risks and benefits from fish and seafood consumption. The mercury exposure in this cohort is strongly related to the consumption of whale meat (Grandjean et al., 1992), on the other hand the frequency of fish dinners (mainly cod) correlated statistically significantly with mercury concentrations in cord blood (r = 0.25) and maternal hair (r = 0.26). The extent of confounding bias was analysed by applying structural equation models. The set of confounders included a series of covariates described previously (Budtz-Jørgensen et al., 2007a; Grandjean et al., 1997). Adjustment for fish intake modified the previously reported mercury regression coefficients (Grandjean et al., 1997; Budtz-Jørgensen et al., 2002; Debes et al., 2006) toward a higher explained variance. PCB exposure was not included as a covariate because of limited impact on the mercury association in previous analyses (Grandjean et al., 2001; Debes et al., 2006). In addition, it was not available for more than half of the cohort members. Fish intake, seen as an indicator for a higher intake of beneficial nutrients, influenced test scores on all five neuropsychological outcome variables (motor, attention, spatial, verbal and memory functions). The association was statistically significant for the motor performance (examination at 7 and 14 years of age) and functioning in tasks for spatial orientation and operations (examination at 14 years of age). The authors discussed the role of possible imprecision of the information about fish consumption on the relationship between exposure and neurological outcomes and concluded that using food frequency questionnaire data might have the highest imprecision, followed by methylmercury exposure estimates based on hair analysis. Assuming a reliability ratio up to 43 % (i.e. percentage of the total variation caused by measurement error > 0.57), the authors concluded that the association between prenatal methylmercury exposure and neurodevelopmental outcomes previously reported in the Faroese Cohort 1 might be underestimated by a factor of up to 2 when beneficial effects of fish consumption and imprecision in the measurement of fish consumption were not taken into account.

Analyses of possible consequences of exposure measurement error (mercury measurement in different matrices at different periods/ages as well as dietary questionnaire data) for confounder identification, model misspecification and for the risk of effect underestimation are available in Budtz-Jørgensen et al. (2003), Grandjean et al. (2004a) and Grandjean and Budtz-Jørgensen (2010).

In the literature search, only one study was identified reporting data from Cohort 2 in relation to mercury (Budtz-Jørgensen et al., 2010). The study combined data from the seven-year follow-up in the two first Faroese cohorts, with a focus on the possible PCB confounding of the associations between neurodevelopmental outcomes and mercury. Most of the results are reported for a combined set of data from the two cohorts, but separate results are given for the two cohorts for the associations when not adjusted for PCB. These results provide some information on whether the Cohort 2 results at seven years of age were confirming the observations from Cohort 1 at that age. Among the outcomes reported for Cohort 2 (Neurobehavioral Evaluation System, finger tapping, reaction time in the Continuous Performance Test (CPT), the Boston Naming Test, the Wechsler Intelligence Scale, and the California Verbal Learning Test) only the results for the Boston Naming Test's negative association with mercury were consistently in line with the observations in Cohort 1. In addition, some aspects of the CPT (reaction time and the total number of missed stimuli) and verbal learning (short and long delay) showed results in similar direction as in Cohort 1. The conclusions that can be made from this are very limited due to the smaller size of Cohort 2 (the analysis included ca 900 children from Cohort 1 and 160 from Cohort 2). As to the possible (positive) confounding from PCB, results of statistical analysis were only given for the combined dataset for the two cohorts. PCB was not statistically significant associated with any of the outcomes. However, when mercury and PCB was included in the models simultaneously, the regression coefficients for mercury decreased for the Boston Naming Test from about 2.1 to about 1.5. It is accordingly difficult to exclude confounding from PCB.

A further discussion on confounding from prenatal exposure to PCB on associations between prenatal mercury exposure and neurobehavioural deficits was provided recently (Grandjean et al., 2012), based on new analyses of PCBs in cord blood from almost all the 923 Faroe 1 Cohort members that participated at the examination at seven years age. Prenatal PCB exposure showed statistically

significant negative associations only with the Boston Naming test. The outcomes from the test battery at seven years were analysed by latent variables for motor and verbally mediated functions in a structural equation model. The PCB effects were weak and not statistically significant, and weakened more when adjusting for prenatal mercury exposure. The associations with prenatal mercury exposure remained significant after adjustment for prenatal PCB-exposure, and the regression coefficients increased marginally after adjustment. The authors concluded that PCB exposure does not explain the methylmercury neurotoxicity previously reported in the cohort.

Julvez et al. (2010) reported the results of the examination using the CPT as a measure of the speed and error rates of visual information processing in the examination of 14 year old Faroese Cohort 1 participants. The CPT-Hit Reaction Time latencies (CPT-HRT) test was applied and the test scores were used as indicators for different neuropsychological functions depending on the time of the task using a computer assisted test. This test assesses several visual-cognitive, attention and motor functions. In multivariate regression analysis with confounder adjustment the duration needed for the CPT task depended on prenatal exposure to methylmercury. The scores of the three stages (HRT-outcomes on 1 - 2, 3 - 6 and 7 - 10 minutes) were highly inter-correlated. The learning phase was less associated with methylmercury exposure than the second phase, which was interpreted to include the functions of speed processing and selective focused attention. The scores of this test phase were strongly associated with prenatal methylmercury exposure, even after controlling for motor speed and simple reaction time. The scores of the third test phase, regarded as indicators of sustained attention by the authors, showed the strongest associations with prenatal methylmercury exposure. Current mercury concentrations (mercury in a proximal 2-cm-hair segment) did not show any clear association structure.

In summary, 14 years follow up and re-analysis of data from the Faroe Islands since the JECFA PTWI was established (FAO/WHO, 2004) consistently indicate a detrimental effect of prenatal methylmercury exposure. The association between prenatal exposure and neurological auditory function was still present at 14 years but with a smaller impact, and not related to the estimates of postnatal exposure. Beneficial effects of fish consumption and imprecision in the measurements might confound the neurotoxic associations in the Faroese studies, causing underestimation of the effects of methylmercury, and this has been estimated to be by a factor up to two. Most of the neurodevelopmental outcomes, but not the neurological auditory function, were evaluated in the smaller Cohort 2 at seven years of age. For most of the associations between neurological outcomes and mercury in Cohort 1, the results could not be confirmed. Assessment of Faroese Cohort 1 and 2 together did not identify major confounding from PCB exposure, but it did not exclude the possibility of an overestimation of the mercury effects in Cohort 1 due to such confounding. Reassessment of the neurodevelopmental endpoints at seven years in the Faroese Cohort 1, including new results on cord blood PCBs in almost all participants, did not identify PCB as a strong confounder in the study.

B. Seychelles

Seychellois consume much and frequent ocean fish (deep-sea and reef fish) and more than 80 % of the population consume fish meals at least once a day as the main source of protein. Consumption of marine mammals is rare. The Seychelles have no major local industrial sources of mercury pollution and the PCB exposure is low. Women's alcohol consumption is low (Myers et al., 2007). Association between mercury exposure and child development has been studied in three different cohorts in the Seychelles, and the studies are called the Seychelles Child Developmental Pilot Study, the Main Study (the Seychelles Child Development Study, SCDS) and the Nutrition Study (SCDNS).

The Seychelles epidemiological study programme started in the mid 1980s with a pilot study including approximately 800 infant-mother pairs in 1986. The pilot study was followed by a main study of 779 mother-infant pairs recruited in 1989 - 1990 on the island of Máhe. The main study objective was to determine whether prenatal methylmercury exposure from fish consumption has adverse associations with the children's neurodevelopment. The children were enrolled when they were six

months old. Mothers reported consuming fish on average 12 meals per week. Prenatal methylmercury exposure was measured as total mercury in maternal hair growing during pregnancy (mean 6.9 mg/kg, SD 4.5 mg/kg). The main cohort has been tested for developmental outcomes at 6, 19 and 29 months and at 5.5, 9, 10.5 and 17 years of age. The longest follow-up available at the evaluation by the JECFA in 2004 was at age 9 years (Myers et al., 2003). Conventional linear regression models were used to analyse the outcome of test batteries which covered neurocognitive, language, memory, motor, perceptual-motor, and behavioural functions. The authors concluded that these data did not support the hypothesis that there is a neurodevelopmental risk from prenatal mercury exposure in this population. The results from analysis at 9 years confirmed those from age 5.5 years, which were used (together with the results from the Faroe Islands) as basis for the derivation of the PTWI (FAO/WHO, 2004).

A third nutrition cohort was established to test if nutrients and dietary status during pregnancy could modulate the neurotoxicity of mercury (Myers et al., 2007; Davidson et al., 2008b). A total of 300 women were recruited in 2001 in their first trimester of pregnancy. At enrolment and at delivery, hair and blood from the mothers and cord blood from the infants was obtained. Prenatal mercury exposure was measured as total mercury in maternal hair covering the gestation period. Nutritional factors that might influence child development were measured in the mother's blood taken at 28 weeks (iodine status measured by thyroid stimulating hormone (TSH) and free T4, iron status and different long-chain polyunsaturated fatty acids (LCPUFAs)). Maternal fish consumption was measured by a food use questionnaire covering the preceding 14 days and a four-day diet diary (two week days and two weekend days) at 28 weeks gestation. Dietary choline intake was estimated from the food diaries and used as an indirect measure of choline status. The mothers consumed on average nine fish meals (537 g) weekly. The mean maternal hair mercury concentration covering the gestation period was 5.7 mg/kg (range 0.2 - 18.5). Child development was tested at 5, 9, 25 and 30 months and at five years of age. The main developmental endpoint was Bayley's scale of infant development-II (BSID-II) at 9 and 30 months, giving two primary endpoints, Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI). Additional assessments at 5, 9 and 25 months examined more specific aspects of cognition. These were at 5 and 9 months the Fagan test of infant intelligence (Fagan Infantest, FTII) measuring novelty preference and the Visual Expectations Paradigm measuring visual recognition memory (VRM). The A-not-B and the Delayed Spatial Alteration tests, measuring aspects of planning, inhibition, attention and working memory, were administered at 25 months.

Since the last evaluation (FAO/WHO, 2004), additional follow-ups as well as several approaches of statistical analysis have been reported for the main cohort. Some additional reanalyses were available at the update in 2006 (FAO/WHO, 2007), and these are also included in the summary below and in Table 24. In addition, results from the nutrition cohort have been published. They are summarised below and in Table 24.

The Main Cohort

Davidson et al. (2004) assessed whether the influences of social and environmental factors on the association between prenatal exposure and infant intelligence at 19 months were present also at the 5.5 years evaluations, and whether the 19 months and 5.5 years results were consistent with each other. The authors concluded that evidence of a small influence by social and environmental variables at 5.5 years was not consistent internally or with earlier results, suggesting that any statistically significant results could be due to chance.

Focussing on those endpoints that had been measured repeatedly, a longitudinal analysis of the results from the main cohort at 19, 29, months and 5.5 and 9 years was performed (Davidson et al., 2006a). The analyses involved global cognition with a measure of developmental quotient or intelligence quotient (IQ), and scholastic achievement, social behaviour and memory. Recent postnatal exposure was also taken into consideration. No statistically significant relationship between prenatal mercury exposure and the endpoints were found. As in the previous cross sectional studies from the same cohort, key covariates such as the home observation for measurement of the environment score

(HOME) and socio-economic status (SES) were statistically significantly associated with the endpoints.

The data from the nine years follow up (Myers et al., 2003), were re-analysed by Huang et al. (2005) by using semi-parametric additive models with different degrees of smoothing in order to see if nonlinear associations of prenatal exposure were present. The results showed evidence of a nonlinear significant relationship between prenatal total mercury levels and one test, the Grooved Pegboard dominant hand score (a test of motor speed and coordination). The modelling suggested that no effect occurs up to 12 mg/kg in maternal hair, but indicates a slight adverse effect above this exposure level although the uncertainty was high. The data are also summarised in a review (Davidson et al., 2006b).

BMDL calculations were performed on the results from the nine years follow up based on the endpoints reported by Myers et al. (2003), with the addition of another seven endpoints. The average $BMDL_{10}$ across the 26 endpoints varied from 20.1 mg Hg/kg in maternal hair (logistic model) to 20.4 mg/kg (k-power model) (van Wijngaarden et al., 2006).

In order to address the possibility of non-homogenous susceptibility, Huang et al. (2007) re-analyzed the data from the nine-years follow up by using a regression tree approach. According to the authors, the results supported the previous analyses and outcomes in Myers et al. (2003), confirming that there is no consistent evidence for effects from prenatal methylmercury exposure in the Seychelles main cohort.

Thurston et al. (2009) used a Bayesian approach for a generalised linear mixed model to allow the exposure effects to differ across outcomes within and across broad outcome classes (so-called domains). Using this approach they investigate the relationship between prenatal methylmercury exposure and multiple neurodevelopmental outcomes in four domains (cognition, memory, motor, and social behaviour) measured at nine years of age as previously reported (Myers et al., 2003). The authors reported findings consistent with the earlier results analysed by conventional linear regression. The study focused mainly on methodological questions and is therefore not as informative for this evaluation.

An alternative analysis of the data from the nine years follow up study grouping 18 individual endpoints into one ordinal outcome variable as well as grouping by developmental domains, followed by ordinal logistic regression, showed no association between prenatal methylmercury exposure and developmental outcomes (van Wijngaarden et al., 2009).

Davidson et al. (2008a) investigated in multiple linear regression, the association between prenatal mercury exposure and visuospatial ability at approximately 10.5 years by use of the Bender Visual Motor Gestalt Test, which yields scores for a copying task and a reproduction task. The same testing and scoring methods as previously used in the Faroe Island study at seven years (Grandjean et al., 1997) was applied. In contrast to the Faroese results, no statistically significant association between prenatal methylmercury exposure and copying task scores was observed. A significant negative association between methylmercury and reproduction task scores was observed when all participants were included, but this was no longer significant after removing one outlier with low exposure and high reproduction task score.

Subsequently, Davidson et al. (2010) investigated whether scholastic achievement was associated with prenatal or recent postnatal mercury exposure after adjustment for covariates. Primary endpoints were Seychelles nationally standardised end-of-year examination scores given when the cohort children were 9 and 17 years of age (n = 643). Additional analyses were done in a subgroup (n = 215) from the main Seychelles cohort that participated in a regional test (Southern and Eastern African Consortium for Monitoring Educational Quality, SACMEQ) at age nine years. Multiple linear regression analyses showed no pattern of associations between prenatal or recent postnatal exposure, and either the 9- or 17-year end-of-year examination scores. No associations between prenatal exposure and the SACMEQ test score results were seen. However, recent exposure was associated with lower test scores in boys.

The authors could not explain this finding and concluded that they would need confirmation by further studies.

Only recently, Davidson et al. (2011) investigated associations between prenatal methylmercury exposure and subjects' performance on 27 endpoints at the 17 years follow-up study (n = 371 to 462, depending on outcome measure). The test battery included several cognitive performance tests and some measures of problematic behaviours of the pupils. Besides the wide range of confounders reported before, the statistical analyses for all endpoints were adjusted for recent postnatal methylmercury exposure. For 21 out of the 27 endpoints there was no association with prenatal exposure. Better scores on four endpoints (Woodcock_Johnson-II mathematical calculation scores, reduced number of trials on the Intra-Extradimensional Shift set on the Cambridge Neuropsychological Test Automated Battery, fewer reports of substance use and lower incidents of problematic behaviour in school) were seen with increasing prenatal mercury exposure. Statistically significant association between prenatal exposure and the lowest level (1 - 3) of referrals to a school counsellor was seen, but no associations between prenatal exposure and having more than three referrals. According to the authors, the improved performance might be associated with beneficial nutrients in fish and is in line with what has been found previously at lower age in the cohort. In conclusion, there was no consistent pattern of adverse associations between prenatal mercury exposure and the tested outcome variables at age 17 years.

The Nutrition cohort

Davidson et al. (2008b) used the endpoints resulting from the BSID-II at 9 and 30 months of age (n = 229 children with complete outcome and covariate data for analysis). The primary analysis examined the associations between methylmercury, maternal nutrition measures (fish consumption and choline intake by questionnaire data, TSH, the n-3 LCPUFA DHA, the n-6 long-chain polyunsaturated fatty acid (n-6-LCPUFA) arachidonic acid (AA) and iron (Fe) measured in maternal blood) and children's scores on the BSID-II. The adjusted results showed a negative regression coefficient between prenatal methylmercury and the mean PDI scores at 30 months (regression coefficient = -0.55, p = 0.04). Neither the association with prenatal methylmercury alone (described as 'borderline significant', regression coefficient = -0.44, p = 0.07), nor those with nutrition factors were statistically significant. The additional assessments at 5, 9 and 25 months showed no statistically significant association with prenatal methylmercury exposure. The authors concluded that nutritional status and methylmercury exposure may simultaneously influence developmental outcomes in opposite directions and suggested that beneficial influences of fish nutrients and of overall diet need to be taken into account to evaluate the risk of neurodevelopmental effects from prenatal methylmercury exposure.

Analysing the same cohort data set as above, Strain et al. (2008) reported the results of an analysis of the influence of different sets of n-3 and n-6 LCPUFAs measured in mothers' blood at 28 weeks gestation and 1 day after delivery on test results for psychomotor and mental development (PDI and MDI of BSID-II) at the age of 9 and 30 month. They used five covariate adjusted linear regression models: Model 1 was adjusted for DHA + AA, Model 2 for DHA + eicosapentaenic acid (EPA) (as a measure of marine n-3 LCPUFAs) and AA, Model 3 was adjusted for n-3 LCPUFAs (DHA + EPA + alpha-linolenic acid (ALA)) and n-6 LCPUFAs (AA + linoleic acid (LA)), whereas model 4 adjusted for AA to DHA ratio and Model 5 for n-6 LCPUFA to n-3 LCPUFA ratio. In contrast to the results in Davidson et al., (2008b), the statistical models were not adjusted for other nutrition variables. The results showed that maternal serum n-3 LCPUFA exhibited a statistical significant effect on the PDI at 9 months of age ($p < 0.02$). As maternal values for n-3 LCPUFA increased, the PDI scores improved. Similarly, the PDI score was statistically significant inversely related to the n-6/n-3 LCPUFA ratio ($p < 0.02$) at 9 months. As the n-6/n-3 LCPUFA ratio increased the PDI scores declined. There were no such significant coefficients in the regression analysis with the MDI at 9 or 30 months and the PDI at the 30-month on the LCPUFA indices with or without adjusting for methylmercury exposure. The associations found were strongest when prenatal methylmercury exposure was included in the analyses. The 30-months PDI, but not the 9 months PDI, decreased statistically significantly ($p < 0.04$)

with increasing prenatal mercury exposure when the LCPUFA measures were included in the regression analysis.

Stokes-Riner et al. (2011) used the same data as Strain et al. (2008) and Davidson et al. (2008b), but instead of analysing the data of the two examinations at age 9 and 30 month separately, they combined the outcomes at the two ages in a longitudinal analysis taking the intra-individual association between the first and the second test results into account. This reflects much better the hypothesis that prenatal methylmercury exposure might influence the individual level of psychomotor performance in childhood. Effectively the power of the study is increased. In addition, the longitudinal model allowed exploration of whether methylmercury, LCPUFA, and/or covariate effects on the PDI change from 9 to 30 months. The results show a statistically significant negative (adverse) effect relationship between maternal hair mercury and the children's psychomotor performance (PDI scale) scores. At the same time a significant beneficial relationship between maternal n-3 LCPUFA (measured by DHA + EPA + ALA or only DHA), and cognitive function was shown. Neither association was changed significantly as the children aged. The authors viewed the combination of a significant positive association of n-3 LCPUFAs together with a significant negative association of methylmercury exposure on the children's development as an indication of the need to adjust for maternal nutrition when studying the potential effects of prenatal methylmercury exposure.

Lynch et al. (2011) fitted varying coefficient function models to explore interaction between outcome data from the Nutrition cohort at 9 and 30 months (BSID-II, MDI, PDI), maternal prenatal hair mercury levels and maternal nutritional status by the five fish nutritional components described by Davidson et al. (2008b). The relationship between the five nutrition components and the outcomes was allowed to change as levels of methylmercury change by allowing the regressions coefficients to change as a function of the methylmercury hair levels considered as effect modifiers. A possible effect modification was modelled as a smooth function (using a penalised spline function) of methylmercury in maternal hair. The results of this statistical analysis indicated that increasing levels of methylmercury exposure are associated with a loss of benefit from the nutritional covariate DHA. This finding is observed for all four outcomes (MDI and PDI at 9 and 30 months) at the higher levels of methylmercury exposure. At approximately 11 mg/kg maternal hair mercury, the slope function became negative for the PDI at 30 months, and DHA was no longer positively associated with outcome. The authors stressed that there were few observations above 11 mg/kg with increased variability in function estimates. DHA seemed to be positively associated with the test results from the PDI at the age of 30 months, while the benefits were outweighed by the negative influence of prenatal methylmercury exposure when the mother's methylmercury hair was above about 11 mg/kg. It should be mentioned that this endpoint was also statistically significant in the analysis of Davidson et al. (2008b). The results of data analysis indicate that the beneficial impact of DHA on developmental outcomes may be increasingly attenuated as the prenatal methylmercury exposure increases.

Recently, the five years follow up, which included a battery of developmental tests giving in total ten outcomes, was published (Strain et al., 2012). The developmental tests measured dexterity and finger tapping speed (dominant and non-dominant hand), language by the Preschool Language Scale Revision Edition (yielding a total language score and scores for verbal ability and auditory comprehension), the Woodstock Johnson Scholastic Achievement Test (letter word recognition and applied problems), and behaviour by the Child Behaviour Checklist. Child's IQ was estimated by the Kaufman Brief Intelligence Test, comprising one subtest for verbal knowledge and one for matrices. Associations between test outcomes and different combinations of maternal LCPUFA status were investigated by covariate-adjusted linear regression models, without and with adjustment for prenatal mercury exposure. Analyses to investigate relationships between prenatal mercury exposure and developmental outcomes without adjusting for maternal LCPUFA status were also conducted. Neither were any statistically significant associations found, nor were there any of the point estimates in an adverse direction. Improved test results on preschool language scores were associated with increasing maternal DHA, and diminished with increasing maternal AA. Of note, in contrast to findings at 9 and 30 months in the Nutrition Cohort, prenatal methylmercury was not significantly associated with any outcome in any of the models applied. This observation was not discussed by the authors in relation to

the previous findings of such associations after adjustments for LCPUFAs (Strain et al., 2008; Lynch et al., 2011; Stokes-Riner et al., 2011).

Summary

In summary, reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the SCDS have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints. Studies in this cohort did not allow for adjustment for n-3 LCPUFAs. The major new developments are coming from the results from the smaller Nutrition Cohort. The new results indicate a negative association between prenatal mercury exposure and neurodevelopmental endpoints at 9 and 30 months when the n-3 LCPUFA concentration in maternal blood was taken into account. A possible effect modification was modelled as a smooth function of methylmercury in maternal hair. The results indicated that increasing levels of methylmercury exposure are associated with a loss of benefit from the nutritional covariate DHA, and an apparent NOEL at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study and a positive association between maternal prenatal DHA and preschool language scores was reported.

C. Other regions

In addition to the large cohort studies previously mentioned, several smaller cohort and cross-sectional studies have been published. These studies are summarised below and in Table 24.

Prenatal high exposure and observations later in life

Possible effects of relatively high mercury exposure have been studied in a birth cohort with Inuit children born in Nunavik, Canada. These children also had a considerable prenatal exposure to PCB. A follow-up of neuromotor function in 109 children at the age of five years only showed statistically significant associations to prenatal mercury in multivariate linear regression analyses (geometric mean total mercury in cord blood: 15.9 µg/L) for a measure of tremor in pointing movements, but no associations were found with other functions or reaction time (Després et al., 2005). No significant confounder-adjusted regression between cord blood mercury concentration and behavioural outcomes from the BSID-II or observational data related to attention and level of activity was seen (Plusquellec et al., 2010). Visual evoked potentials were studied in a subset of 78 children (Saint-Amour et al., 2006). These potentials are responses (to visual stimuli) that can be electrophysiologically measured and recorded. Three components were observed (N75, P100, N150) at three contrasts (95, 30, and 12 %). Increased latency of the P100 component at 30 % contrast was statistically significantly associated with cord blood mercury concentration in confounder-adjusted linear regression analysis, but not with other measures. In contrast, decreased latencies, i.e. not the direction that a priori was thought to be adverse, were associated with current child mercury for both N75 and P100, at both 95 and 30 % contrast. Further, auditory electrophysiological testing was made in 116 Inuit children at the age of 11 years, revealing associations between cord blood mercury and slower reaction times and greater amplitude and delayed latency of the N1 wave in linear regression analyses, suggesting effects of these relatively high exposures on early processing of sensory information (Boucher et al., 2010). In addition, the authors reported that mercury concentrations were not related to any outcomes in a Go/No-go trial, but that prenatal mercury exposure interacted significantly with prenatal lead exposure on certain outcomes (Boucher et al., 2012).

Chevrier et al. (2009) conducted a cross sectional study of visuospatial performance in 395 Amazonian children aged 7 - 12 years from three villages in Brazil (n = 263) and two villages in French Guyana (n = 172). The subscales of the Stanford–Binet Copying test included the active reproduction of three- and two-dimensional designs with pencil and paper. The authors used a relaxed evaluation scheme (avoiding simple solved/unsolved categorisation) for documentation of performance in order to achieve higher discrimination in the test score distribution as well as

information about the types of errors made by the children. Hair-mercury concentration was available for 95 % of these children from the child's own sample and for 68 % from the mother's sample. The main mercury source was oral exposure via fish consumption. The hair mercury results show a dependency of concentration to the vicinity to gold-mining sites. The correlations between maternal and child hair-mercury concentrations was lower in villages in French Guyana (r = 0.09 - 0.28) than in Brazilian villages (r = 0.50 - 0.57). The confounder-adjusted regression analysis on the joint Brazil and the French Guyana data set indicated that the hair-mercury concentrations of both the child and the mother are associated negatively with both the test performance in both subscales (copying and block score). No interaction between sex and mercury exposure was observed for performance. According to the authors, the deficit on the Stanford-Binet Copying task of children with hair mercury of 10 mg/kg compared to children with a 1 mg/kg level corresponds to a developmental delay equivalent of at least two years. Impacts of prenatal and postnatal exposure could not be distinguished.

Prenatal low and moderate exposure and observations later in life

Oken et al. (2005) studied infant cognition by the percent novelty preference on visual recognition memory testing at 6 months of age in a subset of 135 children of a US cohort. The children whose mothers had consumed much fish performed better in a visual recall test than children of mothers with little fish consumption. This association was stronger when the regression was adjusted for mother's hair mercury level. In the adjusted model, each additional weekly fish serving was associated with a 4.0 points higher score (95 % CI: 1.3 - 6.7). An increase of mother's hair mercury level by one mg/kg was associated with a 7.5 points decrement (95 % CI: -13.7 to -1.2) in test score. The mean maternal hair mercury was 0.55 mg/kg with a range of 0.02 - 2.38 mg/kg. A larger number of children from the same cohort (n = 341, possibly including the 135 from the previous study) was followed up at the age of three years, with developmental aspects tested by the Peabody Picture Vocabulary Test, and the Wide Range Assessment of Visual Motor Abilities (Oken et al., 2008). The pattern from the previous study was repeated, with a positive association to fish consumption and a negative association to prenatal mercury exposure, this time assessed through red blood cell mercury concentration. The overall scores for both tests were decreased in children of women with a mercury concentration in the highest decile (> 9.1 ng/g red blood cells, in this cohort roughly corresponding to a hair mercury concentration of 1.2 mg/kg), after adjustment for fish intake. Though the reports provide data on associations with methylmercury exposure, the main focus was on the apparently beneficial effects of fish consumption.

A study on inhabitants living by Lake Ontario (n = 212) focusing on cognitive development and prenatal PCB exposure found no effect of mercury exposure. A statistically significant interaction between cord blood PCBs and maternal hair mercury concentration was however seen on the outcome at 38 months, but not at 4.5 years (137 children were included in the interaction analysis; Stewart et al., 2003). Cognitive performance was assessed by the McCarthy General Cognitive Index. The median maternal mercury in hair was 0.50 mg/kg. At nine years of age, a test was performed by 183 of the children, of which 145 had both methylmercury and PCB data. The test required that the child managed delays and inhibitions in response. Impaired performance was statistically significantly associated with maternal hair mercury ($p = 0.03$ in a regression model controlled for PCB exposure), as well as with maternal PCB ($p = 0.02$, controlled for maternal hair mercury) (Stewart et al., 2006).

A cohort of 151 New York children born in the period after 11 September 2001 had cord blood and maternal blood mercury data. The children were followed at 12, 24, 36 and 48 months of age. No associations were found between cord blood mercury concentration and the BSID-II results at the first three follow-ups, except for an association observed with a reduction in PDI at 36 months (n = 111, $p = 0.002$) when applying linear regression. Data from 48 months showed reduced cognitive performance (on the Wechsler Preschool and Primary Scale of Intelligence, Revised) with increased cord-blood mercury (n = 107, $p < 0.001$). The model contained possibly an excessive number of variables, considering the limited number of individuals studied (Lederman et al., 2008).

Development (BSID-II) was also studied by a case-control design within a birth cohort with 233 children from Krakow, Poland. Thirty-six of the children were categorised as having delayed performance at one year of age (cases). These children's mothers had higher blood mercury during pregnancy than the mothers of children with normal performance (controls) (geometric mean: 0.75 vs. 0.52 µg/L; $p = 0.010$). The same difference was close to statistical significance also for cord blood mercury (Jedrychowski et al., 2006). The cohort was then somewhat increased (n = 374) at examination at two and three years of age and the findings did not confirm results from age one year. Further analysis of the PDI and MDI at the two- and three-year follow-ups showed no statistically significant associations (Jedrychowski et al., 2007a).

In addition to the above studies, Daniels et al. (2004) showed statistically significantly lower odds ratio (OR) when associating low developmental assessment scores with higher frequency of maternal fish intake during pregnancy but found no link to prenatal mercury exposure in a subset of 1 054 children from a larger cohort in Bristol, UK. Cord tissue mercury levels (not cord blood) were used for exposure assessment, making comparisons with other studies difficult.

A Japanese cross-sectional study utilised mothers' hair sampled at the time of the investigation when the children were aged approximately seven years, as a possible proxy for maternal mercury levels during pregnancy. Children of mothers who had changed their dietary habits since pregnancy were not included. The study did not reveal any conclusive association for measures of postural sway, tremor, coordination, reaction time, brainstem evoked potentials or HRV with maternal hair-mercury levels at the time of the examination (Murata et al., 2004a). The median maternal hair mercury was 1.63 mg/kg (range: 0.11 - 6.86 mg/kg). Corresponding values for the children at approximately seven years were 1.65 (0.35 - 6.32) mg/kg.

The association between prenatal mercury exposure and fish intake on the one hand, and Attention Deficit Hyperactivity Disorder (ADHD)-related behaviour on the other hand, was investigated in a birth cohort (recruited in 1993 - 1998) in New Bedford, Massachusetts, US (Sagiv et al., 2012) using regression models. Total hair mercury concentrations were analyzed in maternal hair samples collected approximately 10 days postpartum (n = 421) with a median level of 0.45 mg/kg. There were statistically significant associations observed between hair mercury levels and ADHD-related behaviours at age eight years, including inattention and hyperactivity. For outcomes on the Conners Rating Scale-Teachers and CPT reaction time, the authors determined a so-called 'apparent threshold' of approximately 1 mg Hg/kg for ADHD-related behaviour. On the other hand, slightly negative associations of mercury exposure with ADHD-related behaviour were detected at mercury levels below 1 mg/kg. In addition, for some of the outcomes, associations were primarily found in boys. A protective association for fish consumption was found with ADHD-related behaviours, particularly impulsive/hyperactive behaviours.

Observations at birth

A Japanese study of 498 newborn babies found an association ($p < 0.05$ in multiple regression analysis) between neonatal performance at 3 days of age and maternal hair mercury concentrations of 0.29 - 9.35 mg/kg (median 1.96 mg/kg; Suzuki et al., 2010). The relation was adjusted for maternal PCB level. The slope of the regression became steeper after adjustment for seafood intake, while further adjustment for other potential confounders only had a marginal effect.

A study of 384 babies at 3 days of age, born in the Zhejiang Province, China (geometric mean for maternal hair mercury: 1.2 mg/kg), evaluated associations between neonatal behavioural and maternal mercury exposure. For boys, the probability of not getting full score on behaviour, was statistically significant associated with maternal mercury exposure in a logistic regression model. This was not seen for girls, and not for active and passive tones as endpoint (Gao et al., 2007).

Concluding comments on studies from other regions

For cognitive outcomes, a few, but not all, studies found associations with mercury at levels lower than those reported in the Faroe Islands and Seychelles cohorts, but the overall picture at low-level exposure does not provide information to allow conclusions. In addition, there are indications of beneficial effects of fish consumption. In conclusion, these studies did not provide a better basis for dose response assessment than the studies in the Faroe Islands and Seychelles.

Table 24: Overview of epidemiological data on prenatal mercury exposure and neurodevelopmental and neurotoxic endpoints in children.

Author (country)[c]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[e]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Faroe Islands						
Murata et al. (2004b)	Longitudinal cohort study, Faroese Cohort 1	859 children, age: 14 years	THg in cord blood: GM 22.6 (IQR 13.2-40.8) µg/L (highly correlated to maternal hair). THg in maternal hair: GM 4.22 (IQR 2.55-7.68) mg/kg. THg in hair at 7 years: GM 0.60 (IQR 0.34-1.24) mg/kg. THg in hair at 14 years: GM 0.96 (IQR 0.45-2.29) mg/kg	BAEP	Increased latencies III and V by about 0.012 ms by doubling in cord blood Hg concentration. BMDLs similar as those obtained at 7 years. Child's hair Hg at age 14 years associated with prolonged III-V interpeak latencies. The results indicate that some associations between prenatal exposure and neurotoxic endpoints extend into the teenage period	Age, gender, PCB exposure (from cord tissue of 438 cohort members)
Debes et al. (2006)	Longitudinal cohort study, Faroese Cohort 1	860 children, age: 14 years	THg in cord blood: GM 22.5 (IQR 13.1-40.8) µg/L THg in maternal hair: GM 4.21 (IQR 2.53-7.66) mg/kg THg in hair at7 years: GM 2.99 IQR 1.71-6.20) mg/kg[d] THg in whole blood at 7 years: GM 9.00 (IQR 5.00-18.4) µg/L THg in hair at 14 years: GM 0.96 (IQR 0.45-2.29) mg/kg THg in whole blood at 14 years: GM 4.08 (IQR 2.29-7.46) µg/L	motor, attention, working memory/executive function, language, visuospatial and memory functions and mood status	Prenatal Hg exposure associated with decreased finger tapping speed, reaction time in a CPT, and cued naming, but associations were weaker than at 7 years	Age, gender, maternal Raven score, domicile, maternal and paternal employment, time of the day at testing, used language, computer game experience, the participant's grade in school. Prenatal PCB (cord tissue of 438 cohort members) was considered but not statistically significant

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Faroe Islands (continued)						
Budtz-Jørgensen et al. (2007b)	Longitudinal cohort study, Faroese Cohort 1	917 children, age: 7 years 860 children, age: 14 years	7 years (Grandjean et al., 1997): THg in cord blood: GM 22.9 (IQR 13.4-41.3) µg/L THg in maternal hair: GM 4.27 (IQR 2.6-7.7) mg/kg THg in hair at 7 years: GM 2.99 (IQR 1.7-6.1) mg/kg 14 years: see Debes et al. (2006)	motor, attention, working memory/executive function, language, visuospatial and memory functions and mood status	Fish intake improved test scores statistically significant for the motoric performance (7 and 14 years) and for the functioning in tasks for spatial orientation and operations (14 years).	Not specified, refers to Grandjean et al. (1997) and Budtz-Jørgensen et al. (2007a) PCB exposure was not included as a covariate
Budtz-Jørgensen et al. (2010)	Longitudinal cohort studies Faroese Cohort 1 and Faroese Cohort 2	Faroese Cohort 1: about 860 children, age: 7 years Faroese Cohort 2: about 182 children, age: 7 years	Faroe 1: see Murata et al. (2004b), Debes et al. (2006) Faroe 2 (Steuerwald et al., 2000): THg in cord blood: GM 20.4 (range 1.90-120) µg/L THg in cord serum: GM 2.54 (range 0.70-8.74) µg/L THg in maternal hair: GM 4.08 (range 0.36-16.3) mg/kg	motor, attention, working memory/executive function, language, visuospatial and memory functions	The joint analysis using a structural equation model approach showed statistically significant negative coefficients association between prenatal Hg exposure and the verbal function variable while the motor function variable was close to significance. A very close agreement between the cohorts was seen for the Boston Naming Test, whereas the effect estimates for the other outcomes showed less convinced agreement (although test for equality were non-statistically significant except for 'NES2 Finger tapping – preferred hand).	The effect of PCBs were also investigated and a set of variables identified by Grandjean et al. (1997) were included in the models. Finally, the number of maternal pilot whale dinners during pregnancy was included in the models.
Julvez et al. (2010)	Longitudinal cohort study, Faroese Cohort 1	860 children, age: 14 years	See Murata et al. (2004b), Debes et al. (2006)	CPT-HRT latencies	The test phase regarded as indicators of sustained attention by the authors showed the strongest associations with prenatal Hg exposure. Current proximal hair Hg concentrations did not show any clear association structure.	Similar to Debes et al. (2006). In addition in further analyses, Catsys scores, and CPT-HRT during the first 2 min

Table 24: Continued.

Author (country)[c]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[e]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS)						
Davidson et al. (2004)	Longitudinal cohort study SCDS	711 children, age: 5.5 years	THg in maternal hair: P50: 5.9 (range 0.5-26.7) mg/kg THg in hair at 5.5 years: P50: 5.8 (range 0.9-26) µg/g	Cognitive ability, language development, drawing and copying, Letter-Word recognition, scholastic achievement, and child behaviour.	No consistent associations between prenatal mercury exposure and the measured outcomes.	Caregiver intelligence, the Hollingshead measure of socioeconomic status, home environment, gender, recent postnatal Hg exposure. Low levels of Pb not considered, 28 PCBs below LOD.
Huang et al. (2005)	Longitudinal cohort study SCDS	643 children, age: 9 years Reassessment of results from Myers et al,, 2003	THg in maternal hair: µ ± SD: 6.9 ± 4.5 mg/kg. THg in hair at 9 years: µ ± SD: 6.1 ± 3.5 mg/kg.	neurocognitive, language, memory, motor, perceptual-motor, behavioural functions as described in Myers et al., 2003	Re-analysis by using semi-parametric additive models with different degrees of smoothing showed little evidence for adverse effects from prenatal mercury exposure in the Seychelles main cohort.	Sex, maternal age, examiner, caregiver's intelligence, the child's medical history, family resource scale, number of biological parents living with the child, Hollingshead measure of socioeconomic status, Henderson's early learning process scale, child's age at testing, Home environment during toddlerhood, the child's hearing score, recent postnatal Hg exposure

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS) (continued)						
Davidson et al. (2006a)	Longitudinal cohort study SCDS	738 children, age: 19 months 736 children, age 29 months 711 children, age: 5.5 years 643 children, age: 9 years	THg in maternal hair: μ ± SD: 6.8 ± 4.5 (range 0.5-26.7) mg/kg. THg in hair at 5.5 years: μ ± SD: 6.5 ± 3.3 (range 0.9-25.8) mg/kg THg in hair at 9 years: μ ± SD: 6.1 ± 3.5 (range 0.5-24.8) mg/kg[(a)] THg in hair at 19 and 29 months not reported by Davidson et al. (1995)	global cognition, reading and mathematics scholastic achievement, social behaviour and memory	No statistically significant association between prenatal MeHg exposure and child development.	Sex, maternal age at child's birth, birth weight, the child's medical history, alcohol consumption during pregnancy, the child's hearing status as measured by portable audiometry, the preschool version of the HOME, caregiver intelligence, the Hollingshead measure of socioeconomic status, the Family Resource Scale and the Henderson Environmental Learning Profile Scale
Davidson et al. (2008a)	Longitudinal cohort study SCDS	613 children, age: 10.7 years	THg in maternal hair: μ ± SD: 6.83 ± 4.4 mg/kg THg in hair at 9 years[(b)]: μ ± SD: 6.07 ± 3.5 mg/kg, see additional information in Davidson et al. 2006a	Visuospatial ability	No statistically significant association between prenatal MeHg exposure and visual motor coordination	Sex, maternal age, the child's medical history, the child's age at testing, the tester who administered the Bender, the preschool version of the HOME, caregiver intelligence, the Hollingshead measure of socioeconomic status, the Family Resource Scale, the Henderson Environmental Learning Profile Scale to measure the quality of stimulation in the current home environment, Child's hair THg at 9 years, and the child's hearing status measured by audiometry at age 9 years.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS) (continued)						
Davidson et al. (2010)	Longitudinal cohort study SCDS	643 children, age: 9 and 17 years	THg in maternal hair: µ±SD: 6.89 ± 4.52 mg/kg THg in hair at 9 years: µ±SD: 6.09 ± 3.47 mg/kg, THg in hair at 17 years: µ±SD: 8.00 ± 4.68 mg/kg The SACMEQ subgroup had higher levels of THg in hair at 9 years (µ±SD: 7.48 ± 3.98 vs 5.39 ± 2.94	Scholastic achievements in nationally standardised end-of-year examinations given at 9 and 17 years of age, and a regional test called SACMEQ at 9 years in a subgroup (n = 215)	No pattern of associations between prenatal or recent postnatal exposure with the 9- or 17-year end-of-year examination scores. No associations between prenatal exposure and the SACMEQ test score results were seen. However, recent postnatal exposure had a negative association with these test scores in boys.	From home and family: Family Resource Scale, the Henderson Environmental Learning Profile Scale to measure home environment, caregiver's intelligence, socioeconomic score. From 9 years study on child: sex, region of school attendance, child's IQ, the long delay free recall score from the California Verbal Learning Test, Visual Memory, and the total T score from the child behaviour. For SACMEQ endpoints: teachers competence
Davidson et al.(2011)	Longitudinal cohort study SCDS	371 to 462 children (n depends on the outcome. measure), age: 17 years	THg in maternal hair: µ±SD: 6.89 ± 4.40 (range 0.54 – 22.74) mg/kg. THg in hair at 17 years: 7.98 ± 4.64 (range 0.33-28.33) mg/kg.	Cognigitive functions including verbal learning, memory, learning and reversal learning and attention and measures of problematic behaviours	No consistent pattern of adverse associations between prenatal mercury exposure and the tested outcome variables at age 17 years was found.	All models adjusted for sex, socioeconomic status, maternal intelligence and recent postnatal Hg exposure. All neurocognitive endpoints adjusted for child' age at testing. The youth risk behaviour an problematic behaviour endpoints were adjusted for IQ measures at 107 months.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: nutrition cohort (SCDNS)						
Davidson et al. (2008b)	Longitudinal cohort study SCDNS	229 children, age 5, 9, 25 and 30 months	THg in maternal hair: μ ± SD: 5.7 ± 3.7 (range: 0.2-18.5) mg/kg	Main outcomes tested were mental and psychomotor development (BSID-II) at 9 and 30 months). In addition, novelty preference and VRM at 5 and 9 months. Aspects of planning, inhibition, attention and working memory at 25 months	The adjusted results showed a negative association between prenatal methylmercury and the mean PDI scores on BSID-II at 30 months (r -0.55, p = 0.04). The association with prenatal methylmercury alone was 'borderline statistically significant', (r -0.44, p = 0.07). The additional assessments at 5, 9 and 25 months showed no association with prenatal methylmercury exposure. The results suggest that maternal fish intake is a possible confounder in studies that investigate the associations between prenatal MeHg exposure and child development.	Maternal blood TSH, DHA, AA, Fe, estimated choline intake, fish consumption, socioeconomic status, home environment, maternal intelligence, the tester for each child (except BSID-II), birth weight, maternal age sex, both parents living with the child at 9 months.
Strain et al. (2008)	Longitudinal cohort study SCDNS	229 children, age: 9 and 30 months	See Davidson et al, 2008b	mental and psychomotor development (BSID-II)	Maternal serum n-3 LCPUFA measured during the last trimester was positively associated with the PDI at 9 months of age. PDI score was inversely related to the n-6/n-3 ratio. Associations between maternal measures of n-3 LCPUFA and positive outcome were strengthened when the confounding factor of prenatal exposure to methylmercury was adjusted for in the regression models.	Same as Davidson et al, 2008b, but not including maternal blood TSH, Fe, estimated choline intake and fish consumption

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: nutrition cohort (SCDNS) (continued)						
Lynch et al. (2011)	Longitudinal cohort study SCDNS, longitudinal analysis approach	See Davidson et al., 2008b	See Davidson et al., 2008b	mental and psychomotor development (BSID-II)	The positive effect of DHA on the outcomes (MDI and PDI at 9 and 30 months) was absent or reduced at higher Hg levels (approximately 11 mg/kg). The number of observation with high mercury levels in the study were small.	The same covariates were used as by Davidson et al. (2008b).
Stokes-Riner et al. (2011)	Longitudinal cohort study SCDNS, longitudinal analysis approach	228 children, age 9 and 30 months	See Davidson et al., 2008b	psychomotor development (BSID-II)	Maternal THg was negatively associated with PDI, whereas maternal n-3 LCPUFA was positively associated with PDI. The association was not different at 9 and 30 months of age.	Maternal blood n-3 and n-6 LCPUFAs, socioeconomic status, home environment, maternal intelligence, birth weight, maternal age, sex, both parents living with the child at 9 months
Strain et al. (2012)	Longitudinal cohort study SCDNS	225 children, age: 5 years	THg in maternal hair: μ ± SD: 5.7 ± 3.7 (range: 0.2-18.5) mg/kg	Different outcomes for child development from tests on finger tapping, language, letter word recognition and applied problems, child behaviour, Child's IQ	No statistically significant associations between prenatal mercury exposure and developmental outcomes. Improved test results on preschool language scores were associated with increasing maternal DHA, and diminished with increasing maternal AA.	Sex, number of immediate family members living with the child, maternal age, maternal IQ, socioeconomic status, home environment, child age at testing, birth weight. Different combinations of LCPUFAs in prenatal maternal serum included in different models
South America						
Chevrier et al. (2009) (Brazil and French Guiana)	Cross-sectional study	395 children, age 9.5years,	THg in maternal hair: μ±SE: 10.3 ± 0.5 (range 0.6-41.7) mg/kg THg in hair at 9.5 years: μ±SE: 9.8 ± 0.4 (range 0.5-63.8) mg/kg Correlation child's hair-mother's hair: Higher (r = 0.5-0.57) in Brazil than in French Guiana (r = 0.09-0.28).	Visuospatial ability (Stanford-Binet Copying test)	Mercury exposure negatively associated with scores on the drawing/rotation task: a score reduction of 1.2 (SE 0.3) points was observed in the children with a hair-mercury concentration above 10 mg/kg compared to those with a hair level below 1 mg/kg; the associations appeared to be stronger in the younger children. Components of the test varied according to the study site (e.g. Block organization). Separate impact of pre- and postnatal exposure could not be distinguished	Age, sex, village, maternal marital status, education, alcohol consumption during pregnancy. Maternal Raven Score not determined in the Brazilian study, maternal education used as proxy.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Europe						
Daniels et al. (2004) (United Kingdom)	Longitudinal cohort study	1054 children, age 15 and 18 months	THg in cord tissue: GM ± SD: 0.01±0.4 (IQR of 0.0076-0.0220 mg/kg,	Language and communication development (MCDI) at 15 months, and language, social, fine and gross motor skills (DDST) at 18 months, both assessed by the child's mother and returned by mail.	No association to Hg after adjustments. No crude results given.	Child's age at testing, sex, birth order, fish intake, breastfeeding status, and maternal fish intake, age, education, dental treatment, smoking and alcohol use during pregnancy, and HOME score.
Jedrychowski et al. (2006) (Poland)	Longitudinal cohort study	233 children, age: 1 year	THg in cord blood: P50: 0.85 µg/L, GM: 0.88 (range: 0.10-5.00) µg/L THg in maternal blood: P50: 0.60 µg/L, GM: 0.55 (range: 0.10-3.40) µg/L µg/L	mental and psychomotor development (BSID-II), dichotomised into normal and delayed performance.	36 children with delayed performance had higher maternal blood Hg than those with normal performance (GM: 0.75 vs. 0.52 µg/L; p = 0.010). The same association was close to statistical significance also for cord blood Hg. In a logistic regression model, the RR for delayed performance at maternal blood Hg > 0.50 µg/L was 2.82, 95 % CI 1.17-6.79 (3.58; 1.40-9.14 for cord blood Hg > 0.80 µg/L).	Sex, gestational age, maternal age, and maternal education was used as covariates in the logistic regression model.
Jedrychowski et al.(2007a) (Poland)	Longitudinal cohort study	374 children, age: 1, 2 and 3 years	THg in cord blood and maternal blood. Concentrations not given, but can be assumed to be similar to those in Jedrychowski et al., 2006.	mental and psychomotor development (BSID-II)	Mental and Psychomotor Development Indices showed negative association with cord blood Hg (dichotomised with cut-off at 0.90 µg/L) at 1 year (p = 0.01 and 0.04, respectively), but not at 2 or 3 years (p-values between 0.20 and 0.42)	Sex, environmental tobacco smoke, parity, and maternal education.
North America						
Després et al. (2005) (Canada)	Longitudinal cohort study	109 Inuit children, age: 5.4 years (mean).	THg in cord blood: µ ± SD: 22.2 ± 18.4 µg/L, GM15.9 (range: 1.8-104.0) µg/L	Different measures of neuromotor function	No association to Hg for reaction time, measures related to sway or alternating movements. Both prenatal Hg and current Pb was associated with tremor in pointing movements.	Pb. A range of other covariates considered, including PCB and socioeconomic factors.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Saint-Amour et al. (2006) (Canada)	Longitudinal cohort study	78 Inuit children, age: 5.4 years (mean) (Same cohort as Després et al., 2005)	THg in cord blood: μ ± SD: 24 ± 20 μg/L, GM: 17 (range: 1.8-104) μg/L THg in blood at 5.4 years: μ ± SD: 10 ± 9 μg/L GM: 5.9 (range: 0.2-38) μg/L	Latency (ms) and amplitude (μV) of visual evoked potentials as measured in electrophysiological recordings at three different contrasts, three components each (N75, P100, N150)	Increased latency of the P100 component at 30 % contrast was associated with cord Hg after confounding adjustment. Decreased latencies were associated with current child Hg for both N75 and P100, at both 95 and 30 % contrast.	Considered confounders included socioeconomic variables, caretakers education, n-3 LCPUFA, and PCB.
Boucher et al. (2010) (Canada)	Longitudinal cohort study	116 Inuit children, age: 11 years	THg in cord blood: μ ± SD: 21.5± 18.8 μg/L, P50: 14.2 (range: 1.8-99.3) μg/L μg/L THg in blood at 11 years: μ ± SD: 4.69 ± 4.9 μg/L, P50: 2.8 (range: 0.2-28.1) μg/L	ERPs in EEG recording	MeHg in cord blood was associated with slower reaction times and greater amplitude and delayed latency of the N1 wave. Current blood Hg was not associated with outcome.	DHA, Se, Pb, PCB, breast-feeding. Other factors were considered, e.g. mother's smoking and alcohol consumption.
Plusquellec et al. (2010) (Canada)	Longitudinal cohort study	110 Inuit children, age: 5.4 years, (Same cohort as Després et al., 2005 and Saint-Amour et al., 2006)	THg in cord blood: μ±SD: 22.2 ± 18.4 (range: 1.8-104.0) μg/L THg in blood at 5.4 years: μ ± SD: 9.6 ± 8.9 (range: 0.2-38.2) μg/L	behaviour, attention and emotional expression, (including the Infant Behaviour Rating Scale from BSID-II and observational data).	No associations between outcomes and Hg	Considered confounders included socioeconomic variables, caretakers education, cord and child's Se and LCPUFA, PCB and lead.
Boucher et al. (2012) (Canada)	Longitudinal cohort study (same cohort as Boucher et al., 2010	193 Inuit children, age: 11 years	THg in cord blood: μ ± SD: 21.2 ± 17.6 μg/L, P50: 16.6 (range: 1.0-99.3) μg/L THg in blood at 11 years: μ ± SD: 4.69 ± 4.9 μg/L, P50: 2.8 (range: 0.2-28.1) μg/L	ERPs in EEG recording, but the N1 wave, for which Hg associations have been observed, was not included.	No associations with Hg in adjusted model, but interaction with effects of other contaminants was suggested.	PCB and Pb, which were the pollutants in focus

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Stewart et al. (2003) (USA)	Longitudinal cohort study follow up at 38 months and 4.5 years of age	212 children, age: 38 months and 4.5 years	THg in maternal hair, first half of pregnancy: P50: 0.50 (IQR 0.40-0.60) mg/kg THg in maternal hair, second half of pregnancy: P50: 0.50 (IQR 0.40-0.70) mg/kg	Cognitive performance, as assessed by the McCarthy General Cognitive Index.	No direct association between cognitive performance and Hg was observed, but an interaction between cord blood PCBs and maternal hair Hg was found at 38 months, but not at 4.5 years	A large range of covariates was considered, including maternal and paternal factors, nutrition, drugs, etc, but not variables related to fish consumption or n-3 LCPUFAs.
Oken et al. (2005) (USA)	Prospective cohort study	135 children, age: 6 months.	THg in maternal hair: μ: 0.55 (range: 0.02-2.38) mg/kg	VRM (assessing the magnitude of preference for the child to look at a picture of new face, as compared to a picture of a face the child has seen before).	For each additional weekly fish serving, the VRM score was 4.0 points higher (95 % CI: 1.3-6.7) after adjusting for Hg, for which each mg/kg was associated with a 7.5 points decrement (95 % CI: -13.7 to -1.2).	Participant characteristics, such as maternal age, education, marital status, birth weight, etc.
Stewart et al. (2006) (USA)	Longitudinal cohort study	183 children, age: 9.5 years (from the same cohort as Stewart et al., 2003)	THg in maternal hair at first or second half of pregnancy: μ: 0.56 mg/kg	Performance on a task that requires the child to manage delays in response, a so called differential reinforcement of low rates schedule.	Impaired performance was associated with maternal hair Hg ($p = 0.029$ in a model controlled for PCB exposure).	A large range of covariates was considered, including maternal and paternal factors, nutrition, drugs, etc, and also PCB, but not variables related to fish consumption or n-3 LCPUFAs.
Lederman et al. (2008) (USA)	Longitudinal cohort study	151 children with at least one follow-up (at 1, 2, 3, or 4 years of age) .	THg in cord blood: μ ± SD: 7.82 ± 9.71μg/L, P50: 4.3 (range: <0.2-63) μg/L THg in maternal blood: μ±SD: 2.32 ± 2.3μg/L, P50: 1.7 (range: <0.14-16.4) μg/L	Mental and psychomotor development at 1, 2, and 3years (BSID-II), and performance, verbal and full IQ scores at 4 years (Wechsler Preschool and Primary Scale of Intelligence, Revised).	In an adjusted model of outcome vs. Log Hg no associations with cognitive functions was observed at 1 or 2 years. At 3 years an association was observed with PDI ($p = 0.007$) and at 4 years with Performance ($p = 0.023$), Verbal ($p = 0.023$), and Full IQ scores ($p = 0.002$).	Race, maternal IQ, per capita family income, and child's sex and gestational age at birth. Another model controlled for additional potential confounders.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Oken et al. (2008) (USA)	Prospective cohort study	341 children, age: 3 years (in part same children as in Oken et al., 2005)	THg in maternal red blood cells sampled during the second trimester: μ ± SD: 3.8 ± 3.8 (range: <0.5-21.9) ng/g	Cognitive performance, as assessed by the Peabody Picture Vocabulary Test, and Wide Range Assessment of Visual Motor Abilities	The overall score for both tests were decreased in children of women with Hg in the highest decile (> 9.1 ng/g, in this cohort roughly corresponding to hair Hg 1.2 mg/kg), after adjustment for fish intake, which was associated with increased scoring.	Fish intake and other potential confounders, such as gestational length, primary language, maternal vocabular test score and education.
Sagiv et al. (2012) (USA)	Longitudinal cohort study	421 children, age: 8 years	THg in maternal hair collected about 10 days postpartum: P50: 0.45 (range: 0.03-5.14) mg/kg	Inattentive and impulsive/hyperactive behaviour (teacher rating scale and neuropsychological testing)	Statistically significant associations between maternal THg in hair and ADHD-related behaviours at age 8 years. Threshold associations were detected at approximately 1 mg/kg.	Fish intake and other potential confounders. There was a protective association for fish consumption and ADHD-related behaviours.
Asia and other regions						
Murata et al. (2004a) (Japan)	Cross-sectional	210 Japanese children, age: 6.3-7.5 years (mothers have not reported changes of dietary habits since pregnancy)	THg in current maternal hair: P50: 1.63 (range: 0.11-6.86) mg/kg	Postural sway, tremor, ear-hand coordination, eye-hand coordination, reaction time, brainstem evoked potentials, HRV	Two out of 39 tested correlations were statistically significant (one of 16 sway tests and one of four ear-hand coordination tests).	Age, gender, height
Suzuki et al. (2010) (Japan)	Cross-sectional	498 babies at 3 days of age	THg in maternal hair: μ ± SD: 2.22 ± 1.16 mg/kg, P50: 1.96 (range: 0.29-9.35) mg/kg	behaviour and reflexes according to the NBAS	Impairment related to maternal hair mercury ($p < 0.05$) after adjustment for PCB. Further adjustment for seafood intake increased the magnitude of the association, while further adjustment for potential confounders only marginally affected the association.	Seafood intake, maternal PCB level, as well as a range of other potential confounders, such as maternal age, birth weight, and thyroid related hormones.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Asia and other regions (continued)						
Gao et al. (2007) (China)	Cross-sectional	384 babies at 3 days of age	THg in cord blood: GM: 5.6 (IQR: 4.0-7.8) µg/L THg in maternal hair: GM: 1.2 (0.9-1.7) mg/kg	according to the NBNA scale	In logistic regression analysis, the probability of getting full mark for behaviour score was negatively associated with maternal Hg (both cord blood and hair) for boys but not girls. For cord blood Hg an OR of 1.235 (95 % CI 1.078-1.414) was calculated, presumably for each increment of 1 µg/L. There were no associations for active and passive tones.	Several potential confounders were considered, but only paternal smoking and maternal Hg exposure qualified for the logistic regression model for behaviour score.

µ: mean; AA: arachidonic acid; ADHD: Attention Deficit Hyperactivity Disorder; BAEP: Brainstem Auditory Evoked potentials; BMDL: 95 % benchmark dose lower confidence limit; BSID-II: Bayley Scales of Infant Development-II; CI: confidence interval; CPT: Continuous performance test; CPT-HRT: Continuous Performance Test-Hit Reaction Time latencies; DDST: Denver Development Screening Test; DHA: docosahexaenoic acid; ERP: event-related potential; Fe: iron; GM: geometric mean; Hg: mercury; HOME: Home Observation for Measurement of the Environment; HRV: heart-rate variability; IQ: intelligence quotient; IQR: interquartile range; LCPUFA: long-chain polyunsaturated fatty acids; LOD: limit of detection; MCDI: MacArthur Communicative Development Inventory; MeHg: methylmercury; n.r.: not reported; n-3 LCPUFA: n-3 long-chain polyunsaturated fatty acids; NBAS: Neonatal behaviour assessment scale; NBNA: Neonatal behavioural neurological assessment; OR: odds ratio; P50: 50th percentile; Pb: lead; PCB: polychlorinated biphenyls; PDI: Psychomotor Developmental Index; RR: relative risk; SACMEQ: Southern and Eastern African Consortium for Monitoring Educational Quality; SCDNS: Seychelles Child Development Nutrition Study; SCDS: Seychelles Child Development Study; SD: standard deviation; SE: standard error; SES: socio-economic status; THg: total mercury; TSH: thyroid stimulating hormone; VRM: Visual recognition memory.

(a): values in 143 males with shaved heads were missing at nine years and were substituted by previous measurements;

(b): no concentrations of THg in hair are reported by the authors at 10.7 years of age;

(c): country specified except for the cohorts from the Seychelles and Faroe Islands;

(d): the levels of THg in hair at seven years are reported by both Debes et al. (2006) and Murata et al. (2004b). The CONTAM Panel noted that the levels in both papers are substantially different.

(e): associations were assessed in some cases by correlation, but mostly by (multiple) linear regression of the outcome on the respectively used mercury measures available. However, only the more advances statistical regression methods are mentioned in the table.

7.4.2.1.2. Postnatal exposure and observations in childhood

A cross-sectional study of 72 four-year old boys in Spain (geometric mean mercury level in hair 1.81 mg/kg) found decrements in cognitive abilities (general cognitive, memory and verbal scores) for boys with hair mercury levels above 1 mg/kg – about half of the studied children – compared with those with lower levels (Freire et al., 2010). The authors adjusted for fish consumption and a number of potential confounders.

A study of a cohort of 780 US children enrolled in a clinical trial on treatment of lead-exposed children study did not reveal any cognitive effects of methylmercury at low levels (median blood level 0.5, interquartile range (IQR) 0.4 - 0.8 µg/L). In contrast, the authors noted tendencies for increased IQ and decreased behavioural problems as methylmercury increased. They suggested the possibility that this could be due to nutritional contribution with e.g. n-3 LCPUFAs from fish consumption that was not accounted for in the analyses (Cao et al., 2010).

A cross-sectional study on 355 US children found no statistically significant associations with a range of cognitive outcomes (Surkan et al., 2009). The mercury concentrations in hair were low with a mean of ca. 0.32 mg/kg. Two of the outcomes deviated from linearity in their relation to hair mercury. Modelling these outcomes with smoothed curves suggested positive slopes for hair mercury concentrations below 0.5 mg/kg and negative slopes between 0.5 and 1.5 mg/kg. The number of observations above 0.5 mg/kg was however small and none of the suggested associations in the higher range was statistically significant.

An analysis of the possible influence of postnatal methylmercury exposure from fish consumption (mean ± SD hair level: 6.5 ± 3.3 mg/kg at 5.5 years (n = 694) and 6.1 ± 3.6 mg/kg at 9 years (n = 537)) on multiple outcomes at 5.5 and 9 years of age and association with children's intelligence coefficients at 9 years was reported by Myers et al. (2009). The correlation between maternal and child's hair mercury decreased with the child's age. It ranged from moderate (r = 0.3) at 6 months to low correlation (r = 0.16) at 5.5 years, down to fairly low correlation (r = 0.07) at 9 years. The authors used three different metrics of postnatal exposure in linear regression analyses and included a broad set of confounders. Postnatal mercury exposure metrics did not predict the nine-years intelligence coefficients and the authors concluded that the regression analysis showed no consistent influence of postnatal exposure. Furthermore, the authors acknowledged that the SCDS study might not provide sufficient information on postnatal exposure.

One study of 100 children (Torrente et al., 2005) was not further reviewed because of its limitations in size and lack of confounding adjustment. Two studies of children living in different communities with different exposures (Tavares et al. 2005; de Fonseca et al., 2008) were also not further reviewed because of the limitations in the study designs.

A few studies have specifically focused on ADHD in children. A case-control study from Hong Kong showed higher blood mercury levels among 52 children with ADHD, compared to 59 controls: geometric mean: 3.6 vs. 2.3 µg/L; $p < 0.001$ (Cheuk and Wong, 2006). The analyses were adjusted for age, gender and parental occupational status, but not for variables related to fish consumption.

A cross-sectional study of 1 778 Korean children found no association between ADHD and blood mercury (mean ± SD ca 2.9 ± 1.5 µg/L; Ha et al., 2009). A tendency towards a decreased risk of ADHD with increasing blood mercury appeared ($p = 0.10$).

A cross-sectional study of 83 Romanian children, aged 8 - 12 years, did not find any association between features related to ADHD and blood mercury concentrations ranging between 0.5 and 5 µg/L (Nicolescu et al., 2010).

In addition, Myers et al. (2009) used the Connor's Teacher Ratings Scale ADHD Index in the Seychelles nine year follow-up (n = 537) and observed a highly statistically significant association ($p < 0.0001$) with recent postnatal hair mercury in a regression model.

A number of studies have investigated the relation between mercury levels and autism in children (Holmes et al., 2003; Ip et al., 2004; Adams et al., 2007; Kern et al., 2007; Geier et al., 2010; Hertz-Picciotto et al., 2010; Majewska et al., 2010; Woods et al., 2010; Kaluzna-Czaplinska et al., 2011; Lakshmi Priya and Geetha, 2011; De Palma et al., 2012; Wright et al., 2012). The results of these studies do not give a coherent picture of an association between biomarkers of mercury and autism in children. Associations have been observed in both positive and negative directions, but the studies are generally small. Only two studies attempted to study markers of mercury exposure prior to diagnosis: Adams et al. (2007) measured mercury in baby teeth in 16 children with autism and 11 controls, and Holmes et al. (2003) found lower mercury concentrations in first baby haircut (mean: 0.47 mg/kg) from 94 children with autism than in 45 controls (3.63 mg/kg). The concentration in the control hair samples must however be considered high for USA. The other studies compared children with autism with controls from a cross-sectional study, giving the possibility of bias through an influence of the disorder or its diagnosis on fish consumption or dental amalgam status. Such bias is one of several possible reasons of the differing results. Some studies have focused on porphyrins that may be affected by mercury (Geier and Geier, 2007; Geier et al., 2009a,b; Kern et al., 2010; Woods et al., 2010), but these could not be interpreted in terms of dietary mercury intake. It has been suggested that porphyrins may be associated with autism, but without an association to mercury (Woods et al., 2010). An ecological study of autism and environmental mercury release (Palmer et al., 2006) was not considered relevant for risk assessment of dietary intake.

In conclusion, as regards children's postnatal mercury exposure, the inconsistent observations from the studies above do not give reasons for any increased concern for neurotoxic effects. The studies on autism do not indicate any increased risk from dietary mercury exposure, but for ADHD some studies have found associations with mercury. Taken together, however, the results do not provide information to allow conclusions.

7.4.2.1.3. Neurotoxicity in adults

A range of follow-up studies and reassessment of outcomes from the Minamata area, which also includes control groups from Japan with lower exposure, have been published since the assessment by JECFA (Futatsuka et al., 2005; Ninomiya et al., 2005; Uchino et al., 2005; Ekino et al., 2007; Yorifuji et al., 2008, 2009a, 2009b, 2011; Gilbertson, 2009; Sakamoto et al., 2010). However, the previous methylmercury exposure has been higher than in the Faroese and Seychelles cohorts on which the JECFA PTWI is based. Consequently, the CONTAM Panel does not consider these studies suitable when evaluating if the existing PTWI is sufficiently protective.

In a cross sectional study, Carta et al. (2003) performed neurobehavioural and tremor tests on adult Italian consumers of fresh tuna (n = 22) and non-consumers (n = 22). Colour word reaction time, digit symbol reaction time and finger tapping speed was statistically significantly lower in the tuna fish eaters, and was associated with organic mercury in blood in multiple stepwise regression analysis. However, mercury in blood and urine (total mercury and organic mercury) was available for only 10 consumers and 6 non-consumers (total mercury in blood (µg/L); consumers 44.0 (range 15 - 93); non-consumers 3.9 (range 1.2 - 5.4)). Due to the small sample size the study is regarded as preliminary by the authors, and the CONTAM Panel noted that the exposure in the tuna fish consumers was high.

Neurotoxicity in 240 adults (99 women) living near a chloralkali plant in Taiwan that was closed in 1982 was investigated by Chang et al. (2008). The mean duration of residence was 49.3 years and the majority had age 40 - 70 years. Their current mercury exposure was mainly through fish consumption. Total mercury and methylmercury in blood was measured, and the participants were divided into high exposure (n = 46, mean blood methylmercury 27.0 ± 10.4 µg/L) and low exposure groups (n = 92, 11.6 ± 4.7 µg/L) and matched for age, gender and education. The Cognitive Abilities Screening

Instrument and Mini-Mental State Examination were used to assess the participants' cognitive functions. When comparing the high and low methylmercury groups, lower scores were seen for tests covering remote memory (OR 10.0, 95 % CI 1.7 - 216.1), mental manipulation (OR 5.3, 95 % CI 1.7 - 29.7), orientation (OR 3.3, 95 % CI 1.7 - 9.6) and verbal fluency (OR 5.0, 95 % CI 1.1 - 39.4) in the high exposure group. No differences were seen for tests covering recent memory, attention, abstract thinking, language and drawing.

Choi et al. (2009) studied a group of 41 whaling men (for more details, see Section 7.4.2.2 and Table 25) and found no associations between mercury exposure and BAEPs.

Levels of n-3 LCPUFA or total mercury in whole blood in relation to the risk of dementia or Alzheimer's disease among 149 dementia patients and 514 unaffected participants in the Canadian Study of Health and Aging were investigated (Kröger et al., 2009). No association was found between dementia and n-3 LCPUFA. Mercury in blood in the highest quartile (mean ± SD: 2.48 ± 1.64 µg/L) was associated with a statistically significant lower risk of dementia (0.53, 95 % CI 0.33 - 0.88) in participants with n-3 LCPUFA levels above the median compared to those with lower levels. The authors considered that the results regarding mercury may indicate a spurious association.

In a cross-sectional study on 243 fresh water fish eaters from two regions of Québec, Canada, Philibert et al. (2008) did not observe any association between neuropsychiatric symptoms measured with Brief Symptom Inventory and n-3 LCPUFA in blood, and no interaction of n-3 LCPUFA with mercury. The participants had low n-3 LCPUFA values (median EPA + DHA was 0.11 g/L) and low mercury exposure (median in blood 2.22 µg/L and in hair 0.54 mg/kg).

Twenty scores from 12 neurobehaviour tests were measured in a cross-sectional study on 474 adults (185 women) in the Baltimore Memory Study (50 - 70 years, mean age 59 years and median blood mercury 2.1 µg/L (range 0 - 16 µg/L)) (Weil et al., 2005). In linear regressions, increasing blood mercury was associated with worse performance on a test of visual memory, and with better performance on a test of manual dexterity (finger tapping). The authors concluded that overall, the data did not provide strong evidence for an association between mercury in blood and lower scores on neurobehavioural performance tests in this population.

Benefice et al. (2010) examined neurological abnormalities and blood pressure among two ethnic groups of Amerindian women living along the banks of the Beni River (n = 170). Total mercury in hair (mean 5.5, SD 4.2 mg/kg) and frequency of fish consumption was recorded by a 24-h food recall questionnaire. The authors reported statistically significant associations between the fishing practices or the frequency of fish consumption and hair mercury levels. Women with hair mercury concentration above 5 mg/kg were more likely to have neurological abnormalities (paresthesia, static and dynamic imbalance, poor motor coordination) than women with hair mercury below 5 mg/kg. No relationship was found between blood pressure and mercury levels. Women with higher mercury concentration in hair reported higher rates of infant deaths than did women with lower levels. The women with high mercury concentration and who reported higher infant deaths tended to belong to a population groups practicing traditional fishing and were younger and with poorer health than those with lower mercury levels.

In summary, the studies referred to above do not show relevant associations between mercury exposure, at low levels, and adverse neurological outcomes in the adult population.

7.4.2.2. Cardiovascular effects

When JECFA evaluated methylmercury in 2006, in addition to neurodevelopmental endpoints they also considered cardiovascular outcomes in adults. Five epidemiological studies of mercury concentrations in adults in relation to cardiovascular disease were considered and tabulated (the first five studies in Table 25; FAO/WHO, 2007). It was noted that two of these (Guallar et al., 2002; Virtanen et al., 2005) found an increased risk of acute coronary event or myocardial infarction with higher mercury concentrations; one study (Hallgren et al., 2001) found a decreased risk of myocardial

infarction with higher concentrations of mercury (considered by the authors as a biomarker for fish consumption); and the other two studies (Ahlqwist et al., 1999; Yoshizawa et al., 2002) did not show a statistically significant association between myocardial infarction and mercury concentrations. One study (Salonen et al., 1995) was not included among these five, because it concerned the same cohort as that described by Virtanen et al. (2005).

The JECFA evaluation (FAO/WHO 2007) considered cardiovascular function also in young children with prenatal methylmercury exposure. Two studies of HRV (Grandjean et al., 2004b; Murata et al., 2006), reflecting cardiac autonomy, were reviewed by JECFA. Results suggested that prenatal exposure to methylmercury is associated with impaired cardiac autonomy. The study by Murata et al. (2006) suggested an association already at a median of estimated maternal hair mercury concentration at parturition of 2.24 mg/kg. This value is lower than that for neurodevelopmental endpoints. The value was noted by the JECFA, but did not influence the PTWI.

Cardiovascular disease in adults

Six major epidemiological studies of cardiovascular disease and mercury have been published since 2005 and are summarised in Table 25 (Wennberg et al., 2007; Engström et al., 2011; Mozaffarian et al., 2011; Wennberg et al., 2011; Bergdahl et al., 2012; Virtanen et al., 2012). Of these, one (Engström et al., 2011) evaluated gene-environment interactions in the same individuals as had been studied in other studies (Hallgren et al., 2001; Wennberg et al., 2011). Therefore, these data are not further considered here and the study is not included in Table 25. In addition, a risk-benefit model has been published (Wennberg et al., 2012) for mercury and n-3 LCPUFA based on pooled, previously published, data from Finland and Sweden. One ecological study of Minamata with cardiovascular outcomes during the period 1953 to 1970 (Inoue et al., 2012) was not included in the current review, due to the difficulties of interpreting results in terms of dose-response that follows from the lack of individual exposure information.

Wennberg et al. (2007) studied the risk of a first stroke in relation to mercury, fish consumption and n-3 LCPUFA. The study was a case-control study nested within a cohort study with blood samples stored in a biobank. Hence, 369 cases who had experienced a stroke after their enrolment in the study were identified, and 738 controls were matched by age, sex, time of sampling and place of residence. Total mercury was measured in erythrocytes and n-3 LCPUFA in erythrocyte membranes. Information on fish consumption was obtained from a food frequency questionnaire. The median erythrocyte mercury concentration for the study population (cases and control) was reported as 3.63 ng/g. No association was observed between stroke risk and either mercury (OR: 0.99 per ng Hg/g erythrocytes; 95 % CI: 0.93 - 1.06), or n-3 LCPUFA (OR: 1.08 per % EPA + DHA; 95 % CI 0.92 - 1.28).

Wennberg et al. (2011) studied the risk also of a first acute myocardial infarction in relation to fish consumption. Just like in the stroke study and the study by Hallgren et al. (2001), this was a case-control study nested in a cohort with prospectively collected blood samples. The study comprised 150 female and 350 male cases and 275 female and 350 male controls, matched for sex, age, time of blood sampling, and place of residence. Mercury was measured in erythrocytes and n-3 LCPUFA in plasma phospholipids. The median mercury concentration was reported as 3.54 µg/L. Mercury and n-3 LCPUFA were correlated. Mercury was associated with a decreased risk for acute myocardial infarction. This was interpreted by the authors as a protective effect of fish consumption.

Data from Wennberg et al. (2011) was later combined with data from Hallgren et al. (2001) and Virtanen et al. (2005). When combined, these data provided wider exposure ranges for both mercury and n-3 LCPUFA, which facilitated modelling of acute myocardial risk as a function of both mercury and n-3 LCPUFA (Wennberg et al., 2012). Though this study did not include any new participant, the resulting model illustrates how the risk can be related to both mercury, with an increase in risk, and n-3 LCPUFA, with a decrease in risk. At low serum concentrations of LCPUFAs, a statistically significant association between myocardial risk and hair mercury was seen at hair mercury concentrations above ca 3 mg/kg. Based on readings from a figure, the model indicates a relative risk

(RR) of ca 1.2 at hair-mercury concentrations of 4 - 5 mg/kg, when comparing individuals with the same serum concentrations of LCPUFAs.

Mozaffarian et al. (2011) studied 3 427 cases with cardiovascular disease and 3 427 controls. The study was nested in two cohorts with prospectively collected toenails, in part the same cohort as previously studied by Yoshizawa et al. (2002). The interdecile range for toenail mercury concentration was 0.06 - 0.94 mg/kg in cases and 0.07 - 0.97 mg/kg in controls. Mercury was correlated with fish consumption ($r = 0.39$, $p < 0.001$), but not with any increased risk for coronary heart disease or stroke. Adjustments were made for a number of factors, including intake of n-3 LCPUFA from fish. The latter was not chemically measured but estimated based on data from a dietary questionnaire. Validation studies have shown correlation coefficients of 0.43 - 0.49 between marine n-3 LCPUFA, as assessed from questionnaire data, and on measurements in subcutaneous fat samples (Hunter et al., 1992). No association with cardiovascular outcome was indicated for the estimated n-3 LCPUFA, or for other dietary risk factors, such as trans fatty acids. The study thus found no association between mercury exposure and cardiovascular disease. The highest decile of 0.97 mg/kg in toenails was specifically studied, but revealed no increased cardiovascular risk. The authors indicated that this toenail concentration corresponded to about 2.7 mg/kg in hair.

Bergdahl et al. (2012) followed up the same cohort as was studied earlier by Ahlqwist et al. (1999). The median serum mercury concentration was 1.4 (range: 0.1 - 13) µg/L, reflecting a combination of inorganic and organic mercury at low exposure levels. In accordance with the first study, higher mercury concentration in serum was associated with decreased risk of acute myocardial infarction, i.e. no adverse effect was indicated. When adjustments were made for socioeconomic factors and fish intake (based on 24 hours recall, which is insufficient for a proper adjustment), the association with a reduction in fatal acute myocardial infarction remained statistically significant and an increased risk for stroke appeared, while the association to total acute myocardial infarction incidence did not remain statistically significant. While the study was conducted at low mercury exposure levels and indicated reduced myocardial infarction risks, its main conclusions relate to the relevance for cardiovascular disease, in protective terms, of dental health and/or fish consumption. The results also suggested that effects related to fish consumption and mercury exposure may differ between stroke and acute myocardial infarction, as well as between fatal and non-fatal acute myocardial infarction.

A new follow up (20 years) of the Finnish cohort (described by Salonen et al., 1995 and Virtanen et al., 2005) found 91 new cases of sudden cardiac death (Virtanen et al., 2012). An association with hair mercury was found when treating mercury in hair as a continuous variable, with a 7 % (95 % CI: 3 - 11) increased risk of sudden cardiac death per 0.5 mg/kg increase in mercury. An interaction with n-3 LCPUFA was observed: Among those with hair mercury below the median (1.28 mg/kg), each 0.5 percentage unit increase in the serum n-3 LCPUFA was associated with a hazard ratio of 0.77 (95 % CI: 0.64 - 0.93), whereas no association with n-3 LCPUFA was seen among those with higher hair mercury (p for interaction: 0.01). The authors suggested that an effect of mercury on HRV or oxidative stress may play a role.

Recent literature has suggested an association between persistent organic pollutants present in fish and cardiovascular risks (Goncharov et al., 2011; Lee et al., 2012), none of the studies above control for that.

To summarise the main new results on stroke and cardiac disease, neither the study by Wennberg et al. (2007), at low exposures, nor the one by Mozaffarian et al. (2011), at somewhat higher exposures, indicate any association between stroke and mercury exposure. For acute myocardial infarction, two Swedish studies at low mercury levels (Wennberg et al., 2011 and Bergdahl et al., 2012) showed associations between mercury and decreased risk, suggested by the authors to be caused by beneficial effects of fish consumption. One study (Mozaffarian et al., 2011) showed no association between mercury and the risk of cardiac disease. A study of sudden cardiac disease showed an association with hair mercury (Virtanen et al., 2012). The latter also showed an interaction effect between mercury and n-3 LCPUFA. All these studies are, wholly or in part, based on longer follow-ups of previously

studied cohorts. A model for the acute myocardial infarction risk related to mercury and benefit related to n-3 LCPUFA was described, combining data from Finland and Sweden (Wennberg et al., 2012).

Blood pressure and heart rate variability/cardiac autonomy in adolescents and adults

As mentioned above in this section, results have suggested that fetal exposure to methylmercury is associated with impaired cardiac autonomy. Recently, studies have also been made on adults with relatively high methylmercury exposure in order to find out if there is an effect of current mercury exposure on cardiac autonomy. These studies are summarised below and in Table 25.

A well-functioning cardiac system maintains homeostasis by continuously adjusting heart rate, blood pressure, etc. While doing that, small variations in heart rate can be observed. If the variation in heart rate is too small, this is a sign of poor regulation of the heart. HRV can be used to describe autonomic balance (Akselrod, 1988) and can reflect adaptive mechanisms of the autonomic nervous system (Aubert and Ramaekers, 1999). Activity of the nerves of the autonomic nervous system influence heart rate by means of two pathways: the sympathetic pathway, which causes cardio-acceleration, and the vagal pathway, causing a deceleration in heart rate. Feedback is provided from baroreceptors located in the most important arteries. A shift in the sympatho-vagal balance may become a major risk for cardiac events (Malliani, 2000).

The cardiovascular rhythmicity is usually studied within different frequency domains. Three major spectral components are usually detected, in humans centered at ca 0.00 Hz (very low frequency, VLF), at 0.11 Hz (low frequency, LF), and 0.25 Hz (high frequency, HF), respectively. LF and HF components are evaluated in terms of frequency and amplitude, the latter commonly assessed by the area (i.e. power) of each component. In addition, normalised units are often used, obtained by dividing the power of a given component by the total power (from which VLF has been subtracted) and multiplying by 100, thus giving a percentage. Different frequency bands correspond to modulation of the different branches of the autonomic nervous system. LF oscillations (LF: 0.04 - 0.15 Hz) correspond predominantly to sympathetic modulation, but also vagal influences and the baroreflex, while HF fluctuations (0.16 - 0.4 Hz) are related to vagal or parasympathetic modulation of heart rate.

Valera et al. (2008, 2011a) studied adults with high (total blood mercury up to more than 100 µg/L) and moderate methylmercury exposure. The results showed associations between mercury and decreased HRV, though not completely consistent through crude and adjusted regression models and between the two studies. Another study, comparing an urban and a rural area, the latter with high fish consumption, indicated mercury-related differences in some HRV parameters in teenagers but not in adults (Valera et al., 2011b). However, these results are to a large degree reflecting differences between individuals of two different populations, making conclusions difficult to draw. Choi et al. (2009) studied a group of 41 whaling men and found associations with increased HRV for both high and LF components. However, decreased variability was the hypothesised negative effect of mercury exposure. In a Korean population with moderate exposure levels (mean mercury concentration in hair: 1.02 mg/kg), a large cross-sectional study showed a mercury-associated decrease of the variability in the HF parameter (Lim et al., 2010).

An intervention study in which 27 subjects consumed fish containing 1.08 mg THg/kg (corresponding to 1.0 mg methylmercury/kg) for 14 weeks, showed an increased variability of the LF component, as compared to both baseline observations and a control group (Yaginuma-Sakurai et al., 2010). The individuals in the experimental group were supplied with around 200 g per week bigeye tuna and swordfish meat. The amount of fish supplied to each person was depending on b.w., so that all the 27 exposed individuals would receive a weekly dose of 3.4 µg methylmercury/kg b.w. This consumption resulted after 14 weeks in a mean hair mercury concentration of 8.76 mg/kg. Consumption of fish containing high levels of methylmercury, other than the supplied tuna and swordfish, was restricted. The 27 individuals of the control group were instructed to continue their usual diet. HRV, along with DHA and EPA in plasma, was examined at baseline, week 15, and week 29. The HRV for the LF component for the experimental group was increased at week 15 but had in

week 29, i.e. after a washout time, returned to the baseline level. No such change appeared in the control group. The increase in the LF component was not accompanied by a change in the HF component, thus resulting in an alteration in the ratio between the two components. The plasma concentrations of DHA + EPA showed a small variation between the three observation times, but did not show the same changes in pattern as the HRV. Instead the concentrations in the experimental group were slightly lower in week 29, as compared to baseline, and were at week 15 in-between those. The result for HRV, with an increased variability in the LF component, is in part similar to the results of Choi et al. (2009). However in the intervention study, the LF component increased without a change of the HF component, suggesting a shift in the sympatho-vagal balance towards sympathetic activity. Therefore, this alteration in HRV cannot be considered beneficial, but it is difficult to conclude about its degree of adversity.

Taken together, the studies of cardiac autonomy suggest an influence of mercury on HRV, but the results are not consistent between studies and the implications for health are currently unclear. The well-designed intervention study showed a change in HRV after 14 weeks of a weekly intake of 3.4 µg methylmercury/kg b.w. The variability returned to baseline values after a 15 weeks washout period.

In a study of men and women originating from Greenland (n = 145) and Denmark (n = 41), representing largely varying food consumption patterns, mercury was not associated with systolic blood pressure, but diastolic blood pressure decreased with increased blood mercury. In accord with this, pulse pressure was associated with blood mercury (Pedersen et al., 2005). The mean blood mercury concentration in the Greenlanders was 16.2 µg/L and in the Danes 2.2 µg/L. A study of 545 Amazon Indians with mean hair mercury 4.2 mg/kg (ranging up to ca 40 mg/kg) did not show any consistent association between hair mercury and blood pressure. The statistical analyses did not include adjustments for age, gender, etc (Dórea et al., 2005).

In a study of a non-indigenous fish-eating population in the Brazilian Amazon, Fillion et al. (2006) found an OR of 2.91 (1.26 - 7.28, supposedly denoting 95 % CI) for elevated systolic blood pressure for individuals with hair mercury above 10 mg/kg. In addition, the risk for elevated diastolic blood pressure was increased. A study of Inuit adults showed an association between systolic blood pressure and mercury (ranging up to very high blood concentrations, over 100 µg/L; Valera et al., 2008). A later report on a larger study (Valera et al., 2009), incorporating the individuals from the previous one in addition to others, also showed an association with systolic blood pressure, but with smaller slope (adjusted regression coefficient 2.14, 95 % CI 0.94 - 3.33, $p < 0.001$), suggesting the possibility that the association in the latter study may to some extent be driven by the individuals from the first study. Studies in Canada (Valera et al., 2011a, 2012) and French Polynesia (Valera et al., 2011b) did not show any association between blood pressure and mercury levels after adjustments for potential confounders. A small study (n = 101) of members of a US cohort established to study sleep related factors, found a 4.19 (95 % CI: 1.28 - 13.76) times higher risk for hypertension for individuals with hair mercury exceeding 0.496 mg/kg vs. the other cohort members (Bautista et al., 2009).

A study of 495 older US men did not find any association between systolic or diastolic blood pressure, or pulse pressure, and toenail mercury (Mordukhovich et al., 2012). The point estimates were slightly negative (higher mercury levels related to lower blood pressure), but they were far from statistical significance. The median toenail mercury concentration was 0.22 mg/kg.

A cross-sectional study among adult Inuit in Greenland with high mercury exposure from consumption of marine food showed a relation between lower diastolic blood pressure and higher mercury concentration in blood, but only for men, not for women (Nielsen et al., 2012). The study comprised 1 861 individuals, of which 615 men and 787 women without anti-hypertensive drug therapy were included in linear and logistic regressions of blood pressure and blood mercury. Systolic blood pressure in men gave results in the same direction as for diastolic blood pressure, but not statistically significant. In addition, the risk of hypertension (defined as blood pressure $\geq$ 140/90 mmHg or usage of anti-hypertensive drugs according to guidelines) was decreased in men with high blood mercury, but not in women, and not with consistency throughout the different

statistical models used. Pulse pressure did not show any associations with mercury. The median blood mercury concentration was 18 µg/L, with an inter-quartile range of 8.8 - 34.1 µg/L.

A study of 507 men and 509 women in Sweden with low blood mercury concentrations (median for men: 1.9 µg/L with an IQR of 1.6 µg/L; for women: 1.7 and 1.5 µg/L, respectively) showed no association to systolic blood pressure (Olsén et al., 2012), but increased LDL-cholesterol and decreased high-density lipoprotein (HDL)-cholesterol. Smoking was however associated with blood mercury but was not adjusted for. It is unknown to what extent the mercury stemmed from methylmercury contaminated food or inorganic mercury from dental amalgams. The study of 41 whaling men from the Faroe Islands (Choi et al., 2009) also found statistically significant associations between blood pressure and biomarkers of mercury exposure. The latter study also found an association with carotid intima-media thickness, in line with previous findings by Salonen et al. (2000).

Blood pressure in relation to mercury was studied in US women (Vupputuri et al., 2005), showing no associations among fish consumers, but non-fish consumers of the highest mercury quintile (blood mercury from 2.1 µg/L) had ca 5 mmHg higher systolic blood pressure, as compared to the lower quintiles. As this occurred in non-fish consumers it must be assumed that the major source of mercury was not the diet but rather dental amalgam.

In addition, blood pressure in adolescents was studied in relation to prenatal exposure in the Seychelles cohort (Thurston et al., 2007). An association was found for diastolic blood pressure in boys at 15 years of age (slope: 0.36; SE 0.12 mmHg) but no associations were found at the age of 12 years or in girls.

Some studies report on resting heart rate in relation to mercury. This outcome has not been considered in this review. An increase was reported in a recent study (Valera et al., 2012), but is not in accordance with previous studies in adults with environmental mercury exposure.

In all, the observations on blood pressure give a somewhat inconsistent picture, e.g. as regards whether diastolic or systolic blood pressure may be affected. There is no firm basis for assessment of a dose-response relationship.

Concluding comments

At the time of the evaluation by the JECFA in 2006, there were only two major epidemiological studies that indicate an association between methylmercury and increased the risk of cardiovascular disease (Guallar et al., 2002; Virtanen et al., 2005). Both these concern acute coronary events or myocardial infarction. Reported mercury levels ranged from 0.14 to 0.57 mg/kg in toenails (Guallar et al., 2002) and from 0 to 15.7 mg/kg in hair (mean: 1.9 mg/kg) (Virtanen et al., 2005). Results in the same direction were found in a recent study on sudden cardiac death (Virtanen et al., 2012) from a longer follow up of the cohort previously studied by Virtanen et al. (2005). The negative results of Yoshizawa et al. (2002) have been further strengthened by the recent study by Mozaffarian et al. (2011), in which no increased cardiovascular risk was observed even in the group with hair mercury > 2.7 mg/kg. Some other studies have dealt with lower exposure levels and provided negative findings.

The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. The studies by Yoshizawa et al. (2002) and Mozaffarian et al. (2011) have based the correction for n-3 LCPUFA confounding on dietary questionnaires, while the studies by Guallar et al. (2002) and Virtanen et al. (2005) have used biochemical measurements, and this may explain part of the discrepancy.

Thus, the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, but still not conclusive.

Table 25: Overview of epidemiological data on cardiovascular effects.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
CVD considered by JECFA (adapted from FAO/WHO, 2007)						
Guallar et al. (2002) Eight European countries and Israel	Case-control	Cases: 684 men Controls: 724 men	THg in toenail: range 0.14-0.57 mg/kg (authors presented averages in control patients across study centers) (toenails collected after occurrence of MI, analysed in 1991-1992)	First acute MI	Adjusted OR for MI: highest quintile of Hg compared with lowest quintile: 2.16 (95 % CI 1.09-4.29)	
Yoshizawa et al. (2002) USA	Case-control within prospective cohort study	Cases: 470 men Controls: 464 men matched on age and smoking status	THg in toenail : controls: range: 0.03-14.6 mg/kg dentists: μ±SD: 0.91±1.47 mg/kg others: μ±SD: 0.45±0.40 mg/kg (toenails collected before the onset of CHD, analysed in 1987)	CHD	Adjusted OR for CHD: Highest quintile of Hg compared with lowest quintile in dentists: 0.97 (95 % CI, 0.63-1.50) Adjusted OR for CHD: Highest quintile of Hg compared with lowest quintile, excluding dentists: 1.27 (95 % CI, 0.62 to 2.59)	
Hallgren et al. (2001) Sweden	Case-control within a prospective cohort study	Cases: 78 men and women	THg in erythrocytes: range: 0.6-67 ng/g (blood samples stored in 1985 for future research purposes, analysed 1998) N.B. Slightly incorrect: stored after 1984 would be correct.	First MI	Adjusted OR for MI: Intermediate Hg (3-6 ng/g) compared with lowest Hg (< 3 ng/g): 0.9. Highest Hg (< 6 ng/g) compared with lowest Hg (< 3 ng/g): 0.4 (95 % CI, 0.19-0.95)	
Ahlqwist et al. (1999) Sweden	Prospective cohort study of women	1462 women, enrolled in 1968-1969	Serum THg (blood samples collected in 1968-69, then 1980-81 for future research; mostly used earlier samples)	MI (n = 87, 39 died); all-cause death (n = 253)	An inverse, but not statistically significant correlation between serum Hg and MI was found. A statistically significant negative correlation between serum Hg and death from all causes was found after adjusting for age and education.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
CVD considered by JECFA (adapted from FAO/WHO, 2007) (continued)						
Virtanen et al. (2005) Eastern Finland	Prospective cohort study of men, 14 year follow-up	1871 men who were free of CVD at baseline (1984-1989)	THg in hair: μ: 1.9 (range: 0-15.7) mg/kg (hair collected before onset of disease or death, analysed in 1992-1993)	Acute CE (n = 282); Death from CVD (n = 132), Death from CHD (n = 91), All-cause death (n = 525)	Adjusted RR for acute CE: Middle third of Hg compared with lowest third: 1.1. Highest third of Hg compared with lowest third: 1.7*. Adjusted RR for CVD death: Middle third of Hg compared with lowest third: 0.7. Highest third of Hg compared with lowest third: 1.3. Adjusted RR for CHD death: Middle third of Hg compared with lowest third: 0.6. Highest third of Hg compared with lowest third: 1.2. Adjusted RR for any death: Middle third of Hg compared with lowest third: 0.9. Highest third of Hg compared with lowest third: 1.3* *range of 95 % CI above 1.0.	
Recent CVD studies, not considered by JECFA						
Wennberg et al. (2007) Sweden	Case-control within prospective cohort study	Cases: 369 men and women. Controls: 738 men and women	THg in erythrocyte: P50: 3.63 (range up to 24) ng/g. Hg in erythrocytes sampled after 1984 and before any diagnosed stroke	First stroke	No association to Hg or EPA+DHA.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Recent CVD studies, not considered by JECFA (continued)						
Mozaffarian et al. (2011) USA	Case-control within two prospective cohort studies (nurses and male health professionals)	Cases: 1211 men, 2216 women. Controls 1211+2216	THg in toenail: IDR: 0.06-0.94 mg/kg in cases and 0.07-0.97 mg/kg in controls. Prospectively collected	CHD, stroke	RRs for fifth quintile of Hg vs. the first: CHD: 0.85 (95 % CI 0.69-1.06); stroke: 0.83 (95 % CI 0.30-1.15)	Matched for age, sex, race, smoking, time of toenail sampling. Adjusted for BMI, physical activity, alcohol, diabetes, hypertension, cholesterol, estimated intake of EPA and DHA.
Wennberg et al. (2011) Sweden	Case-control within prospective cohort study	Cases: 150 women and 350 men. Controls: 275 women and 350 men.	THg in erythrocyte: P50: 3.54 (range 0.01-87) µg/L. (sampled after 1984 and before any diagnosed MI)	First MI	OR for > 4.98 µg/L (adjusted model): 0.55, after adjustment for EPA+DHA: 0.61 (the latter not statistically significant).	
Bergdahl et al. (2012) Sweden (Gothenburg)	Prospective cohort study of women. New follow up of Ahlqwist et al. (1999)	1397 adult women with serum Hg, total 1462 in cohort	THg in serum: P50: 1.4 (range: 0.1-13) µg/L. Serum Hg	Mortality, AMI, stroke	HR for highest quartile (from 1.8 µg/L) adjusted only for age: Total mortality: 0.76; 95 % CI: 0.59–0.97; incident AMI: 0.56; 95 % CI: 0.34–0.93, fatal AMI: 0.31; 95 % CI: 0.15–0.66; stroke: 1.26; 95 % CI: 0.81–1.97. After adjustments only fatal AMI 0.43 (0.19–0.98) and stroke (1.80; 1.11–2.92) was statistically significant. Confirms indications from Ahlqwist et al. (1999). Lower risk of AMI associated with S-Hg.	Age, number of teeth, social class, education, serum triglycerides, wine consumption. (Considered but not related to exposure and therefore not potential confounders: smoking, waist/hip ratio, serum cholesterol, hypertension, and diabetes.)

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Recent CVD studies, not considered by JECFA (continued)						
Virtanen et al., (2012) Finland	Prospective cohort study of men, 20 year follow-up	1857 men who were free of CVD at baseline (1984-1989)	THg in hair: μ: 1.91 (range: 0-15.67) mg/kg. (hair collected before onset of disease or death, analysed in 1992-1993)	Sudden cardiac death (n = 91)	HR in highest tertile (2-15.67 mg/kg) vs. the lowest: 1.48 (95 % CI: 0.87-2.54). In continuous model: HR changed 1.07 (95 % CI: 1.03-1.11) for each 0.5 μg/g. Both results come from adjusted models. EPA+DPA+DHA was associated with decreased risk in individuals below the median hair Hg concentration (1.28 μg/g): HR: 0.77 (95 % CI: 0.64-0.93) for each 0.5 percentage unit increase in n-3 LCPUFA, while not so in individuals with hair Hg concentration at or above the median: HR: 1.02 (95 % CI: 0.95-1.09).	Association between sudden cardiac death and Hg was adjusted for age, examination year, body mass index, pack-years of smoking, alcohol intake, EPA+DPA+DHA content in serum.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness						
Dórea et al. (2005), Brazil	Cross-sectional	621 (545 with Hg data) Amazon Indians, men, women and children, age ca 14-80 years	THg in hair: μ: 4.2 (range ca 0-40) mg/kg. Hair Hg	BP	Hair Hg was not associated with BP, except when the village with highest exposure was excluded.	None

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Pedersen et al. (2005) Greenland and Denmark	Cross-sectional	Men and women originating from Greenland (n = 145) and Denmark (n = 41)	THg in blood: Greenlanders: μ: 16.2 μg/l Danes: μ: 2.2 μg/L, Range up to ca 150 μg/L.	BP, Pulse pressure	Diastolic, but not SBP, was decreased with increasing log blood Hg (p = 0.014). Pulse pressure increased with increasing log blood Hg (p = 0.001).	Age, BMI, gender, residence.
Vupputuri et al. (2005) US (NHANES)	Cross-sectional	1240 women, 16-49 years	THg in blood: μ: 1.8μg/L; P50: 0.9 (range: 0.1-21.4) μg/L.	BP	No association among fish consumers, but in non-fish consumers, the highest Hg quintile (from 2.1 μg/L) had ca 5 mmHg higher SBP vs. other groups (95 % CI available only for model estimates).	Age, race, income, BMI, pregnancy status, and dietary sodium, potassium, and total calories.
Fillion et al. (2006) Brazilian Amazon	Cross-sectional	118 women, 133 men, adults >=15 years	THg in hair: μ: 17.8 (range 0.21-77.2) mg/kg	Blood pressure	OR 2.91 [1.26-7.28, supposedly 95 % CI] for elevated SBP (>=130 mmHg) with hair Hg >=10 mg/kg. OR 2.29 [0.95-6.06] for DBP (>=90 mmHg)	Age, sex, BMI, smoking, community
Thurston et al. (2007) Seychelles	Prospective	343 girls 336 boys BP at age 12 and 15. Hg exposure *in utero*.	THg in maternal hair: μ: 7.0 (girls), 6.5-6.6 (boys); range 0.5-26.7 mg/kg.	BP	DBP at 15 years increased in boys only (slope: 0.36 mmHg; SE: 0.12). No associations at 12 years or in girls.	Birth weight, BMI, height, maternal hypertension
Valera et al. (2008) Canada, Nunavik	Cross-sectional	120 women 85 men Inuit adults > 40 years	Range of blood Hg: 0.5-152 μg/L.	BP, HRV	BP: SBP (also pulse pressure) positively associated with Hg. DBP close to statistical significance. SDANN negatively associated with Hg. Both after adjustments. Other HRV variables negatively associated with Hg in crude model.	Potential confounders considered: gender, age, waist circumference, insulin sensitivity, LDL- and HDL-cholesterol, triglycerides, smoking, alcohol, physical leisure-time activity, income, n-3 LCPUFA in erythrocyte membranes. For BP also blood Se.

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Bautista et al. (2009) US (sleep cohort study)	Cross-sectional	48 women 53 men adults	THg in hair: GM: 270 mg/kg; P75: 496 mg/kg THg in blood: GM: 1.16 µg/L, P75: 2.01 µg/L.	Hypertension, vasodilating function	4.19 (95 % CI: 1.28-13.76) higher risk for hypertension for those in the highest hair Hg quartile vs. others. Corresponding for blood Hg: 1.93 (0.66-5.65).	Sex, age, BMI, fish intake.
Choi et al. (2009) Faroe Islands	Cross-sectional	41 whaling men	THg in blood: GM: 29.5 (range: 5.19-128.4) µg/L THg in hair: GM: 7.31 (range: 4.52 -13.4) mg/kg; THg in toenail: GM: 2.04 (range: 1.35-3.29) mg/kg.	HRV, BP, carotid intima-media thickness, BAEP	Structural equation models showed statistically significant associations between some, but not all, Hg biomarkers and blood pressure and carotid intima-media thickness. An association with slight delays of BAEP latencies was also observed. Associations with measures of HRV were partly in the opposite direction vs. expected (i.e. increased variability).	Age, smoking, BMI, consumption of alcohol and fish, cholesterol, triglycerides and PCB were considered, though not all included in the model.
Valera et al. (2009) Canada, Nunavik	Cross-sectional	413 women 319 men > 18 years Includes the 205 of Valera et al. (2008)	THg in blood: range: 0-240 µg/L	BP	SBP associated with Hg, but with smaller regression and correlation coefficients, as compared to the 2008 article, suggesting that the association is mainly driven by the same individuals as in the previous article.	Potential confounders considered, as in Valera et al. (2008) with minor additions.
Lim et al. (2010)	Cross-sectional	Mainly adults, but 10-20 % children. 852 females 737 males	THg in hair: µ: 1.02 (range 0.01-13.36) mg/kg	HRV	The HF parameter decreased by 8.4 % (95 % CI: 2.2-15.1 %) with an 1 mg/kg increase in hair Hg.	Age, heart rate, history of diabetes, smoking. Other variables, e.g. cholesterol and triglycerides were considered.
Yaginuma-Sakuri et al. (2010)	Intervention	Adult volunteers 26 women 28 men	Controlled MeHg intake. THg in hair: µ at week 15: 8.76 mg/kg µ in control group: 2.14 mg/kg	HRV	14 weeks intake at Japan's PTWI 3.4 µg/kg b.w. LF component CV increased at 15 weeks, compared to both baseline and control group.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Valera et al. (2011a) Canada, James Bay	Cross-sectional	724 adults (663 with HRV data) (> 18 years) from Cree communities	THg in blood: IQR: 1-9 µg/L THg in hair: IQR: 0.2-1.6 mg/kg.	BP, HRV	BP associated with Hg only in crude data, not after adjustments. HRV: SDANN and other parameters negatively associated in unadjusted analysis, but not in adjusted models. In contrast, LF, HF and LF/HF associated with Hg in adjusted models.	Potential confounders considered: sex, age, waist circumference, fasting glucose, triglycerides, smoking, physical activity, PCB 153, lead, selenium, n-3 LCPUFAs.
Valera et al. (2011b) French Polynesia	Cross-sectional	157 adults 82 teenagers Recruited from an urban area and a rural area, representing different Hg exposure and different life-styles	THg in blood: IQR: 8.5-22 µg/L	BP, HRV	No effects observed in adults on BP or any HRV variable. In teenagers: Tertile 3 vs 2 showed lower square root of the mean squared differences of successive R-R intervals (rMSSD), lower HF, though not in normalised units, higher LF/HF ratio.	Age, gender, triglycerides, fasting glucose, obesity, selenium, n-3 LCPUFAs. Smoking and alcohol consumption was considered but not adjusted for, due to lack of statistically significant associations.
Mordukhovich et al., 2012 USA	Cross-sectional	495 older men with mean age 72 years	THg in toenail: P50: 0.22 (range: 2.40; IQR: 0.31) mg/kg	BP	The point estimates for Hg in relation to SBP and DBP, as well as pulse pressure, were all negative, but far from statistical significance.	Age, smoking, season and year of clinical visit, BMI, education, race/ethnicity, alcohol and fish intake.
Nielsen et al., 2012 Greenland	Cross-sectional	805 men and 1040 women with Hg data. All were Inuit aged 30-69.	THg in blood: P50: 18 (IQR: 8.8-34.1) µg/L.	BP	Lower DBP, was associated with higher Hg in men but not in women. Weaker and non-statistically significant results in the same direction was found for SBP, but no associations were shown for pulse pressure. The risk for hypertension decreased with blood Hg in men only, but not with statistical significance in all chosen models.	Age, smoking, selenium, ratio of n-3/n-6 LCPUFA, waist circumference.
Olsén et al., 2012 Sweden	Cross-sectional	507 men and 509 women at age 70.	THg in blood: P50 for men: 1.9 (IQR: 1.6) µg/L; for women 1.7 (1.5) µg/L.	BP	No association was found to SBP (but with increased LDL-cholesterol and decreased HDL-cholesterol.	Gender and kidney function (glomerular filtration rate)

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Valera et al. (2012) Canada, Nunavik	Cross-sectional	313 adults with complete data on potential confounders	THg in blood: P50: 17 (IQR: 9.0-28.4; range: 0.8-112.0) µg/L.	BP, resting heart rate	No statistically significant associations between Hg and SBP, DBP, or pulse pressure. Resting heart rate increased (p for trend: 0.02), with 6.9 beats per minute more in the fourth vs. the first quartile.	Age, sex, fasting glucose, LDL-cholesterol, HDL-cholesterol, triacylglycerol, alcohol, smoking, physical activity, anti-hypertensive treatment, lead, PCB, and n-3 LCPUFAs were all considered, but only those that changed the regression coefficient more than 10 % were retained in the model.

µ: mean; AMI: acute myocardial infarction; BAEP: Brainstem Auditory Evoked potentials; BMI: body mass index; BP: blood pressure; CE: coronary event; CHD: coronary heart disease; CI: confidence interval; CVD: cardiovascular disease; DBP: diastolic blood pressure; DHA: docosahexaenoic acid; DPA: docosapentaenoic acid; EPA: eicosapentaenoic acid; GM: geometric mean; HDL: high-density lipoprotein; HF: high frequency; Hg: mercury; HR: hazard ratio; HRV: heart-rate variability; IQR: interquartile range; LCPUFA: long-chain polyunsaturated fatty acids; LDL: low-density lipoprotein; LF: low frequency; MeHg: methylmercury; MI: myocardial infarction; n-3 LCPUFA: n-3 long-chain polyunsaturated fatty acids; n-6 LCPUFA: n-6 long-chain polyunsaturated fatty acids; NHANES: National Health and Nutrition Examinations Survey; OR: odds ratio; P50: 50th percentile; PCB: polychlorinated biphenyls; PTWI: provisional tolerable weekly intake; RR: relative risk; SBP: systolic blood pressure; SD: standard deviation; SDANN: standard deviation of the average R-R intervals calculated over 5-minute periods; SE: standard error; SES: socio-economic status; THg: total mercury.

7.4.2.3. Other endpoints

Immunotoxicity

A Canadian study compared immunological status between newborns in a maritime population (n = 48) with a reference group which comprised newborns from a coastal urban centre (n = 60) (Belles-Isles et al., 2002). The maritime population had three times higher levels of PCBs and two times higher levels of mercury in cord blood (mean levels of mercury were 1.8 µg/L and 0.9 µg/L, respectively). Compared to the reference group, in the maritime population the proportion of a subset of naive helper T-cells was negatively correlated to mercury and PCBs, T-cell proliferation following an *in vitro* mitogenic stimulation was negatively associated with PCBs, and plasma IgM levels were negatively correlated to mercury, while IgG levels showed a positive correlation with PCBs.

For evaluation of the hypothesised association between exposure to methylmercury and titers of total Igs and specific antibodies in mothers and fetuses, maternal as well as cord serum samples were analysed in a cross-sectional study including 61 mother-infant pairs from the Brazilian Amazon region (Nyland et al., 2011). The total mercury level was higher in the cord blood as compared to the maternal blood (geometric means 9.63 µg/L and 6.90 µg/L, respectively). Total IgG levels were statistically significantly correlated with both maternal (r = 0.60) and cord blood mercury levels (r = 0.61), but IgG isotypes were not.

Antinuclear antibodies (ANA) were compared between two Amazon populations; high fish eaters (n = 105) and an urban control group with a low intake of fish (n = 105) (Alves et al., 2006). The mean mercury levels in hair were significantly higher among the fish eaters (35.4 mg/kg) as compared to the control group (1.0 mg/kg). Although positive serum ANA was more frequently observed in fish eaters (12.4 %) than controls (2.9 %), there was no statistically significant association between hair mercury and ANA. The authors concluded that an autoimmune dysfunction is unlikely to occur as a result of mercury exposure due to fish consumption.

A population-based study in Korea investigated the hypothesised association between mercury exposure and prevalence of atopic dermatitis in an adult population (Park and Kim, 2011). The investigated population consisted of 1990 adults, of which 10.9 % had a history of atopic dermatitis. Blood mercury concentrations were positively associated with lifetime prevalence of atopic dermatitis (OR for highest [> 6.04 µg/L] vs lowest [3.56 µg/L] tertile was 1.50, 95 % CI 1.02 - 2.21; p for trend = 0.057). The association was stronger for one-year atopic dermatitis prevalence (OR 1.82, 95 % CI 1.17 - 2.83; p for trend = 0.026).

The association between mercury levels in maternal and children's hair and the risk of wheeze and eczema were investigated among 582 Japanese children at 29 - 39 months of age (Miyake et al., 2011). The range of mercury levels was 0.26 - 6.05 mg/kg in mothers and 0.13 - 9.51 mg/kg in children. The adjusted ORs of wheeze and eczema were not statistically significantly different between exposure groups whether maternal or children's hair mercury levels were used.

In a birth cohort from the Faroe Islands that was recruited in 1999 - 2001 (the Faroese Cohort 3) sensitization and development of allergic disease was studied in relation to exposure to PCBs and methylmercury, and duration of breast feeding (Grandjean et al., 2010b). The study included 464 children who were clinical examined at five and seven years of age regarding asthma and atopic dermatitis. PCB and mercury concentrations were determined in blood samples obtained at parturition and at follow-up. The geometric mean mercury concentrations were: maternal hair 2.21 mg/kg; cord blood 11.3 µg/L; child's blood at five years of age 2.65 µg/L; child's blood at seven years of age 2.01 µg/L. Whereas positive associations were observed between duration of breast feeding and PCB concentrations on the one hand and some of the outcomes on the other hand, there was a positive association (protective) between prenatal methylmercury concentrations and grass-specific serum IgE concentrations.

Heilmann et al. (2010) studied serum concentrations of antibodies against vaccine toxoids at age five and seven years in the same cohort (the Faroese Cohort 3) as Grandjean et al. (2010b). Associations were seen between increased PCB exposure and reduction in antibody titres after diphtheria and to a less extent tetanus vaccination, but prenatal or recent postnatal mercury exposure did not seem to affect the outcomes.

Reproductive toxicity

A study from the Michigan communities, US, found an association between mercury levels and the prevalence of preterm births (Xue et al., 2007). The study comprised 1 024 women from the Pregnancy Outcomes and Community Health study and the mean level of total mercury in hair was 0.29 mg/kg (range 0.01 to 2.50). Women who delivered before 35 weeks´ gestation were more likely to have hair mercury levels at or above the 90th percentile (≥ 0.55 mg/kg) compared with women delivering at 37 weeks or later (OR 3.0, 95 % CI 1.3 - 6.7).

A study among 1 425 women from the National Health and Nutrition Examinations Survey (NHANES), 1999 - 2002, investigated the hypothesised associations between metals and endometriosis and uterine myomas (Jackson et al., 2008). The women included in the study were between 20 and 49 years of age, premenopausal and neither pregnant nor breastfeeding. Regarding blood mercury after taking potential confounders into account, there were no statistically significant associations with the outcomes. The mean blood level of mercury was 1.00 µg/L (95 % CI 0.94 - 1.05).

Within the BioCycle Study in Buffalo, New York, US, the associations between metals and reproductive hormones and anovulation in 252 premenopausal women were investigated (Pollack et al., 2011). The geometric mean for mercury in blood was 1.03 µg/L (IQR 0.58 - 2.10). There were no statistically significant associations between mercury and the outcomes investigated.

The association between methylmercury and semen parameters was investigated among 195 fishermen from Sweden (Rignell-Hydbom et al., 2007). The group of men was selected according to relatively high intake of locally caught fish. Blood levels of methylmercury were calculated as the difference between the concentrations of total mercury and inorganic mercury in blood and ranged from 0.11 to 16.59 µg/L (median 2.25 µg/L). Methylmercury in blood was not associated with the outcomes investigated (sperm motility, total sperm count, sperm chromatin integrity, and the proportion of Y-chromosome bearing sperms). Within the project it was also investigated whether an interaction between methylmercury exposure and PCB-153 (2,2',4,4',5,5'-hexachlorobiphenyl) was present, but no interaction was observed.

A study in Hong Kong included 111 males of infertile couples undergoing *in vitro* fertilization treatment (Choy et al., 2002). The mean blood mercury concentration was 8.3 µg/L and the mean seminal fluid mercury concentration was 4.4 µg/L. Neither the overall percentage of motile sperm nor sperm concentrations were correlated with mercury concentrations. On the other hand, seminal fluid mercury concentrations were statistically significantly ($p < 0.05$) correlated with abnormal sperm morphology ($r_s = 0.26$), particularly head ($r_s = 0.49$) and midpiece defects ($r_s = 0.30$). Also some sperm motion characteristics were statistically significantly correlated with seminal fluid mercury concentrations.

Developmental toxicity other than neurotoxicity and immunotoxicity

In the EDEN mother-child-cohort, fish intake was estimated through a questionnaire and hair mercury levels were analysed among 691 French women (Drouillet-Pinard et al., 2010). The relation between these two parameters and fetal growth was estimated. The median mercury level for the mothers was 0.52 mg/kg and no association was found between mercury and fetal growth in the whole sample of women.

In a Canadian study, the associations between n-3 LCPUFA and environmental contaminants (such as mercury, lead and PCBs) and gestational age and birth weight were investigated (Lucas et al., 2004). n-3 LCPUFA and contaminant concentrations were measured in cord plasma in a seafood eating population (Nunavik, n = 454) and in a comparison group from southern Québec (n = 29). There were positive associations between n-3 LCPUFA and the birth outcomes (statistically significant for gestational age but not for birth weight), whereas there was no evidence that contaminants had negative effects on the birth outcomes. The geometric mean of cord blood mercury concentrations was about 18 times higher in the Nunavik population as compared to the population from the Southern Québec (14.1 vs 0.8 µg/L).

A study among women from Korea suggested that the interactions of mercury with GSTM1 and GSTT1 play a role in reducing birth weight (Lee et al., 2010). The study included 417 Korean women and newborns in the Mothers and Children´s Environmental Health study and the geometric means of total mercury concentrations (µg/L) were 3.67 in early pregnancy maternal blood, 3.30 in late pregnancy maternal blood, and 5.53 in cord blood, respectively. For mothers with the GSTT1 null genotype, elevated mercury levels in maternal blood during late pregnancy were associated with an increased risk of lower birth weight. For mothers with both GSTM1 and GSTT1 null genotype, both maternal and cord blood mercury levels were associated with lower birth weight.

A study which investigated the relation between cord mercury levels and early child development in a World Trade Centre Cohort (New York), found no significant associations between exposure and birth outcomes (birth weight, length, head circumference, and gestational duration) (Lederman et al., 2008).

Cace et al. (2011) measured cerebellum length and width in 30 newborn babies of mothers with hair mercury levels above 1 mg/kg (mean: 2.37 mg/kg) and compared to 107 controls (mean: 0.46 mg/kg). The children of mothers with high mercury levels had shorter cerebellum, compared to the controls (18.4 vs. 20 mm, $p = 0.019$). No difference was observed for cerebellum width.

A study within the INMA Valencia cohort, Spain, investigated the association between total cord blood mercury concentrations and birth outcomes among 554 infants born 2004 to 2006 (Ramón et al., 2009). The geometric mean concentration of total mercury was 9.4 µg/L. Newborns in the highest quartile of total mercury weighed statistically significantly less (143.7 g) and had higher odds of being small for gestational age (OR 5.3, 95 % CI 1.2 - 23.9, $p = 0.03$) compared to those in the lowest quartile. In the statistical analyses consumption of fish was included as covariate together with others.

Miscellaneous

A cross-sectional study included 135 adult volunteers recruited from 12 fish-eating communities in the Brazilian Amazon had the objective to examine possible relations between different biomarkers of mercury exposure and oxidative stress using linear regression (Grotto et al., 2010). Medians of mercury were in blood 40.5 µg/L (range 1.70 to 179.3), in plasma 4.7 µg/L (0.2 to 30.9), and in hair 10.1 mg/kg (1.0 to 57.8). The study showed statistically significant inverse relations between glutathione peroxidase, glutathione, catalase, δ-aminolevulinate dehydratase (ALA-D) activity and blood mercury or hair mercury ($p < 0.05$), ALA-D reactivation index was significantly positively related to blood mercury ($p < 0.0001$). Plasma mercury was directly related to ALA-D reactivation index and inversely associated with glutathione peroxidase, glutathione, and ALA-D activity ($p < 0.05$). There were, however, some gender differences.

An earlier study in the Amazonas region in Brazil evaluated the association between hair mercury levels and the strengths of antioxidant defences (evaluated by glutathione levels and catalase activity) (Pinheiro et al., 2008). The study comprised women from three populations, two 'exposed' and one 'non-exposed'. In total, 87 women participated and the levels in the exposed populations were much higher. The geometric means for hair mercury varied between 9.81 mg/kg and 17.32 mg/kg for different age groups in the 'exposed' populations and between 2.72 mg/kg and 3.89 mg/kg for the

different age groups among the 'non-exposed' populations. A statistically significant correlation was found between higher mercury content, higher glutathione level, and lower catalase activity.

Age-related cataract is a cause of impaired vision among elderly populations. Within the Amazonas region in Brazil, 211 participants from 12 regions were investigated in a cross-sectional study regarding the hypothesised association between exposure to mercury and selenium (Se) on the one hand and the prevalence of age-related cataract on the other hand (Lemire et al., 2010). For the individuals with plasma Se below the 25th percentile (110 µg/L) and blood mercury above the 25th percentile (25 µg/L), the prevalence of age-related cataract was statistically significantly increased for individuals younger than 65 years compared to individuals with plasma Se above 110 µg/L and blood mercury below 25 µg/L. However, the increase was not statistically significant for individuals of 65 years or older. Due to the limited number of participants and the relative low number of cases (n = 69), the results must be interpreted with caution.

One study which included 81 mother-newborn pairs from Paris, France, reported a relationship between calcium pump activity in pregnant women and their newborns on the one hand and mercury exposure on the other hand (Huel et al., 2008). Mercury explained about 7 % of total variance of calcium pump activity in mothers and newborns using stepwise linear regression. The median mother hair mercury level was 1.20 mg/kg.

The relationship between minerals and metabolic syndrome by analysis of hair tissue minerals was investigated among 343 subjects from Korea (Park et al., 2009). The mean concentration of hair mercury was 1.7 mg/kg in the normal group (n = 270) and 2.9 mg/kg in the metabolic syndrome group (n = 73). When subjects in the highest mercury quartile were compared with the subjects in the lowest mercury quartile group an OR of 7.35 (95 % CI 1.73 - 31.1) was obtained.

Cho and colleagues (2012) investigated the association between heavy metals and bone mineral density and osteoporosis in 481 postmenopausal Korean women. The women with highest blood mercury concentrations (upper quartile ≥ 5.23 µg/L) had a decreased prevalence of osteoporosis as compared to the women in the lowest concentrations (lowest quartile < 2.67 µg/L). An OR of 0.36 (95 % CI 0.19 - 0.68) was obtained.

Among 59 non-occupationally exposed women from northern Japan (mean age 20 years), total mercury levels in hair, toenail, and urine were investigated in relation to renal tubular function (Ohno et al., 2007). Mean mercury levels in the women were 1.51 mg/kg in hair, 0.59 mg/kg in toenail, and 0.86 mg/kg creatinine in urine. Among the women, the N-acetyl-β-D-glucosaminidase activity and the α1-microglobulin were positively correlated (although weakly) with both the daily mercury intake (estimated using a food frequency questionnaire) and mercury levels in hair, toenail, and urine ($p < 0.001$).

Within the NHANES in the US the hypothesised association between mercury and homocysteine in 1 005 children aged three to five years was examined, differentiated by higher and lower methylmalonic acid (an indicator of vitamin B-12 deficiency) and folate status (Gallagher and Meliker, 2011). An inverse association was observed in the subgroup of boys with higher methylmalonic acid and lower folate (n = 135), but not in other children. Children with mercury > 700 µg/L showed 189 µg/L lower homocysteine ($p < 0.001$) relative to the lowest quartile (≤ 140 µg/L).

Summary

There are a number of outcomes that have been investigated in single or few studies and the importance of the findings from these studies is accordingly difficult to evaluate. In addition, some of the studies are relatively small and other studies have investigated a number of outcomes, which raise the question about chance findings.

7.4.2.4. Summary of new developments since the last EFSA opinion of 2004

The new epidemiological observations in relation to methylmercury are as follows:

- The results of the new nutrition cohort suggest an effect of methylmercury at age 9 and 30 months, but not at five years, after adjustment for the beneficial effects related to n-3 LCPUFA. The previous interpretation from the main Seychelles cohort that there were no effects on children's cognitive performance following prenatal methylmercury exposure needs to be reconsidered. The results from the main cohort were not adjusted for n-3 LCPUFA.

- New results from the Faroese Cohort 1 show that the association between prenatal methylmercury exposure and neurodevelopmental outcomes was still present, although weaker, at the age of 14 years. In addition, results from a smaller Cohort 2 have become available. Most of the associations between neurological outcomes and mercury in Cohort 1 at seven years of age could not be confirmed in Cohort 2.

- Adjustment for the beneficial effects related to maternal fish consumption in the statistical analyses of the Faroese Cohort 1 indicated that the effects of prenatal methylmercury exposure may have previously been underestimated. Assessment of the Faroese Cohorts 1 and 2 together and further analyses in the Faroese Cohort 1 did not identify major confounding from PCB exposure.

- New studies of cardiac autonomy suggest an influence of mercury on HRV. In addition to a number of epidemiological studies, a well-designed intervention study found a change in HRV after a weekly intake of 3.4 µg methylmercury/kg b.w. However, the results are not consistent between studies and the implications for health are currently unclear.

- A recent study from Finland showed an association between mercury and sudden cardiac death. No other new epidemiological studies of cardiovascular disease have been identified that indicate an association between methylmercury and increased risk of cardiovascular disease.

- The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. The previous studies indicating an association between methylmercury and myocardial infarction risk, based the correction for n-3 LCPUFA confounding on biochemical measurements. One recent large study indicated no increased risk of cardiovascular disease associated with methylmercury, but adjustment for dietary n-3 LCPUFA was based on dietary questionnaires, and this may explain part of the discrepancy.

- Thus, the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, but still not conclusive.

7.4.3. Epidemiological data on inorganic mercury

Human data on the adverse health effects of oral exposure to inorganic mercury mainly consist of case reports that cannot be used to identify a dose-response relationship, as summarised in (FAO/WHO, 2011b). Case reports and epidemiological studies addressing the toxicity after oral exposure to inorganic mercury, and that were not included in (FAO/WHO, 2011b) were summarised in a report of an EFSA contractor and this was used as a starting point (Hassauer et al., 2012). The epidemiological studies report on effects on the immune system, liver, kidney, endocrine systems and cyto-genotoxicity. The CONTAM Panel finds that these epidemiological studies suffer from several limitations, such as small study group, insufficient control for confounders, inadequate exposure assessment and insufficient differentiation between mercury compounds and routes of exposure. Therefore, the existing human data could not form the basis for a risk assessment of inorganic mercury.

7.5. Derivation of Health-based Guidance Value

7.5.1. Methylmercury

In the present opinion the CONTAM Panel has evaluated new developments in methylmercury toxicity since the last EFSA opinion from 2004, which referred to the PTWI of 1.6 μg/kg b.w. set by JECFA (FAO/WHO, 2004). This PTWI was based on neurodevelopmental endpoints from epidemiological studies. The point of departure behind this PTWI was based on the mean of the highest NOEL for prenatal exposure in the Seychelles main cohort (15.3 mg/kg in maternal hair) and the $BMDL_{05}$ for neurodevelopmental effects at age seven years in the Faroese Cohort 1 (12 mg/kg in maternal hair), giving a point of departure of 14 mg/kg in maternal hair.

A recent study in rats on developmental immunotoxicity indicated effects at low doses and the $BMDL_{05}$ for reduction in antibody response was 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury) (Tonk et al., 2010). The Panel noted that the BMD is below the lowest dose tested. These data need to be confirmed, and the Panel has therefore not identified any new experimental animal studies that could provide a better primary basis than the human epidemiological data for a health-based guidance value. The reported associations between methylmercury exposure and cardiovascular disease were addressed by JECFA in their update in 2006 (FAO/WHO, 2007), and additional studies have become available. Although the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, they are still not conclusive. Consequently, after carefully considering endpoints other than neurodevelopmental outcomes, and in particular cardiovascular disease, the CONTAM Panel concludes that associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value for methylmercury.

A major development since the previous EFSA opinion from 2004 is the understanding of confounding by beneficial factors in fish on associations between prenatal methylmercury exposure and neurodevelopmental endpoints. In the results from a new cohort from the Seychelles and in re-analysis of previous results from the Faroe Islands, confounding from fish consumption has been investigated. The new information partly modifies the interpretation of the previous results.

The previously derived NOEL of 15.3 mg/kg in maternal hair from the Seychelles main cohort did not take the concomitant intake of n-3 LCPUFAs into consideration. Results from the newer nutrition cohort at 9 and 30 months examinations indicated that at a mercury concentration in maternal hair of above approximately 11 mg/kg, the positive effects from n-3 LCPUFA intake can no longer outweigh detrimental effects from methylmercury exposure. However, the number of observations above this exposure level was low, increasing the uncertainty. Of note, at the follow up examination when the children's age was five years, positive associations between prenatal n-3 LCPUFA exposure and improved neurodevelopmental scores were seen, and inclusion of mercury in the regression did not affect the results. Based on the observations in the Seychelles nutrition cohort at 9 and 30 months, the CONTAM Panel finds that a methylmercury concentration of 11 mg/kg hair is an apparent NOEL which has been adjusted for maternal blood concentration of n-3 LCPUFA, and therefore forms a better point of departure than the unadjusted NOEL (15.3 mg/kg) derived from the Seychelles main cohort.

The new results presented from the Faroese cohorts are limited, and of note, the results at seven years in the Faroese Cohort 2 did not confirm the results of the Faroese Cohort 1, and this can not be only explained by a lower statistical power in the smaller Cohort 2. The question concerning confounding by PCB exposure in the Faroese cohorts was addressed by analysing the Faroese Cohorts 1 and 2 together, and the evidence for confounding by PCB exposure is considered as weak. Although some evidence for confounding by the beneficial effects of maternal fish consumption has been presented from the Faroese Cohort 1, the evidence for confounding from maternal blood n-3 LCPUFA is stronger in the nutrition cohort from the Seychelles. Even though the CONTAM Panel noted these

additions to the previous results from the Faroese Cohorts, it could not identify a better point of departure from the Faroese studies than the $BMDL_{05}$ of 12 mg/kg in maternal hair that has been selected previously by JECFA.

Based on what is summarised above, the CONTAM Panel decided to use the mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese Cohort 1 at age seven years (12 mg/kg in maternal hair), giving 11.5 mg/kg maternal hair as the basis for derivation of a health-based guidance value.

By use of a one-compartment toxicokinetic model as described in formula (i) (WHO, 1990), the JECFA calculated the steady state concentration in blood related to an average daily intake of mercury (FAO/WHO, 2004).

$$\text{(i)} \qquad C = (d*A*f*b.w.)/(b*V)$$

JECFA incorporated some refinements in the parameters used by the WHO in order to better reflect the situation in pregnant women. The following parameters were used by the JECFA:

C = concentration of mercury in blood (µg/L)
d = daily dietary mercury intake (µg/kg b.w. per day)
A = absorption factor (0.95)
f = the absorbed fraction distributed to the blood (0.05)
b.w. = body weight (65 kg for a pregnant woman)
b = elimination rate constant (ln 2 / half-life in blood = 0.014 per day)
V = blood volume (9 % of the body weight in a pregnant female).

By application of a maternal hair to maternal blood ratio of 250, the maternal hair concentration associated with no appreciable adverse effect (11.5 mg/kg) was converted into a maternal blood concentration of 46 µg/L. Using a one-compartment toxicokinetic model the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w.

A data-derived factor of 2 for variation in hair to blood ratio was applied by JECFA (FAO/WHO, 2004). Interindividual variation in toxicokinetics when converting the steady state concentration of mercury in blood to an estimated daily intake was taken into account by a standard factor of 3.2 ($10^{0.5}$).

The CONTAM Panel did not identify studies providing a sufficient basis to change the parameters in the one-compartment model and the uncertainty factors used by JECFA (FAO/WHO, 2004).

Therefore, the CONTAM Panel established a tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w., expressed as mercury. The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response reported by Tonk et al. in rats (Tonk et al., 2010).

7.5.2. Inorganic mercury

As summarised in Section 7.4.3 and by FAO/WHO (2011b) the human data on toxicity after oral exposure to inorganic mercury were not suitable for dose-response assessment, but they clearly indicated that kidney effects observed in experimental animals are relevant for humans. The JECFA review (FAO/WHO, 2011b) noted that kidney effects are consistently observed in various experimental animal species (weight changes, proximal tubule damage and progressive nephropathy) and that relative kidney weight increases observed in rats following exposure to mercuric chloride are also associated with a dose-dependent increase in renal mercury accumulation and with significant changes in the renal cortex, including increases in both proximal tubule and glomerular volumes. The JECFA therefore considered it appropriate to model kidney weight changes, which generally occurred at doses similar to or lower than other renal effects. The 6-month exposure was deemed sufficient to establish a health-based guidance value because the half-life of mercuric chloride in rats is estimated

at less than 30 days, steady-state renal mercury concentrations were reached by 4 - 6 months, and exposures in the same dose range for longer durations produced early mortality (FAO/WHO, 2011b).

The JECFA calculated BMD and BMDL values for a BMR of a 10 % increase in relative kidney weight. The EFSA Scientific Committee has recommended that a default BMR value of 5 % should be used for continuous data from animal studies, and that this could be modified based on statistical or toxicological considerations (EFSA, 2009). The CONTAM Panel noted that in the NTP study, statistically significant increases in relative kidney weight, all of approximately 120 % of control, were reported in male rats at 0.625, 1.25. 2.5 and 5.0 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.46, 0.92, 1.9 and 3.7 mg/kg b.w. per day, expressed as mercury) (Table 26). At 0.312 mg/kg b.w. per day, expressed as mercuric chloride (equivalent to 0.23 mg/kg b.w. per day, expressed as mercury) the relative kidney weight was 110 % of control, which was not statistically significantly different. The lowest dose at which there was an increase in nephropathy was 0.625 mg mercuric chloride/kg b.w. per day (equivalent to 0.46 mg/kg b.w. per day). The CONTAM Panel concluded that, in this study, a 10 % increase in relative kidney weight was not accompanied by nephropathological changes and therefore represented an appropriate BMR.

The JECFA based its PTWI on the changes in relative kidney weights in male rats, because rats were more sensitive than mice and the data for male rats gave lower BMD and BMDL values than the data for female rats. The lowest BMD_{10} was 0.220 mg/kg b.w. per day, expressed as mercuric chloride with a corresponding $BMDL_{10}$ of 0.112 mg/kg b.w. per day, expressed as mercuric chloride (see Figure 9[39]). After correction of these values for the amount of mercury in mercuric chloride (73.9 %) and an adjustment to account for 5 days per week dosing, rather than 7 days per week dosing, these values result in a BMD_{10} of 0.12 mg/kg b.w. per day, expressed as mercury and a $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury. After application of a 100-fold uncertainty factor to this $BMDL_{10}$ and converting to a weekly basis with rounding to one significant figure, the JECFA established a PTWI for inorganic mercury of 4 µg kg b.w., expressed as mercury (FAO/WHO, 2011b). The Panel confirmed these BMD calculations.

[39] Reprinted from FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2011. Safety evaluation of certain food additives and contaminants. Methylmercury. WHO Food Additives Series, 63, 605-684, with permission from WHO.

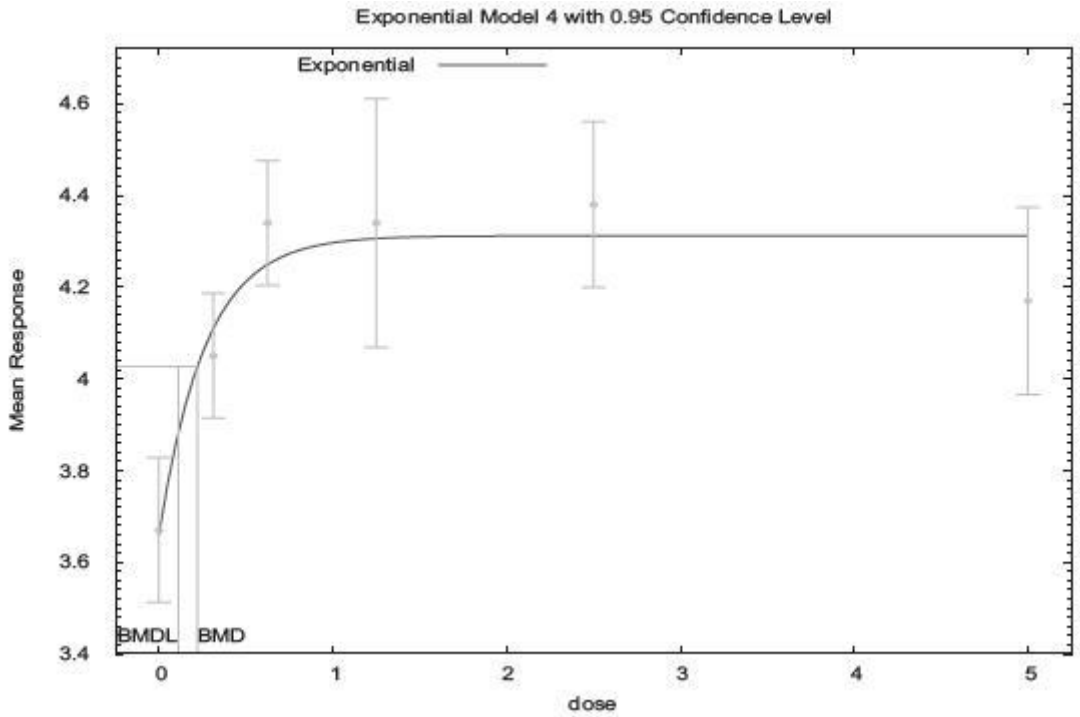


Figure 9: Exponential four-parameter model of relative kidney weight data in male F344 rats from 6-month NTP (1993) study (reprinted from FAO/WHO, 2011b[39]). Notes: Mean response = relative kidney weight (g); BMD(L)s are expressed as mercuric chloride and have not been corrected for dosing schedule.

Table 26: Results from US NTP study for rats gavaged with mercuric chloride for 6 months (modified from FAO/WHO, 2011b): Relative kidney weights in males and females and kidney pathology in males.

Dose (mg $HgCl_2$/kg b.w. per day)	Dose (mg Hg/kg b.w. per day)	n	Relative (to body weight) kidney weights (g)					Male nephropathy	
			Males			Females		minimal	mild
			mean	SE	SD	mean	SE		
0	0	10	3.67	0.07	0.22	3.80	0.07	8/10	0/10
0.312	0.23	10	4.05	0.06	0.19	4.09	0.10	10/10	0/10
0.625	0.46	10	4.34[(b)]	0.06	0.19	4.29[(a)]	0.05	9/10	1/10
1.25	0.92	10	4.34[(b)]	0.12	0.38	4.46[(a)]	0.09	6/10	4/10[(a)]
2.5	1.9	10	4.38[(b)]	0.08	0.25	4.57[(a)]	0.11	7/10	3/10
5.0	3.7	10	4.17[(b)]	0.09	0.28	4.62[(a)]	0.11	6/10	4/10[(a)]

$HgCl_2$: mercuric chloride; n: number of animals; SD: standard deviation; SE: standard error.
(a) : $p \leq 0.05$
(b) : $p < 0.01$
Source: NTP (1993)

Having considered the more recent data on experimental animals exposed to inorganic mercury, the Panel has not identified any studies in experimental animals exposed to inorganic mercury indicating effects on the kidney at doses lower than the $BMDL_{10}$ of 0.112 mg mercuric chloride/kg b.w. per day identified for effects on kidney weight in the NTP (1993) study, and from which the $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury was derived (FAO/WHO, 2011b).

The Panel noted that some recent studies (Huang et al., 2011; Lukačínová et al., 2011, 2012) have reported ototoxicity and reproductive toxicity at relatively low doses. These studies had some limitations, which have been discussed in Sections 7.2.2.3. and 7.2.2.4, and were not taken into further consideration. The Panel therefore agreed with the rationale of JECFA in setting a health-based guidance value of 4 µg/kg b.w. per week (FAO/WHO, 2011b), based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day for kidney weight changes in male rats as the pivotal effect and application of a total uncertainty factor of 100 to account for intra- and interspecies differences. The CONTAM Panel therefore established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

8. RISK CHARACTERISATION

8.1. Risk characterisation of methylmercury

Dietary exposure to methylmercury was calculated from fish and other seafood only, and since the data available for methylmercury were too limited, total mercury was regarded as methylmercury in fish, and 80 % in other seafood. Less than 10 % of the total mercury occurrence data were LC and since there were practically no differences between the UB and the LB dietary exposure estimates, the MB dietary exposure to methylmercury has been used in the risk characterisation.

The medians of mean methylmercury dietary exposures across surveys showed low variation between the age groups and were between 0.24 (adults) and 0.32 µg Hg/kg b.w. per week (other children), which is well below the TWI of 1.3 µg/kg b.w. The mean dietary exposure for adults ranged from 0.07 to 1.08 µg Hg/kg b.w. per week across European surveys and was highest for toddlers and other children, ranging from 0.09 to 1.57 µg Hg/kg b.w. per week. This indicates that a proportion of children with mean exposure can exceed the TWI. Also the medians of 95th percentile dietary exposures across surveys showed low variation between age groups, and were between 1.13 µg Hg/kg b.w. per week and 1.6 µg Hg/kg b.w. per week, which is close to or slightly exceeding the TWI for all age groups. The 95th percentile dietary exposure for adults ranged from 0.51 to 3.04 µg Hg/kg b.w. per week across European surveys and the dietary exposure was highest for other children and adolescents, ranging from 0.42 to 5.05 µg Hg/kg b.w. per week. For the 95th percentile dietary exposure, the maximum across surveys exceeded the TWI in all age groups.

The food category 'Fish meat' contributed most to methylmercury dietary exposure, and people with high and frequent fish consumption are at higher risk of exceeding the TWI. When only fish meat consumers were included in the exposure assessment, the intake estimates were generally two-fold higher compared to those for the total population. The highest dietary exposure of high consumers of fish meat across surveys and European countries was for other children at 7.48 µg Hg/kg b.w. per week, which is approximately six-fold the TWI.

Since the TWI is based on neurodevelopmental effects after prenatal dietary exposure, it is of importance that pregnant women have dietary exposure below the TWI in order to protect the unborn child. The women aged 18 - 45 years participating in the consumption surveys appeared to have similar dietary exposure as the general adult population. In the adult population, the median dietary exposure among high consumers of fish meat was 2.08 µg Hg/kg b.w. per week, but ranged up to 6.17 µg Hg/kg b.w. per week (4.7-fold the TWI).

Dietary exposure to methylmercury from human milk was calculated based on few observations. The mean weekly dietary exposure to methylmercury for infants with an average milk consumption ranged from 0.09 to 0.62 µg Hg/kg b.w. per week, and for infants with a high milk consumption the range was from 0.14 to 0.94 µg Hg/kg b.w. per week. This is below the TWI. However, since both the contribution of methylmercury to total mercury in human milk and the concentrations of total mercury in human milk shows high variation, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

In order to validate the exposure assessment to methylmercury, the CONTAM Panel calculated the level of mercury in blood that would correspond with the calculated dietary exposure for adults and

compared it with the observed concentration of total mercury in blood and hair in Europe. Using a similar one-compartment kinetic model as described in Section 7.5.1., but with blood volume as in non-pregnant adults, and the MB mean and 95th percentile exposure values for adults (Table 11), the corresponding levels in blood were calculated (Table 27).

Table 27: Predicted concentration of mercury in blood (µg/L) based on calculated chronic dietary middle bound mean and 95th percentile exposure to methylmercury across European dietary studies among adults as described in Table 11.

	Mean[(a)]	P95[(a)]
Minimum	0.48	3.5
Median	1.7	7.8
Maximum	7.5	21

P95: 95th percentile.

(a): Calculations are based on the following assumptions: C = d*A*f*b.w./(b*V), where C = mercury concentration in blood (µg/L), d = daily mercury intake (µg/kg b.w. per day), b = elimination constant (0.014 days-1), V = blood volume in the body (5 L in adults of 70 kg b.w), A = absorption factor (0.95), f = fraction of daily intake distributed to the blood (0.05), b.w. = body weight (70 kg).

As described in Section 7.4.1., the mean concentration of total mercury in blood among adults and elderly is in the range 0.2 - 4.85 µg/L (Table 23). The mean concentrations reported among adults in Europe are therefore in the same range and possibly a little lower than the means that can be predicted from the dietary exposure (Table 27). The high percentile concentrations were approximately 10 - 15 µg/L, although up to 40 µg/L was reported (see Appendix F, Tables F1 and F2). This is also in accordance with the predicted values from the 95th percentile exposures (Table 27).

The mean mercury levels in blood are supported by the mean hair concentrations in Europe, which ranged from 0.17 to 1.45 in the adult population (Table 23). With few exceptions, hair mercury concentrations in the higher percentiles in different studies were below 10 mg/kg. The reported hair concentrations of mercury in the European population are therefore, with a few exceptions, lower than the highest concentrations (point of departure) associated with low risk.

Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered then the potential beneficial effects of fish consumption should also be taken into account.

8.2. Risk characterisation of inorganic mercury

The dietary exposure assessment was based on occurrence of total mercury. The CONTAM Panel allocated 20 % of total mercury in fish and 50 % in crustaceans and molluscs. In all other foods 100 % was regarded as inorganic mercury. This was done in order to not underestimate dietary exposure. For human milk, the concentration of inorganic mercury was calculated as the difference between total and methylmercury, since the mean contribution of inorganic mercury to total mercury was not evaluated as sufficiently robust to form basis for exposure assessment. More than 60 % of the occurrence data on total mercury in food were reported as below LOD or LOQ (LC), and the CONTAM Panel decided to use the LB and UB to represent a possible range within which the real dietary exposure would fall for its risk characterisation.

Dietary mean LB to UB estimates of exposure to inorganic mercury across European surveys and countries varied widely. The mean dietary exposure for adults ranged from 0.14 to 0.70 µg Hg/kg b.w. per week (minimum LB – maximum UB) across European surveys and was the highest for toddlers, ranging from 0.27 to 2.16 µg Hg/kg b.w. per week. The 95th percentile dietary exposure for adults ranged from 0.36 to 1.83 µg Hg/kg b.w. per week (minimum LB – maximum UB) across European surveys and was the highest for toddlers and other children, ranging from 0.50 to 4.06 µg Hg/kg b.w. per week. Mean and 95th percentile UB dietary exposures are well below the TWI of 4 µg/kg b.w in most of the studies. Although the highest UB 95th percentile dietary exposure for toddlers is similar to

the TWI, this value represents an overestimate and is associated with high uncertainty, as indicated by the wide LB to UB ranges.

Based on limited data on the occurrence of inorganic mercury in human milk in Europe, the dietary exposure for a 3 month old exclusively breast-fed infant is approximately 0.17 to 1.29 µg/kg b.w. per week with mean human milk consumption and at mean occurrence. For high consuming breast-fed infants, the intake ranged from 0.25 to 1.94 µg/kg b.w. per week. This is below the TWI. However, since both the contribution of inorganic mercury to total mercury in human milk and the concentrations of total mercury in human milk shows high variation, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

The estimated dietary exposure to inorganic mercury in Europe does not indicate a concern. Outgassing from amalgam fillings will increase total mercury exposure. Since elemental mercury is oxidised in the human body to mercuric mercury, a high number of amalgam fillings is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded. Exposure from ambient air can be considered negligible. Mercury-containing skin care products are not permitted in the EU but would be an additional source and might be a concern if used.

9. UNCERTAINTY ANALYSIS

The evaluation of the inherent uncertainties in the assessment of exposure to methylmercury and inorganic mercury has been performed following the guidance of the Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment (EFSA, 2006). In addition, the report on 'Characterizing and Communicating Uncertainty in Exposure Assessment' has been considered (WHO/IPCS, 2008). According to the guidance provided by the EFSA opinion (2006) the following sources of uncertainties have been considered: Assessment objectives, exposure scenario, exposure model, and model input (parameters).

9.1. Assessment objectives

The objectives of the assessment were defined in the terms of reference. The CONTAM Panel considered the new developments regarding the toxicity of inorganic mercury and methylmercury to evaluate whether the PTWIs established by JECFA of 1.6 µg/kg b.w. for methylmercury and of 4 µg/kg b.w. for inorganic mercury are still considered appropriate. The CONTAM Panel also assessed human dietary exposure, taking into account specific sensitive groups and considered the non-dietary sources of exposure to mercury. There was no uncertainty in addressing the objectives as outlined in the terms of reference.

9.2. Exposure scenario/Exposure model

In response to the EFSA call for data on mercury, 59 650 data points from the period 2002 to 2011 from 20 European countries were included in the analyses. The major contributors of the data were Slovakia (35 %), followed by Germany (26 %) and Norway (11 %), while several other countries contributed a very low number of results. There is an uncertainty in possible regional differences in mercury contamination of food commodities and it is evident that the dataset is not fully representative of food on the EU market.

There are considerable differences in the number of analytical results reported across the food groups with the most samples belonging to the fish and seafood category, followed by meat and meat products category and only few samples on other food categories (e.g. composite food, snacks, herbs etc.), which created uncertainty for the inorganic mercury dietary exposure estimate.

Only when results were ten times higher than the second highest value and significantly influenced the mean concentration, they were excluded. However, there was uncertainty whether some included high values were really measured or erroneously reported and they might lead to an overestimation of the dietary exposure.

The occurrence data come from monitoring programmes, and also from routine measurements within the frame of official food controls, so they originated from both random and targeted sampling and this might lead to overestimation.

The majority of the data were reported as total mercury and only a limited number of results were available for methylmercury (n = 1 083) and inorganic mercury (n = 3). For this reason the conversion factors based on contributions of methylmercury and inorganic mercury to total mercury derived from the literature data were applied in order to achieve the contribution of methylmercury and inorganic mercury to total mercury. The CONTAM Panel used a conservative approach and assumed that 100 % of mercury in fish is in the form of methylmercury and 20 % inorganic mercury. In seafood it was assumed that 80 % of total mercury is methylmercury and 50 % inorganic mercury. And in all other food categories it was assumed that 0 % is methylmercury and 100 % inorganic mercury. These assumptions resulted in an overestimation of dietary exposure.

For human milk, the exposure assessment was based on a low number of studies reporting concentrations of total and methylmercury. The limited available data on the contribution of methylmercury to total mercury in human milk showed a wide variation, and the mean contribution was not considered sufficiently robust to form a basis for exposure assessment. Therefore, concentrations of methylmercury in human milk were used and the difference between total mercury and methylmercury concentrations in human milk was used for inorganic mercury exposure assessment. However, a study reporting only total mercury in human milk has shown higher concentrations than the studies that provided speciation analyses (about 5 to 11 fold higher). Therefore, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

Some types of food processing have been shown to have an influence on the concentration of methylmercury in fish due to weight (moisture and fat) change but the change will depend on the method of cooking and processing.

The significant proportion of samples with values below LOD/LOQ introduced considerable uncertainties to the overall dietary exposure estimate, particularly for inorganic mercury. The use of the LB in this opinion tends to underestimate, while UB tends to overestimate the dietary exposure.

Two specific population subgroups (women in childbearing age and high and frequent fish consumers) were considered separately in the assessment. Since the number of women of childbearing age participating in the surveys was low (less than 500 participants in 10 out of 15 surveys), there will be uncertainty in extrapolation to the wider European population. Similar uncertainty exists in the age group of infants where only two surveys with low number of participants were available.

When the survey duration covers a low number of days and the dietary exposure is assessed for ‘consumers only’, this can lead to some overestimation of dietary exposure in high and frequent consumers of fish meat. This is especially true for countries where these food commodities are consumed rarely or seasonally. As the duration of surveys increase, the observed percentage of subjects reporting consumption of commonly and rarely eaten foods becomes larger, whereas the observed mean and high percentiles consumption, in consumers only, decreases (Merten et al., 2011).

9.3. Other uncertainties

Methylmercury

The TWI is based on neurodevelopmental endpoints associated with mercury exposure in the cohort studies from the Seychelles and the Faroe Islands. Whereas the Seychelles population are exposed to methylmercury via fish consumption, the main source is whale meat in the Faroe Islands, with a minor contribution coming from fish consumption. Since confounding from the beneficial effects of fish consumption is addressed, and the mercury source is fish in only one of the cohorts, such confounding

might affect the outcomes differently in these cohorts, which might increase the uncertainty in the assessment.

The point of departure from the nutrition cohort in the SCDS was at a level with few observations, this also increases the uncertainty in the risk assessment.

A developmental immunotoxicity study in rats indicated that immunosuppressive effects might be the most sensitive endpoint (see Section 7.2.1.3.). Immunotoxicity is not well characterised in epidemiological studies, increasing the uncertainty in whether the TWI has been based on the most sensitive endpoint.

Observations in humans on myocardial infarction and HRV are of potential importance, which contributes to the uncertainty regarding whether the TWI has been based on the most sensitive endpoint, and whether only pregnant women and fetuses belong to the groups at risk.

There is high inter-study and inter-individual variation in the ratio between total mercury in hair and blood, and a mean ratio of 250:1 was used for converting the concentration of total mercury in hair into its concentration in blood. A data-derived factor of 2 for variation in hair to blood ratio was applied and the new data available for hair to blood ratio from adults, including the critical group of women in child bearing age, indicated that the factor covers the variance. There are, however, some indications that the total mercury hair to blood ratio is higher in children, and this might lead to an underestimation of the risk if postnatal effects of exposure were of higher significance. There is uncertainty connected to the half-life of methylmercury in blood and the absorbed fraction distributed to the blood, which are parameters used for the conversion of blood levels to dietary intake in the one-compartment toxicokinetic model.

Inorganic mercury

The TWI established by the Panel is based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, for effects on kidney weight in male rats dosed with mercuric chloride for 6 months (see Section 7.2.2.2.). Selection of this value as the point of departure is supported by results from other studies that have investigated effects on the kidney, for which effect levels were all higher, including those for the immune-type kidney reaction in the Brown Norway rat, which is considered a sensitive animal model.

Some more recent laboratory animal studies have reported other effects at low levels of exposure to mercuric chloride, for which NOAELs or BMDLs could not be identified. The lowest effect level in these studies was 0.022 – 0.029 mg/kg b.w. per day, expressed as mercury for reproductive parameters (see Section 7.2.2.4.). These studies had limitations, discussed earlier, and therefore were not used to derive the TWI.

9.4. Summary of uncertainties

In Tables 28 and 29, a summary of the uncertainty evaluation is presented for methylmercury and inorganic mercury respectively, highlighting the main sources of uncertainty and indicating an estimate of whether the respective source of uncertainty might have led to an over- or underestimation of the exposure or the resulting risk.

Table 28: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure of methylmercury.

Sources of uncertainty	Direction
Measurement uncertainty of analytical results	+/-[(a)]
Extrapolation of occurrence data to whole Europe	+/-
Use of analytical data from both targeted and random sampling	+
Applying conversion factors to convert total mercury to methylmercury	+
Not including exposure from food groups other than fish and other seafood	-
Exposure estimation from rarely consumed food and/or in high consumers	+/-
Exposure from human milk based on limited data	+/-
Value of point of departure from the Seychelles and the Faroe Islands cohorts	+/-
Possibility that other endpoints are more sensitive (e.g. developmental immunotoxicity and cardiovascular effects)	-

(a): + = uncertainty with potential to cause over-estimation of exposure/risk; - = uncertainty with potential to cause under-estimation of exposure/risk.

Table 29: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure of inorganic mercury.

Sources of uncertainty	Direction
Measurement uncertainty of analytical results	+/-[(a)]
Extrapolation of occurrence data to whole Europe	+/-
Use of analytical data from both targeted and random sampling	+
Applying conversion factors to convert total mercury to inorganic mercury	+
Use of LB and UB occurrence data in the dietary exposure estimations	+/-
Limited occurrence data from several food groups	+/-
Exposure from human milk based on limited data	+/-

LB: lower bound; UB: upper bound.

(a): + = uncertainty with potential to cause over-estimation of exposure/risk; - = uncertainty with potential to cause under-estimation of exposure/risk.

The CONTAM Panel concluded that the impact of the uncertainties on the risk assessment of exposure to methylmercury and inorganic mercury is considerable and that the assessment is likely to be conservative.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Background

- Mercury is a metal that is released into the environment from both natural and anthropogenic sources. Once released into the environment, mercury undergoes a series of complex transformations and cycles between atmosphere, ocean and land.

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

- In 2003, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed the provisional tolerable weekly intake (PTWI) for methylmercury and established a revised PTWI of 1.6 µg/kg body weight (b.w.).

- In 2010, the JECFA reviewed the PTWI for total mercury and established a PTWI of 4 µg/kg b.w. for inorganic mercury.

Sampling and methods of analysis

- For total mercury, cold vapour - atomic absorption spectrometry (CV-AAS) or cold vapour - atomic fluorescence spectrometry and increasingly inductively coupled plasma mass spectrometry (ICP-MS) are the most widely used techniques. Two European standardised methods with CV-AAS and ICP-MS detection are available.

- For speciation analysis, gas chromatography coupled to mass spectrometry or ICP-MS is the most widely used technique. High-performance liquid chromatography techniques are increasingly being used but usually, gas chromatography methods have higher sensitivity than liquid chromatography. No fully validated or standardised methods are available for the separation and detection of mercury species.

- Several standard or certified reference materials are available for both total mercury and methylmercury. Regular proficiency testing schemes are organised by a number of providers for both total mercury and methylmercury in foodstuffs to demonstrate and maintain analytical quality assurance.

Occurrence

- Following a call for data, 20 European countries submitted approximately 60 000 analytical results of mercury concentrations, covering the period from 2002 to 2011; 98 % of the data were on total mercury.

- The food group 'Fish and other seafood' (12 % left-censored (LC) data) dominated the total number of samples. This food category was followed by 'Meat and meat products' (56 % LC data) and 'Grains and grain products' (60 % LC data). The percentage of samples below the limit of detection or limit of quantification in the individual food groups at FoodEx Level 1 ranged between 12 % to 90 %.

- The highest mean total mercury concentrations were detected in the following food commodities: fish and other seafood, particularly in fish meat (especially swordfish and sharks), wild mushrooms and dietary supplements.

- Mercury can be transferred into human milk. In the literature, mean concentrations of total mercury between 0.3 and 3.53 µg/L in Europe are reported.

- The contribution of methylmercury to total mercury is typically 80 - 100 % in fish and 50 - 80 % in seafood other than fish. In other foods, mercury is presumed to be present as inorganic mercury.

- Three European studies were identified in which both methylmercury and total mercury were analysed in human milk and the mean contribution of methylmercury to total mercury ranged from 26 to 63 %.

- There is little impact on the content of mercury in foods resulting from cooking or processing. Therefore data for mercury in raw foods are suitable to use for dietary exposure estimates.

Human dietary exposure

- For dietary exposure to methylmercury, the EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) used a conservative approach by assuming that 100 % of total mercury in fish and 80 % in seafood other than fish is in the form of methylmercury.

- For dietary exposure to inorganic mercury, the CONTAM Panel used a conservative approach by assuming that 20 % of total mercury in fish and 50 % in seafood other than fish and 100 % in other foods is in the form of inorganic mercury.

- In order to estimate dietary exposure, the consumption data of each individual within the surveys were multiplied by the mean occurrence data for the relevant food categories, resulting in a distribution of exposure, from which the mean and 95th percentile were identified for each survey and age class.

- For human milk, the limited available data on the contribution of methylmercury to total mercury showed a wide variation, and the mean contribution was not evaluated as sufficiently robust to form a basis for dietary exposure assessment. Therefore, concentrations of methylmercury in human milk were used for methylmercury dietary exposure assessment and the difference between total mercury and methylmercury concentrations in human milk was used for inorganic mercury dietary exposure assessment.

Methylmercury

- Only the consumption of fish and other seafood was considered relevant and therefore was used for assessment of dietary exposure to methylmercury from food (other than human milk).

- The estimation of dietary exposure to methylmercury was based on middle bound (MB) data since there was virtually no difference between lower bound (LB) and upper bound (UB).

- The mean MB methylmercury dietary exposure varied from the lowest minimum of 0.06 µg/kg b.w. per week seen in elderly and very elderly to the highest maximum of 1.57 µg/kg b.w. per week in toddlers.

- The 95th percentile MB dietary exposure ranged from the lowest minimum of 0.14 µg/kg b.w. per week in very elderly to the highest maximum of 5.05 µg/kg b.w. per week in adolescents. For consumers that report consumption of fish meat during the course of the surveys, the 95th percentile MB dietary exposure ranged from the lowest minimum of 0.54 µg/kg b.w. per week in elderly to the highest maximum of 7.48 µg/kg b.w. per week in other children.

- Dietary exposure for the child age groups (toddlers and other children) was higher compared to the adult age groups, and this is explained by the higher food consumption in relation to their body weight.

- Based on the reported mean concentrations of methylmercury in human milk, the mean weekly dietary exposure to methylmercury for infants with an average milk consumption ranges from 0.09 to 0.62 µg/kg b.w. per week and from 0.14 to 0.94 µg/kg b.w. per week for infants with a high milk consumption. However, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

- Dietary exposure of women of child-bearing age did not differ appreciably from dietary exposure of the general adult population.

- Fish meat, particularly tuna, swordfish, cod and whiting, and pike were identified as the most important contributors for all age groups with hake also being important for children because of high consumption in some population groups.

Inorganic mercury

- All main food categories were considered for the dietary exposure to inorganic mercury.

- The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations.

- The mean dietary exposure to inorganic mercury ranged from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers.

- The 95th percentile dietary exposure ranged from the lowest minimum LB of 0.25 µg/kg b.w. per week in elderly and very elderly to the highest maximum UB of 4.06 µg/kg b.w. per week in toddlers.

- The 95th percentile dietary exposure, to inorganic mercury from dietary supplements (consumers only) was up to 0.24 µg/kg b.w. per week (UB), and dietary supplements were not considered a major source.

- Dietary exposure for the child age groups (toddlers and other children) was higher compared to the adult age groups, and this is explained by the higher food consumption in relation to their body weight.

- At FoodEx Level 1, 'Fish and other seafood', 'Non-alcoholic beverages' and 'Composite food' were the most important contributors to inorganic mercury dietary exposure in the European population. Dietary exposure to inorganic mercury was driven by high concentrations in the case of fish and other seafood and composite food (where a high proportion of the data were LC), but was more likely driven by high consumption in the case of non-alcoholic beverages.

- At FoodEx Level 2, different groups of food commodities were estimated as the major contributors to inorganic mercury dietary exposure: (i) tea (infusion), driven by high consumption; (ii) fish meat, cereal-based dishes, prepared salads, wild mushrooms, when the contribution was based on high mercury concentration; (iii) ready to eat soups, driven by high percentage of LC data; and (iv) fruit juices and bread and rolls, driven by both high consumption and high percentage of LC data.

- Based on mean concentrations of inorganic mercury in human milk, the mean weekly dietary exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week and from 0.25 to 1.94 µg/kg b.w. per week for infants with a high milk consumption. However, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

Human non-dietary exposure

- Non-dietary exposure to methylmercury is likely to be of minor importance for the general population in the European Union.

- In the case of a high number of amalgam fillings, exposure to elemental mercury via the outgassing of dental amalgam is believed to strongly contribute to the internal inorganic mercury exposure.

Hazard identification and characterisation

Toxicokinetics

- After oral intake, methylmercury is much more extensively and rapidly absorbed than mercuric and mercurous mercury.

- In human blood mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma, whereas methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes.

- Due to its low lipophilicity, mercuric mercury does not readily cross the placental, the blood-brain or the blood-cerebrospinal fluid (CSF) barrier, whereas organic mercury species are able to enter the hair follicle, and to cross the placenta as well as the blood-brain and blood-CSF barriers, allowing accumulation in hair, the fetus and the brain.

- Mercuric mercury in the brain is generally the result of either in situ demethylation of organic mercury species or oxidation of elemental mercury.

- Excretion of absorbed mercuric mercury occurs mainly via urine, whereas the main pathway of excretion of absorbed methylmercury is via faeces (in the form of mercuric mercury).

- Urinary total mercury might be a suitable biomarker of inorganic (and elemental) mercury, but not for methylmercury exposure. Total mercury in hair and blood are routinely used as biomarkers to assess long term methylmercury exposure. A frequently cited total mercury blood to hair ratio is 1:250, however large variations exist, especially in people with infrequent fish consumption.

Toxicity

Methylmercury

- A recent developmental study applying only one low dose in mice indicated effects on body weight gain, locomotor function and auditory function. A large study in rats showed developmental immunotoxic effects at low doses, and the lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 0.01 mg/kg b.w. per day, expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day, expressed as mercury) for the specific antibody response in rats was the lowest BMDL.

- Methylmercury exerts genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent.

Inorganic mercury

- The critical target for toxicity of inorganic mercury is the kidney.

- Other targets include the liver, nervous system, immune system, reproductive and developmental systems.

- Effects on reproduction have been reported at a low dose ($BMDL_{10}$ for kidney weight) but the study had limitations and the CONTAM Panel did not consider the data sufficiently robust to be used as a basis for establishing a health-based guidance value.

- From repeated-dose studies, no effects were observed on the kidney at 0.23 mg/kg b.w. per day, expressed as mercury or below. The CONTAM Panel confirmed the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, for effects on kidney weight calculated by JECFA.

- Mercuric mercury exerts genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent.

Mode of action

- Most of the *in vitro* and *in vivo* studies used methylmercuric chloride, which differs in bioavailability, tissue distribution and toxicity from methylmercury species present in fish.

- Molecular mechanisms of methylmercury toxicity include protein binding, disturbances in calcium homeostasis and oxidative stress including lipid peroxidation. The modes of action described are mitochondrial dysfunction, disruption of the neurotransmitter systems, neuronal and vascular/cardiovascular cell damage possibly leading to adverse effects such as inflammation, thrombosis, dyslipidemia, vascular smooth muscle and endothelial damage, neurotoxicity and neurodevelopmental toxicity.

- The most likely mechanism of genotoxicity appears to be via oxidative stress, which would be expected to be thresholded. Inorganic and organic mercury species have been shown to bind covalently to isolated DNA but the formation of such DNA adducts has not been investigated in cell systems or *in vivo* and therefore the consequences of this interaction for genotoxicity have not been elucidated.

Observations in humans

Methylmercury

- In the European population, mean concentrations of total mercury ranged from 0.86 to 13.9 µg/L in cord blood, from 0.2 to 4.85 µg/L in blood from adults and elderly, from 0.17 to 1.45 mg/kg in hair from adults and elderly and from 0.14 (geometric mean) to 1.99 mg/kg in hair from children.

- New data from the Faroe Islands Cohort 1 at children's age 14 years indicated that the association between prenatal exposure and neurological auditory function was still present at 14 years, but with a smaller impact than at seven years, and not related to the estimates of recent postnatal exposure. Reassessment of the data from the Faroese Cohort 1 participants at age seven years indicated that beneficial effects of fish consumption together with imprecision in the measurements of fish consumption and determination of mercury in hair might underestimate the effects of methylmercury by a factor up to two.

- Most of the assessments of the neurobehavioural outcomes in the smaller Faroe Islands Cohort 2 at age seven years could not confirm the associations between neurological outcomes and mercury found in the Faroese Cohort 1. Assessment of the Faroese Cohorts 1 and 2 together and further analyses in the Faroese Cohort 1 did not identify major confounding from polychlorinated biphenyls exposure.

- Reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the Seychelles Child Developmental Study have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints.

- Results from the smaller Nutrition Cohort in the Seychelles Child Developmental Study indicated an association between prenatal mercury exposure and decreased scores on neurodevelopmental indices at 9 and 30 months after adjustment for prenatal blood maternal n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFA). An apparent no-observed-effect level (NOEL) at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study. However, a positive association between maternal prenatal docosahexaenoic acid and preschool language scores was reported from the five years follow up.

- A few, but not all, studies from other regions found associations between prenatal mercury exposure and cognitive outcomes at lower mercury levels than those reported in the Faroe Islands and Seychelles cohorts, but the overall picture at low-level exposure does not provide information to allow conclusions.

- As regards children's postnatal mercury exposure, the inconsistent observations from the identified studies do not give reasons for increased concern for neurological effects. The studies on autism do not indicate increased risk from dietary mercury exposure, but for attention deficit hyperactivity disorder some studies have found associations with mercury. Taken together, the results do not provide information to allow conclusions.

- In the adult population, no association is observed between low levels of mercury exposure and adverse neurological outcomes.

- The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident.

- Studies on stroke in relation to mercury exposure do not suggest an association.

- Some studies indicate an association between methylmercury and increased risk for acute myocardial infarction and acute cardiac death. Other studies do not show increased cardiac disease risk. The studies that showed association had used biochemical measurements as basis for adjustment for n-3 LCPUFA, while the ones that found no association had based adjustments on dietary questionnaire data. Some additional studies have dealt with lower exposure levels and provided no associations.

- The observations related to myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, but still not conclusive.

- Endpoints other than neurodevelopmental toxicity, neurotoxicity and cardiovascular toxicity have been investigated only in single or few studies and the importance of the findings from these studies are accordingly difficult to evaluate.

Inorganic mercury

- Human data on the adverse health effects from oral exposure to inorganic mercury mainly consist of case reports that are not suitable to identify a dose-response relationship and they could not form the basis for a risk assessment of inorganic mercury.

Derivation of Health-based Guidance Values

Methylmercury

- The CONTAM Panel has not identified any new, experimental animal studies that could provide a better primary basis than the human epidemiological data for a health-based guidance value.
- Associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value.
- The mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese cohort 1 at age seven years (12 mg/kg in maternal hair), resulting in 11.5 mg/kg maternal hair, was used as basis for derivation of a health-based guidance value.
- By application of a maternal hair to maternal blood ratio of 250, the maternal hair mercury concentration with no appreciable adverse effect was converted into a maternal blood mercury concentration of 46 µg/L.
- Using a one-compartment toxicokinetic model the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w.
- A data-derived uncertainty factor of 2 was applied to account for variation in the hair to blood ratio. In addition a standard factor of 3.2 was applied to account for interindividual variation in toxicokinetics, resulting in a total uncertainty factor of 6.4.
- The CONTAM Panel established a tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w. expressed as mercury.
- The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response in rats.

Inorganic mercury

- Having considered the data on inorganic mercury, including some recent studies not reviewed by JECFA in its evaluation of 2010, the Panel agrees with the rationale of JECFA in setting a health-based guidance value, based on kidney weight changes in male rats as the pivotal effect.
- Based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury and an uncertainty factor of 100 to account for inter and intra species differences with conversion to a weekly basis and rounding to one significant figure, the Panel established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

Risk characterisation

Methylmercury

- The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The medians of 95th percentile dietary exposures across surveys are close to or above the TWI for all age groups.
- High consumers of fish meat may exceed the TWI by up to approximately six-fold.

- Unborn children constitute the most vulnerable group for developmental effects of methylmercury exposure, and pregnant women can be present in the group of high and frequent fish consumers.

- Biomonitoring data on blood and hair concentrations indicate that in the general European population, methylmercury exposure is generally below the TWI. However, higher levels in blood and hair are also observed, confirming higher dietary exposure in some population groups.

- Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered then the potential beneficial effects of fish consumption should also be taken into account.

Inorganic mercury

- The estimated exposure to inorganic mercury in Europe from the diet alone does not exceed the TWI. Inhaled elemental mercury vapour from dental amalgam, which after absorption is converted to inorganic mercury, is an additional source that is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded.

RECOMMENDATIONS

- There is a need to develop certified reference materials and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood.

- Further effort should be made to increase the number of methylmercury and inorganic mercury data in all food groups that contribute significantly to overall exposure.

- In order to decrease the uncertainty in the point of departure derived from the epidemiological studies, more reliable definition of the dose response taking confounding factors into account is needed.

- Future studies should elucidate the relevance of additional endpoints, such as immunological and cardiovascular endpoints.

REFERENCES

Abballe A, Ballard TJ, Dellatte E, di Domenico A, Ferri F, Fulgenzi AR, Grisanti G, Iacovella N, Ingelido AM, Malisch R, Miniero R, Porpora MG, Risica S, Ziemacki G and De Felip E, 2008. Persistent environmental contaminants in human milk: concentrations and time trends in Italy. Chemosphere, 73, S220-227.

Abdelouahab N, Huel G, Suvorov A, Foliguet B, Goua V, Debotte G, Sahuquillo J, Charles MA and Takser L, 2010. Monoamine oxidase activity in placenta in relation to manganese, cadmium, lead, and mercury at delivery. Neurotoxicolgy and Teratology, 32, 256-261.

Abrankó L, Kmellár B and Fodor P, 2007. Comparison of extraction procedures for methylmercury determination by a SPME-GC-AFS system. Microchemical Journal, 85, 122-126.

Adams JB, Romdalvik J, Ramanujam VM and Legator MS, 2007. Mercury, lead, and zinc in baby teeth of children with autism versus controls. Journal of Toxicology and Environmental Health. Part A, 70, 1046-1051.

Agah H, Leermakers M, Elskens M, Fatemi SMR and Baeyens W, 2007. Total mercury and methyl mercury concentrations in fish from the Persian Gulf and the Caspian Sea. Water Air and Soil Pollution, 181, 95-105.

Ahlqwist M, Bengtsson C, Lapidus L, Gergdahl IA and Schutz A, 1999. Serum mercury concentration in relation to survival, symptoms, and diseases: results from the prospective population study of women in Gothenburg, Sweden. Acta Odontologica Scandinavica, 57, 168-174.

Airaksinen R, Turunen AW, Rantakokko P, Mannisto S, Vartiainen T and Verkasalo PK, 2010. Blood concentration of methylmercury in relation to food consumption. Public Health Nutrition, 1-10.

Akselrod S, 1988. Spectral analysis of fluctuations in cardiovascular parameters: a quantitative tool for the investigation of autonomic control. Trends in Pharmacological Sciences, 9, 6-9.

al-Shahristani H and Shihab KM, 1974. Variation of biological half-life of methylmercury in man. Archives of Environmental Health, 28, 342-344.

Alves MF, Fraiji NA, Barbosa AC, De Lima DS, Souza JR, Dorea JG and Cordeiro GW, 2006. Fish consumption, mercury exposure and serum antinuclear antibody in Amazonians. International Journal of Environmental Health Research, 16, 255-262.

Amouroux D, Seby F, Monperrus M, Pannier F, Mendiguchia C, Benoit-Bonnemason C and Donard OFX, 2011. Chapter 5. Chemical Species. In: Chemical Marine Monitoring: Policy Framework and Analytical Trends, First edition. Eds Quevauviller P, Roose P and Verreet G. John Wiley & Sons, Ltd., Chichester, UK, doi:10.1002/9781119990826.ch5

Andres P, 1984. IgA-IgG disease in the intestine of Brown-Norway rats ingesting mercuric chloride. Clinical Immunology and Immunopathology, 30, 488-494.

Arnich N, Sirot V, Riviere G, Jean J, Noël L, Guérin T and Leblanc JC, 2012. Dietary exposure to trace elements and health risk assessment in the 2nd French Total Diet Study. Food and Chemical Toxicology, 50, 2432-2449.

Aschner M, Onishchenko N and Ceccatelli S, 2010. Toxicology of alkylmercury compounds. Metal Ions in Life Sciences, 7, 403-434.

Ask K, Åkesson A, Berglund M and Vahter M, 2002. Inorganic mercury and methylmercury in placentas of Swedish women. Environmental Health Perspectives, 110, 523-526.

Atkinson A, Thompson SJ, Khan AT, Graham TC, Ali S, Shannon C, Clarke O and Upchurch L, 2001. Assessment of a two-generation reproductive and fertility study of mercuric chloride in rats. Food and Chemical Toxicology, 39, 73-84.

ATSDR (Agency for Toxic Substances and Disease Registry), 1999. Toxicological Profile for Mercury March 1999. CAS#: 7439-97-6. U.S. Department of Health and Human Services, Atlanta, Georgia. Available from http://www.atsdr.cdc.gov/toxprofiles/tp46.pdf.

ATSDR (Agency for Toxic Substances and Disease Registry), 2009. Children's exposure to elemental mercury: a national review of exposure events. Atlanta, Georgia, U. S. Department of Health and Human Services, Center of Disease Control and Prevention, Public Health Service.

Aubert AE and Ramaekers D, 1999. Neurocardiology: the benefits of irregularity. The basics of methodology, physiology and current clinical applications. Acta Cardiologica, 54, 107-120.

Azevedo BF, Furieri LB, Pecanha FM, Wiggers GA, Vassallo PF, Simoes MR, Fiorim J, de Batista PR, Fioresi M, Rossoni L, Stefanon I, Jesus Alonso M, Salaices M and Vassallo DV, 2012. Toxic Effects of Mercury on the Cardiovascular and Central Nervous Systems. Journal of Biomedicine and Biotechnology, doi:10.1155/2012/949048.

Baeyens W, Leermakers M, Papina T, Saprykin A, Brion N, Noyen J, De Gieter M, Elskens M and Goeyens L, 2003. Bioconcentration and biomagnification of mercury and methylmercury in North Sea and Scheldt estuary fish. Archives of Environmental Contamination and Toxicology, 45, 498-508.

Ballatori N and Clarkson TW, 1985. Biliary secretion of glutathione and of glutathione-metal complexes. Fundamental and Applied Toxicology, 5, 816-831.

Baralkiewicz D, Gramowska H and Gołdyn R, 2006. Distribution of total mercury and methyl mercury in water, sediment and fish from Swarzedzkie lake. Chemistry and Ecology, 22, 59-64.

Barregard L, Hogstedt B, Schutz A, Karlsson A, Sallsten G and Thiringer G, 1991. Effects of occupational exposure to mercury vapor on lymphocyte micronuclei. Scandinavian Journal of Work, Environment & Health, 17, 263-268.

Bates CJ, Prentice A, Birch MC and Delves HT, 2007. Dependence of blood indices of selenium and mercury on estimated fish intake in a national survey of British adults. Public Health Nutrition, 10, 508-517.

Batista BL, Rodrigues JL, de Souza SS, Oliveira Souza VC and Barbosa Jr F, 2011. Mercury speciation in seafood samples by LC–ICP-MS with a rapid ultrasound-assisted extraction procedure: Application to the determination of mercury in Brazilian seafood samples. Food Chemistry, 126, 2000-2004.

Bautista LE, Stein JH, Morgan BJ, Stanton N, Young T and Nieto FJ, 2009. Association of blood and hair mercury with blood pressure and vascular reactivity. WMJ, 108, 250-252.

Becker K, Müssig-Zufika M, Conrad A, Lüdecke A, Schulz C, Seiwert M and Kolossa-Gehring M 2008. German Environmental Survey for Children 2003/06 - GerES IV. Human biomonitoring. Levels of selected substances in blood and urine of children in Germany. Environmental Research of the Environment, Nature Conservation and Nuclear Safety. Research Report 202 62 219. UBA-FB 001026. Federal Environmental Agency (Umweltbundesamt), Dessau-Rosslau, January 2008. Available from www.umweltbundesamt.de.

Belles-Isles M, Ayotte P, Dewailly E, Weber JP and Roy R, 2002. Cord blood lymphocyte functions in newborns from a remote maritime population exposed to organochlorines and methylmercury. Journal of Toxicology and Environmental Health. Part A, 65, 165-182.

Benefice E, Luna-Monrroy S and Lopez-Rodriguez R, 2010. Fishing activity, health characteristics and mercury exposure of Amerindian women living alongside the Beni River (Amazonian Bolivia). International Journal of Hygiene and Environmental Health, 213, 458-464.

Bergdahl IA, Ahlqwist M, Barregard L, Bjorkelund C, Blomstrand A, Skerfving S, Sundh V, Wennberg M and Lissner L, 2012. Mercury in serum predicts low risk of death and myocardial infarction in Gothenburg women. International Archives of Occupational and Environmental Health, doi:10.1007/s00420-00012-00746-00428.

Berglund M, Lind B, Bjornberg KA, Palm B, Einarsson O and Vahter M, 2005. Inter-individual variations of human mercury exposure biomarkers: a cross-sectional assessment. Environmental Health, 4, 20.

Berlin M, Zalups RK and Fowler BA, 2007. Chapter 33 - Mercury. In: Handbook on the Toxicology of Metals (Third Edition). Eds Nordberg GF, Fowler BA, Nordberg M and Friberg LT. Elsevier, New York, 675-729.

Bernaudin JF, Druet E, Druet P and Masse R, 1981. Inhalation or ingestion of organic or inorganic mercurials produces auto-immune disease in rats. Clinical Immunology and Immunopathology, 20, 129-135.

Bernhoft RA, 2012. Mercury toxicity and treatment: a review of the literature. Journal of Environmental and Public Health, 2012, 460-508.

Berntssen MH, Hylland K, Lundebye AK and Julshamn K, 2004. Higher faecal excretion and lower tissue accumulation of mercury in Wistar rats from contaminated fish than from methylmercury chloride added to fish. Food and Chemical Toxicology, 42, 1359-1366.

Berzas Nevado JJ, Rodrígues Martín-Doimeadios RC, Guzmán Bernardo FJ, Jiménez Moreno MJ, Patiño Ropero MJ and de Marcos Serrano A, 2011. Mercury speciation in fish tissues from a

Mediterranean River basin: the Tagus River (central Spain) as a case study. Archives of Environmental Contamination and Toxicology, 61, 642-652.

Björkman L, Lundekvam BF, Laegreid T, Bertelsen BI, Morild I, Lilleng P, Lind B, Palm B and Vahter M, 2007. Mercury in human brain, blood, muscle and toenails in relation to exposure: an autopsy study. Environmental Health, 6, 30.

Björnberg KA, Vahter M, Berglund B, Niklasson B, Blennow M and Sandborgh-Englund G, 2005. Transport of methylmercury and inorganic mercury to the fetus and breast-fed infant. Environmental Health Perspectives, 113, 1381-1385.

Bocca B, Mattei D, Pino A and Alimonti A, 2010. Italian network for human biomonitoring of metals: preliminary results from two Regions. Annali dell'Istituto Superiore di Sanita, 46, 259-265.

Boening DW, 2000. Ecological effects, transport, and fate of mercury: a general review. Chemosphere, 40, 1335-1351.

Boischio AA and Cernichiari E, 1998. Longitudinal hair mercury concentration in riverside mothers along the Upper Madeira river (Brazil). Environmental Research, 77, 79-83.

Bolann BJ, Rahil-Khazen R, Henriksen H, Isrenn R and Ulvik RJ, 2007. Evaluation of methods for trace-element determination with emphasis on their usability in the clinical routine laboratory. Scandinavian Journal of Clinical and Laboratory Investigation, 67, 353-366.

Bose R, Onishchenko N, Edoff K, Janson Lang AM and Ceccatelli S, 2012. Inherited effects of low-dose exposure to methylmercury in neural stem cells. Toxicological Sciences, doi:10.1093/toxsci/kfs1257.

Boucher O, Bastien CH, Saint-Amour D, Dewailly E, Ayotte P, Jacobson JL, Jacobson SW and Muckle G, 2010. Prenatal exposure to methylmercury and PCBs affects distinct stages of information processing: an event-related potential study with Inuit children. Neurotoxicology, 31, 373-384.

Boucher O, Burden MJ, Muckle G, Saint-Amour D, Ayotte P, Dewailly E, Nelson CA, Jacobson SW and Jacobson JL, 2012. Response inhibition and error monitoring during a visual go/no-go task in inuit children exposed to lead, polychlorinated biphenyls, and methylmercury. Environmental Health Perspectives, 120, 608-615.

Boujbiha MA, Ben Salah G, Ben Feleh A, Saoudi M, Kamoun H, Bousslema A, Ommezzine A, Said K, Fakhfakh F and El Feki A, 2012. Hematotoxicity and genotoxicity of mercuric chloride following subchronic exposure through drinking water in male rats. Biological Trace Element Research, 148, 76-82.

Bourdineaud JP, Fujimura M, Laclau M, Sawada M and Yasutake A, 2011. Deleterious effects in mice of fish-associated methylmercury contained in a diet mimicking the Western populations' average fish consumption. Environment International, 37, 303-313.

Bowles KC, Apte SC, Maher WA, Kawei M and Smith R, 2001. Bioaccumulation and biomagnification of mercury in Lake Murray, Papua New Guinea. Canadian Journal of Fisheries and Aquatic Sciences, 58, 888-897.

Bramanti E, Lomonte C, Onor M, Zamboni R, D'Ulivo A and Raspi G, 2005. Mercury speciation by liquid chromatography coupled with on-line chemical vapour generation and atomic fluorescence spectrometric detection (LC-CVGAFS). Talanta, 66, 762-768.

Brantsæter AL, Haugen M, Thomassen Y, Ellingsen DG, Ydersbond TA, Hagve TA, Alexander J and Meltzer HM, 2010. Exploration of biomarkers for total fish intake in pregnant Norwegian women. Public Health Nutrition, 13, 54-62.

Bridges CC and Zalups RK, 2010. Transport of inorganic mercury and methylmercury in target tissues and organs. Journal of Toxicology and Environmental Health. Part B, 13, 385-410.

Budtz-Jorgensen E, Debes F, Weihe P and Grandjean P, 2010. Structural equation models for meta-analysis in environmental risk assessment. Environmetrics, 21, 510-527.

Budtz-Jorgensen E, Grandjean P and Weihe P, 2007b. Separation of risks and benefits of seafood intake. Environmental Health Perspectives, 115, 323-327.

Budtz-Jorgensen E, Grandjean P, Jorgensen PJ, Weihe P and Keiding N, 2004. Association between mercury concentrations in blood and hair in methylmercury-exposed subjects at different ages. Environmental Research, 95, 385-393.

Budtz-Jorgensen E, Keiding N, Grandjean P and Weihe P, 2002. Estimation of health effects of prenatal methylmercury exposure using structural equation models. Environmental Health, 1, 2.

Budtz-Jorgensen E, Keiding N, Grandjean P and Weihe P, 2007a. Confounder selection in environmental epidemiology: assessment of health effects of prenatal mercury exposure. Annals of Epidemiology, 17, 27-35.

Budtz-Jorgensen E, Keiding N, Grandjean P, Weihe P and White RF, 2003. Consequences of exposure measurement error for confounder identification in environmental epidemiology. Statistics in Medicine, 22, 3089-3100.

Burger J, Dixon C, Boring CS and Gochfeld M, 2003. Effect of deep-frying fish on risk from mercury. Journal of Toxicology and Environmental Health. Part A, 66, 817-828.

Cace IB, Milardovic A, Prpic I, Krajina R, Petrovic O, Vukelic P, Spiric Z, Horvat M, Mazej D and Snoj J, 2011. Relationship between the prenatal exposure to low-level of mercury and the size of a newborn's cerebellum. Medical Hypotheses, 76, 514-516.

Cairns E, Tharumakulasingam K, Athar M, Yousaf M, Cheng I, Huang Y, Lu J and Yap D, 2011. Source, concentration, and distribution of elemental mercury in the atmosphere in Toronto, Canada. Environmental Pollution, 159, 2003-2008.

Cao Y, Chen A, Jones RL, Radcliffe J, Caldwell KL, Dietrich KN and Rogan WJ, 2010. Does background postnatal methyl mercury exposure in toddlers affect cognition and behavior? Neurotoxicology, 31, 1-9.

Carbonell G, Bravo JC, Fernandez C and Tarazona JV, 2009. A new method for total mercury and methyl mercury analysis in muscle of seawater fish. Bulletin of Environmental Contamination and Toxicology, 83, 210-213.

Carrasco L, Diez S, Soto DX, Catalan J and Bayona JM, 2008. Assessment of mercury and methylmercury pollution with zebra mussel (Dreissena polymorpha) in the Ebro River (NE Spain) impacted by industrial hazardous dumps. The Science of the Total Environment, 407, 178-184.

Carta P, Flore C, Alinovi R, Ibba A, Tocco MG, Aru G, Carta R, Girei E, Mutti A, Lucchini R and Randaccio FS, 2003. Sub-clinical neurobehavioral abnormalities associated with low level of mercury exposure through fish consumption. Neurotoxicology, 24, 617-623.

Castaño A, Sánchez-Rodríguez JE, Canas A, Esteban M, Navarro C, Rodríguez-García AC, Arribas M, Díaz G and Jiménez-Guerrero JA, 2012. Mercury, lead and cadmium levels in the urine of 170 Spanish adults: a pilot human biomonitoring study. International Journal of Hygiene and Environmental Health, 215, 191-195.

Castoldi AF, Onishchenko N, Johansson C, Coccini T, Roda E, Vahter M, Ceccatelli S and Manzo L, 2008. Neurodevelopmental toxicity of methylmercury: Laboratory animal data and their contribution to human risk assessment. Regulatory Toxicology and Pharmacology, 51, 215-229.

Cava-Montesinos P, Ródenas-Torralba E, Morales-Rubio Á, Luisa Cervera M and de la Guardia M, 2004. Cold vapour atomic fluorescence determination of mercury in milk by slurry sampling using multicommutation. Analytica Chimica Acta, 506, 145-153.

Cebulska-Wasilewska A, Panek A, Zabinski Z, Moszczynski P and Au WW, 2005. Occupational exposure to mercury vapour on genotoxicity and DNA repair. Mutation Research, 586, 102-114.

Ceccatelli S, Dare E and Moors M, 2010. Methylmercury-induced neurotoxicity and apoptosis. Chemico-Biological Interactions, 188, 301-308.

Čejchanová M, Spěvácková V, Kratzer K, Wranová K, Spěvácek V and Beneš B, 2008. Determination of mercury and methylmercury in hair of the Czech children's population. Biological Trace Element Research, 121, 97-105.

CEN (European Committee for Standardization), 2002. EN 13804:2002. Foodstuffs - Determination of trace elements - Performance criteria, general considerations and sample preparation.

CEN (European Committee for Standardization), 2003. EN 13806:2003. Foodstuffs - Determination of trace elements - Determination of total mercury by cold-vapour atomic absorption spectrometry (CVAAS) after pressure digestion.

CEN (European Committee for Standardization), 2010. EN 15763:2010. Foodstuffs - Determination of trace elements - Determination of arsenic, cadmium, mercury and lead in foodstuffs by inductively coupled plasma mass spectrometry (ICP-MS) after pressure digestion.

CEN (European Committee for Standardization), 2012. PR NF EN 13804:2012. Foodstuffs - Determination of elements and their chemical species - General considerations and specific requirements. Available in French and in English at http://www.boutique.afnor.org/NEL5DetailNormeEnLigne.aspx?&nivCtx=NELZNELZ1A10A101A107&aff=1&ts=9607348&CLE_ART=FA175124.

Cernichiari E, Toribara TY, Liang L, Marsh DO, Berlin MW, Myers GJ, Cox C, Shamlaye CF, Choisy O, Davidson P and et al., 1995. The biological monitoring of mercury in the Seychelles study. Neurotoxicology, 16, 613-628.

Chan TY, 2011. Inorganic mercury poisoning associated with skin-lightening cosmetic products. Clinical Toxicology, 49, 886-891.

Chang JW, Pai MC, Chen HL, Guo HR, Su HJ and Lee CC, 2008. Cognitive function and blood methylmercury in adults living near a deserted chloralkali factory. Environmental Research, 108, 334-339.

Chapman L and Chan HM, 2000. The influence of nutrition on methyl mercury intoxication. Environmental Health Perspectives, 108 Suppl 1, 29-56.

Chen C, Qu L, Li B, Xing L, Jia G, Wang T, Gao Y, Zhang P, Li M, Chen W and Chai Z, 2005. Increased oxidative DNA damage, as assessed by urinary 8-hydroxy-2'-deoxyguanosine concentrations, and serum redox status in persons exposed to mercury. Clinical Chemistry, 51, 759-767.

Chen YW and Belzile N, 2010. High performance liquid chromatography coupled to atomic fluorescence spectrometry for the speciation of the hydride and chemical vapour-forming elements As, Se, Sb and Hg: a critical review. Analytica Chimica Acta, 671, 9-26.

Cheng J, Gao L, Zhao W, Liu X, Sakamoto M and Wang W, 2009. Mercury levels in fisherman and their household members in Zhoushan, China: impact of public health. The Science of the Total Environment, 407, 2625-2630.

Cheuk DK and Wong V, 2006. Attention-deficit hyperactivity disorder and blood mercury level: a case-control study in Chinese children. Neuropediatrics, 37, 234-240.

Chevrier C, Sullivan K, White RF, Comtois C, Cordier S and Grandjean P, 2009. Qualitative assessment of visuospatial errors in mercury-exposed Amazonian children. Neurotoxicology, 30, 37-46.

Chicourel EL, Sakuma AM, Zenebon O and Tenuta-Filho A, 2001. Inefficacy of cooking methods on mercury reduction from shark. Archivos Latinoamericanos de Nutricion, 51, 288-292.

Cho GJ, Park HT, Shin JH, Hur JY, Kim SH, Lee KW and Kim T, 2012. The relationship between blood mercury level and osteoporosis in postmenopausal women. Menopause, 19, 576-581.

Choi AL, Weihe P, Budtz-Jorgensen E, Jorgensen PJ, Salonen JT, Tuomainen TP, Murata K, Nielsen HP, Petersen MS, Askham J and Grandjean P, 2009. Methylmercury exposure and adverse cardiovascular effects in Faroese whaling men. Environmental Health Perspectives, 117, 367-372.

Chojnacka K, Mikulewicz M, Michalak I, Saeid A, Grecka H and Górecki H, 2011. Biomonitoring release of elements from water pipes using hair mineral analysis. Polish Journal of Environmental Studies, 20, 1419-1432.

Choy CM, Yeung QS, Briton-Jones CM, Cheung CK, Lam CW and Haines CJ, 2002. Relationship between semen parameters and mercury concentrations in blood and in seminal fluid from subfertile males in Hong Kong. Fertility and Sterility, 78, 426-428.

Christie NT, Cantoni O, Sugiyama M, Cattabeni F and Costa M, 1986. Differences in the effects of Hg(II) on DNA repair induced in Chinese hamster ovary cells by ultraviolet or X-rays. Molecular Pharmacology, 29, 173-178.

Chudzynski K, Jarzynska G, Stefanska A and Falandysz J, 2011. Mercury content and bio-concentration potential of Slippery Jack, Suillus luteus, mushroom. Food Chemistry, 125, 986-990.

Chuu JJ, Hsu CJ and Lin-Shiau SY, 2001. Abnormal auditory brainstem responses for mice treated with mercurial compounds: involvement of excessive nitric oxide. Toxicology, 162, 11-22.

Claisse D, Cossa D, Bretaudeau-Sanjuan J, Touchard G and Bombled B, 2001. Methylmercury in molluscs along the French coast. Marine Pollution Bulletin, 42, 329-332.

Clarkson TW and Magos L, 2006. The toxicology of mercury and its chemical compounds. Critical Reviews in Toxicology, 36, 609-662.

Clarkson TW, 2002. The three modern faces of mercury. Environmental Health Perspectives, 110 Suppl 1, 11-23.

Clémens S, Monperrus M, Donard OF, Amouroux D and Guerin T, 2011. Mercury speciation analysis in seafood by species-specific isotope dilution: method validation and occurrence data. Analytical and Bioanalytical Chemistry, 401, 2699-2711.

Clémens S, Monperrus M, Donard OF, Amouroux D and Guérin T, 2012. Mercury speciation in seafood using isotope dilution analysis: a review. Talanta, 89, 12-20.

Cossa D, Martin JM, Takayanagi K and Sanjuan J, 1997. The distribution and cycling of mercury species in the western Mediterranean. Deep-Sea Research Part II - Topical Studies in Oceanography, 44, 721-740.

Crespo-Lopez ME, Macedo GL, Arrifano GP, Pinheiro Mda C, do Nascimento JL and Herculano AM, 2011. Genotoxicity of mercury: contributing for the analysis of Amazonian populations. Environment International, 37, 136-141.

Crespo-Lopez ME, Macedo GL, Pereira SI, Arrifano GP, Picanco-Diniz DL, do Nascimento JL and Herculano AM, 2009. Mercury and human genotoxicity: critical considerations and possible molecular mechanisms. Pharmacological Research, 60, 212-220.

da Silva MJ, Paim AP, Pimentel MF, Cervera ML and de la Guardia M, 2010. Determination of mercury in rice by cold vapor atomic fluorescence spectrometry after microwave-assisted digestion. Analytica Chimica Acta, 667, 43-48.

Daniels JL, Longnecker MP, Rowland AS, Golding J and Alspac Study Team University of Bristol Institute of Child Health, 2004. Fish intake during pregnancy and early cognitive development of offspring. Epidemiology, 15, 394-402.

Davidson PW, Cory-Slechta DA, Thurston SW, Huang LS, Shamlaye CF, Gunzler D, Watson G, van Wijngaarden E, Zareba G, Klein JD, Clarkson TW, Strain JJ and Myers GJ, 2011. Fish

consumption and prenatal methylmercury exposure: cognitive and behavioral outcomes in the main cohort at 17 years from the Seychelles child development study. Neurotoxicology, 32, 711-717.

Davidson PW, Jean Sloane R, Myers GJ, Hansen ON, Huang LS, Georger LA, Cox C, Thurston SW, Shamlaye CF and Clarkson TW, 2008a. Association between prenatal exposure to methylmercury and visuospatial ability at 10.7 years in the Seychelles Child Development Study. Neurotoxicology, 29, 453-459.

Davidson PW, Leste A, Benstrong E, Burns CM, Valentin J, Sloane-Reeves J, Huang LS, Miller WA, Gunzler D, van Wijngaarden E, Watson GE, Zareba G, Shamlaye CF and Myers GJ, 2010. Fish consumption, mercury exposure, and their associations with scholastic achievement in the Seychelles Child Development Study. Neurotoxicology, 31, 439-447.

Davidson PW, Myers GJ, Cox C, Shamlaye CF, Marsh DO, Tanner MA, Berlin M, Sloane-Reeves J, Cernichiari E, Choisy O, Choi A and Clarkson TW, 1995. Longitudinal neurodevelopmental study of Seychellois children following in utero exposure to methylmercury from maternal fish ingestion: outcomes at 19 and 29 months. Neurotoxicology, 16, 677-688.

Davidson PW, Myers GJ, Cox C, Wilding GE, Shamlaye CF, Huang LS, Cernichiari E, Sloane-Reeves J, Palumbo D and Clarkson TW, 2006a. Methylmercury and neurodevelopment: longitudinal analysis of the Seychelles child development cohort. Neurotoxicology and Teratology, 28, 529-535.

Davidson PW, Myers GJ, Shamlaye C, Cox C and Wilding GE, 2004. Prenatal exposure to methylmercury and child development: influence of social factors. Neurotoxicology and Teratology, 26, 553-559.

Davidson PW, Myers GJ, Weiss B, Shamlaye CF and Cox C, 2006b. Prenatal methyl mercury exposure from fish consumption and child development: a review of evidence and perspectives from the Seychelles Child Development Study. Neurotoxicology, 27, 1106-1109.

Davidson PW, Strain JJ, Myers GJ, Thurston SW, Bonham MP, Shamlaye CF, Stokes-Riner A, Wallace JM, Robson PJ, Duffy EM, Georger LA, Sloane-Reeves J, Cernichiari E, Canfield RL, Cox C, Huang LS, Janciuras J and Clarkson TW, 2008b. Neurodevelopmental effects of maternal nutritional status and exposure to methylmercury from eating fish during pregnancy. Neurotoxicology, 29, 767-775.

Day JJ, Reed MN and Newland MC, 2005. Neuromotor deficits and mercury concentrations in rats exposed to methyl mercury and fish oil. Neurotoxicology and Teratology, 27, 629-641.

de Fonseca MF, Dorea JG, Bastos WR, Marques RC, Torres JP and Malm O, 2008. Poor psychometric scores of children living in isolated riverine and agrarian communities and fish-methylmercury exposure. Neurotoxicology, 29, 1008-1015.

De Palma G, Catalani S, Franco A, Brighenti M and Apostoli P, 2012. Lack of correlation between metallic elements analyzed in hair by ICP-MS and autism. Journal of Autism and Developmental Disorders, 42, 342-353.

Debes F, Budtz-Jorgensen E, Weihe P, White RF and Grandjean P, 2006. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. Neurotoxicology and Teratology, 28, 363-375.

Denny MF and Atchison WD, 1996. Mercurial-induced alterations in neuronal divalent cation homeostasis. Neurotoxicology, 17, 47-61.

Després C, Beuter A, Richer F, Poitras K, Veilleux A, Ayotte P, Dewailly E, Saint-Amour D and Muckle G, 2005. Neuromotor functions in Inuit preschool children exposed to Pb, PCBs, and Hg. Neurotoxicology and Teratology, 27, 245-257.

Di Leo A, Cardellicchio N, Giandomenico S and Spada L, 2010. Mercury and methylmercury contamination in Mytilus galloprovincialis from Taranto Gulf (Ionian Sea, Southern Italy): risk evaluation for consumers. Food and Chemical Toxicology, 48, 3131-3136.

Díez S and Bayona JM, 2008. Determination of Hg and organomercury species following SPME: a review. Talanta, 77, 21-27.

Díez S, Delgado S, Aguilera I, Astray J, Pérez-Gómez B, Torrent M, Sunyer J and Bayona JM, 2009. Prenatal and early childhood exposure to mercury and methylmercury in Spain, a high-fish-consumer country. Archives of Environmental Contamination and Toxicology, 56, 615-622.

Djedjibegovic J, Larssen T, Skrbo A, Marjanovic A and Sober M, 2012. Contents of cadmium, copper, mercury and lead in fish from the Neretva river (Bosnia and Herzegovina) determined by inductively coupled plasma mass spectrometry (ICP-MS). Food Chemistry, 131, 469-476.

Domingo JL, Perello G and Gine Bordonaba J, 2012. Dietary intake of metals by the population of Tarragona County (Catalonia, Spain): results from a duplicate diet study. Biological Trace Element Research, 146, 420-425.

Dórea JG, de Souza JR, Rodrigues P, Ferrari I and Barbosa AC, 2005. Hair mercury (signature of fish consumption) and cardiovascular risk in Munduruku and Kayabi Indians of Amazonia. Environmental Research, 97, 209-219.

Dougherty CP, Henricks Holtz S, Reinert JC, Panyacosit L, Axelrad DA and Woodruff TJ, 2000. Dietary exposures to food contaminants across the United States. Environmental Research, 84, 170-185.

Drouillet-Pinard P, Huel G, Slama R, Forhan A, Sahuquillo J, Goua V, Thiébaugeorges O, Foliguet B, Magnin G, Kaminski M, Cordier S and Charles MA, 2010. Prenatal mercury contamination: relationship with maternal seafood consumption during pregnancy and fetal growth in the 'EDEN mother-child' cohort. British Journal of Nutrition, 104, 1096-1100.

Druet P, Druet E, Potdevin F and Sapin C, 1978. Immune type glomerulonephritis induced by $HgCl_2$ in the Brown Norway rat. Annales d'Immunologie, 129 C, 777-792.

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to mercury and methylmercury in food. The EFSA Journal, 34, 1-14.

EFSA (European Food Safety Authority), 2006. Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment. The EFSA Journal, 438, 1-54.

EFSA (European Food Safety Authority), 2008. Mercury as undesirable substance in animal feed. Scientific Opinion of the Panel on Contaminants in the Food Chain. The EFSA Journal, 654, 1-74.

EFSA (European Food Safety Authority), 2009. Use of the benchmark dose in risk assessment. The EFSA Journal, 1150, 1-72.

EFSA (European Food Safety Authority), 2010. Management of left-censored data in dietary exposure assessment of chemical substances. EFSA Journal, 2010; 8(3):1557, 96 pp.

EFSA (European Food Safety Authority), 2011a. Evaluation of the FoodEx, the food classification system applied to the development of the EFSA Comprehensive European Food Consumption Database. EFSA Journal, 2011; 9(3):1970, 27 pp.

EFSA (European Food Safety Authority), 2011b. Use of the EFSA Comprehensive European Food Consumption Database in exposure assessment. EFSA Journal, 2011; 9(3):2097, 34 pp.

Ekino S, Susa M, Ninomiya T, Imamura K and Kitamura T, 2007. Minamata disease revisited: an update on the acute and chronic manifestations of methyl mercury poisoning. Journal of the Neurological Sciences, 262, 131-144.

Endo T, Haraguchi K, Hotta Y, Hisamichi Y, Lavery S, Dalebout ML and Baker CS, 2005. Total mercury, methyl mercury, and selenium levels in the red meat of small cetaceans sold for human consumption in Japan. Environmental Science and Technology, 39, 5703-5708.

Engström KS, Wennberg M, Strömberg U, Bergdahl IA, Hallmans G, Jansson JH, Lundh T, Norberg M, Rentschler G, Vessby B, Skerfving S and Broberg K, 2011. Evaluation of the impact of genetic polymorphisms in glutathione-related genes on the association between methylmercury or n-3 polyunsaturated long chain fatty acids and risk of myocardial infarction: a case-control study. Environmental Health, 10, 33.

EURL-CEFAO (United States Environmental Protection Agency), 2011. Report of the 14th Proficiency Test. Part A: Third Round on Frozen Fish. Cadmium, Lead, total Arsenic and Mercury, Istituto Superiore di Sanità, 1-59. This report is available at the EURL-CEFAO website - Restricted area.

European Commission 2005a. Communiy Strategy Concerning Mercury. COM (2005) 20 final, 28.01.2005. Available from http://eur-lex.europa.eu/LexUriServ/site/en/com/2005/com2005_0020en01.pdf

European Commission 2005b. Commission Staff working Paper. Annex to the Comunication from the Commission to the Council and the European Parliament on Community Strategy Concerning Mercury. Extended Impact Assessment. COM (2005) 20 final, 28.01.2005. 174 pp.

Evans EH, Day JA, Palmer C, Price WJ, Smith CMM and Tyson JF, 2006. Atomic spectrometry update. Advances in atomic emission, absorption and fluorescence spectrometry, and related techniques. Journal of Analytical Atomic Spectrometry, 21, 592-625.

Ewers U, Boening D, Albrecht J, Rädel R, Peter G and Uthoff T, 2004. Risk assessment of soil contamination in a residential area: the importance and role of human biological monitoring--a case report. Gesundheitswesen, 66, 536-544.

Falcó G, Bocio A, Llobet JM and Domingo JL, 2005. Health risks of dietary intake of environmental pollutants by elite sportsmen and sportswomen. Food and Chemical Toxicology, 43, 1713-1721.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 1972. Evaluation of mercury, lead, cadmium and the food additives amaranth, diethylpyrocarbamate, and octyl gallate. World Health Organization, Geneva. WHO Food Additives Series, 4, 605-683.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2004. Safety evaluation of certain food additives and contaminants. Methylmercury. WHO Food Additives Series, 52, 565-623.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2007. Safety evaluation of certain food additives and contaminants. Methylmercury. WHO Food Additives Series, 58, 269-315.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2011a. Report of the Joint FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption. Rome, Food and Agriculture Organization of the United Nations; Geneva, World Health Organization. WHO Food Additives Series, 50 pp.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2011b. Safety evaluation of certain food additives and contaminants. Methylmercury. WHO Food Additives Series, 63, 605-684.

Farias LA, Favaro DI, Santos JO, Vasconcellos MB, Pessoa A, Aguiar J and Yuyama L, 2010. Cooking process evaluation on mercury content in fish. Acta Amazonica, 40, 741-748.

Farina M, Aschner M and Rocha JB, 2011b. Oxidative stress in MeHg-induced neurotoxicity. Toxicology and Applied Pharmacology, 256, 405-417.

Farina M, Rocha JB and Aschner M, 2011a. Mechanisms of methylmercury-induced neurotoxicity: evidence from experimental studies. Life Sciences, 89, 555-563.

Fauser P, Saarinen K, Aasestad K and Danielssen H, 2011. Emission of mercury, PAHs, dioxins and PCBs related to NFR 3. 86 pp.

Fillion M, Mergler D, Sousa Passos CJ, Larribe F, Lemire M and Guimaraes JR, 2006. A preliminary study of mercury exposure and blood pressure in the Brazilian Amazon. Environmental Health, 5, 29.

Forsyth DS, Casey V, Dabeka RW and McKenzie A, 2004. Methylmercury levels in predatory fish species marketed in Canada. Food Additives & Contaminants, 21, 849-856.

Francesconi KA, 2007. Toxic metal species and food regulations--making a healthy choice. Analyst, 132, 17-20.

Franchi E, Loprieno G, Ballardin M, Petrozzi L and Migliore L, 1994. Cytogenetic monitoring of fishermen with environmental mercury exposure. Mutation Research, 320, 23-29.

Freire C, Ramos R, Lopez-Espinosa MJ, Diez S, Vioque J, Ballester F and Fernandez MF, 2010. Hair mercury levels, fish consumption, and cognitive development in preschool children from Granada, Spain. Environmental Research, 110, 96-104.

Fromme H, Buescher O, Matzen W, Drasch G, Roscher E and Nitschke L, 2011. Indoor air contamination after the breakage of mercury-containing compact fluorescent lamps (CFLs). Gefahrstoffe Reinhaltung der Luft, 71, 215-220.

FSA (Food Standards Agency), 2003. Multi-element survey of infant foods. Food Survey Information Sheet No. 42/03.

FSA (Food Standards Agency), 2006. Survey of metals in weaning foods and formulae for infants. Food Survey Information Sheet No. 17/06 September 2006. Available from http://www.food.gov.uk/multimedia/pdfs/fsis1706.pdf.

FSANZ (Food Standards Australia New Zealand), 2003. 20th Australian Total Diet Study. Available from http://www.foodstandards.gov.au/_srcfiles/Final_20th_Total_Diet_Survey.pdf.

FSANZ (Food Standards Australia New Zealand), 2011. 23rd Australian Total Diet Study. Available from http://www.foodstandards.gov.au/_srcfiles/FSANZ%2023rd%20ATDS_v5.pdf.

Furieri LB, Fioresi M, Junior RF, Bartolome MV, Fernandes AA, Cachofeiro V, Lahera V, Salaices M, Stefanon I and Vassallo DV, 2011b. Exposure to low mercury concentration in vivo impairs myocardial contractile function. Toxicology and Applied Pharmacology, 255, 193-199.

Furieri LB, Galan M, Avendano MS, Garcia-Redondo AB, Aguado A, Martinez S, Cachofeiro V, Bartolome MV, Alonso MJ, Vassallo DV and Salaices M, 2011a. Endothelial dysfunction of rat coronary arteries after exposure to low concentrations of mercury is dependent on reactive oxygen species. British Jornal of Pharmacology, 162, 1819-1831.

Futatsuka M, Kitano T, Shono M, Nagano M, Wakamiya J, Miyamoto K, Ushijima K, Inaoka T, Fukuda Y, Nakagawa M, Arimura K and Osame M, 2005. Long-term follow-up study of health status in population living in methylmercury-polluted area. Environmental Sciences, 12, 239-282.

Gallagher CM and Meliker JR, 2010. Blood and urine cadmium, blood pressure, and hypertension: a systematic review and meta-analysis. Environmental Health Perspectives, 118, 1676-1684.

Gao Y, Yan CH, Tian Y, Wang Y, Xie HF, Zhou X, Yu XD, Yu XG, Tong S, Zhou QX and Shen XM, 2007. Prenatal exposure to mercury and neurobehavioral development of neonates in Zhoushan City, China. Environmental Research, 105, 390-399.

García-Esquinas E, Pérez-Gómez B, Fernández MA, Pérez-Meixeira AM, Gil E, de Paz C, Iriso A, Sanz JC, Astray J, Cisneros M, de Santos A, Asensio A, García-Sagredo JM, García JF, Vioque J, Pollán M, López-Abente G, González MJ, Martínez M, Bohigas PA, Pastor R and Aragonés N, 2011. Mercury, lead and cadmium in human milk in relation to diet, lifestyle habits and sociodemographic variables in Madrid (Spain). Chemosphere, 85, 268-276.

Garrecht M and Austin DW, 2011. The plausibility of a role for mercury in the etiology of autism: a cellular perspective. Toxicological and Environmental Chemistry, 93, 1251-1273.

Geier DA and Geier MR, 2007. A prospective study of mercury toxicity biomarkers in autistic spectrum disorders. Journal of Toxicology and Environmental Health. Part A, 70, 1723-1730.

Geier DA, Audhya T, Kern JK and Geier MR, 2010. Blood mercury levels in autism spectrum disorder: Is there a threshold level? Acta Neurobiologiae Experimentalis (Warsaw), 70, 177-186.

Geier DA, Kern JK and Geier MR, 2009b. A prospective blinded evaluation of urinary porphyrins verses the clinical severity of autism spectrum disorders. Journal of Toxicology and Environmental Health. Part A, 72, 1585-1591.

Geier DA, Kern JK, Garver CR, Adams JB, Audhya T, Nataf R and Geier MR, 2009a. Biomarkers of environmental toxicity and susceptibility in autism. Journal of the Neurological Sciences, 280, 101-108.

Gerstenberger SL, Martinson A and Kramer JL, 2010. An evaluation of mercury concentrations in three brands of canned tuna. Environmental Toxicology and Chemistry, 29, 237-242.

Gibb H, Haver C, Kozlov K, Centeno JA, Jurgenson V, Kolker A, Conko KM, Landa ER and Xu H, 2011. Biomarkers of mercury exposure in two eastern Ukraine cities. Journal of Occupational and Environmental Hygiene, 8, 187-193.

Gibičar D, Horvat M, Nakou S, Sarafidou J and Yager J, 2006. Pilot study of intrauterine exposure to methylmercury in Eastern Aegean islands, Greece. The Science of the Total Environment, 367, 586-595.

Gilbertson M, 2009. Index of congenital Minamata disease in Canadian areas of concern in the Great Lakes: an eco-social epidemiological approach. Journal of Environmental Science and Health. Part C: Environmental Carcinogenesis & Ecotoxicology Reviews, 27, 246-275.

Glover CN, Zheng D, Jayashankar S, Sales GD, Hogstrand C and Lundebye AK, 2009. Methylmercury speciation influences brain gene expression and behavior in gestationally-exposed mice pups. Toxicological Sciences, 110, 389-400.

Goncharov A, Pavuk M, Foushee HR and Carpenter DO, 2011. Blood pressure in relation to concentrations of PCB congeners and chlorinated pesticides. Environmental Health Perspectives, 119, 319-325.

Goullé JP, Saussereau E, Mahieu L, Bouige D, Groenwont S, Guerbet M and Lacroix C, 2009. Application of Inductively Coupled Plasma Mass Spectrometry Multielement Analysis in Fingernail and Toenail as a Biomarker of Metal Exposure. Journal of Analytical Toxicology, 33, 92-98.

Grandjean P and Budtz-Jorgensen E, 2010. An ignored risk factor in toxicology: The total imprecision of exposure assessment. Pure and Applied Chemistry, 82, 383-391.

Grandjean P, Budtz-Jorgensen E, Keiding N and Weihe P, 2004a. Underestimation of risk due to exposure misclassification. International Journal of Occupational Medicine and Environmental Health, 17, 131-136.

Grandjean P, Murata K, Budtz-Jorgensen E and Weihe P, 2004b. Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort. Journal of Pediatrics, 144, 169-176.

Grandjean P, Poulsen LK, Heilmann C, Steuerwald U and Weihe P, 2010b. Allergy and sensitization during childhood associated with prenatal and lactational exposure to marine pollutants. Environmental Health Perspectives, 118, 1429-1433.

Grandjean P, Satoh H, Murata K and Eto K, 2010a. Adverse effects of methylmercury: environmental health research implications. Environmental Health Perspectives, 118, 1137-1145.

Grandjean P, Weihe P, Burse VW, Needham LL, Storr-Hansen E, Heinzow B, Debes F, Murata K, Simonsen H, Ellefsen P, Budtz-Jorgensen E, Keiding N and White RF, 2001. Neurobehavioral

deficits associated with PCB in 7-year-old children prenatally exposed to seafood neurotoxicants. Neurotoxicology and Teratology, 23, 305-317.

Grandjean P, Weihe P, Jorgensen PJ, Clarkson T, Cernichiari E and Videro T, 1992. Impact of maternal seafood diet on fetal exposure to mercury, selenium and lead. Archives of Environmental Health, 47, 185-195.

Grandjean P, Weihe P, Nielsen F, Heinzow B, Debes F and Budtz-Jorgensen E, 2012. Neurobehavioral deficits at age 7 years associated with prenatal exposure to toxicants from maternal seafood diet. Neurotoxicology and Teratology, 34, 466-472.

Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, Murata K, Sorensen N, Dahl R and Jorgensen PJ, 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicology and Teratology, 19, 417-428.

Grotto D, Barcelos GR, Valentini J, Antunes LM, Angeli JP, Garcia SC and Barbosa FJr, 2009a. Low levels of methylmercury induce DNA damage in rats: protective effects of selenium. Archives of Toxicology, 83, 249-254.

Grotto D, de Castro MM, Barcelos GR, Garcia SC and Barbosa FJr, 2009b. Low level and sub-chronic exposure to methylmercury induces hypertension in rats: nitric oxide depletion and oxidative damage as possible mechanisms. Archives of Toxicology, 83, 653-662.

Grotto D, Valentini J, Fillion M, Passos CJ, Garcia SC, Mergler D and Barbosa FJr, 2010. Mercury exposure and oxidative stress in communities of the Brazilian Amazon. The Science of the Total Environment, 408, 806-811.

Grotto D, Valentini J, Serpeloni JM, Monteiro PA, Latorraca EF, de Oliveira RS, Antunes LM, Garcia SC and Barbosa FJr, 2011. Evaluation of toxic effects of a diet containing fish contaminated with methylmercury in rats mimicking the exposure in the Amazon riverside population. Environmental Research, 111, 1074-1082.

Guallar E, Sanz-Gallardo MI, van't Veer P, Bode P, Aro A, Gomez-Aracena J, Kark JD, Riemersma RA, Martin-Moreno JM, Kok FJ and Heavy Metals and Myocardial Infarction Study Group, 2002. Mercury, fish oils, and the risk of myocardial infarction. The New England Journal of Medicine, 347, 1747-1754.

Gundacker C, Frohlich S, Graf-Rohrmeister K, Eibenberger B, Jessenig V, Gicic D, Prinz S, Wittmann KJ, Zeisler H, Vallant B, Pollak A and Husslein P, 2010a. Perinatal lead and mercury exposure in Austria. The Science of the Total Environment, 408, 5744-5749.

Gundacker C, Gencik M and Hengstschlager M, 2010b. The relevance of the individual genetic background for the toxicokinetics of two significant neurodevelopmental toxicants: mercury and lead. Mutation Research, 705, 130-140.

Gundacker C, Komarnicki G, Zodl B, Forster C, Schuster E and Wittmann K, 2006. Whole blood mercury and selenium concentrations in a selected Austrian population: does gender matter? The Science of the Total Environment, 372, 76-86.

Gundacker C, Scheinast M, Damjanovic L, Fuchs C, Rosner M and Hengstschlager M, 2012. Proliferation potential of human amniotic fluid stem cells differently responds to mercury and lead exposure. Amino Acids, 43, 937-949.

Guzman-Mar JL, Hinojosa-Reyes L, Serra AM, Hernandez-Ramirez A and Cerda V, 2011. Applicability of multisyringe chromatography coupled to cold-vapor atomic fluorescence spectrometry for mercury speciation analysis. Analytica Chimica Acta, 708, 11-18.

Ha M, Kwon HJ, Lim MH, Jee YK, Hong YC, Leem JH, Sakong J, Bae JM, Hong SJ, Roh YM and Jo SJ, 2009. Low blood levels of lead and mercury and symptoms of attention deficit hyperactivity in children: a report of the children's health and environment research (CHEER). Neurotoxicology, 30, 31-36.

Hajeb P, Jinap S and Ahmad I, 2010. Biomagnifications of mercury and methylmercury in tuna and mackerel. Environmental Monitoring and Assessment, 171, 205-217.

Hajeb P, Jinap S, Abu Bakar F and Bakar J, 2009a. Optimizing conditions for methylmercury extraction from fish samples for GC analysis using response surface methodology. Food Additives & Contaminants. Part A, 26, 829-838.

Hajeb P, Jinap S, Ismail A, Fatimah AB, Jamilah B and Rahim MA, 2009b. Assessment of mercury level in commonly consumed marine fishes in Malaysia. Food Control, 20, 79-84.

Hallgren CG, Hallmans G, Jansson JH, Marklund SL, Huhtasaari F, Schutz A, Stromberg U, Vessby B and Skerfving S, 2001. Markers of high fish intake are associated with decreased risk of a first myocardial infarction. British Journal of Nutrition, 86, 397-404.

Hansen S, Nieboer E, Sandanger TM, Wilsgaard T, Thomassen Y, Veyhe AS and Odland JO, 2011. Changes in maternal blood concentrations of selected essential and toxic elements during and after pregnancy. Journal of Environmental Monitoring, 13, 2143-2152.

Hansteen IL, Ellingsen DG, Clausen KO and Kjuus H, 1993. Chromosome aberrations in chloralkali workers previously exposed to mercury vapor. Scandinavian Journal of Work, Environment & Health, 19, 375-381.

Harada M, 1995. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. Critical Reviews in Toxicology, 25, 1-24.

Harada Y, Miyamoto Y, Nonaka I, Ohta S and Ninomiya T, 1968. Electroencephalographic studies of Minamata disease in children. Developmental Medicine and Child Neurology, 10, 257-258.

Harris HH, Pickering IJ and George GN, 2003. The chemical form of mercury in fish. Science, 301, 1203.

Hassauer. M, Kaiser. E, Schneider K and Schuhmacher-Wolz U, 2012. Collate the literature on toxicity data on mercury in experimental animals and humans, Part I. Data on organic mercury. Part II – Data on inorganic mercury. External scientific report prepared for EFSA by Forschungs- und Beratungsinstitut Gefahrstoffe GmbH (FoBIG). Supporting Publications 2012:EN-297, 360 pp.

He Q, Zhu Z, Hu S and Jin L, 2011. Solution cathode glow discharge induced vapor generation of mercury and its application to mercury speciation by high performance liquid chromatography-atomic fluorescence spectrometry. Journal of Chromatography. A, 1218, 4462-4467.

Health Canada, 1995. Assessment of mercury exposure and risks from dental amalgam. Prepared by GM Richardson on behalf of the Bureau of Medical Devices, Health Protection Branch Health Canada. 109 pp.

Heilmann C, Budtz-Jorgensen E, Nielsen F, Heinzow B, Weihe P and Grandjean P, 2010. Serum concentrations of antibodies against vaccine toxoids in children exposed perinatally to immunotoxicants. Environmental Health Perspectives, 118, 1434-1438.

Hertz-Picciotto I, Green PG, Delwiche L, Hansen R, Walker C and Pessah IN, 2010. Blood mercury concentrations in CHARGE Study children with and without autism. Environmental Health Perspectives, 118, 161-166.

Hight SC and Cheng J, 2006. Determination of methylmercury and estimation of total mercury in seafood using high performance liquid chromatography (HPLC) and inductively coupled plasma-mass spectrometry (ICP-MS): Method development and validation. Analytica Chimica Acta, 567, 160-172.

Hippler J, Hoppe HW, Mosel F, Rettenmeier AW and Hirner AV, 2009. Comparative determination of methyl mercury in whole blood samples using GC-ICP-MS and GC-MS techniques. Journal of chromatography. B, 877, 2465-2470.

Hirner AV and Rettenmeier AW, 2010. Methylated metal(loid) species in humans. Metal Ions in Life Sciences, 7, 465-521.

Hohenblum P, Steinbichl P, Raffesberg W, Weiss S, Moche W, Vallant B, Scharf S, Haluza D, Moshammer H, Kundi M, Piegler B, Wallner P and Hutter HP, 2012. Pollution gets personal! A first population-based human biomonitoring study in Austria. International Journal of Hygiene and Environmental Health, 215, 176-179.

Holcer JN and Vitale K, 2009. How to set up a public health campaign: Croatian example of environmental mercury exposure. Periodicum Biologorum, 111, 99-105.

Holmes AS, Blaxill MF and Haley BE, 2003. Reduced levels of mercury in first baby haircuts of autistic children. International Journal of Toxicology, 22, 277-285.

Holsbeek L, Das HK and Joiris CR, 1997. Mercury speciation and accumulation in Bangladesh freshwater and anadromous fish. The Science of the Total Environment, 198, 201-210.

Houston MC, 2011. Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. Journal of Clinical Hypertension, 13, 621-627.

Hrubá F, Strömberg U, Černá M, Chen C, Harari F, Harari R, Horvat M, Koppová K, Kos A, Krsková A, Krsnik M, Laamech J, Li YF, Löfmark L, Lundh T, Lundström NG, Lyoussi B, Mazej D, Osredkar J, Pawlas K, Pawlas N, Prokopowicz A, Rentschler G, Spěváčková V, Spiric Z, Tratnik J, Skerfving S and Bergdahl IA, 2012. Blood cadmium, mercury, and lead in children: an international comparison of cities in six European countries, and China, Ecuador, and Morocco. Environment International, 41, 29-34.

Hsiao HW, Ullrich SM and Tanton TW, 2011. Burdens of mercury in residents of Temirtau, Kazakhstan I: hair mercury concentrations and factors of elevated hair mercury levels. Sci Total Environ, 409, 2272-2280.

Huang CF, Hsu CJ, Liu SH and Lin-Shiau SY, 2008. Neurotoxicological mechanism of methylmercury induced by low-dose and long-term exposure in mice: oxidative stress and down-regulated Na+/K(+)-ATPase involved. Toxicology Letters, 176, 188-197.

Huang CF, Liu SH, Hsu CJ and Lin-Shiau SY, 2011. Neurotoxicological effects of low-dose methylmercury and mercuric chloride in developing offspring mice. Toxicology Letters, 201, 196-204.

Huang LS, Cox C, Myers GJ, Davidson PW, Cernichiari E, Shamlaye CF, Sloane-Reeves J and Clarkson TW, 2005. Exploring nonlinear association between prenatal methylmercury exposure from fish consumption and child development: evaluation of the Seychelles Child Development Study nine-year data using semiparametric additive models. Environmental Research, 97, 100-108.

Huang LS, Myers GJ, Davidson PW, Cox C, Xiao F, Thurston SW, Cernichiari E, Shamlaye CF, Sloane-Reeves J, Georger L and Clarkson TW, 2007. Is susceptibility to prenatal methylmercury exposure from fish consumption non-homogeneous? Tree-structured analysis for the Seychelles Child Development Study. Neurotoxicology, 28, 1237-1244.

Huel G, Sahuquillo J, Debotte G, Oury JF and Takser L, 2008. Hair mercury negatively correlates with calcium pump activity in human term newborns and their mothers at delivery. Environmental Health Perspectives, 116, 263-267.

Hunter DJ, Rimm EB, Sacks FM, Stampfer MJ, Colditz GA, Litin LB and Willett WC, 1992. Comparison of measures of fatty acid intake by subcutaneous fat aspirate, food frequency questionnaire, and diet records in a free-living population of United States men. American Journal of Epidemiology, 135, 418-427.

IAEA (International atomic Energy Agency), 2010. World-wide Intercomparison Exercice On the Determination of Trace Elements in IAEA-452 Biota sample. Report No. IAEA/192, IAEA/MEL/83. 1-105.

IMEP 109. Scientific and Technical Reports 2010. Report of the ninth interlaboratory comparison organised by the European Union Reference Laboratory for Heavy Metals in Feed and Food. Total

cadmium, lead, arsenic and mercury as well as methylmercury and inorganic arsenic in seafood. 1-56.

IMEP 110. Scientific and Technical Reports 2010. Report of the tenth interlaboratory comparison organised by the European Union Reference Laboratory for Heavy Metals in Feed and Food. Total arsenic, cadmium, mercury and lead in vegetable food. 1-52.

IMEP 30. JRC Scientific and Technical Reports 2010. Total cadmium, lead, arsenic and mercury as well as methylmercury and inorganic arsenic in seafood. Interlaboratory Comparison Report. 1-70.

Inoue S, Yorifuji T, Tsuda T and Doi H, 2012. Short-term effect of severe exposure to methylmercury on atherosclerotic heart disease and hypertension mortality in Minamata. The Science of the Total Environment, 417-418, 291-293.

Ip P, Wong V, Ho M, Lee J and Wong W, 2004. Mercury exposure in children with autistic spectrum disorder: case-control study. Journal of Child Neurology, 19, 431-434.

Ipolyi I, Massanisso P, Sposato S, Fodor P and Morabito R, 2004. Concentration levels of total and methylmercury in mussel samples collected along the coasts of Sardinia Island (Italy). Analytica Chimica Acta, 505, 145-151.

Jackson B, Taylor V, Baker RA and Miller E, 2009. Low-level mercury speciation in freshwaters by isotope dilution GC-ICP-MS. Environmental Science & Technology, 43, 2463-2469.

Jackson LW, Zullo MD and Goldberg JM, 2008. The association between heavy metals, endometriosis and uterine myomas among premenopausal women: National Health and Nutrition Examination Survey 1999-2002. Human Reproduction, 23, 679-687.

Jagtap R, Krikowa F, Maher W, Foster S and Ellwood M, 2011. Measurement of methyl mercury (I) and mercury (II) in fish tissues and sediments by HPLC-ICPMS and HPLC-HGAAS. Talanta, 85, 49-55.

Janzen R, Schwarzer M, Sperling M, Vogel M, Schwerdtle T and Karst U, 2011. Adduct formation of Thimerosal with human and rat hemoglobin: a study using liquid chromatography coupled to electrospray time-of-flight mass spectrometry (LC/ESI-TOF-MS). Metallomics, 3, 847-852.

Jarosińska D, Horvat M, Sallsten G, Mazzolai B, Dąbkowska B, Prokopowicz A, Biesiada M and Barregård L, 2008. Urinary mercury and biomarkers of early renal dysfunction in environmentally and occupationally exposed adults: a three-country study. Environmental Research, 108, 224-232.

Jarzynska G and Falandysz J, 2011. The determination of mercury in mushrooms by CV-AAS and ICP-AES techniques. Journal of Environmental Science and Health. Part A, 46, 569-573.

Jedrychowski W, Jankowski J, Flak E, Skarupa A, Mroz E, Sochacka-Tatara E, Lisowska-Miszczyk I, Szpanowska-Wohn A, Rauh V, Skolicki Z, Kaim I and Perera F, 2006. Effects of prenatal exposure to mercury on cognitive and psychomotor function in one-year-old infants: epidemiologic cohort study in Poland. Annals of Epidemiology, 16, 439-447.

Jedrychowski W, Perera F, Jankowski J, Rauh V, Flak E, Caldwell KL, Jones RL, Pac A and Lisowska-Miszczyk I, 2007a. Fish consumption in pregnancy, cord blood mercury level and cognitive and psychomotor development of infants followed over the first three years of life: Krakow epidemiologic study. Environment International, 33, 1057-1062.

Jedrychowski W, Perera F, Rauh V, Flak E, Mroz E, Pac A, Skolicki Z and Kaim I, 2007b. Fish intake during pregnancy and mercury level in cord and maternal blood at delivery: an environmental study in Poland. International Journal of Occupational Medicine and Environmental Health, 20, 31-37.

Jenssen MT, Brantsaeter AL, Haugen M, Meltzer HM, Larssen T, Kvalem HE, Birgisdottir BE, Thomassen Y, Ellingsen D, Alexander J and Knutsen HK, 2012. Dietary mercury exposure in a population with a wide range of fish consumption - Self-capture of fish and regional differences are important determinants of mercury in blood. The Science of the Total Environment, 439C, 220-229.

Jewett SC and Duffy LK, 2007. Mercury in fishes of Alaska, with emphasis on subsistence species. The Science of the Total Environment, 387, 3-27.

Jin L, Liang L, Jiang G and Xu Y, 2006. Methylmercury, total mercury and total selenium in four common freshwater fish species from Ya-Er Lake, China. Environmental Geochemistry and Health, 28, 401-407.

Jin X, Hidiroglou N, Lok E, Taylor M, Kapal K, Ross N, Sarafin K, Lau A, De Souza A, Chan HM and Mehta R, 2012. Dietary selenium (Se) and vitamin E (V(E)) supplementation modulated methylmercury-mediated changes in markers of cardiovascular diseases in rats. Cardiovascular Toxicology, 12, 10-24.

Johansson C, Castoldi AF, Onishchenko N, Manzo L, Vahter M and Ceccatelli S, 2007. Neurobehavioural and molecular changes induced by methylmercury exposure during development. Neurotoxicity Research, 11, 241-260.

Joiris CR, Ali IB, Holsbeek L, Kanuya-Kinoti M and Tekele-Michael Y, 1997. Total and organic mercury in Greenland and Barents Seas demersal fish. Bulletin of Environmental Contamination and Toxicology, 58, 101-107.

Joiris CR, Holsbeek L and Otchere FA, 2000. Mercury in the bivalves Crassostrea tulipa and Perna perna from Ghana. Marine Pollution Bulletin, 40, 457-460.

Jorhem L, 2004. Certified reference materials as a quality tool in food control: much used - often misused - sometimes abused. Accreditation and Quality Assurance, 9, 305-310.

Julvez J, Debes F, Weihe P, Choi A and Grandjean P, 2010. Sensitivity of continuous performance test (CPT) at age 14 years to developmental methylmercury exposure. Neurotoxicology and Teratology, 32, 627-632.

Kałużna-Czaplińska J, Socha E, Michalska M and Rynkowski J, 2011. Urinary level of homovanillic acid and mercury in autistic children. Toxicological and Environmental Chemistry, 93, 199-206.

Kannan K, Smith RG, Jr., Lee RF, Windom HL, Heitmuller PT, Macauley JM and Summers JK, 1998. Distribution of total mercury and methyl mercury in water, sediment, and fish from south Florida estuaries. Archives of Environmental Contamination and Toxicology, 34, 109-118.

Karch H, Dobler L, Eckard R, Günsel A, Langel D, Müller A and Organowski M 2011. Umweltprobenbank des Bundes - Teilbank Humanproben und Datenbank. Jahresbericht 2010/11. Westfälische Wilhelms-Universität Münster. 157 pp.

Kaur P, Aschner M and Syversen T, 2011. Biochemical factors modulating cellular neurotoxicity of methylmercury. Journal of Toxicology, 2011, 721987.

Kehrig HA, Costa M, Moreira I and Malm O, 2002. Total and methylmercury in a Brazilian estuary, Rio de Janeiro. Marine Pollution Bulletin, 44, 1018-1023.

Kerin EJ, Gilmour CC, Roden E, Suzuki MT, Coates JD and Mason RP, 2006. Mercury methylation by dissimilatory iron-reducing bacteria. Applied and Environmental Microbiology, 72, 7919-7921.

Kern JK, Geier DA, Adams JB and Geier MR, 2010. A biomarker of mercury body-burden correlated with diagnostic domain specific clinical symptoms of autism spectrum disorder. BioMetals, 23, 1043-1051.

Kern JK, Grannemann BD, Trivedi MH and Adams JB, 2007. Sulfhydryl-reactive metals in autism. Journal of Toxicology and Environmental Health. Part A, 70, 715-721.

Kershaw TG, Clarkson TW and Dhahir PH, 1980. The relationship between blood levels and dose of methylmercury in man. Archives of Environment Health, 35, 28-36.

Khan AT, Atkinson A, Graham TC, Thompson SJ, Ali S and Shireen KF, 2004. Effects of inorganic mercury on reproductive performance of mice. Food and Chemical Toxicology, 42, 571-577.

Kim BM, Lee BE, Hong YC, Park H, Ha M, Kim YJ, Kim Y, Chang N, Kim BN, Oh SY, Yoo M and Ha EH, 2011. Mercury levels in maternal and cord blood and attained weight through the 24 months of life. The Science of the Total Environment, 410-411, 26-33.

Kröger E, Verreault R, Carmichael PH, Lindsay J, Julien P, Dewailly E, Ayotte P and Laurin D, 2009. Omega-3 fatty acids and risk of dementia: the Canadian Study of Health and Aging. American Journal of Clinical Nutrition, 90, 184-192.

Kružiková K, Randák T, Kenšova R, Kroupová H, Leontovyčová D and Svobodová Z, 2008. Mercury and Methylmercury Concentrations in Muscle Tissue of Fish Caught in Major Rivers of the Czech Republic. Acta Veterinaria Brno, 77, 637-643.

Kuballa T, Moellers M, Schoeberl K and Lachenmeier DW, 2011. Survey of methylmercury in fish and seafood from the southwestern German market. European Food Research and Technology, 232, 737-742.

Kuban P, Houserova P, Kuban P, Hauser PC and Kuban V, 2007. Mercury speciation by CE: a review. Electrophoresis, 28, 58-68.

Kuban P, Pelcova P, Margetinova J and Kuban V, 2009. Mercury speciation by CE: an update. Electrophoresis, 30, 92-99.

Lakshmi Priya MD and Geetha A, 2011. Level of trace elements (copper, zinc, magnesium and selenium) and toxic elements (lead and mercury) in the hair and nail of children with autism. Biological Trace Element Research, 142, 148-158.

Landaluze JS, de Diego A, Raposo JC and Madariaga JM, 2004. Methylmercury determination in sediments and fish tissues from the Nerbioi-lbaizabal estuary (Basque Country, Spain). Analytica Chimica Acta, 508, 107-117.

Laurier FJG, Mason RP, Gill GA and Whalin L, 2004. Mercury distributions in the North Pacific Ocean - 20 years of observations. Marine Chemistry, 90, 3-19.

Leblanc JC, Guerin T, Noel L, Calamassi-Tran G, Volatier JL and Verger P, 2005. Dietary exposure estimates of 18 elements from the 1st French Total Diet Study. Food Additives & Contaminants, 22, 624-641.

Lederman SA, Jones RL, Caldwell KL, Rauh V, Sheets SE, Tang D, Viswanathan S, Becker M, Stein JL, Wang RY and Perera FP, 2008. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. Environmental Health Perspectives, 116, 1085-1091.

Lee BE, Hong YC, Park H, Ha M, Koo BS, Chang N, Roh YM, Kim BN, Kim YJ, Kim BM, Jo SJ and Ha EH, 2010. Interaction between GSTM1/GSTT1 polymorphism and blood mercury on birth weight. Environmental Health Perspectives, 118, 437-443.

Lee DH, Lind PM, Jacobs DR, Jr., Salihovic S, van Bavel B and Lind L, 2012. Background exposure to persistent organic pollutants predicts stroke in the elderly. Environment International, 47, 115-120.

Lee HS, Cho YH, Park SO, Kye SH, Kim BH, Hahm TS, Kim M, Lee JO and Kim C, 2006. Dietary exposure of the Korean population to arsenic, cadmium, lead and mercury. Journal of Food Composition and Analysis, 19, S31-S37.

Lemire M, Fillion M, Frenette B, Mayer A, Philibert A, Passos CJ, Guimaraes JR, Barbosa FJ and Mergler D, 2010. Selenium and mercury in the Brazilian Amazon: opposing influences on age-related cataracts. Environmental Health Perspectives, 118, 1584-1589.

Leopold K, Foulkes M and Worsfold P, 2010. Methods for the determination and speciation of mercury in natural waters--a review. Analytica Chimica Acta, 663, 127-138.

Levy LS, Jones K, Cocker J, Assem FL and Capleton AC, 2007. Background levels of key biomarkers of chemical exposure within the UK general population - pilot study. International Journal of Hygiene and Environmental Health, 210, 387-391.

Li Y, Jiang Y and Yan XP, 2006. Probing mercury species-DNA interactions by capillary electrophoresis with on-line electrothermal atomic absorption spectrometric detection. Anal Analytical Chemistry, 78, 6115-6120.

Lim S, Chung HU and Paek D, 2010. Low dose mercury and heart rate variability among community residents nearby to an industrial complex in Korea. Neurotoxicology, 31, 10-16.

Limke TL, Heidemann SR and Atchison WD, 2004. Disruption of intraneuronal divalent cation regulation by methylmercury: are specific targets involved in altered neuronal development and cytotoxicity in methylmercury poisoning? Neurotoxicology, 25, 741-760.

Lindberg A, Bjornberg KA, Vahter M and Berglund M, 2004. Exposure to methylmercury in non-fish-eating people in Sweden. Environmental Research, 96, 28-33.

Lindberg S, Bullock R, Ebinghaus R, Engstrom D, Feng X, Fitzgerald W, Pirrone N, Prestbo E, Seigneur C and Panel on Source Attribution of Atmospheric Mercury, 2007. A synthesis of progress and uncertainties in attributing the sources of mercury in deposition. Ambio, 36, 19-32.

Link B, 1999. Richtwerte für die Innenraumluft - Quecksilber. Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz, 2•99, 168-174.

Link B, Gabrio T, Zöllner I, Jaroni H, Piechotowski I, Schilling B, Felder-Kennel A, Flicker-Klein A, Konig M, Maisner V, Schick KH and Fischer G, 2012. Decrease of internal exposure to chlororganic compounds and heavy metals in children in Baden-Wurttemberg between 1996/1997 and 2008/2009. International Journal of Hygiene and Environmental Health, 215, 196-201.

Liu J, Shi JZ, Yu LM, Goyer RA and Waalkes MP, 2008. Mercury in traditional medicines: is cinnabar toxicologically similar to common mercurials? Experimental Biology and Medicine, 233, 810-817.

Llop S, Guxens M, Murcia M, Lertxundi A, Ramon R, Riaño I, Rebagliato M, Ibarluzea J, Tardon A, Sunyer J, Ballester F and Project I, 2012. Prenatal exposure to mercury and infant neurodevelopment in a multicenter cohort in Spain: study of potential modifiers. American Journal of Epidemiology, 175, 451-465.

Lopez I, Cuello S, Camara C and Madrid Y, 2010. Approach for rapid extraction and speciation of mercury using a microtip ultrasonic probe followed by LC-ICP-MS. Talanta, 82, 594-599.

Lucas M, Dewailly E, Muckle G, Ayotte P, Bruneau S, Gingras S, Rhainds M and Holub BJ, 2004. Gestational age and birth weight in relation to n-3 fatty acids among Inuit (Canada). Lipids, 39, 617-626.

Lukačínová A, Benacka R, Sedlakova E, Lovasova E and Nistiar F, 2012. Multigenerational lifetime low-dose exposure to heavy metals on selected reproductive parameters in rats. Journal of Environmental Science and Health. Part A, 47, 1280-1287.

Lukačínová A, Racz O, Lovasova E and Nistiar F, 2011. Effect of lifetime low dose exposure to heavy metals on selected serum proteins of Wistar rats during three subsequent generations. Ecotoxicology and Environment Safety, 74, 1747-1755.

Lynch ML, Huang LS, Cox C, Strain JJ, Myers GJ, Bonham MP, Shamlaye CF, Stokes-Riner A, Wallace JM, Duffy EM, Clarkson TW and Davidson PW, 2011. Varying coefficient function models to explore interactions between maternal nutritional status and prenatal methylmercury toxicity in the Seychelles Child Development Nutrition Study. Environmental Research, 111, 75-80.

Mabille V, Roels H, Jacquet P, Leonard A and Lauwerys R, 1984. Cytogenetic examination of leucocytes of workers exposed to mercury vapour. International Archives of Occupational and Environmental Health, 53, 257-260.

Madeddu A and Sciacca S, 2008. Biological tracking on the presence of Hg, PCB and HCG in milk and hair of women resident in a region with high incidence of children born with malformation (Augusta). Annali di Igiene, 20, 59-64.

Mahaffey KR, Clickner RP and Bodurow CC, 2004. Blood organic mercury and dietary mercury intake: National Health and Nutrition Examination Survey, 1999 and 2000. Environmental Health Perspectives, 112, 562-570.

Majewska MD, Urbanowicz E, Rok-Bujko P, Namyslowska I and Mierzejewski P, 2010. Age-dependent lower or higher levels of hair mercury in autistic children than in healthy controls. Acta Neurobiologiae Experimentalis, 70, 196-208.

Malliani A, 2000. Principles of Cardiovascular neural Regulation in Health and Disease. Kluwer Academic Press, 222 pp.

Marusczak N, Larose C, Dommergue A, Paquet S, Beaulne JS, Maury-Brachet R, Lucotte M, Nedjai R and Ferrari CP, 2011. Mercury and methylmercury concentrations in high altitude lakes and fish (Arctic charr) from the French Alps related to watershed characteristics. The Science of the Total Environment, 409, 1909-1915.

Mason RP, Rolfhus KR and Fitzgerald WF, 1998. Mercury in the North Atlantic. Marine Chemistry, 61, 37-53.

Maulvault AL, Machado R, Afonso C, Lourenco HM, Nunes ML, Coelho I, Langerholc T and Marques A, 2011. Bioaccessibility of Hg, Cd and As in cooked black scabbard fish and edible crab. Food and Chemical Toxicology, 49, 2808-2815.

Maxson P, 2009. Global mercury supply and trade. Ad hoc open-ended working group to prepare for the intergovernmental negociating committee on mercury. Bankok, Kingdom of Thailand. Available from http://www.chem.unep.ch/mercury/WGprep.1/documents/Overview%20of%20Supply%20-%20Maxson%20presentation_ppt.pdf.

Mazzaron Barcelos GR, de Marco KC, Grotto D, Valentini J, Garcia SC, Leite Braga GU and Barbosa FJr, 2012. Evaluation of glutathione S-transferase GSTM1 and GSTT1 polymorphisms and methylmercury metabolism in an exposed Amazon population. Journal of Toxicology and Environmental Health, Part A, 75, 960-970.

McElwee MK and Freedman JH, 2011. Comparative toxicology of mercurials in Caenorhabditis elegans. Environmental Toxicology and Chemistry, 30, 2135-2141.

McKelvey W, Jeffery N, Clark N, Kass D and Parsons PJ, 2011. Population-based inorganic mercury biomonitoring and the identification of skin care products as a source of exposure in New York City. Environmental Health Perspectives, 119, 203-209.

Melchart D, Köhler W, Linde K, Zilker T, Kremers L, Saller R and Halbach S, 2008. Biomonitoring of mercury in patients with complaints attributed to dental amalgam, healthy amalgam bearers, and amalgam-free subjects: a diagnostic study. Clinical Toxicology, 46, 133-140.

Mergler D, Anderson HA, Chan LH, Mahaffey KR, Murray M, Sakamoto M, Stern AH, Panel on Health R and Toxicological Effects of M, 2007. Methylmercury exposure and health effects in humans: a worldwide concern. Ambio, 36, 3-11.

Merten C, Ferrari P, Bakker M, Boss A, Hearty A, Leclercq C, Lindtner O, Tlustos C, Verger P, Volatier JL and Arcella D, 2011. Methodological characteristics of the national dietary surveys carried out in the European Union as included in the European Food Safety Authority (EFSA) Comprehensive European Food Consumption Database. Food Additives & Contaminants. Part A, 28, 975-995.

Mieiro CL, Pacheco M, Pereira ME and Duarte AC, 2009. Mercury distribution in key tissues of fish (Liza aurata) inhabiting a contaminated estuary-implications for human and ecosystem health risk assessment. Journal of Environmental Monitoring, 11, 1004-1012.

Mikac N, Kwokal Z, Martinčić D and Branica M, 1996. Uptake of mercury species by transplanted mussels Mytilus galloprovincialis under estuarine conditions (Krka river estuary). The Science of the Total Environment, 184, 173-182.

Miklavčič A, Casetta A, Snoj Tratnik J, Mazej D, Krsnik M, Mariuz M, Sofianou K, Spiric Z, Barbone F and Horvat M, in press. Mercury, arsenic and selenium exposure levels in relation to fish consumption in the Mediterranean area. Environmental Research, doi:10.1016/j.envres.2012.1008.1010.

Miklavčič A, Cuderman P, Mazej D, Snoj Tratnik J, Krsnik M, Planinsek P, Osredkar J and Horvat M, 2011b. Biomarkers of low-level mercury exposure through fish consumption in pregnant and lactating Slovenian women. Environmental Research, 111, 1201-1207.

Miklavčič A, Stibilj V, Heath E, Polak T, Tratnik JS, Klavž J, Mazej D and Horvat M, 2011a. Mercury, selenium, PCBs and fatty acids in fresh and canned fish available on the Slovenian market. Food Chemistry, 124, 711-720.

Millour S, Noel L, Kadar A, Chekri R, Vastel C and Guerin T, 2011a. Simultaneous analysis of 21 elements in foodstuffs by ICP-MS after closed-vessel microwave digestion: Method validation. Journal of Food Composition and Analysis, 24, 111-120.

Millour S, Noel L, Kadar A, Chekri R, Vastel C, Sirot V, Leblanc J-C and Guerin T, 2011b. Pb, Hg, Cd, As, Sb and Al levels in foodstuffs from the 2nd French total diet study. Food Chemistry, 126, 1787-1799.

Mishra S, Bhalke S, Saradhi IV, Suseela B, Tripathi RM, Pandit GG and Puranik VD, 2007. Trace metals and organometals in selected marine species and preliminary risk assessment to human beings in Thane Creek area, Mumbai. Chemosphere, 69, 972-978.

Miyake Y, Tanaka K, Yasutake A, Sasaki S and Hirota Y, 2011. Lack of association of mercury with risk of wheeze and eczema in Japanese children: the Osaka Maternal and Child Health Study. Environmental Research, 111, 1180-1184.

Montgomery KS, Mackey J, Thuett K, Ginestra S, Bizon JL and Abbott LC, 2008. Chronic, low-dose prenatal exposure to methylmercury impairs motor and mnemonic function in adult C57/B6 mice. Behavioural Brain Research, 191, 55-61.

Mordukhovich I, Wright RO, Hu H, Amarasiriwardena C, Baccarelli A, Litonjua A, Sparrow D, Vokonas P and Schwartz J, 2012. Associations of toenail arsenic, cadmium, mercury, manganese, and lead with blood pressure in the normative aging study. Environmental Health Perspectives, 120, 98-104.

Morel FMM, Kraepiel AML and Amyot M, 1998. The chemical cycle and bioaccumulation of mercury. Annual Review of Ecology and Systematics, 29, 543-566.

Mori N, Yasutake A, Marumoto M and Hirayama K, 2011. Methylmercury inhibits electron transport chain activity and induces cytochrome c release in cerebellum mitochondria. Journal of Toxicological Sciences, 36, 253-259.

Morton J, Mason HJ, Ritchie KA and White M, 2004. Comparison of hair, nails and urine for biological monitoring of low level inorganic mercury exposure in dental workers. Biomarkers, 9, 47-55.

Mousavi HZ, Asghari A and Shirkhanloo H, 2010. Determination of Hg in water and wastewater samples by CV-AAS following on-line preconcentration with silver trap. Journal of Analytical Chemistry, 65, 935-939.

Mozaffarian D, Shi P, Morris JS, Spiegelman D, Grandjean P, Siscovick DS, Willett WC and Rimm EB, 2011. Mercury exposure and risk of cardiovascular disease in two U.S. cohorts. The New England Journal of Medicine, 364, 1116-1125.

Muñoz O, Bastias JM, Araya M, Morales A, Orellana C, Rebolledo R and Velez D, 2005. Estimation of the dietary intake of cadmium, lead, mercury, and arsenic by the population of Santiago (Chile) using a Total Diet Study. Food and Chemical Toxicology, 43, 1647-1655.

Munthe J, Wängberg I, Rognerud S, Fjeld E, Verta M, Porvari P and Meili M 2007. Mercury in Nordic ecosystems IVL Swedish Environmental Research Institute Ltd. IVL Report B1761. Available from http://www.norden.org/en/nordic-council-of-ministers/councils-of-ministers/nordic-council-of-ministers-for-the-environment-mr-m/institutes-co-operative-bodies-and-working-groups/working-groups/working-group-for-aquatic-ecosystem-aeg/mercury-in-nordic-ecosystems.

Murata K, Dakeishi M, Shimada M and Satoh H, 2007. Assessment of intrauterine methylmercury exposure affecting child development: messages from the newborn. Tohoku Journal of Experimental Medicine, 213, 187-202.

Murata K, Sakamoto M, Nakai K, Dakeishi M, Iwata T, Liu XJ and Satoh H, 2006. Subclinical effects of prenatal methylmercury exposure on cardiac autonomic function in Japanese children. International Archives of Occupational and Environmental Health, 79, 379-386.

Murata K, Sakamoto M, Nakai K, Weihe P, Dakeishi M, Iwata T, Liu XJ, Ohno T, Kurosawa T, Kamiya K and Satoh H, 2004a. Effects of methylmercury on neurodevelopment in Japanese children in relation to the Madeiran study. International Archives of Occupational and Environmental Health, 77, 571-579.

Murata K, Weihe P, Budtz-Jorgensen E, Jorgensen PJ and Grandjean P, 2004b. Delayed brainstem auditory evoked potential latencies in 14-year-old children exposed to methylmercury. Journal of Pediatrics, 144, 177-183.

Musaiger AO and D'Souza R, 2008. The effects of different methods of cooking on proximate, mineral and heavy metal composition of fish and shrimps consumed in the Arabian Gulf. Archivos Latinoamericanos de Nutricion, 58, 103-109.

Mutter J, Naumann J and Guethlin C, 2007. Comments on the article "The toxicology of mercury and its chemical compounds" by Clarkson and Magos (2006). Critical Reviews in Toxicology, 37, 537-549.

Myers GJ, Davidson PW and Strain JJ, 2007. Nutrient and methyl mercury exposure from consuming fish. Journal of Nutrition, 137, 2805-2808.

Myers GJ, Davidson PW, Cox C, Shamlaye CF, Palumbo D, Cernichiari E, Sloane-Reeves J, Wilding GE, Kost J, Huang LS and Clarkson TW, 2003. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study. Lancet, 361, 1686-1692.

Myers GJ, Thurston SW, Pearson AT, Davidson PW, Cox C, Shamlaye CF, Cernichiari E and Clarkson TW, 2009. Postnatal exposure to methyl mercury from fish consumption: a review and new data from the Seychelles Child Development Study. Neurotoxicology, 30, 338-349.

Nakamura M, Yasutake A, Fujimura M, Hachiya N and Marumoto M, 2011. Effect of methylmercury administration on choroid plexus function in rats. Archives of Toxicology, 85, 911-918.

Nardi EP, Evangelista FS, Tormen L, SaintPierre TD, Curtius AJ, de Souza SS and Barbosa F, Jr., 2009. The use of inductively coupled plasma mass spectrometry (ICP-MS) for the determination of toxic and essential elements in different types of food samples. Food Chemistry, 112, 727-732.

Nasreddine L, Hwalla N, El Samad O, LeBlanc JC, Hamze M, Sibiril Y and Parent-Massin D, 2006. Dietary exposure to lead, cadmium, mercury and radionuclides of an adult urban population in Lebanon: a total diet study approach. Food Additives & Contaminants, 23, 579-590.

Nevado JJ, Martin-Doimeadios RC, Krupp EM, Bernardo FJ, Farinas NR, Moreno MJ, Wallace D and Ropero MJ, 2011. Comparison of gas chromatographic hyphenated techniques for mercury speciation analysis. Journal of Chromatography. A, 1218, 4545-4551.

Ni M, Li X, Yin Z, Sidoryk-Wegrzynowicz M, Jiang H, Farina M, Rocha JB, Syversen T and Aschner M, 2011. Comparative study on the response of rat primary astrocytes and microglia to methylmercury toxicity. Glia, 59, 810-820.

Nicolescu R, Petcu C, Cordeanu A, Fabritius K, Schlumpf M, Krebs R, Krämer U and Winneke G, 2010. Environmental exposure to lead, but not other neurotoxic metals, relates to core elements of ADHD in Romanian children: performance and questionnaire data. Environmental Research, 110, 476-483.

Nielsen AB, Davidsen M and Bjerregaard P, 2012. The association between blood pressure and whole blood methylmercury in a cross-sectional study among Inuit in Greenland. Environmental Health, 11, 44.

Ninomiya T, Imamura K, Kuwahata M, Kindaichi M, Susa M and Ekino S, 2005. Reappraisal of somatosensory disorders in methylmercury poisoning. Neurotoxicology and Teratology, 27, 643-653.

Noël L, Chafey C, Testu C, Pinte J, Velge P and Guérin T, 2011a. Contamination levels of lead, cadmium and mercury in imported and domestic lobsters and large crab species consumed in France: Differences between white and brown meat. Journal of Food Composition and Analysis, 24, 368-375.

Noël L, Testu C, Chafey C, Velge P and Guérin T, 2011b. Contamination levels for lead, cadmium and mercury in marine gastropods, echinoderms and tunicates. Food Control, 22, 433-437.

NRC (National Research Council), 2000. Toxicological effects of methylmercury. Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, Commission on Life Sciences, National Research Council. Washington, DC: National Academy Press.

NTP (National Toxicology Program), 1993. Toxicology and carcinogenesis studies of mercuric chloride (CAS n° 7487-94-7) in F344/N rats and B6C3F mice (feed studies) U.S. Technical Report Series n°345. Department of Health and Human Services. Research Triangle Park. Available from http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr408.pdf.

Nyland JF, Wang SB, Shirley DL, Santos EO, Ventura AM, de Souza JM and Silbergeld EK, 2011. Fetal and maternal immune responses to methylmercury exposure: a cross-sectional study. Environmental Research, 111, 584-589.

Ohno T, Sakamoto M, Kurosawa T, Dakeishi M, Iwata T and Murata K, 2007. Total mercury levels in hair, toenail, and urine among women free from occupational exposure and their relations to renal tubular function. Environmental Research, 103, 191-197.

Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, Hu H and Gillman MW, 2008. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. American Journal of Epidemiology, 167, 1171-1181.

Oken E, Wright RO, Kleinman KP, Bellinger D, Amarasiriwardena CJ, Hu H, Rich-Edwards JW and Gillman MW, 2005. Maternal fish consumption, hair mercury, and infant cognition in a U.S. Cohort. Environmental Health Perspectives, 113, 1376-1380.

Olsén L, Lind PM and Lind L, 2012. Gender differences for associations between circulating levels of metals and coronary risk in the elderly. International Journal of Hygiene and Environmental Health, 215, 411-417.

Onishchenko N, Karpova N, Sabri F, Castren E and Ceccatelli S, 2008. Long-lasting depression-like behavior and epigenetic changes of BDNF gene expression induced by perinatal exposure to methylmercury. Journal of Neurochemistry, 106, 1378-1387.

Onishchenko N, Spulber S and Ceccatelli S, 2012. Behavioural effects of exposure to methylmercury during early development. In: Methylmercury and Neurotoxicity. Eds Ceccatelli S and Aschner M. Springer, New York Dordrecht Heidelberg London, 163-198.

Ortega-Garcia JA, Rodriguez K, Calatayud M, Martin M, Velez D, Devesa V, Sanchez-Alarcon MC, Torres Cantero AM, Galindo-Cascales C, Gil-Vazquez JM, Sanchez-Sauco MF, Sanchez-Solis M, Alfonso-Marsilla B and Romero-Braquehais F, 2009. Estimated intake levels of methylmercury in children, childbearing age and pregnant women in a Mediterranean region, Murcia, Spain. European Journal of Pediatrics, 168, 1075-1080.

Ouédraogo O and Amyot M, 2011. Effects of various cooking methods and food components on bioaccessibility of mercury from fish. Environmental Research, 111, 1064-1069.

Oyama Y, Yamazaki Y, Okada Y, Takahama K, Satoh M and Hayashi H, 2000. Toxicity of methylmercury conjugated with L-cysteine on rat thymocytes and human leukemia K562 cells in comparison with that of methylmercury chloride. Environmental Toxicology and Pharmacology, 9, 49-55.

Pacyna EG, Pacyna JM, Steenhuisen F and Wilson S, 2006. Global anthropogenic mercury emission inventory for 2000. Atmospheric Environment, 40, 4048-4063.

Pacyna EG, Pacyna JM, Sundseth K, Munthe J, Kindbom K, Wilson S, Steenhuisen F and Maxson P, 2010. Global emission of mercury to the atmosphere from anthropogenic sources in 2005 and projections to 2020. Atmospheric Environment, 44, 2487-2499.

Pacyna JM, Pacyna EG and Aas W, 2009. Changes of emissions and atmospheric deposition of mercury, lead, and cadmium. Atmospheric Environment, 43, 117-127.

Paletz EM, Craig-Schmidt MC and Newland MC, 2006. Gestational exposure to methylmercury and n-3 fatty acids: effects on high- and low-rate operant behavior in adulthood. Neurotoxicology and Teratology, 28, 59-73.

Palkovicova L, Ursinyova M, Masanova V, Yu Z and Hertz-Picciotto I, 2008. Maternal amalgam dental fillings as the source of mercury exposure in developing fetus and newborn. Journal of Exposure Science and Environmental Epidemiology, 18, 326-331.

Palkovicova L, Ursinyova M, Masanova V, Yu Z and Hertz-Picciotto I, 2008. Maternal amalgam dental fillings as the source of mercury exposure in developing fetus and newborn. Journal of Exposure Science and Environmental Epidemiology, 18, 326-331.

Palmer RF, Blanchard S, Stein Z, Mandell D and Miller C, 2006. Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas. Health & Place, 12, 203-209.

Park H and Kim K, 2011. Association of blood mercury concentrations with atopic dermatitis in adults: a population-based study in Korea. Environmental Research, 111, 573-578.

Park SB, Choi SW and Nam AY, 2009. Hair tissue mineral analysis and metabolic syndrome. Biological Trace Element Research, 130, 218-228.

Passos CJ, Mergler D, Lemire M, Fillion M and Guimaraes JR, 2007. Fish consumption and bioindicators of inorganic mercury exposure. The Science of the Total Environment, 373, 68-76.

Pedersen EB, Jørgensen ME, Pedersen MB, Siggaard C, Sørensen TB, Mulvad G, Hansen JC, Asmund G and Skjoldborg H, 2005. Relationship between mercury in blood and 24-h ambulatory blood pressure in Greenlanders and Danes. American Journal of Hypertension, 18, 612-618.

Pereiro IR and Diaz AC, 2002. Speciation of mercury, tin, and lead compounds by gas chromatography with microwave-induced plasma and atomic-emission detection (GC-MIP-AED). Analytical and Bioanalytical Chemistry, 372, 74-90.

Perelló G, Marti-Cid R, Llobet JM and Domingo JL, 2008. Effects of various cooking processes on the concentrations of arsenic, cadmium, mercury, and lead in foods. Journal of Agricultural and Food Chemistry, 56, 11262-11269.

Phelps RW, Clarkson TW, Kershaw TG and Wheatley B, 1980. Interrelationships of blood and hair mercury concentrations in a North American population exposed to methylmercury. Archives of Environmental Health, 35, 161-168.

Philibert A, Bouchard M and Mergler D, 2008. Neuropsychiatric symptoms, omega-3, and mercury exposure in freshwater fish-eaters. Archives of Environmental & Occupational Health, 63, 143-153.

Pinheiro MC, Macchi BM, Vieira JL, Oikawa T, Amoras WW, Guimaraes GA, Costa CA, Crespo-Lopez ME, Herculano AM, Silveira LC and do Nascimento JL, 2008. Mercury exposure and antioxidant defenses in women: a comparative study in the Amazon. Environmental Research, 107, 53-59.

Plusquellec P, Muckle G, Dewailly E, Ayotte P, Begin G, Desrosiers C, Despres C, Saint-Amour D and Poitras K, 2010. The relation of environmental contaminants exposure to behavioral indicators in Inuit preschoolers in Arctic Quebec. Neurotoxicology, 31, 17-25.

Pollack AZ, Schisterman EF, Goldman LR, Mumford SL, Albert PS, Jones RL and Wactawski-Wende J, 2011. Cadmium, lead, and mercury in relation to reproductive hormones and anovulation in premenopausal women. Environmental Health Perspectives, 119, 1156-1161.

Popescu HI, Negru L and Lancranjan I, 1979. Chromosome aberrations induced by occupational exposure to mercury. Archives of Environmental Health, 34, 461-463.

Pouzaud F, Ibbou A, Blanchemanche S, Grandjean P, Krempf M, Philippe HJ and Verger P, 2010. Use of advanced cluster analysis to characterize fish consumption patterns and methylmercury dietary exposures from fish and other sea foods among pregnant women. Journal of Exposure Science & Environmental Epidemiology, 20, 54-68.

Puklová V, Krsková A, Černá M, Čejchanová M, Řehůřková I, Ruprich J, Kratzer K, Kubínová R and Zimová M, 2010. The mercury burden of the Czech population: An integrated approach. International Journal of Hygiene and Environmental Health, 213, 243-251.

Qiu G, Feng X, Li P, Wang S, Li G, Shang L and Fu X, 2008. Methylmercury accumulation in rice (Oryza sativa L.) grown at abandoned mercury mines in Guizhou, China. Journal of Agricultural and Food Chemistry, 56, 2465-2468.

Qiu G, Feng X, Wang S, Fu X and Shang L, 2009. Mercury distribution and speciation in water and fish from abandoned Hg mines in Wanshan, Guizhou province, China. The Science of the Total Environment, 407, 5162-5168.

Ralston NV and Raymond LJ, 2010. Dietary selenium's protective effects against methylmercury toxicity. Toxicology, 278, 112-123.Ramón R, Ballester F, Aguinagalde X, Amurrio A, Vioque J, Lacasana M, Rebagliato M, Murcia M and Iniguez C, 2009. Fish consumption during pregnancy, prenatal mercury exposure, and anthropometric measures at birth in a prospective mother-infant cohort study in Spain. American Journal of Clinical Nutrition, 90, 1047-1055.

Ramon R, Ballester F, Aguinagalde X, Amurrio A, Vioque J, Lacasana M, Rebagliato M, Murcia M and Iniguez C, 2009. Fish consumption during pregnancy, prenatal mercury exposure, and anthropometric measures at birth in a prospective mother-infant cohort study in Spain. American Journal of Clinical Nutrition, 90, 1047-1055.

Ramón R, Murcia M, Aguinagalde X, Amurrio A, Llop S, Ibarluzea J, Lertxundi A, Alvarez-Pedrerol M, Casas M, Vioque J, Sunyer J, Tardon A, Martinez-Arguelles B and Ballester F, 2011. Prenatal mercury exposure in a multicenter cohort study in Spain. Environment International, 37, 597-604.

Rees JR, Sturup S, Chen C, Folt C and Karagas MR, 2007. Toenail mercury and dietary fish consumption. Journal of exposure science & environmental epidemiology, 17, 25-30.

Reis MF, Sampaio C, Brantes A, Aniceto P, Melim M, Cardoso L, Gabriel C, Simão F and Miguel JP, 2007. Human exposure to heavy metals in the vicinity of Portuguese solid waste incinerators - Part

1: biomonitoring of Pb, Cd and Hg in blood of the general population. International Journal of Hygiene and Environmental Health, 210, 439-446.

Richardson GM, Wilson R, Allard D, Purtill C, Douma S and Graviere J, 2011. Mercury exposure and risks from dental amalgam in the US population, post-2000. The Science of the Total Environment, 409, 4257-4268.

Rignell-Hydbom A, Axmon A, Lundh T, Jönsson BA, Tiido T and Spano M, 2007. Dietary exposure to methyl mercury and PCB and the associations with semen parameters among Swedish fishermen. Environmental Health, 6, 14.

Ritchie KA, Burke FJ, Gilmour WH, Macdonald EB, Dale IM, Hamilton RM, McGowan DA, Binnie V, Collington D and Hammersley R, 2004. Mercury vapour levels in dental practices and body mercury levels of dentists and controls. British Dental Journal, 197, 625-632; discussion 621.

Ritchie KA, Gilmour WH, Macdonald EB, Burke FJ, McGowan DA, Dale IM, Hammersley R, Hamilton RM, Binnie V and Collington D, 2002. Health and neuropsychological functioning of dentists exposed to mercury. Occupational and Environmental Medicine, 59, 287-293.

Rodrigues JL, de Souza SS, de Oliveira Souza VC and Barbosa FJr, 2010a. Methylmercury and inorganic mercury determination in blood by using liquid chromatography with inductively coupled plasma mass spectrometry and a fast sample preparation procedure. Talanta, 80, 1158-1163.

Rodrigues JL, Serpeloni JM, Batista BL, Souza SS and Barbosa FJr, 2010b. Identification and distribution of mercury species in rat tissues following administration of thimerosal or methylmercury. Archives of Toxicology, 84, 891-896.

Roman HA, Walsh TL, Coull BA, Dewailly E, Guallar E, Hattis D, Marien K, Schwartz J, Stern AH, Virtanen JK and Rice G, 2011. Evaluation of the cardiovascular effects of methylmercury exposures: current evidence supports development of a dose-response function for regulatory benefits analysis. Environmental Health Perspectives, 119, 607-614.

Roos DH, Puntel RL, Lugokenski TH, Ineu RP, Bohrer D, Burger ME, Franco JL, Farina M, Aschner M, Rocha JB and de Vargas Barbosa NB, 2010. Complex methylmercury-cysteine alters mercury accumulation in different tissues of mice. Basic & Clinical Pharmacology & Toxicology, 107, 789-792.

Rose M, Baxter M, Brereton N and Baskaran C, 2010. Dietary exposure to metals and other elements in the 2006 UK Total Diet Study and some trends over the last 30 years. Food Additives & Contaminants. Part A, 27, 1380-1404.

Rubio C, Gutierrez A, Burgos A and Hardisson A, 2008. Total dietary intake of mercury in the Canary Islands, Spain. Food Addit Contam Part A Chem Anal Control Expo Risk Assess, 25, 946-952.

Sagiv SK, Thurston SW, Bellinger DC, Amarasiriwardena C and Korrick SA, 2012. Prenatal Exposure to Mercury and Fish Consumption During Pregnancy and Attention-Deficit/Hyperactivity Disorder-Related Behavior in Children. Archives of Pediatrics & Adolescent Medicine, 1-9.

Sahuquillo I, Lagarda MJ, Silvestre MD and Farre R, 2007. Methylmercury determination in fish and seafood products and estimated daily intake for the Spanish population. Food Additives & Contaminants, 24, 869-876.

Saint-Amour D, Roy MS, Bastien C, Ayotte P, Dewailly E, Despres C, Gingras S and Muckle G, 2006. Alterations of visual evoked potentials in preschool Inuit children exposed to methylmercury and polychlorinated biphenyls from a marine diet. Neurotoxicology, 27, 567-578.

Sakamoto M, Chan HM, Domingo JL, Kawakami S and Murata K, 2012. Mercury and docosahexaenoic acid levels in maternal and cord blood in relation to segmental maternal hair mercury concentrations at parturition. Environment International, 44, 112-117.

Sakamoto M, Kaneoka T, Murata K, Nakai K, Satoh H and Akagi H, 2007. Correlations between mercury concentrations in umbilical cord tissue and other biomarkers of fetal exposure to methylmercury in the Japanese population. Environmental Research, 103, 106-111.

Sakamoto M, Kubota M, Liu XJ, Murata K, Nakai K and Satoh H, 2004. Maternal and fetal mercury and n-3 polyunsaturated fatty acids as a risk and benefit of fish consumption to fetus. Environmental Science & Technology, 38, 3860-3863.

Sakamoto M, Kubota M, Murata K, Nakai K, Sonoda I and Satoh H, 2008. Changes in mercury concentrations of segmental maternal hair during gestation and their correlations with other biomarkers of fetal exposure to methylmercury in the Japanese population. Environmental Research, 106, 270-276.

Sakamoto M, Murata K, Kubota M, Nakai K and Satoh H, 2010. Mercury and heavy metal profiles of maternal and umbilical cord RBCs in Japanese population. Ecotoxicology and Environment Safety, 73, 1-6.

Salonen JT, Seppanen K, Lakka TA, Salonen R and Kaplan GA, 2000. Mercury accumulation and accelerated progression of carotid atherosclerosis: a population-based prospective 4-year follow-up study in men in eastern Finland. Atherosclerosis, 148, 265-273.

Salonen JT, Seppanen K, Nyyssonen K, Korpela H, Kauhanen J, Kantola M, Tuomilehto J, Esterbauer H, Tatzber F and Salonen R, 1995. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in eastern Finnish men. Circulation, 91, 645-655.

Salthammer T, Uhde E, Omelan A, Luedecke A and Moriske HJ, 2012. Estimating human indoor exposure to elemental mercury from broken compact fluorescent lamps (CFLs). Indoor Air, 22, 289-298.

Sanchez-Rodas D, Corns WT, Chen B and Stockwell PB, 2010. Atomic Fluorescence Spectrometry: a suitable detection technique in speciation studies for arsenic, selenium, antimony and mercury. Journal of Analytical Atomic Spectrometry, 25, 933-946.

Sanzo JM, Dorronsoro M, Amiano P, Amurrio A, Aguinagalde FX, Azpiri MA and EPIC Group of Spain, 2001. Estimation and validation of mercury intake associated with fish consumption in an EPIC cohort of Spain. Public Health Nutrition, 4, 981-988.

Sardans J, Montes F and Penuelas J, 2010. Determination of As, Cd, Cu, Hg and Pb in biological samples by modern electrothermal atomic absorption spectrometry. Spectrochimica Acta. Part B, 65, 97-112.

Schlüter K, 2000. Review: evaporation of mercury from soils. An integration and synthesis of current knowledge. Environmental Geology, 39, 249-271.

Schober SE, Sinks TH, Jones RL, Bolger PM, McDowell M, Osterloh J, Garrett ES, Canady RA, Dillon CF, Sun Y, Joseph CB and Mahaffey KR, 2003. Blood mercury levels in US children and women of childbearing age, 1999-2000. JAMA: the Journal of the American Medical Association, 289, 1667-1674.

Schulz C, Conrad A, Becker K, Kolossa-Gehring M, Seiwert M and Seifert B, 2007. Twenty years of the German Environmental Survey (GerES): human biomonitoring--temporal and spatial (West Germany/East Germany) differences in population exposure. International Journal of Hygiene and Environmental Health, 210, 271-297.

Selin NE, 2009. Global Biogeochemical Cycling of Mercury: A Review. In: Annual Review of Environment and Resources. 43-63.

Senila M, Levei E, Senila L, Cadar O, Oprea G and Roman C, 2011. Comparative study of mercury determination in soil and vegetable by methods based on thermal decomposition-AAS and wet digestion CV-AFS. Studia Universitatis Babes-Bolyai Chemia, 56, 27-34.

Sherwani SI, Pabon S, Patel RB, Sayyid MM, Hagele T, Kotha SR, Magalang UJ, Maddipati KR and Parinandi NL, 2011. Eicosanoid Signaling and Vascular Dysfunction: Methylmercury-Induced Phospholipase D Activation in Vascular Endothelial Cells. Cell Biochemistry and Biophysics, doi:10.1007/s12013-12011-19304-12013.

Sirot V, Guérin T, Mauras Y, Garraud H, Volatier JL and Leblanc JC, 2008. Methylmercury exposure assessment using dietary and biomarker data among frequent seafood consumers in France CALIPSO study. Environmental Research, 107, 30-38.

Slowey AJ and Brown GE, Jr., 2007. Transformations of mercury, iron, and sulfur during the reductive dissolution of iron oxyhydroxide by sulfide. Geochimica et Cosmochimica Acta, 71, 877-894.

Smart ER, 1986. Mercury vapour levels in a domestic environment following breakage of a clinical thermometer. The Science of the Total Environment, 57, 99-103.

Spada L, Annicchiarico C, Cardellicchio N, Giandomenico S and Di Leo A, 2012. Mercury and methylmercury concentrations in Mediterranean seafood and surface sediments, intake evaluation and risk for consumers. International Journal of Hygiene and Environmental Health, 215, 418-426.

Sprovieri F, Pirrone N, Ebinghaus R, Kock H and Dommergue A, 2010. A review of worldwide atmospheric mercury measurements. Atmospheric Chemistry and Physics, 10, 8245-8265.

Stein ED, Cohen Y and Winer AM, 1996. Environmental distribution and transformation of mercury compounds. Critical Reviews in Environmental Science and Technology, 26, 1-43.

Stern AH and Smith AE, 2003. An assessment of the cord blood:maternal blood methylmercury ratio: implications for risk assessment. Environmental Health Perspectives, 111, 1465-1470.

Stern AH, 2005. A revised probabilistic estimate of the maternal methyl mercury intake dose corresponding to a measured cord blood mercury concentration. Environmental Health Perspectives, 113, 155-163.

Steuerwald U, Weihe P, Jorgensen PJ, Bjerve K, Brock J, Heinzow B, Budtz-Jorgensen E and Grandjean P, 2000. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. Journal of Pediatrics, 136, 599-605.

Stewart PW, Reihman J, Lonky EI, Darvill TJ and Pagano J, 2003. Cognitive development in preschool children prenatally exposed to PCBs and MeHg. Neurotoxicology and Teratology, 25, 11-22.

Stewart PW, Sargent DM, Reihman J, Gump BB, Lonky E, Darvill T, Hicks H and Pagano J, 2006. Response inhibition during Differential Reinforcement of Low Rates (DRL) schedules may be sensitive to low-level polychlorinated biphenyl, methylmercury, and lead exposure in children. Environmental Health Perspectives, 114, 1923-1929.

Stokes-Riner A, Thurston SW, Myers GJ, Duffy EM, Wallace J, Bonham M, Robson P, Shamlaye CF, Strain JJ, Watson G and Davidson PW, 2011. A longitudinal analysis of prenatal exposure to methylmercury and fatty acids in the Seychelles. Neurotoxicology and Teratology, 33, 325-328.

Storelli MM, 2008. Potential human health risks from metals (Hg, Cd, and Pb) and polychlorinated biphenyls (PCBs) via seafood consumption: estimation of target hazard quotients (THQs) and toxic equivalents (TEQs). Food and Chemical Toxicology, 46, 2782-2788.

Storelli MM, Barone G, Cuttone G, Giungato D and Garofalo R, 2010b. Occurrence of toxic metals (Hg, Cd and Pb) in fresh and canned tuna: public health implications. Food and Chemical Toxicology, 48, 3167-3170.

Storelli MM, Garofalo R, Giungato D and Giacominelli-Stuffler R, 2010a. Intake of essential and non-essential elements from consumption of octopus, cuttlefish and squid. Food Additives & Contaminants. Part B, 3, 14-18.

Storelli MM, Giachi L, Giungato D and Storelli A, 2011. Occurrence of heavy metals (Hg, Cd, and Pb) and polychlorinated biphenyls in salted anchovies. Journal of Food Protection, 74, 796-800.

Storelli MM, Giacominelli-Stuffler R and Marcotrigiano G, 200a2. Mercury accumulation and speciation in muscle tissue of different species of sharks from Mediterranean Sea, Italy. Bulletin of Environmental Contamination and Toxicology, 68, 201-210.

Storelli MM, Giacominelli-Stuffler R and Marcotrigiano GO, 2002b. Total and methylmercury residues in cartilaginous fish from Mediterranean Sea. Marine Pollution Bulletin, 44, 1354-1358.

Storelli MM, Giacominelli-Stuffler R, Storelli A, D'Addabbo R, Palermo C and Marcotrigiano GO, 2003. Survey of total mercury and methylmercury levels in edible fish from the Adriatic Sea. Food Additives and Contaminants, 20, 1114-1119.

Storelli MM, Storelli A, Giacominelli-Stuffler R and Marcotrigiano GO, 2005. Mercury speciation in the muscle of two commercially important fish, hake (Merluccius merluccius) and striped mullet (Mullus barbatus) from the Mediterranean sea: estimated weekly intake. Food Chemistry, 89, 295-300.

Strain JJ, Davidson PW, Bonham MP, Duffy EM, Stokes-Riner A, Thurston SW, Wallace JM, Robson PJ, Shamlaye CF, Georger LA, Sloane-Reeves J, Cernichiari E, Canfield RL, Cox C, Huang LS, Janciuras J, Myers GJ and Clarkson TW, 2008. Associations of maternal long-chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. Neurotoxicology, 29, 776-782.

Strain JJ, Davidson PW, Thurston SW, Harrington D, Mulhern MS, McAfee AJ, van Wijngaarden E, Shamlaye CF, Henderson J, Watson GE, Zareba G, Cory-Slechta DA, Lynch M, Wallace JM, McSorley EM, Bonham MP, Stokes-Riner A, Sloane-Reeves J, Janciuras J, Wong R, Clarkson TW and Myers GJ, 2012. Maternal PUFA Status but Not Prenatal Methylmercury Exposure Is Associated with Children's Language Functions at Age Five Years in the Seychelles. Journal of Nutrition, 142, 1943-1949.

Strom S, Helmfrid I, Glynn A and Berglund M, 2011. Nutritional and toxicological aspects of seafood consumption--an integrated exposure and risk assessment of methylmercury and polyunsaturated fatty acids. Environmental Research, 111, 274-280.

Suda I and Hirayama K, 1992. Degradation of methyl and ethyl mercury into inorganic mercury by hydroxyl radical produced from rat liver microsomes. Archives of Toxicology, 66, 398-402.

Sun J, Wang C, Song X, Wu Y, Yuan B and Liu P, 2011. Dietary intake of mercury by children and adults in Jinhu area of China. International Journal of Hygiene and Environmental Health, 214, 246-250.

Surkan PJ, Wypij D, Trachtenberg F, Daniel DB, Barregard L, McKinlay S and Bellinger DC, 2009. Neuropsychological function in school-age children with low mercury exposures. Environmental Research, 109, 728-733.

Suzuki K, Nakai K, Sugawara T, Nakamura T, Ohba T, Shimada M, Hosokawa T, Okamura K, Sakai T, Kurokawa N, Murata K, Satoh C and Satoh H, 2010. Neurobehavioral effects of prenatal exposure to methylmercury and PCBs, and seafood intake: neonatal behavioral assessment scale results of Tohoku study of child development. Environmental Research, 110, 699-704.

Syversen T and Kaur P, 2012. The toxicology of mercury and its compounds. Journal of Trace Elements in Medicine and Biology, doi:10.1016/j.jtemb.2012.1002.1004.

Takeuchi T, Eto K and Tokunaga H, 1989. Mercury level and histochemical distribution in a human brain with Minamata disease following a long-term clinical course of twenty-six years. Neurotoxicology, 10, 651-657.

Tamm C, Duckworth J, Hermanson O and Ceccatelli S, 2006. High susceptibility of neural stem cells to methylmercury toxicity: effects on cell survival and neuronal differentiation. Journal of Neurochemistry, 97, 69-78.

Tamm C, Duckworth JK, Hermanson O and Ceccatelli S, 2008. Methylmercury inhibits differentiation of rat neural stem cells via Notch signalling. Neuroreport, 19, 339-343.

Tang ASP, Kwong KP, Chung SWC, Ho YY and Xiao Y, 2009. Dietary exposure of Hong Kong secondary school students to total mercury and methylmercury from fish intake. Food Additives & Contaminants. Part B, 2, 8-14.

Tavares LM, Camara VM, Malm O and Santos EC, 2005. Performance on neurological development tests by riverine children with moderate mercury exposure in Amazonia, Brazil. Cadernos de Saude Publica, 21, 1160-1167.

Thurston SW, Bovet P, Myers GJ, Davidson PW, Georger LA, Shamlaye C and Clarkson TW, 2007. Does prenatal methylmercury exposure from fish consumption affect blood pressure in childhood? Neurotoxicology, 28, 924-930.

Thurston SW, Ruppert D and Davidson PW, 2009. Bayesian models for multiple outcomes nested in domains. Biometrics, 65, 1078-1086.

Tonk EC, de Groot DM, Penninks AH, Waalkens-Berendsen ID, Wolterbeek AP, Slob W, Piersma AH and van Loveren H, 2010. Developmental immunotoxicity of methylmercury: the relative sensitivity of developmental and immune parameters. Toxicological Sciences, 117, 325-335.

Torrente M, Colomina MT and Domingo JL, 2005. Metal concentrations in hair and cognitive assessment in an adolescent population. Biological Trace Element Research, 104, 215-221.

Torres DP, Frescura VLA and Curtius AJ, 2009. Simple mercury fractionation in biological samples by CV AAS following microwave-assisted acid digestion or TMAH pre-treatment. Microchemical Journal, 93, 206-210.

Torres-Escribano S, Ruiz A, Barrios L, Velez D and Montoro R, 2011. Influence of mercury bioaccessibility on exposure assessment associated with consumption of cooked predatory fish in Spain. Journal of the Science of Food and Agriculture, 91, 981-986.

Uchino M, Hirano T, Satoh H, Arimura K, Nakagawa M and Wakamiya J, 2005. The severity of Minamata disease declined in 25 years: temporal profile of the neurological findings analyzed by multiple logistic regression model. Tohoku Journal of Experimental Medicine, 205, 53-63.

Ullrich SM, Tanton TW and Abdrashitova SA, 2001. Mercury in the aquatic environment: A review of factors affecting methylation. Critical Reviews in Environmental Science and Technology, 31, 241-293.

UNEP (United Nations Environment Programme), 2002. Global mercury assessment. UNEP Chemicals, Geneva, Switzerland, December 2002. Available from http://www.chem.unep.ch/mercury/report/GMA-report-TOC.htm

Ursinyova M and Masanova V, 2005. Cadmium, lead and mercury in human milk from Slovakia. Food Additives and Contaminants, 22, 579-589.

US-EPA (United States Environmental Protection Agency), 1995. Mercuric chloride (HgCl2). Washington, DC, United States Environmental Protection Agency, Integrated Risk Information System. Available from http://www.epa.gov/ncea/iris/subst/0692.htm.

US-EPA (United States Environmental Protection Agency), 1997. Mercury study report to Congress EPA-452/R-97-004. Volume 5: Health Effects of Mercury and Mercury Compounds. Washington, DC, United States Environmental Protection Agency. Available from http://www.epa.gov/ttn/oarpg/t3/reports/volume5.pdf.

US-EPA (United States Environmental Protection Agency), 2001a. Integrated Risk Information System. Methylmercury (MeHg) (CASRN 22967-2-6).

US-EPA (United States Environmental Protection Agency), 2001b. EPA-823-R-001. January 2001. Water quality criterion for the protection of human health: methylmercury. Final. 303 pp.

US-EPA (United States Environmental Protection Agency), 2007. Inorganic mercury. TEACH Chemical summary. Available from http://www.epa.gov/teach/chem_summ/mercury_org_summary.pdf.

US-FDA (United States Food and Drug Administration), 2009. Center for Biologics Evaluation and Research. Thimerosal in vaccines. [Internet]; 2009 Jan; [cited 2009 Jan 27]. Available from http://www.fda.gov/cber/vaccine/thimerosal.htm#1/.

Valent F, Pisa F, Mariuz M, Horvat M, Gibicar D, Fajon V, Mazej D, Daris F and Barbone F, 2011. Fetal and perinatal exposure to mercury and selenium: baseline evaluation of a cohort of children in Friuli Venezia Giulia, Italy. Epidemiologia e Prevenzione, 35, 33-42.

Valera B, Dewailly E and Poirier P, 2008. Cardiac autonomic activity and blood pressure among Nunavik Inuit adults exposed to environmental mercury: a cross-sectional study. Environmental Health, 7, 29.

Valera B, Dewailly E and Poirier P, 2009. Environmental mercury exposure and blood pressure among Nunavik Inuit adults. Hypertension, 54, 981-986.

Valera B, Dewailly E and Poirier P, 2011a. Impact of mercury exposure on blood pressure and cardiac autonomic activity among Cree adults (James Bay, Quebec, Canada). Environmental Research, 111, 1265-1270.

Valera B, Dewailly E and Poirier P, 2012. Association between methylmercury and cardiovascular risk factors in a native population of Quebec (Canada): A retrospective evaluation. Environmental Research.

Valera B, Dewailly E, Poirier P, Counil E and Suhas E, 2011b. Influence of mercury exposure on blood pressure, resting heart rate and heart rate variability in French Polynesians: a cross-sectional study. Environmental Health, 10, 99.

van Wijngaarden E, Beck C, Shamlaye CF, Cernichiari E, Davidson PW, Myers GJ and Clarkson TW, 2006. Benchmark concentrations for methyl mercury obtained from the 9-year follow-up of the Seychelles Child Development Study. Neurotoxicology, 27, 702-709.

van Wijngaarden E, Myers GJ, Thurston SW, Shamlaye CF and Davidson PW, 2009. Interpreting epidemiological evidence in the presence of multiple endpoints: an alternative analytic approach using the 9-year follow-up of the Seychelles child development study. International Archives of Occupational and Environmental Health, 82, 1031-1041.

Velge P, Pinte J, Noël L and Guérin T, 2010. Bilan de la surveillance 2008 des niveaux de contamination en mercure dans les produits de la pêche – Evolution des recommandations de consommation. Bulletin Epidémiologique, 36, 10-13.

Verschaeve L, Kirsch-Volders M, Susanne C, Groetenbriel C, Haustermans R, Lecomte A and Roossels D, 1976. Genetic damage induced by occupationally low mercury exposure. Environmental Research, 12, 306-316.

Verschaeve L, Tassignon JP, Lefevre M, De Stoop P and Susanne C, 1979. Cytogenetic investigation on leukocytes of workers exposed to metallic mercury. Environmental Mutagenesis, 1, 259-268.

Virtanen JK, Laukkanen JA, Mursu J, Voutilainen S and Tuomainen TP, 2012. Serum long-chain n-3 polyunsaturated fatty acids, mercury, and risk of sudden cardiac death in men: a prospective population-based study. PLoS ONE, 7, e41046.

Virtanen JK, Voutilainen S, Rissanen TH, Mursu J, Tuomainen TP, Korhonen MJ, Valkonen VP, Seppanen K, Laukkanen JA and Salonen JT, 2005. Mercury, fish oils, and risk of acute coronary events and cardiovascular disease, coronary heart disease, and all-cause mortality in men in eastern Finland. Arteriosclerosis, thrombosis, and vascular biology, 25, 228-233.

Voegborlo RB, Matsuyama A, Adimado AA and Akagi H, 2011. Determination of methylmercury in marine and freshwater fish in Ghana using a combined technique of dithizone extraction and gas-liquid chromatography with electron capture detection. Food Chemistry, 124, 1244-1248.

Vupputuri S, Longnecker MP, Daniels JL, Guo X and Sandler DP, 2005. Blood mercury level and blood pressure among US women: results from the National Health and Nutrition Examination Survey 1999-2000. Environmental Research, 97, 195-200.

Wagner C, Sudati JH, Nogueira CW and Rocha JB, 2010. In vivo and in vitro inhibition of mice thioredoxin reductase by methylmercury. BioMetals, 23, 1171-1177.

Warfvinge K, 2000. Mercury distribution in the neonatal and adult cerebellum after mercury vapor exposure of pregnant squirrel monkeys. Environmental Research, 83, 93-101.

Watras CJ, Morrison KA, Rubsam JL and Rodger B, 2009. Atmospheric mercury cycles in northern Wisconsin. Atmospheric Environment, 43, 4070-4077.

Wegner R, Radon K, Heinrich-Ramm R, Seemann B, Riess A, Koops F, Poschadel B and Szadkowski D, 2004. Biomonitoring results and cytogenetic markers among harbour workers with potential exposure to river silt aerosols. Occupational and Environmental Medicine, 61, 247-253.

Weil M, Bressler J, Parsons P, Bolla K, Glass T and Schwartz B, 2005. Blood mercury levels and neurobehavioral function. JAMA, 293, 1875-1882.

Welch AA, Lund E, Amiano P, Dorronsoro M, Brustad M, Kumle M, Rodriguez M, Lasheras C, Janzon L, Jansson J, Luben R, Spencer EA, Overvad K, Tjonneland A, Clavel-Chapelon F, Linseisen J, Klipstein-Grobusch K, Benetou V, Zavitsanos X, Tumino R, Galasso R, Bueno-De-Mesquita HB, Ocke MC, Charrondiere UR and Slimani N, 2002. Variability of fish consumption within the 10 European countries participating in the European Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutrition, 5, 1273-1285.

Wennberg M, Bergdahl IA, Hallmans G, Norberg M, Lundh T, Skerfving S, Stromberg U, Vessby B and Jansson JH, 2011. Fish consumption and myocardial infarction: a second prospective biomarker study from northern Sweden. American Journal of Clinical Nutrition, 93, 27-36.

Wennberg M, Bergdahl IA, Stegmayr B, Hallmans G, Lundh T, Skerfving S, Stromberg U, Vessby B and Jansson JH, 2007. Fish intake, mercury, long-chain n-3 polyunsaturated fatty acids and risk of stroke in northern Sweden. British Journal of Nutrition, 98, 1038-1045.

Wennberg M, Stromberg U, Bergdahl IA, Jansson JH, Kauhanen J, Norberg M, Salonen JT, Skerfving S, Tuomainen TP, Vessby B and Virtanen JK, 2012. Myocardial infarction in relation to mercury and fatty acids from fish: a risk-benefit analysis based on pooled Finnish and Swedish data in men. American Journal of Clinical Nutrition, 96, 706-713.

WHO (World Health Organization), 1990. Methylmercury. Environmental Health criteria 101. Available from http://www.inchem.org/documents/ehc/ehc/ehc101.htm.

WHO (World Health Organization), 1991. Inorganic mercury. Environmental Health criteria 118. Available from http://www.inchem.org/documents/ehc/ehc/ehc118.htm.

WHO (World Health Organization), 2000. Air Quality Guidelines for Europe, Copenhagen, Denmark, WHO Regional Office for Europe. Available from http://www.euro.who.int/__data/assets/pdf_file/0005/74732/E71922.pdf.

WHO (World Health Organization), 2003. Instructions for electronic submission of data on chemical contaminants in food and the diet. Global Environment Monitoring System - Food Contamination Monitoring and Assessment Programme (GEMS/Food). Available from http://www.who.int/foodsafety/publications/chem/en/gemsmanual.pdf.

WHO (World Health Organization), 2008. Guidance for Identifying Populations at Risk from Mercury Exposure. August 2008. Issued by UNEP DTIE Chemicals Branch and WHO Department of Food Safety, Zoonoses and Foodborne Diseases. 176 pp.

WHO (World Health Organization), 2009. Environmental Health Criteria 240. Principles and methods for the assessment of chemicals in food. Available from http://www.who.int/foodsafety/chem/principles/en/index1.html.

WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2008. Uncertainty and data quality in exposure assessment. Harmonisation project document No. 6. ISBN 978 92 4 156376 5.

WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 1991. Inorganic mercury. Geneva, World Health Organization, International Programme on Chemical Safety, Environmental Health Criteria 118. Available from http://www.inchem.org/documents/ehc/ehc/ehc118.htm.

WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2003. Elemental mercury and inorganic mercury compounds: human health aspects. Geneva, World Health Organization, International Programme on Chemical Safety, Concise International Chemical Assessment Document 50. Available from http://www.who.int/ipcs/publications/cicad/en/cicad50.pdf.

Wickre JB, Folt CL, Sturup S and Karagas MR, 2004. Environmental exposure and fingernail analysis of arsenic and mercury in children and adults in a Nicaraguan gold mining community. Archives of Environmental Health, 59, 400-409.

Wilhelm M, Schulz C and Schwenk M, 2006. Revised and new reference values for arsenic, cadmium, lead, and mercury in blood or urine of children: basis for validation of human biomonitoring data in environmental medicine. International Journal of Hygiene and Environmental Health, 209, 301-305.

Wood MD, Punt A and Leah RT, 2008. Assessment of the mercury concentrations in soil and vegetation, including crops, around crematoria to determine the impact of mercury emissions on food safety. Ref. No. C02070. A report by the University of Liverpool's Institute for SWIMMER and Enviros Consulting Ltd. Available from http://www.foodbase.org.uk/results.php?f_category_id=&f_report_id=323.

Woods JS, Armel SE, Fulton DI, Allen J, Wessels K, Simmonds PL, Granpeesheh D, Mumper E, Bradstreet JJ, Echeverria D, Heyer NJ and Rooney JP, 2010. Urinary porphyrin excretion in neurotypical and autistic children. Environmental Health Perspectives, 118, 1450-1457.

Wright B, Pearce H, Allgar V, Miles J, Whitton C, Leon I, Jardine J, McCaffrey N, Smith R, Holbrook I, Lewis J, Goodall D and Alderson-Day B, 2012. A comparison of urinary mercury between children with autism spectrum disorders and control children. PLoS ONE, 7, e29547.

Wulf HC, Kromann N, Kousgaard N, Hansen JC, Niebuhr E and Alboge K, 1986. Sister chromatid exchange (SCE) in Greenlandic Eskimos. Dose-response relationship between SCE and seal diet, smoking, and blood cadmium and mercury concentrations. The Science of the Total Environment, 48, 81-94.

Xia H, Liu X, Huang K, Gao Y, Gan L, He C and Hou X, 2010. Matrix-Assisted UV-Photochemical Vapor Generation for AFS Determination of Trace Mercury in Natural Water Samples: A Green Analytical Method. Spectroscopy Letters, 43, 550-554.

Xiong C and Hu B, 2007. Online YPA4 resin microcolumn separation/preconcentration coupled with inductively coupled plasma optical emission spectrometry (ICP-OES) for the speciation analysis of mercury in seafood. Journal of Agricultural and Food Chemistry, 55, 10129-10134.

Xu M, Yan C, Tian Y, Yuan X and Shen X, 2010. Effects of low level of methylmercury on proliferation of cortical progenitor cells. Brain Research, 1359, 272-280.

Xue F, Holzman C, Rahbar MH, Trosko K and Fischer L, 2007. Maternal fish consumption, mercury levels, and risk of preterm delivery. Environmental Health Perspectives, 115, 42-47.

Yaginuma-Sakurai K, Murata K, Iwai-Shimada M, Nakai K, Kurokawa N, Tatsuta N and Satoh H, 2012. Hair-to-blood ratio and biological half-life of mercury: experimental study of methylmercury exposure through fish consumption in humans. Journal of Toxicological Sciences, 37, 123-130.

Yaginuma-Sakurai K, Murata K, Shimada M, Nakai K, Kurokawa N, Kameo S and Satoh H, 2010. Intervention study on cardiac autonomic nervous effects of methylmercury from seafood. Neurotoxicology and Teratology, 32, 240-245.

Yaginuma-Sakurai K, Shimada M, Ohba T, Nakai K, Suzuki K, Kurokawa N, Kameo S and Satoh H, 2009. Assessment of exposure to methylmercury in pregnant Japanese women by FFQ. Public Health Nutrition, 12, 2352-2358.

Yorifuji T, Kashima S, Tsuda T and Harada M, 2009a. What has methylmercury in umbilical cords told us? - Minamata disease. The Science of the Total Environment, 408, 272-276.

Yorifuji T, Tsuda T, Inoue S, Takao S and Harada M, 2011. Long-term exposure to methylmercury and psychiatric symptoms in residents of Minamata, Japan. Environment International, 37, 907-913.

Yorifuji T, Tsuda T, Takao S and Harada M, 2008. Long-term exposure to methylmercury and neurologic signs in Minamata and neighboring communities. Epidemiology, 19, 3-9.

Yorifuji T, Tsuda T, Takao S, Suzuki E and Harada M, 2009b. Total mercury content in hair and neurologic signs: historic data from Minamata. Epidemiology, 20, 188-193.

Yoshizawa K, Rimm EB, Morris JS, Spate VL, Hsieh CC, Spiegelman D, Stampfer MJ and Willett WC, 2002. Mercury and the risk of coronary heart disease in men. The New England journal of medicine, 347, 1755-1760.

Yu RQ, Flanders JR, Mack EE, Turner R, Mirza MB and Barkay T, 2012. Contribution of coexisting sulfate and iron reducing bacteria to methylmercury production in freshwater river sediments. Environmental Science & Technology, 46, 2684-2691.

APPENDICES

A. OCCURRENCE

Table A1: Statistical description of the total mercury occurrence data by food group (μg/kg).

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Grains and grain-based products	4 545	60	0	1.0	1.6	0.9	2.0	3.1	4.0	5.3	10	5.5	9.6	12	9.0	12	20	254
Vegetables and vegetable products	4 299	62	0	0.8	1.2	6.0	7.0	7.8	8.3	10	11	19	20	20	96	96	100	2 080
Starchy roots and tubers	1 234	75	0	0.5	1.0	0.2	0.8	1.4	0.8	2.5	5.0	1.5	5.0	10	3.0	5.7	10	20
Legumes, nuts and oilseeds	1 311	51	0	1.0	2.0	2.3	2.8	3.3	9.6	10	10	12	13	14	18	19	20	257
Fruit and fruit products	1 368	74	0	0.6	1.0	0.3	1.2	2.1	1.0	5.0	9.6	1.9	5.1	10	9.7	10	20	37
Meat and meat products	10 304	56	0	1.1	2.0	1.9	2.7	3.5	9.0	10	11	14	15	17	28	28	30	233
Fish and other seafood	21 539	12	40	43	48	131	133	136	540	540	540	852	852	852	1 400	1 400	1 400	6 890
Milk and dairy products	3 345	64	0	0.3	0.4	0.9	1.5	2.1	4.3	8.0	11	12	12	16	17	17	20	50
Eggs and egg products	798	58	0	0.6	1.0	0.6	1.2	1.8	3.2	4.6	6.3	4.4	5.0	10	7.0	7.0	10	13
Sugar and confectionery	1 617	73	0	1.0	1.7	0.6	2.6	4.7	2.9	10	20	4.9	10	20	10	30	60	60
Animal and vegetable fats and oils	835	61	0	0.6	0.9	1.1	1.6	2.0	6.0	6.0	6.0	8.0	10	10	12	22	23	100
Fruit and vegetable juices	651	89	0	0.5	1.0	0.1	3.2	6.2	0.4	10	20	0.7	10	20	2.1	10	20	20
Non-alcoholic beverages	699	46	0.1	1.0	2.0	3.4	4.0	4.5	16	16	20	21	21	21	31	31	31	87
Alcoholic beverages	652	79	0	0.2	0.3	0.1	0.4	0.7	0.3	1.0	2.0	0.7	1.5	2.1	1.7	1.7	3.0	6.0
Drinking water	1 637	90	0	0.1	0.1	0.0	0.1	0.2	0.1	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0.6	5.0
Herbs, spices and condiments	529	47	0.4	2.0	2.0	3.1	4.3	5.5	10	13	20	17	20	23	41	41	50	160
Food for infants and small children	834	63	0	1.0	1.0	0.6	1.6	2.5	3.0	5.0	6.0	6.0	6.0	11	9.0	9.0	11	50
Products for special nutritional use	1 608	68	0	2.9	5.0	96	99	102	35	38	43	64	64	76	300	300	300	64 000
Composite food	304	41	3.0	6.6	10	16	18	19	59	59	59	101	101	101	274	274	274	486
Snacks, desserts, and other foods	451	54	0	0.5	0.5	1.2	1.5	1.9	3.0	4.7	5.0	5.0	5.0	10	16	16	20	110

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A2: Statistical description of concentrations of total mercury for the food group 'Grains and grain-based products' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Grains for human consumption	2 680	52	0	1.0	2.0	1.0	2.1	3.2	4.0	5.5	10	6.3	8.0	12	12	15	20	63
Grain milling products	671	65	0	1.0	1.2	0.6	1.6	2.6	3.6	4.5	9.0	5.0	5.5	9.0	6.0	10	10	20
Bread and rolls	596	75	0	0.5	1.0	0.7	1.7	2.7	1.6	4.5	9.0	2.6	4.5	9.0	5.0	5.0	9.0	254
Pasta (raw)	81	77	0	1.5	3.0	0.5	2.2	4.0	3.0	4.9	9.0	4.0	5.0	10	5.0	5.0	10	10
Breakfast cereals	230	82	0	2.1	3.0	0.5	3.1	5.6	3.0	12	23	5.5	12	23	10	12	23	23
Fine bakery wares	287	73	0	0.5	1.0	0.5	1.7	2.9	3.0	10	20	4.0	10	20	6.0	10	20	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A3: Statistical description of concentrations of total mercury for the food group 'Vegetables and vegetable products (including fungi)' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Vegetable and vegetable products	103	47	0.1	0.4	0.4	0.5	1.0	1.4	1.6	3.0	3.0	3.0	10	10	4.8	10	20	20
Root vegetables	724	71	0	0.7	1.2	0.4	1.5	2.6	1.3	5.0	10	3.5	5.0	10	10	10	10	23
Bulb vegetables	325	76	0	0.5	1.0	0.1	1.2	2.3	0.6	5.0	10	1.1	5.0	10	2.0	5.0	10	10
Fruiting vegetables	669	70	0	0.5	1.0	0.2	0.9	1.6	0.8	2.5	5.0	1.0	5.0	10	2.0	5.0	10	100
Brassica vegetables	481	61	0	0.4	0.4	0.4	0.8	1.3	1.6	2.5	5.0	4.5	5.0	5.0	8.0	8.0	9.5	14
Leaf vegetables	339	83	0	1.5	2.0	0.5	2.1	3.8	2.1	5.0	10	3.9	5.0	10	8.9	17	17	100
Legume vegetables	13	46	0.1	0.2	0.3	0.3	0.6	0.9	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0
Stem vegetables (fresh)	246	91	0	0.5	1.0	0.1	1.5	2.9	0.2	5.0	10	0.3	5.0	10	2.0	5.0	10	100
Sugar plants	65	22	0.2	0.2	0.3	0.7	0.7	0.8	2.1	2.1	2.1	3.3	3.3	3.3	16	16	16	16
Sea weeds	1	100	0	2.5	5.0	0	2.5	5.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0
Tea and herbs for infusions (solid)	85	68	0	5.0	9.7	6.0	7.7	9.5	20	20	20	43	43	43	110	110	110	110
Cocoa beans and cocoa products	126	56	0	2.5	3.2	1.7	3.7	5.7	7.0	10	20	12	12	20	24	24	24	30
Coffee beans and coffee products (solid)	298	49	0.4	0.9	1.0	1.4	1.7	1.9	6.4	6.4	6.4	11	11	11	15	15	15	20
Coffee imitates (solid)	13	46	0.5	0.7	0.9	0.7	0.9	1.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.1
Vegetable products	139	55	0	0.3	0.3	13	13	13	6.8	6.8	6.8	22	22	22	395	395	395	973
Fungi, cultivated	508	32	3.0	4.0	5.0	9.1	10	11	26	26	26	54	54	54	102	102	102	620
Fungi, wild, edible	165	19	5.0	8.0	8.3	105	106	107	575	575	575	1 083	1 083	1 083	1 640	1 640	1 640	2 080

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A4: Statistical description of concentrations of total mercury for the food group 'Starchy root and tubers' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Potatoes and potatoes products	421	92	0	0.6	1.1	0.1	1.1	2.1	0.3	5.0	10	0.8	5.0	10	1.5	5.0	10	16
Other starchy roots and tubers	813	67	0	0.3	0.3	0.3	0.6	1.0	0.9	1.0	2.0	2.0	2.6	2.6	5.2	10	10	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A5: Statistical description of concentrations of total mercury for the food group 'Legumes, nuts and oilseeds' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Legumes, beans, green, without pods	102	75	0	0.6	1.2	0.4	1.0	1.5	3.0	3.0	5.0	3.0	3.0	5.0	4.0	4.0	5.0	9.0
Legumes, beans, dried	483	53	0	0.5	1.0	1.4	1.8	2.2	7.0	7.0	7.7	9.0	9.0	10	11	11	14	45
Tree nuts	170	65	0	1.0	2.0	2.6	3.8	4.9	5.3	7.0	8.6	7.0	18	20	21	21	38	257
Oilseeds	556	39	0.9	1.9	2.0	3.2	3.7	4.2	12	12	13	16	16	18	23	23	23	42

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A6: Statistical description of concentrations of total mercury for the food group 'Fruit and fruit products' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fruit and fruit products	3	33	0.1	0.2	0.3	0.1	0.2	0.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Citrus fruits	150	69	0	0.2	0.3	0.1	0.6	1.1	0.6	2.5	5.0	0.9	3.0	6.0	1.6	3.0	6.0	6.0
Pome fruits	349	63	0	0.3	0.3	0.2	0.6	0.9	0.6	1.0	2.0	1.2	2.0	3.0	2.4	2.5	5.0	37
Stone fruits	143	72	0	0.5	1.0	0.1	1.0	1.9	0.7	2.5	5.0	1.0	5.0	5.0	2.2	5.0	10	10
Berries and small fruits	358	87	0	1.0	1.8	0.1	1.5	2.9	1.0	5.0	10	1.0	5.0	10	4.0	5.0	10	10
Miscellaneous fruits	149	89	0	0.5	1.0	0.1	1.0	1.9	0.5	2.5	5.0	1.0	2.7	5.0	2.0	5.0	10	10
Dried fruits	33	73	0	2.7	5.3	0.2	1.7	3.2	1.0	2.7	5.3	1.1	2.7	5.3	1.1	2.7	5.3	5.3
Jam, marmalade and other fruit spreads	57	44	1.0	4.6	8.9	3.3	5.6	7.8	13	13	20	14	14	20	18	18	20	20
Other fruit products	126	75	0	0.6	1.0	0.2	1.3	2.5	1.1	3.6	5.0	1.8	10	20	1.9	10	20	21

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A7: Statistical description of concentrations of total mercury for the food group 'Meat and meat products (including edible offal)' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Meat and meat products	23	61	0	0.5	1.0	0.7	1.3	1.9	1.7	6.1	6.1	6.1	10	20	6.1	10	20	20
Livestock meat	3 078	66	0	0.7	1.0	0.8	1.7	2.5	3.0	5.0	9.7	6.1	8.0	12	13	17	18	100
Poultry	1 450	66	0	1.3	2.0	1.2	2.3	3.5	5.1	6.5	10	10	10	16	32	33	33	100
Game mammals	1 613	54	0	1.4	2.0	2.4	3.3	4.3	11	11	15	17	17	20	30	30	30	123
Game birds	376	81	0	1.9	3.6	0.6	2.0	3.4	2.7	3.0	4.3	4.5	5.1	5.1	12	12	13	40
Mixed meat	382	46	0.3	0.5	1.0	0.9	1.1	1.3	4.3	4.3	4.4	6.5	6.5	6.5	8.9	8.9	8.9	12
Edible offal, farmed animals	2 453	38	1.0	2.0	2.6	3.1	3.6	4.1	11	11	11	17	17	17	30	30	30	124
Edible offal, game animals	259	30	4.0	4.4	5.0	11	11	12	35	35	35	40	40	40	190	190	190	233
Preserved meat	174	65	0	1.0	2.0	1.0	2.9	4.9	7.0	13	25	12	13	25	16	16	25	25
Sausages	364	63	0	0.5	0.5	0.8	1.4	1.9	3.2	3.2	5.0	8.0	8.0	8.0	20	20	20	40
Meat specialities	27	33	0.2	0.2	0.2	0.9	0.9	1.0	5.0	5.0	5.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Pastes, pâtés and terrines	96	33	0.4	0.5	0.5	1.3	1.4	1.5	4.1	4.1	4.1	15	15	15	30	30	30	30
Meat imitates	9	56	0	1.0	1.4	1.2	1.4	1.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A8: Statistical description of concentrations of total mercury for the food group 'Fish and other seafood' in µg/kg (FoodEx Level 2).

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fish and other seafood, unspecified[(b)]	1 968	3	64	64	65	100	100	101	273	273	273	423	423	423	672	672	672	2 143
Fish meat	13 737	7	53	53	60	177	178	180	710	710	710	1 043	1 043	1 043	1 775	1 775	1 775	6 890
Fish products	241	8	22	22	22	37	38	38	109	109	109	233	233	233	310	310	310	622
Fish offal	158	58	0	15	28	12	19	26	67	67	70	88	88	88	92	92	92	121
Crustaceans	1 478	21	17	20	20	43	47	50	189	189	189	282	282	282	374	374	374	1 040
Molluscs	3 926	26	16	21	25	31	36	41	100	100	100	160	160	160	300	300	300	955
Amphibians, reptiles, snails, insects	31	48	0.8	2.5	3.7	19	20	21	140	140	140	280	280	280	280	280	280	280

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

(a): The 95th, P97.5th and P99th percentile obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

(b): Data available only on FoodEx Level 1.

Table A9: Statistical description of concentrations of total mercury for the food group 'Fish meat' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(c)]			P97.5[(c)]			P99[(c)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Anchovy	110	33	50	50	60	73	83	92	200	200	200	291	291	291	891	891	891	1 249
Angler fish	61	30	78	78	100	186	195	204	551	551	551	920	920	920	2 900	2 900	2 900	2 900
Babel	10	0	205	205	205	211	211	211	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	430
Barracuda	1	0	340	340	340	340	340	340	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	340
Bass	78	10	89	89	97	199	203	206	698	698	698	1 000	1 000	1 000	4 169	4 169	4 169	4 169
Bonito	25	8	400	400	400	580	583	586	1 920	1 920	1 920	2 080	2 080	2 080	2 080	2 080	2 080	2 080
Bream	253	11	135	135	135	224	225	226	883	833	883	1 124	1 124	1 124	1 400	1 400	1 400	2 909
Capelin	11	82	0	4.4	8.3	2.0	5.0	8.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10
Carp	338	5	28	28	29	55	55	55	194	194	194	244	244	244	403	403	403	985
Char	8	0	37	37	37	32	32	32	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	40
Cod, whiting	1 308	18	54	54	56	91	94	96	340	340	340	460	460	460	590	590	590	1 000
Dentex	3	0	832	832	832	2 019	2 019	2 019	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4 450
Eel	487	2	130	130	130	177	178	178	461	461	461	719	719	719	1 100	1 100	1 100	1 880
Flounder	23	17	40	50	70	85	91	97	185	185	185	205	205	205	578	578	578	578
Garfish	3	0	590	590	590	590	590	590	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 000
Grenadier	3	0	98	98	98	104	104	104	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	137
Grey mullet	52	23	85	85	100	152	159	167	566	566	566	784	784	784	1 000	1 000	1 000	1 000
Grouper	2	0	195	195	195	195	195	195	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	320
Gurnard	4	25	75	75	75	103	109	116	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	262
Hake	131	16	90	90	100	130	136	142	420	420	420	510	510	510	620	620	620	660
Halibut	1 713	0	170	170	170	209	209	209	610	610	610	710	710	710	860	860	860	2 280
Herring	1 272	0	30	30	30	36	36	36	78	78	78	94	94	94	120	120	120	400
Jack mackerel	3	0	110	110	110	127	127	127	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	170
John Dory	6	0	212	212	212	302	302	302	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	620
Lizardfish	2	0	611	611	611	611	611	611	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	650
Luvarus	1	0	590	590	590	590	590	590	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	590
Mackerel	1 348	5	40	40	40	106	108	109	520	520	520	735	735	735	976	976	976	1 560
Meagre	2	50	145	170	195	145	170	195	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	290
Perch	423	0	130	130	130	165	165	165	370	370	370	490	490	490	560	560	560	780
Pike	267	0	290	290	290	394	394	394	979	979	979	1 200	1 200	1 200	3 276	3 276	3 276	5 139
Plaice	194	2	46	46	46	64	64	65	160	160	160	200	200	200	240	240	240	400
Ray	32	3	108	108	108	229	229	230	1 170	1 170	1 170	1 350	1 350	1 350	1 350	1 350	1 350	1 350

Table A9: Continued.

Food category	N	% LC	Median			Mean			P95[c]			P97.5[c]			P99[c]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Redfish	221	0	100	100	100	189	189	189	676	676	676	847	847	847	940	940	940	1 574
Roach	17	0	113	113	113	122	122	122	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	240
Salmon, trout	1 741	7	30	30	30	31	33	35	57	57	70	67	67	67	100	100	100	950
Sardine and pilchard	399	18	16	27	30	32	38	44	116	116	116	127	127	127	153	153	153	244
Scorpion fish	1	0	422	422	422	422	422	422	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	422
Sea bass	10	0	288	288	288	300	300	300	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	610
Sea catfish, wolf-fish	67	54	0	10	13	103	109	114	770	770	770	850	850	850	950	950	950	950
Shad	1	0	173	173	173	173	173	173	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	173
Shark	272	11	495	495	495	688	691	695	1 900	1 900	1 900	2 720	2 720	2 720	3 518	3 518	3 518	5 560
Smelt	2	0	325	325	325	325	325	325	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	370
Sole	49	24	48	50	64	69	77	84	180	180	180	325	325	325	500	500	500	500
Sprat	107	1	19	19	19	21	21	21	50	50	50	84	84	84	100	100	100	117
Sturgeon	4	50	36	61	79	40	52	65	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	86
Swordfish	264	5	1 010	1 010	1 010	1 210	1 212	1 214	3 300	3 300	3 300	4 500	4 500	4 500	5 300	5 300	5 300	6 760
Tuna	849	5	189	189	189	286	290	291	850	850	850	1 182	1 182	1 182	1 620	1 620	1 620	3 370
Turbot	4	0	56	56	56	62	62	62	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	89
Weever	11	0	741	741	741	763	763	763	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 927
Whitefish	37	16	70	70	80	77	85	93	250	250	250	260	260	260	260	260	260	260
Wrasse	12	0	427	427	427	511	511	511	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 730
Fish meat, unspecified, as reported[a]	1 502	10	57	57	57	279	280	280	1 194	1 194	1 194	1 900	1 900	1 900	3 270	3 270	3 270	6 890
Fish meat, overall results[b]	12 235	10	117	117	118	164	166	168	499	500	501	661	661	665	922	922	922	6 760

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): Data described as reported.

(b): Data calculated on overall concentrations of individual specified fish species excluding fish meat unspecified and such used for exposure calculation.

(c): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A10: Statistical description of concentrations of methylmercury for the food group 'Fish and other seafood' in µg/kg (FoodEx Level 2).

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fish meat	969	6	39	50	54	131	135	139	598	598	598	810	810	810	1 213	1 213	1 213	5 740
Fish products	33	12	23	23	23	39	39	40	95	95	95	538	538	538	538	538	538	538
Fish offal	4	100	26	26	26	23	23	23	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	26
Crustaceans	42	48	0	50	100	70	102	134	280	280	280	309	309	309	970	970	970	970
Molluscs	35	57	0	50	100	15	61	107	151	151	151	390	390	390	390	390	390	390

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A11: Statistical description of concentrations of methylmercury for the food group 'Fish meat' in µg/kg **(FoodEx Level 3).**

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Anchovy	5	80	0	50	100	22	62	102	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	112
Angler fish	3	33	148	148	148	173	190	206	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	370
Bass	5	60	0	50	100	31	61	91	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	104
Bream	4	50	51	76	101	61	86	111	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	141
Carp	33	21	10	10	10	13	13	13	39	39	39	51	51	51	51	51	51	51
Cod and whiting	183	4	10	10	10	19	19	20	51	51	54	74	74	74	106	106	106	400
Eel	8	0	93	93	93	172	172	172	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	455
Flounder	45	0	50	50	50	66	66	66	167	167	167	202	202	202	205	205	205	205
Grey mullet	8	88	0	50	100	18	62	106	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	144
Hake	11	64	0	50	100	32	64	96	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	200
Halibut	61	0	79	79	79	127	127	127	400	400	400	624	624	624	1 213	1 213	1 213	1 213
Herring	39	0	26	26	26	30	30	30	63	63	63	63	63	63	63	63	63	63
Mackerel	122	9	29	34	34	123	127	132	547	547	547	598	598	598	905	905	905	1 114
Perch	2	0	56	56	56	56	56	56	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	77
Salmon and trout	28	50	3.5	50	100	13	38	63	39	50	100	106	106	106	106	106	106	106
Sardine and pilchard	16	88	0	50	100	14	58	102	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	121
Sea catfish, wolf-fish	1	0	121	121	121	121	121	121	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	121
Shark	4	0	1 510	1 510	1 510	1 520	1 520	1 520	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 730
Smelt	1	0	73	73	73	73	73	73	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	73
Sole	4	0	0	50	100	0	50	100	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	100
Sprat	25	0	8	8	8	8	8	8	16	16	16	18	18	18	18	18	18	18
Swordfish	10	0	795	795	795	819	819	819	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 079
Tuna	125	2	133	133	133	220	221	221	784	784	784	880	880	880	1 162	1 162	1 162	1 728
Fish meat, unspecified	226	1	113	113	113	225	225	225	700	700	700	1 079	1 079	1 079	1 414	1 414	1 414	5 740

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A12: Statistical description of concentrations of total mercury for the food group 'Milk and dairy products' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Milk and dairy products	32	97	0	8.0	16	0.0	6.7	13	0	8.0	16	1.0	10	20	1.0	10	20	20
Liquid milk	1 624	74	0	0.2	0.3	0.2	0.7	1.1	2.0	2.5	4.3	2.0	5.0	10	3.1	8.0	16	16
Milk based beverages	3	33	0.2	0.2	0.2	2.9	3.0	3.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	8.7
Concentrated milk	96	55	0	0.3	0.3	0.8	1.1	1.3	4.6	4.6	4.6	5.0	6.7	6.7	13	13	20	20
Whey and whey products	2	100	0	0.2	0.3	0	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Cream and cream products	140	60	0	0.2	0.3	0.5	0.7	0.9	3.0	3.0	4.9	4.0	4.0	5.0	4.8	4.8	5.0	8.1
Fermented milk products	323	67	0	0.5	0.8	0.4	2.1	3.8	2.5	10	20	3.5	10	20	4.3	10	20	20
Cheese	1 095	49	0.1	0.5	0.5	2.0	2.4	2.8	14	14	14	17	17	17	20	20	20	23
Milk and milk product imitates	30	90	0	2.0	4.0	2.0	3.6	5.3	8.3	8.3	10	50	50	50	50	50	50	50

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A13: Statistical description of concentrations of total mercury for the food group 'Eggs and egg products' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Eggs, fresh	790	58	0	0.5	1.0	0.6	1.2	1.8	3.2	4.5	6.0	4.4	5.0	10	7.0	7.0	10	13
Eggs, powder	8	88	0	1.0	2.0	0.4	1.8	3.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A14: Statistical description of concentrations of total mercury for the food group 'Sugar and confectionery' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Sugar and confectionery	15	93	0	0.5	1.0	0.1	1.0	1.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1.2
Sugars	51	82	0	0.2	0.3	0.1	0.3	0.4	0.8	0.8	0.8	0.8	0.8	0.8	3.0	3.0	3.0	3.0
Sugar substitutes	2	50	0.2	0.2	0.3	0.2	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Chocolate (Cocoa) products	314	60	0	1.5	2.0	1.4	2.1	3.2	7.2	9.5	10	7.4	10	20	9.5	10	20	20
Confectionery (non-chocolate)	280	73	0	1.5	2.2	0.5	4.3	8.1	2.4	30	60	3.7	30	60	4.8	30	60	60
Dessert sauces	11	45	0.5	0.9	0.9	1.1	1.4	1.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4.0
Molasses and other syrups	52	60	0	0.2	0.3	0.2	0.3	0.5	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3
Honey	892	64	0	1.0	2.0	0.5	2.7	4.8	1.4	10	20	3.9	10	20	14	14	20	32

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A15: Statistical description of concentrations of total mercury for the food group 'Animal and vegetable fats and oils' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Animal and vegetable fats and oils	3	0	3.0	3.0	3.0	3.6	3.6	3.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	6.2
Animal fat	396	52	0	0.5	0.5	1.1	1.3	1.5	5.0	5.0	5.0	7.0	7.0	7.0	23	23	23	44
Fish oil	103	99	0	0.7	1.4	0.2	1.5	2.9	0	1.8	3.6	0	13	16	0	16	25	100
Vegetable fat	36	75	0	0.2	0.3	0.9	1.1	1.3	6.8	6.8	6.8	12	12	12	12	12	12	12
Vegetable oil	268	56	0	0.5	0.6	1.5	2.1	2.6	6.3	8.0	9.0	10	12	12	18	25	25	100
Margarine and similar products	29	72	0	0.2	0.3	0.6	0.7	0.8	3.3	3.3	3.3	5.3	5.3	5.3	5.3	5.3	5.3	5.3

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A16: Statistical description of concentrations of total mercury for the food group 'Fruit and vegetable juices' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fruit and vegetable juices	44	89	0	0.2	0.3	0.1	0.3	0.5	0.5	1.0	2.0	0.6	1.0	2.0	1.0	1.0	2.0	2.0
Fruit juice	416	63	0	0.5	1.0	0.1	2.9	5.7	0.4	10	20	0.5	10	20	1.8	10	20	20
Concentrated juice fruit	27	26	0	10	20	0	7.6	15	0	10	20	0	10	20	0	10	20	20
Fruit nectar	44	64	0	0.2	0.3	0.4	3.5	6.7	0.6	10	20	6.0	10	20	9.5	10	20	20
Mixed fruit juice	35	23	0	10	20	0	7.8	16	0	10	20	0	10	20	0	10	20	20
Dehydrated/powdered fruit juice	23	70	0	0.2	0.3	0.2	0.4	0.6	0.3	1.5	2.9	2.9	2.9	3.0	2.9	2.9	3.0	3.0
Vegetable juice	49	88	0	2.0	2.0	0.2	2.2	4.2	2.0	5.0	10	2.0	5.0	10	2.1	10	20	20
Mixed vegetable juice	4	50	0	5.3	11	0	5.3	11	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Mixed fruit and vegetable juice	9	0	0	10	20	1.1	10	19	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A17: Statistical description of concentrations of total mercury for the food group 'Non-alcoholic beverages (excepting milk based beverages)' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Non-alcoholic beverages	17	47	0	0.5	0.5	0.1	3.7	7.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Soft drinks	301	71	0	0.2	0.3	0.0	0.8	1.6	0.4	10	20	0.7	10	20	1.2	10	20	20
Tea (Infusion)	369	20	4.0	4.0	4.0	6.4	6.6	6.8	20	21	21	24	25	29	35	35	38	87
Coffee (Beverage)	12	33	0.8	0.8	1.0	1.9	2.0	2.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A18: Statistical description of concentrations of total mercury for the food group 'Alcoholic beverages' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Beer and beer-like beverage	256	79	0	0.2	0.3	0.1	0.4	0.8	0.3	1.5	3.0	0.9	1.5	3.0	2.0	2.0	3.0	6.0
Wine	359	77	0	0.2	0.3	0.1	0.4	0.7	0.3	1.0	2.0	0.6	1.0	2.0	1.2	1.2	2.0	5.5
Fortified and liqueur wines	2	50	0.1	0.1	0.1	0.1	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Wine-like drinks	16	88	0	0.2	0.3	0.1	0.4	0.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3.0
Spirits	19	95	0	0.5	1.0	0.0	0.6	1.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A19: Statistical description of concentrations of total mercury for the food group 'Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)' in µg/kg.

Food category	N	% LC	Median			Mean			P95 [(a)]			P97.5 [(a)]			P99 [(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Drinking water	73	99	0	0.1	0.2	0.0	0.1	0.2	0.0	0.1	0.2	0	0.1	0.2	0.5	0.5	0.5	0.5
Tap water	22	77	0	0.1	0.2	0.1	0.2	0.2	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Well water	422	76	0	0.1	0.1	0.0	0.1	0.2	0.2	0.3	0.5	0.5	0.5	0.5	0.5	0.5	0.6	2.0
Bottled water	1 120	95	0	0.1	0.1	0.0	0.1	0.2	0	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0.6	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A20: Statistical description of concentrations of total mercury for the food group 'Herbs, spices and condiments' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Herbs, spices and condiments	3	67	0	8.0	16	27	32	37	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	80
Herbs	34	62	0	2.0	4.0	13	15	17	94	94	94	160	160	160	160	160	160	160
Spices	174	37	2.0	3.9	5.0	3.7	5.3	6.8	13	13	20	18	18	20	31	31	31	41
Herb and spice mixtures	38	66	0	4.8	7.4	2.3	7.3	12	12	25	50	20	25	50	20	25	50	50
Seasoning or extracts	69	61	0	0.5	1.0	1.4	1.9	2.3	5.0	5.0	8.0	8.0	8.0	10	17	17	17	17
Condiment	54	61	0	0.2	0.3	0.8	0.9	1.0	4.0	4.0	4.0	8.0	8.0	8.0	10	10	10	10
Dressing	22	45	0.8	0.8	1.0	2.1	2.2	2.2	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0
Chutney and pickles	3	0	1.3	1.3	1.3	0.9	0.9	0.9	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1.5
Savoury sauces	5	60	0	0.2	0.3	0.1	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.4
Flavourings or essences	8	50	0.1	1.2	1.2	0.7	4.0	7.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	40
Baking ingredients	119	33	1.0	1.1	1.3	1.8	1.9	2.1	6.7	6.7	6.7	7.5	7.5	7.5	8.0	8.0	8.0	13

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A21: Statistical description of concentrations of total mercury for the food group 'Food for infants and small children' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Food for infants and small children	222	11	1.0	1.0	1.0	1.1	1.2	1.3	3.9	3.9	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Infant formulae, powder	144	79	0	2.5	3.4	1.0	2.2	3.5	8.0	8.0	11	10	10	11	12	12	12	13
Infant formulae, liquid	1	100	0	0.2	0.4	0	0.2	0.4	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.4
Follow-on formulae, powder	128	86	0	2.5	5.0	0.7	2.7	4.7	8.0	8.0	8.0	8.0	9.0	9.0	11	12	12	50
Cereal-based food for infants and young children	102	90	0	0.5	1.0	0.2	1.3	2.4	1.3	2.7	5.3	3.0	4.0	5.3	4.0	5.0	10	11
Ready-to-eat meal for infants and young children	228	77	0	0.3	0.4	0.1	1.0	1.9	0.4	3.0	5.3	0.7	5.5	11	2.0	5.5	11	11
Yoghurt, cheese and milk-based dessert for infants and young children	8	100	0	0.1	0.1	0	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Fruit juice and herbal tea for infants and young children	1	0	6.0	6.0	6.0	6.0	6.0	6.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	6.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A22: Statistical description of concentrations of total mercury for the food group 'Products for special nutritional use' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Products for special nutritional use	82	52	0	0.1	1.0	1.0	2.6	4.2	2.0	10	20	2.5	10	20	17	17	20	20
Food for weight reduction	15	80	0	1.5	3.0	0.6	2.0	3.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Dietary supplements[(b)]	1 233	66	0	3.0	5.7	123	126	129	38	40	45	75	75	80	410	410	410	64 000
Food for sports people	168	57	0	2.5	4.0	19	22	25	57	57	60	116	116	116	600	600	600	1 236
Dietetic food for diabetics	51	96	0	0.5	1.0	0.3	0.8	1.3	0	1.5	3.0	0.1	1.5	3.0	17	17	17	17
Medical food	59	95	0	0.5	3.0	0.2	1.7	3.3	1.7	2.5	5.0	4.0	4.0	5.0	8.0	8.0	8.0	8.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; UB: upper bound; MB: middle bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

(b): Correct values: mean values are higher than P95 values because of right-skewed distribution.

Table A23: Statistical description of concentrations of total mercury for the food group 'Composite food (including frozen products)' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Composite food	83	66	0	0.5	1.0	2.8	4.6	6.4	13	13	20	21	25	33	33	33	50	50
Cereal-based dishes	15	13	0.2	10	13	6.9	9.7	12	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	25
Potato based dishes	2	0	1.3	1.3	1.3	1.3	1.3	1.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.0
Beans-based meals	5	100	0	0.2	0.3	0	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Meat-based meals	37	35	0	2.8	2.8	4.6	6.6	8.6	13	13	20	61	61	61	61	61	61	61
Fish and seafood based meals	84	4	21	23	23	42	42	43	126	126	126	274	274	274	486	486	486	486
Vegetable-based meals	3	67	0	5.0	5.6	1.9	3.7	5.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10
Ready to eat soups	33	73	0	0.5	1.0	11	11	12	13	13	20	321	321	321	321	321	321	321
Prepared salads	42	7	11	11	11	15	15	15	41	41	41	41	41	41	74	74	74	74

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A24: Statistical description of concentrations of total mercury for the food group 'Snacks, desserts, and other foods' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Snacks, desserts, and other foods	1	100	0	0.1	0.1	0	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Snack food	248	58	0	0.5	0.6	0.7	0.9	1.2	3.1	3.1	3.1	5.0	5.0	5.0	7.5	7.5	7.5	15
Ices and desserts	135	43	0.2	0.2	0.3	0.8	0.8	0.9	2.5	2.5	2.5	2.8	2.8	2.8	9.0	9.0	9.0	30
Other foods	31	68	0	2.5	5.0	8.3	10	12	86	86	86	110	110	110	110	110	110	110

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

B. RELATIONSHIP BETWEEN CONCENTRATIONS OF TOTAL MERCURY AND METHYLMERCURY

Table B1: Overview of previously reported literature data on relationship between concentrations of total mercury and methylmercury in fish.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Largetooth flounder (*Pseudorhombus arsicus*)	The Persian Gulf	Sea	4	28	23-34	27	18-39	96.4[(f)]	64-100	1
Spotfin flathead (*Gramnopolites suppositus*)	The Persian Gulf	Sea	8	39	14-73	34	11-60	87.2[(f)]	83-100	1
Spotfin flathead (*Gramnopolites suppositus*)	The Persian Gulf	Sea	7	27	22-32	17	14-21	63.0[(f)]	63-67	1
Japanese threadfin bream (*Nemipterus japonicus*)	The Persian Gulf	Sea	8	49	30-87	48	25-97	98.0[(f)]	84-100	1
Greater Lizardfish (*Saurida tumbil*)	The Persian Gulf	Sea	9	43	12-86	47	11-100	109.3[(f)]	92-100	1
Greater Lizardfish (*Saurida tumbil*)	The Persian Gulf	Sea	12	17	15-20	18	15-17	105.9[(f)]	100	1
Giant Seacatfish (*Arius thalassinus*)	The Persian Gulf	Sea	10	45	30-78	45	30-74	100.0[(f)]	95-100	1
Elongate Sole (*Solea elongata*)	The Persian Gulf	Sea	5	28	18-42	23	17-32	82.1[(f)]	75-99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [(a)]	3	20	n.r.	20	n.r.	100.0[(f)]	100	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [(a)]	3	108	n.r.	107	n.r.	99.1[(f)]	99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [(a)]	3	10.2	n.r.	10	n.r.	98.0[(f)]	99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [(a)]	3	20	n.r.	19.5	n.r.	97.5[(f)]	97	1
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	2.95	n.r.	2.63	n.r.	89.2[(f)]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.38	n.r.	0.34	n.r.	89.5[(f)]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.6	n.r.	0.59	n.r.	98.3[(f)]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.25	n.r.	0.18	n.r.	72[(f)]	n.r.	2
Chub (*Leuciscus cephalus*)	Czech rivers, Dyje - Pohansko	Fresh	7	97[(c)]	n.r.	76	n.r.	78.4[(f)]	n.r.	3
Chub (*Leuciscus cephalus*)	Czech rivers, Labe - Obristvi	Fresh	10	263[(d)]	n.r.	256	n.r.	97.3[(f)]	n.r.	3
Shad (*Hilsa ilisha*)	Padma river and Moheshkhali, Cox Bazar, Bangladesh	Fresh/ Sea	64	19[(e)]	2-60	6[(e)]	1-13	31.6[(f)]	n.r.	4
Shad (*Hilsa kelee*)	Padma river, Bangladesh	Fresh	30	21[(e)]	7-52	4[(e)]	3-13	19.0[(f)]	n.r.	4
Jewelled shad (*Ilisha indica*)	Padma river, Bangladesh	Fresh	15	15[(e)]	4-43	4[(e)]	3-7	26.7[(f)]	n.r.	4
Jewelled shad (*Ilisha filigera*)	Moheshkhali, Bangladesh	Sea	15	16[(e)]	7-40	4[(e)]	2-7	25.0[(f)]	n.r.	4
Major carp (*Catla catla*)	Aurial Beel, Bangladesh	Fresh	30	29[(e)]	10-70	21[(e)]	7-58	72.4[(f)]	n.r.	4
Major carp (*Labeo rohita*)	Buriganga river, Bangladesh	Fresh	18	42[(e)]	28-70	29[(e)]	16-59	69.0[(f)]	n.r.	4
Feather back (*Notopterus notopterus*)	Aurial Beel, Bangladesh	Fresh	20	64[(e)]	33-154	48[(e)]	20-138	75.0[(f)]	n.r.	4
Minor carp (*Puntius sarana*)	Aurial Beel, Bangladesh	Fresh	19	21[(e)]	9-50	14[(e)]	6-34	66.7[(f)]	n.r.	4
Catfish (*Heteropneustes fossilis*)	Aurial Beel, Bangladesh	Fresh	28	34[(e)]	18-83	27[(e)]	13-79	79.4[(f)]	n.r.	4
Perch (*Pama pama*)	Meghna river, Bangladesh	Fresh	15	55[(e)]	35-97	30[(e)]	13-54	54.5[(f)]	n.r.	4

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Perch (*Pama pama*)	Meghna river, Bangladesh	Fresh	15	67[e]	27-108	28[e]	13-73	41.8[f]	n.r.	4
Perch (*Tilapia nilotica*)	Dhanmondi lake, Bangladesh	Fresh	26	26[e]	20-42	19[e]	6-35	73.1[f]	n.r.	4
Catfish (*Mystus seenghala*)	Meghna river, Bangladesh	Fresh	42	104[e]	29-427	82[e]	67-402	78.8[f]	n.r.	4
Catfish (*Silonia silondia*)	Meghna river, Bangladesh	Fresh	30	145[e]	51-302	124[e]	32-295	85.5[f]	n.r.	4
Catfish (*Wallago attu*)	Padma river, Bangladesh	Fresh	8	145[e]	60-320	126[e]	42-305	86.9[f]	n.r.	4
Murrel (*Channa punctatus*)	Aurial Beel, Bangladesh	Fresh	21	88[e]	49-148	73[e]	27-142	83.0[f]	n.r.	4
Spiny eel (*Mastacembalus armatus*)	Buriganga river, Bangladesh	Fresh	21	134[e]	83-240	121[e]	67-238	90.3[f]	n.r.	4
Southest European nase (*Chondrostoma miegii*)	Tagus river, Spain	Fresh	10	270[g]	116-532[g]	227[g]	97-440[g]	84.1[f]	n.r.	5
Carp (*Cyprinus carpio*)	Tagus river, Spain	Fresh	3	630[g]	200-1240[g]	530[g]	120-1090[g]	84.1[f]	n.r.	5
Carp (*Cyprinus carpio*)	Tagus river, Spain	Fresh	5	1057[g]	451-1335[g]	917[g]	381-1158[g]	86.8[f]	n.r.	5
Catfish (*Ameiurus melas*)	Tagus river, Spain	Fresh	4	460[g]	150-850[g]	340[g]	110-590[g]	73.9[f]	n.r.	5
Catfish (*Ameiurus melas*)	Tagus river, Spain	Fresh	12	159[g]	38-321[g]	122[g]	31-268[g]	76.7[f]	n.r.	5
Hardhead catfish (*Arius felis*)	Biscayne Bay, Florida	Sea	1[h]	1580[g]	n/a	1960[g]	n/a	124.1[f]	n/a	6
Hardhead catfish (*Arius felis*)	Tampa Bay, Florida	Sea	3[h]	2090[g]	720-4640[g]	1700[g]	250-4420[g]	81.3[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Charlotte Harbour, Florida	Sea	2[h]	1310[g]	1120-1500[g]	1000[g]	n.r.	76.3[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Florida Bay, Florida	Sea	7[h]	2640[g]	1790-3900[g]	1680[g]	1460-1800[g]	63.6[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Pine Island Sound, Florida	Sea	2[h]	400[g]	340-450[g]	300[g]	180-410[g]	75.0[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Whitewater Bay, Florida	Sea	1[h]	3390[g]	n/a	3540[g]	n/a	104.4[f]	n/a	6
Hardhead catfish (*Arius felis*)	Boca Ciega Bay, Florida	Sea	2[h]	860[g]	440-1280[g]	840[g]	360-1320[g]	97.7[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Card Sound, Florida	Sea	1[h]	2120[g]	n/a	2000[g]	n/a	94.3[f]	n/a.	6
White grunt (*Haemulon plumieri*)	Biscayne Bay, Florida	Sea	2[h]	870[g]	710-1030[g]	900[g]	800-990[g]	103.4[f]	n.r.	6
White grunt (*Haemulon plumieri*)	Florida Bay, Florida	Sea	7[h]	390[g]	280-470[g]	390[g]	320-530[g]	100.0[f]	n.r.	6
White grunt (*Haemulon plumieri*)	Cudjoe Basin, Florida	Sea	1[h]	440[g]	n/a	310[g]	n/a	70.5[f]	n/a	6
Sand perch (*Diplectrum formosum*)	Tampa Bay, Florida	Sea	2[h]	470[g]	400-540[g]	390[g]	380-400[g]	83.0[f]	n.r.	6
Sand perch (*Diplectrum formosum*)	Florida Bay, Florida	Sea	1[h]	490[g]	n/a	490[g]	n/a	100.0[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Florida Bay, Florida	Sea	4[h]	830[g]	300-1200[g]	860[g]	330-1270[g]	103.6[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Pine Island Sound, Florida	Sea	2[h]	360[g]	350-360[g]	340[g]	290-380[g]	94.4[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Sarasota Bay, Florida	Sea	2[h]	280[g]	220-340[g]	260[g]	190-320[g]	92.9[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Tampa Bay, Florida	Sea	2[h]	4000[g]	2620-5400[g]	2240[g]	2060-2420[g]	56.0[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Charlotte Harbour, Florida	Sea	3[h]	1700[g]	860-2160[g]	1490[g]	720-2270[g]	87.6[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Florida Bay, Florida	Sea	1[h]	3130[g]	n/a	1640[g]	n/a	52.4[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Pine Island Sound, Florida	Sea	2[h]	960[g]	760-1160[g]	920[g]	n.r.	95.8[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Hillsborough Channels, Florida	Sea	1[h]	4980[g]	n/a	4500[g]	n/a	90.4[f]	n/a	6
Gafftopsail catfish (B*agre marinus*)	Boca Ciega Bay, Florida	Sea	1[h]	1650[g]	n/a	1300[g]	n/a	78.8[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Caloosahatchee river, Florida	Sea	1[h]	1320[g]	n/a	1140[g]	n/a	86.4[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Gordon river, Florida	Sea	1[h]	10100[g]	n/a	2000[g]	n/a	19.8[f]	n/a	6

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Pinfish (*Lagodon rhomboides*)	Charlotte harbour, Florida	Sea	1[(h)]	320[(g)]	n/a	200[(g)]	n/a	62.5[(f)]	n/a	6
Pinfish (*Lagodon rhomboides*)	Florida bay, Florida	Sea	1[(h)]	1 060[(g)]	n/a	900[(g)]	n/a	84.9[(f)]	n/a	6
Pinfish (*Lagodon rhomboides*)	Pine Island Sound, Florida	Sea	3[(h)]	430[(g)]	410-460[(g)]	370[(g)]	270-430[(g)]	86.0[(f)]	n.r.	6
Pinfish (*Lagodon rhomboides*)	Sarasota Bay, Florida	Sea	2[(h)]	550[(g)]	460-630[(g)]	430[(g)]	320-530[(g)]	78.2[(f)]	n.r.	6
Spot (*Leiostomus xanthurus*)	Pine Island Sound, Florida	Sea	1[(h)]	330[(g)]	n/a	260[(g)]	n/a	78.8[(f)]	n/a	6
Spot (*Leiostomus xanthurus*)	Boca Ciega Bay, Florida	Sea	1[(h)]	110[(g)]	n/a	60[(g)]	n/a	54.5[(f)]	n/a	6
Spot (*Leiostomus xanthurus*)	Gordon river, Florida	Sea	1[(h)]	430[(g)]	n/a	40[(g)]	n/a	9.3[(f)]	n/a	6
Pigfish (*Orthopristis chrysoptera*)	Pine Island Sound, Florida	Sea	1[(h)]	380[(g)]	n/a	310[(g)]	n/a	81.6[(f)]	n/a	6
Sand seatrout (*Cynoscion arenarius*)	Tampa Bay, Florida	Sea	2[(h)]	2410[(g)]	2210-2610[(g)]	2040[(g)]	1600-2470[(g)]	84.6[(f)]	n.r.	6
Brown shrimp (*Penaeus aztecus*)	Charlotte Harbour, Florida	Sea	2[(h)]	180[(g)]	160-190[(g)]	130[(g)]	120-140[(g)]	72.2[(f)]	n.r.	6
Fresh trout (*Onchorchynchus mykiss*)	unknown		1	45		42		93	n.r.	7
Fresh tuna (*Thunnus thynnus*)	Indonesia		3	596	162-1110	559	n.r.	93	81-101	7
Fresh salmon (*Salmo salar*)	Norway, Holland		3	36	33- 40	27	15- 39	74	45-98	7
Fresh Euoropean flounder (*Platichthys flesus*)	Holland, Denmark		1	14	n/a	10	n/a	71	n/a	7
Fresh euoropean flounder (*Platichthys flesus*)	Holland, Denmark		1	5	n/a	2	n/a	40	n/a	7
Fresh Cod (*Gadus morhua*)	Holland, Denmark, Croatia		4	69	31 – 139	66	20–149	87	54-107	7
Fresh squid (*Lolligu vulgaris*)	France		1	47	n/a	31	n/a	66	n/a	7
Fresh Conger (*Conger conger*)	Croatia		1	864	n/a	731	n/a	85	n/a	7
Fresh octopus (*Octopus vulgaris*)	Phillipines		1	12	n/a	11	n/a	92	n/a	7
Fresh turbot (*Psetta maxima*)	Spain		1	42	n/a	36	n/a	86	n/a	7
Fresh angler (*Lophius piscatorius*)	Croatia		3	291	71–678)	287	45-702	86.00	63-104	7
Feresh Scorpaena (*Scorpaena scrofa*)	Morocco		1	134	n/a	134	n/a	100	n/a	7
Feresh Scorpaena (*Scorpaena scrofa*)	Morocco		1	371	n/a	265	n/a	71	n/a	7
Fresh goatfish (*Mullus barbatus*)	Croatia		1	210	n/a	221	n/a	105	n/a	7
Fresh goatfish (*Mullus barbatus*)	Croatia		1	108	n/a	80	n/a	74	n/a	7
Fresh common pandora (*Pagellus eruthinus*)	Croatia		1	70	n/a	76	n/a	109	n/a	7
Fresh common pandora (*Pagellus eruthinus*)	Croatia		1	936	n/a	719	n/a	77	n/a	7
Fresh grey mullet (*Mugil chepalus*)	Croatia		1	69	n/a	76	n/a	110	n/a	7
Fresh grey mullet (*Mugil chepalus*)	Croatia		2	31	n.r.	23	n.r.	74	n.r.	7
Fresh atlantic herring (*Clupea harengus*)	Denmark		1	40	n/a	40	n/a	100	n/a	7
Fresh Atlantic herring (*Clupea harengus*)	Denmark		2	38	n.r.	26	n.r.	68	n.r.	7

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Fresh trout (*Salmo trutta*)	Slovenia		1	25	n/a	25	n/a	100	n/a	7
Fresh trout (*Salmo trutta*)	Slovenia		1	37	n/a	25	n/a	68	n/a	7
Fresh Nile perch (*Lates niloticus*)	Tanzania		1	134	n/a	118	n/a	88	n/a	7
Fresh Nile perch (*Lates niloticus*)	Tanzania		1	45	n/a	46	n/a	102	n/a	7
Fresh Atlantic chub mackerel (*Scomber scomber*)	Slovenia		1	56	n/a	54	n/a	96	n/a	7
Fresh Atlantic chub mackerel (*Scomber scomber*)	Slovenia		1	35	n/a	19	n/a	54	n/a	7
Fresh sea bass (*Dicentrachus labrax*)	Croatia		1	137	n/a	92	n/a	67	n/a	7
Fresh sea bass (*Dicentrachus labrax*)	Croatia		1	66	n/a	45	n/a	68	n/a	7
Fresh dover sole (*Solea vulgaris*)	Denmark		1	24	n/a	25	n/a	104	n/a	7
Fresh common dentex (*Dentex dentex*)	Morocco		1	77	n/a	64	n/a	83	n/a	7
Fresh common dentex (*Dentex dentex*)	Morocco		1	53	n/a	32	n/a	60	n/a	7
Fresh gilt head bream (*Sparus aurata*)	Turkey, Croatia, unknown		4	138	103-159	109	79-134	82.00	50-102	7
Fresh sparidae (*Lithognathus mormyrus*)	Croatia		1	238	n/a	246	n/a	103	n/a	7
Fresh sparidae (*Lithognathus mormyrus*)	Croatia		1	78	n/a	40	n/a	51	n/a	7
Fresh John Dory (*Zeus faber*)	Morocco		1	66	n/a	68	n/a	103	n/a	7
Fresh pilchard (*Clupea pilchardus*)	Slovenia		1	70	n/a	77	n/a	110	n/a	7
Fresh pilchard (*Clupea pilchardus*)	Slovenia		1	143	n/a	66	n/a	46	n/a	7
Fresh swordfish (*Xiphias gladius*)	Croatia		1	1 160	n/a	1 080	n/a	93	n/a	7
Fresh European hake (*Merluccius merluccius*)	Croatia		1	52	n/a	56	n/a	108	n/a	7
Canned tuna in vegetable oil	Spain, Thailand, Croatia(i), Thailand(i)		9	125	17-384	93	7-323	68	41-88	7
Canned sardine in vegetable oil	France(i), Croatia(i), Thailand(i)		8	94	4-144	70	2-109	71	42-109	7
Canned anchovy in vegetable oil	Spain(i)		1	22	n/a	16	n/a	73	n/a	7
Canned tuna in olive oil	Italy(i), Spain(i), Thailand		15	243	22-800	212	14-654	85	64-105	7
Canned mackerel in olive oil	Portugal(i)		1	44	n/a	18	n/a	41	n/a	7
Canned mackerel in seed oil	Croatia(i)		1	63	n/a	59	n/a	94	n/a	7
Canned tuna in sunflower oil	Cote d'Ivoire		3	129	103-180	112	92-151	87	84-89	7
Canned mackerel	Slovenia(i)		1	46	n/a	27	n/a	59	n/a	7
Canned tuna in own juice	France(i), Italy(i), Thailand, Thailand(i), Cote d'Ivoire		8	118	24-238	93	16-259	74	57-109	7
Canned mackerel with white wine aroma	France(i)		1	49	n/a	24	n/a	49	n/a	7

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Canned tuna with vegetables	France[(i)], Italy[(i)], Spain[(i)], Thailand[(i)], Slovenia[(i)], Spain[(i)] Cote d'Ivoire, Thailand		17	132	21-858	122	10-862	90	45 -109	7
Canned sardine with vegetables	Croatia[(i)], Thailand		3	62	3-93	35	30-55	71	53-100	7
Canned cod	Croatia[(i)]		1	111	n/a	46	n/a	41	n/a	7
Canned salmon with vegetables	Thailand		1	27	n/a	22	n/a	81	n/a	7
Canned sardines in seed oil	Croatia[(i)]		1	75	n/a	48	n/a	64	n/a	7
Canned salmon in own juice	USA		1	29	n/a	20	n/a	69	n/a	7
Canned herring in tomato sauce	Austria[(i)]		1	51	n/a	26	n/a	51	n/a	7
Canned mackerel with vegetables	Slovenia[(i)]		3	29	18-39	20	10-31	70	51-103	7
Grass carp (*Ctenopharyngodon idella Valenciennes)*	Wanshan, China	fresh	12[(b)]	292	61-680	60	24-98	28.4	7.4-93	8
Blackmouth dogfish (*Galeus melastomus*)	Adriatic Sea, Italy	sea	164	2 660	680-5 030	2 110	470-3 700	79.8	57-100	9
Blackmouth dogfish (*Galeus melastomus*)	Adriatic Sea, Albania	sea	164	1 010	250-2 060	1 010	230-1 990	92.3	72-100	9
Blackmouth dogfish (*Galeus melastomus*)	Ionian Sea	sea	273	820	250-2 840	740	250-2 200	91.5	72-100	9
Blackmouth dogfish (*Galeus melastomus*)	Aegean Sea	sea	218	2 140	850-5 470	1 550	580-4 320	70.3	43-100	9
Small spotted shark (*Scyliorhinus canicula*)	Adriatic Sea, Italy	sea	70	1 490	790-2 560	1 230	680-2 000	82.6	77-89.5	9
Kitefin shark (*Dalatias licha*)	Ionian Sea	sea	3	4 380	3 580-6 000	3 810	3 240-5 000	88	78-95	9
Gulper shark (*Centrophorus granulosus*)	Adriatic Sea, Albania	sea	25	9 660	8 750-10 510	9 090	7 900-10 000	92.9	89.4-96.9	9
Longnose spurdog (*Squalus blainvillei*)	Adriatic Sea, Albania	sea	20	4 530	3 900-7 440	4 050	3 220-7 240	91.8	81-98	9
Velvet belly (*Etmopterus spinax*)	Ionian Sea	sea	120	630	170-1 070	580	170-970	90.8	86.3-100	9
Sharpnose sevengill (*Heptranchias perlo*)	Adriatic Sea, Italy	sea	15	1 270	1 130-1 410	1 200	1 000-1 410	91.3	86.3-100	9
Smoothhound (*Mustelus mustelus*)	Ionian Sea	sea	8	310	230-370	230	180-280	75	69-80	9
Hammerhead (*Sphyrna zygaena*)	Ionian Sea	Sea	1	18 290	n/a	16 060	n/a	87.7	n/a	9
Bokkem (*Trachurus trachurus*)	central and southern Adriatic Sea	sea	100	230	ND-1 870	180	ND-1 210	94	65-100	10
Gilt sardine (*Sardinella aurita*)	central and southern Adriatic Sea	sea	150	90	ND-300	80	ND-300	93	56-100	10
Pilchard (*Sardina pilchardus*)	central and southern Adriatic Sea	sea	300	130	ND-400	90	ND-300	87	80-100	10
Sprat (*Sprattus sprattus*)	central and southern Adriatic Sea	sea	70	60	ND-140	60	ND-140	100	100	10

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Pandora (*Pagellus erythrinus*)	central and southern Adriatic Sea	sea	170	220	ND-700	200	ND-540	93	73-100	10
Megrim (*Lepidorhombus whiffjagonis*)	central and southern Adriatic Sea	sea	150	390	90-1 170	300	90-870	70	54-100	10
Four spotted megrim (*Lepidorhombus bosci*)	central and southern Adriatic Sea	sea	180	350	140-690	350	14-690	100	100	10
Red fish (*Helicolenus dactylopterus*)	central and southern Adriatic Sea	sea	220	420	110-840	400	110-610	98	70-100	10
Striped mullet (*Mullus barbatus*)	central and southern Adriatic Sea	sea	270	390	ND-1 740	370	ND-1 740	89	65-100	10
Skate (*Starry ray*)	central and southern Adriatic Sea	sea	120	730	90-1 780	710	50–1460	80	68-100	10
Forkbeard (*Phycis blennoides*)	central and southern Adriatic Sea	sea	330	360	160-570	260	140-390	71	52-82	10
Goldline (*Sarpa salpa*)	central and southern Adriatic Sea	sea	140	80	60-160	80	60-160	100	100	10
Frost fish (*Lepidopus caudatus*)	central and southern Adriatic Sea	sea	300	610	90-1 610	600	50-1 510	99	78-100	10
Angler fish (*Lophius budegassa*)	central and southern Adriatic Sea	sea	200	760	190-1 770	640	130-1 660	83	67-100	10
Picarel (*Spicara flexuosa*)	central and southern Adriatic Sea	sea	180	200	90-600	120	50–330	77	63-100	10
Hake (*Merluccius merluccius*)	Ionian Sea	sea	n.r.	90	ND-300	90	ND-300	98.3	73-100	11
Hake (*Merluccius merluccius*)	Aegean Sea	sea	n.r.	180	40-480	160	40-480	90.8	60-100	11
Striped mullet (*Mullus barbatus*)	Ionian Sea	sea	n.r.	400	ND-1 500	400	ND-1 500	98.9	92-100	11
Striped mullet (*Mullus barbatus*)	Aegean Sea	sea	n.r.	490	80-1 740	440	80-1 740	79.8	68-100	11
Long rough dab (*Hippoglossoides platessoides*)	Barents Sea, Arctic water	sea	4	160[(e, g)]	n.r.	47[(e, g)]	10-130	29.4[(e)]	9-67	12
Long rough dab (*Hippoglossoides platessoides*)	Barents Sea, Atlantic water	sea	14	290[(e, g)]	n.r.	47[(e, g)]	10-400	16.2[(e)]	3- >100	12
Long rough dab (*Hippoglossoides platessoides*)	Greenland Sea	sea	9	900[(e, g)]	n.r.	440[(e,g)]	10-930	48.9[(e)]	16-49	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Barents Sea, Arctic water	sea	1	70[(e, g)]	n.r.	13[(e, g)]	n/a	18.6[(e)]	n/a	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Barents Sea, Atlantic water	sea	2	310[(e, g)]	n.r.	40[(e, g)]	40-40	12.9[(e)]	1-17	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Greenland Sea	sea	8	1 360[(e, g)]	n.r.	53[(e, g)]	260-1 630	3.9[(e)]	24-53	12
Halibut (*Hippoglossus hippoglossus*)	Barents Sea, Arctic water	sea	8	210[(e, g)]	n.r.	80[(e, g)]	70-200	38.1[(e)]	24->100	12
Halibut (*Hippoglossus hippoglossus*)	Barents Sea, Atlantic water	sea	1	200[(e, g)]	n.r.	760[(e,g)]	n/a	68[(e)]	n/a	12
Starry ray (*Raja radiata*)	Barents Sea, Atlantic water	sea	1	200[(e, g)]	n.r.	8[(e, g)]	n/a	4[(e)]	n/a	12
Atlantic cod (*Gadus morhua*)	Barents Sea, Atlantic water	sea	6	110[(e, g)]	n.r.	21[(e, g)]	10-50	19.1[(e)]	11-57	12
Atlantic cod (*Gadus morhua*)	Barents Sea, Atlantic water	sea	6	150[(e, g)]	n.r.	15[(e, g)]	10-40	10.0[(e)]	6-30	12
Plaice (*Pleuronectes platessa*)	Southern North Sea	sea	5	300[(e, g)]	n.r.	150[(e, g)]	120-440	50.0[(e)]	43-100	12
Angler	greater North Sea	sea	20	87	n.r.	80	n.r.	92.5	n.r.	13

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Lesser spotted dogfish	greater North Sea	sea	20	613	n.r.	598	n.r.	97	n.r.	13
Thornback ray	greater North Sea	sea	19	39	n.r.	37	n.r.	97.8	n.r.	13
Lemon sole	greater North Sea	sea	20	52	n.r.	49	n.r.	95.7	n.r.	13
Pouting	greater North Sea	sea	5	172	n.r.	160	n.r.	92.4	n.r.	13
Whiting	greater North Sea	sea	5	101	n.r.	91	n.r.	90.9	n.r.	13
Atlantic cod (*Gadus morhua*)	greater North Sea	sea	5	53	n.r.	49	n.r.	93.2	n.r.	13
Brill	greater North Sea	sea	5	64	n.r.	59	n.r.	91.8	n.r.	13
Ling	greater North Sea	sea	5	117	n.r.	106	n.r.	91	n.r.	13
Saithe	greater North Sea	sea	5	91	n.r.	88	n.r.	97.4	n.r.	13
Dab	greater North Sea	sea	13	101	n.r.	98	n.r.	97.2	n.r.	13
Sand sole	greater North Sea	sea	9	327	n.r.	308	n.r.	94.4	n.r.	13
Plaice (*Pleuronectes platessa*)	greater North Sea	sea	17	45	n.r.	43	n.r.	97	n.r.	13
Common sole	greater North Sea	sea	16	88	n.r.	86	n.r.	96.2	n.r.	13
Megrim (*Lepidorhombus whiffjagonis*)	greater North Sea	sea	6	83	n.r.	80	n.r.	96.7	n.r.	13
Ghostshark (*Chimaera monstruosa*)	South Adriatic Sea	sea	10[(h)]	3 140	1 300-5 160	2 670	1 140-4 560	83.6	74-97	14
Electric ray (*Torpedo nobiliana*)	South Adriatic Sea	sea	3[(h)]	2 420	1 650-3 590	1 900	1 150-2 760	81	51-97	14
Eagle ray (*Myliobatis aquila*)	South Adriatic Sea	sea	2[(h)]	830	670-1 010	630	400-840	71.6	61-83	14
Herring (*Nematalosa flyensis*)	Lake Murray, Papua New Guinea	fresh	11	49	n.r.	26	n.r.	54	n.r.	15
Herring (*Nematalosa papuensis*)	Lake Murray, Papua New Guinea	fresh	14	48	n.r.	26	n.r.	56	n.r.	15
Groove snouted catfish (*Arius berneyi*)	Lake Murray, Papua New Guinea	fresh	15	230	n.r.	181	n.r.	75	n.r.	15
Seven spotted archerfish (*Toxotes chatareus*)	Lake Murray, Papua New Guinea	fresh	8	360	n.r.	289	n.r.	80	n.r.	15
Sepic garpike (*Strongylura kreffti*)	Lake Murray, Papua New Guinea	fresh	9	380	n.r.	382	n.r.	94	n.r.	15
Giant freshwater anchovy (*Thryssa scratchleyi*)	Lake Murray, Papua New Guinea	fresh	5	380	n.r.	337	n.r.	79	n.r.	15
Barramundi (*Lates calcarifer*)	Lake Murray, Papua New Guinea	fresh	33	500	n.r.	458	n.r.	88	n.r.	15
Silver carp (*Hypophtalmichthys molitrtix*)	Ya-Er lake, China	fresh	13	429	205-928	195	57-360	48	27-72	16
Common carp (*Cyprinus carpio*)	Ya-Er lake, China	fresh	10	79	24-210	39	5-126	44	18-85	16
Crucian carp (*Carassius carassius*)	Ya-Er lake, China	fresh	11	423	131-1 360	185	52 -644	43	29-55	16
Snakehead fish (*Ophiocephalus argus cantor*)	Ya-Er lake, China	fresh	6	827	429-1 199	371	164-499	46	38-54	16
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, reference	estuarine	15	63[(g)]	n.r.	70[(g)]	n.r.	94	n.r.	17
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, moderately contaminated	estuarine	15	120[(g)]	n.r.	110[(g)]	n.r.	97	n.r.	17

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, heavily contaminated	estuarine	15	240[(g)]	n.r.	200[(g)]	n.r.	85	n.r.	17

n: number of samples; w.w.: wet weight; THg: total mercury; MeHg: methylmercury; Ref.: reference; n.r.: not reported; n/a: not applicable; ND: not detected.
(a): semi saline;
(b): samples from mercury mining area;
(c): result from the sampling site with the lowest concentration;
(d): result from the sampling site with the highest concentration;
(e): median;
(f): calculated from the mean (or median) THg and MeHg concentrations;
(g): reported as dry weight;
(h): each sample represents a pooled sample;
(i): country or producer, unknown origin.

References: 1: Agah et al. (2007); 2: Baralkiewicz et al. (2006); 3: Kružiková et al. (2008); 4 Holsbeek et al. (1997); 5: Berzas Nevado et al. (2011); 6: Kannan et al. (1998); 7: Miklavčič et al. (2011a); 8: Qiu et al. (2009); 9: Storelli et al. (2002a); 10: Storelli et al. (2003); 11: Storelli et al. (2005); 12: Joiris et al. (1997); 13: Baeyens et al. (2003); 14: Storelli et al. (2002b); 15: Bowles et al. (2001); 16: Jin et al. (2006); 17: Mieiro et al. (2009).

Table B2: Overview of previously reported literature data on relationship between concentrations of total mercury and methylmercury in seafood.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (small)	F	20	750.3	695.4-805.2	n.r.	n.r.	78.5	n.r.	1
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (medium)	F	50	442.7	410.3-475.1	308[a]	220-589	59.4	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (large)	F	40	381.3	353.4-409.2	n.r.	n.r.	49.6	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (small)	F	9	127.9	118.5 -137.2	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (medium)	F	27	38.4	35.6-41.2	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (large)	F	50	31.7	29.4-34.0	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (small)	F	7	45.7	42.4-49.1	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (medium)	F	40	21.1	19.4-22.4	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (large)	F	30	16	14.8-17.1	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Meander (large)	F	12	106.8	84.6-141.4	n.r.	n.r.	n.r.	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 1	S	n.r.	559[b]	n.r.	150[b]	n.r.	26[b]	n.r.	2
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 2	S	n.r.	320[b]	n.r.	90[b]	n.r.	28[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 3	S	n.r.	410[b]	n.r.	93[b]	n.r.	23[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 4	S	n.r.	236[b]	n.r.	75[b]	n.r.	32[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 5	S	n.r.	360[b]	n.r.	141[b]	n.r.	39[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 6	S	n.r.	383[b]	n.r.	66[b]	n.r.	17[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 7	S	n.r.	434[b]	n.r.	155[b]	n.r.	36[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 8	S	n.r.	370[b]	n.r.	105[b]	n.r.	28[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 9	S	n.r.	262[b]	n.r.	75[b]	n.r.	29[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 10	S	n.r.	280[b]	n.r.	137[b]	n.r.	49[b]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	10 locations on Sardinian coast, campaign 1	S	n.r.	n.r.	35 – 115[b,c]	39[b]	15-51[b,c]	n.r.	33-91[b,c]	3
Mediterranean mussel (*Mytilus galloprovincialis*)	10 locations on Sardinian coast, campaign 2	S	n.r.	n.r.	40-830[b,c]	65[b]	17 – 116[b,c]	n.r.	14-98[b,c]	
Dall's porpoise (*Phocoenoides dalli*)	Japan	S	9	1 230	830-2 390	1 020	680-1 950	84	n.r.	4
Short-finned pilot whale (*Globicephala macrorhynchus*),northern form	Japan	S	8	1 500	790-2 240	1 250	500-1 880	81	n.r.	
Baird's beaked whale (*Berardius bairdii*),	Japan	S	22	1 770	750-6 460	1 250	560-3 470	78	n.r.	
pantropical spotted dolphin (*Stenella attenuata*)	Japan	S	4	4 870	4 280-5 320	2 620	2 010-3 160	54	n.r.	
Risso's dolphin (*Grampus griseus*)	Japan	S	17	4 460	1 710-9 210	3 150	1 330-8 780	74	n.r.	
Rough-toothed dolphin (*Steno bredanensis*)	Japan	S	5	5 020	1 220-9 980	3 510	1 110-6 060	74	n.r.	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Striped dolphin (*Stenella coeruleoalba*)	Japan	S	20	8 550	1 040-63 400	3 740	970-26 200	63	n.r.	
Short-finned pilot whale (*Globicephala macrorhynchus*), southern form	Japan	S	34	11 600	1 210-37 600	6 450	930-17 200	64	n.r.	
Bottlenose dolphin (*Tursiops truncatus*),	Japan	S	37	17 800	590-98 900	6 830	580-15 400	54	n.r.	
False killer whale (*Pseudorca crassidens*)	Japan	S	4	39 500	17 400-81 000	11 200	9 020-13300	36	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 1	E	1[(d)]	18.6	n/a	6.2	n/a	33	n/a	5
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 2	E	1[(d)]	16.3	n/a	7.2	n/a	44	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 3	E	1[(d)]	14.5	n/a	8.5	n/a	59	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 4	E	1[(d)]	30.2	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 1	E	1[(d)]	21.1	n/a	5.3	n/a	25	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 2	E	1[(d)]	17.4	n/a	6.1	n/a	35	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 3	E	1[(d)]	15.6	n/a	6.5	n/a	42	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 4	E	1[(d)]	27.7	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 1	E	1[(d)]	22.3	n/a	5.1	n/a	23	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 2	E	1[(d)]	20.1	n/a	5.3	n/a	26	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 3	E	1[(d)]	15.9	n/a	6.7	n/a	42	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 4	E	1[(d)]	28.3	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 1	S	1[(d)]	23.7	n/a	4.1	n/a	17	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 2	S	1[(d)]	22.9	n/a	4.8	n/a	21	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 3	S	1[(d)]	20.2	n/a	5.1	n/a	25	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 4	S	1[(d)]	22.6	n/a	n.r.	n/a	n.r.	n/a	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Dunkirk and Calais	S	12[(d)]	84[(b)]	n.r.	56[(b)]	n.r.	66[(b)]	n.r.	6
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Boulogne and Canche	S	4[(d)]	97[(b)]	n.r.	65[(b)]	n.r.	65[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Authie and Somme	S	7[(d)]	65[(b)]	n.r.	34[(b)]	n.r.	54[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Caux region	S	12[(d)]	287[(b)]	n.r.	98[(b)]	n.r.	45[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Seine estuary	S	16[(d)]	176[(b)]	n.r.	73[(b)]	n.r.	44[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Calvados	S	15[(d)]	152[(b)]	n.r.	75[(b)]	n.r.	53[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Veys bay, St Vaast	S	10[(d)]	131[(b)]	n.r.	67[(b)]	n.r.	54[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cherbourg	S	4[(d)]	127[(b)]	n.r.	53[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	West Cotentin	S	6[(d)]	78[(b)]	n.r.	38[(b)]	n.r.	51[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cancale	S	8[(d)]	125[(b)]	n.r.	40[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Arguenon-Fresnaye	S	4[(d)]	58[(b)]	n.r.	20[(b)]	n.r.	35[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Saint Brieuc	S	11[(d)]	75[(b)]	n.r.	34[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Paimpol-Perros-Guirec	S	4[(d)]	92[(b)]	n.r.	48[(b)]	n.r.	52[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Lannion	S	4[(d)]	102[(b)]	n.r.	62[(b)]	n.r.	61[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Morlaix	S	8[(d)]	128[(b)]	n.r.	70[(b)]	n.r.	55[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Benoit Aber	S	4[(d)]	78[(b)]	n.r.	26[(b)]	n.r.	34[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Brest	S	16[(d)]	145[(b)]	n.r.	64[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Concarneau	S	4[(d)]	107[(b)]	n.r.	76[(b)]	n.r.	68[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Aven-Belon-Laita	S	4[(d)]	131[(b)]	n.r.	86[(b)]	n.r.	65[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Lorient	S	4[(d)]	153[(b)]	n.r.	11[(b)]	n.r.	74[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Etel	S	3[(d)]	138[(b)]	n.r.	77[(b)]	n.r.	57[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Gulf of Morbihan	S	12[(d)]	134[(b)]	n.r.	63[(b)]	n.r.	49[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Vilaine	S	16[(d)]	121[(b)]	n.r.	48[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	loire and Bourgneuf	S	19[(d)]	129[(b)]	n.r.	52[(b)]	n.r.	41[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Vendee	S	4[(d)]	329[(b)]	n.r.	99[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Pertuis Breton	S	8[(d)]	232[(b)]	n.r.	76[(b)]	n.r.	35[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Pertuis de Antioche	S	4[(d)]	253[(b)]	n.r.	51[(b)]	n.r.	21[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Marennes-Oleron	S	24[(d)]	207[(b)]	n.r.	54[(b)]	n.r.	28[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Gironde	S	11[(d)]	211[(b)]	n.r.	61[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Arcachon	S	16[(d)]	222[(b)]	n.r.	71[(b)]	n.r.	32[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Basque region	S	16[(d)]	199[(b)]	n.r.	94[(b)]	n.r.	52[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Roussillon	S	14[(d)]	103[(b)]	n.r.	43[(b)]	n.r.	41[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Languedoc	S	13[(d)]	132[(b)]	n.r.	88[(b)]	n.r.	64[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Rhone delta and Fos	S	16[(d)]	155[(b)]	n.r.	86[(b)]	n.r.	57[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Marseille	S	4[(d)]	169[(b)]	n.r.	70[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Toulon-St Raphael	S	6[(d)]	220[(b)]	n.r.	73[(b)]	n.r.	37[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cannes-Menton	S	6[(d)]	124[(b)]	n.r.	49[(b)]	n.r.	42[(b)]	n.r.	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	West Corsica-Ajaccio	S	4[(d)]	173[(b)]	n.r.	83[(b)]	n.r.	53[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	East Corsica	S	7[(d)]	99[(b)]	n.r.	45[(b)]	n.r.	45[(b)]	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	20	41.1	n.r.	12.2	n.r.	29.6	n.r.	7
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	10	29.2	n.r.	8.9	n.r.	30.5	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	20	25.3	n.r.	8.5	n.r.	32.9	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	32.7	n.r.	11.5	n.r.	35.2	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	18.6	n.r.	5.9	n.r.	31.9	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	11.6	n.r.	4.5	n.r.	38.4	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	25	48.3	n.r.	13.8	n.r.	28.7	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	29	51.3	n.r.	18.0	n.r.	35.1	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	10	45.4	n.r.	21.0	n.r.	46.2	n.r.	
Oyster (*Crassostrea tulipa*)	Ghana, Benya lagoon, dry season	S	54	210[(b,e, f)]	100-470[(b,f)]	130[(b,e)]	30-390[(b)]	54[(e)]	19->100	8
Oyster (*Crassostrea tulipa*)	Ghana, Benya lagoon, wet season	S	15	140[(b,e,g)]	100-310[(b,g)]	90[(b,e)]	30-240[(b)]	36[(e)]	17->100	
Oyster (*Crassostrea tulipa*)	Ghana, Sakumo lagoon, dry season	S	25	130[(b,e)]	80-180[(b)]	100[(b,e)]	60-230[(b)]	80[(e)]	39->100	
Oyster (*Crassostrea tulipa*)	Ghana, Sakumo lagoon, wet season	S	45	120[(b,e,h)]	60-230[(b,h)]	50[(b,e,i)]	30-130[(b,i)]	39[(e)]	17-68	
Oyster (*Crassostrea tulipa*)	Ghana, Ningo lagoon, dry season	S	19	160[(b,e,j)]	30-230[(b,j)]	80[(b,e,j)]	40-190[(b,j)]	50[(e)]	17->100	
Oyster (*Crassostrea tulipa*)	Ghana, Ningo lagoon, wet season	S	5	130[(b,e,k)]	100-160[(b,k)]	50[(b,e)]	40-90[(b)]	47[(e)]	40-58	
Common mussel (*Perna perna*)	Ghana, Benya lagoon, dry season	S	30	370[(b,e)]	190-660[(b)]	160[(b,e,l)]	70-550[(b,l)]	43[(e)]	12->100	
Common mussel (*Perna perna*)	Ghana, Benya lagoon, wet season	S	14	200[(b,e,m)]	110-300[(b,m)]	90[(b,e,n)]	40-190[(b,n)]	38[(e)]	14-79	
Common mussel (*Perna perna*)	Ghana, Sakumo lagoon, dry season	S	15	330[(b,e,o)]	200-530[(b,o)]	100[(b,e,o)]	40-180[(b,o)]	29[(e)]	9-50	
Common mussel (*Perna perna*)	Ghana, Sakumo lagoon, wet season	S	10	260[(b,e,p)]	170-760[(b,p)]	70[(b,e)]	30-180[(b)]	33[(e)]	28-100	

n: number of samples or sampling sites; ww: wet weight; THg: total mercury; MeHg: methylmercury; Ref.: reference; n.r.: not reported; n/a: not applicable; F: freshwater; S: seawater; E: estuarine.

(a): MeHg only analysed in samples from the sampling site that showed the highest concentrations of THg;
(b): reported as dry weight;
(c): results are mean values from 2 measurements on the same station at different times;
(d): each sample represents a pooled sample;
(e): median;
(f): n = 59;
(g): n = 24;
(h): n = 55;

(i): n = 71;
(j): n = 31;
(k): n = 12;
(l): n = 35;
(m): n = 30;
(n): n = 25;
(o): n = 19;
(p): n = 18.

References: 1: Carrasco et al. (2008); 2: Di Leo et al. (2010); 3: Ipolyi et al. (2004); 4: Endo et al. (2005); 5: Mikac et al. (1996); 6: Claisse et al. (2001); 7: Kehrig et al. (2002); 8: Joiris et al. (2000).

C. CONSUMPTION

Table C1: Overview on 'Fish and other seafood' consumption (g/day) in the total population by age class. Minimum, median and maximum of the mean and 95th percentile values across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Mean consumption in the total population (g/day)							
Minimum	0.5	3.2	5.2	5.6	8.8	5.5	5.2
Median	1.3	5.2	10.3	17.3	25.9	27.7	25.8
Maximum	2.2	32.6	40.2	48.9	75.3	46.1	33.8
P95 consumption in the total population (g/day)[(a)]							
Minimum	-	20.5	35.0	42.0	54.7	50.0	45.8
Median	-	26.1	44.0	72.8	100.0	120.5	99.7
Maximum		33.3	132.0	169.5	194.3	137.5	117.4

P95: 95th percentile.
(a): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C2: Overview on 'Fish and other seafood' consumption (g/day) in the consumers only by age class. Minimum, median and maximum of the mean, 95th percentile values and percentage of consumers across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Percentage of consumers (%)[(a)]							
	7.1	31.6	44.2	50.2	55.2	54.0	52.3
Mean consumption in the consumers only (g/day)							
Minimum	17.2	13.9	14.6	14.5	20.3	25.9	30.2
Median	21.8	18.6	28.8	51.7	62.7	67.4	55.1
Maximum	26.5	74.5	58.8	74.5	83.4	74.9	68.9
P95 consumption in the consumers only (g/day)[(b)]							
Minimum	-	35.7	40.5	43.2	54.4	57.5	87.1
Median	-	63.3	62.5	138.7	150.0	158.8	134.8
Maximum	-	90.9	154.7	181.8	201.1	180.1	150.0

P95: 95th percentile.
(a): Based on average of percentages from all included surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C3: Overview on 'Fish meat' consumption (g/day) in the total population by age class. Minimum, median and maximum of the mean and 95th percentile values across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Mean consumption in the total population (g/day)							
Minimum	0.5	1.2	2.2	4.4	4.8	5.5	5.2
Median	1.3	4.1	7.9	12.6	16.9	21.8	21.0
Maximum	2.2	29.0	30.8	36.4	57.3	35.5	26.3
P95 consumption in the total population (g/day)[(a)]							
Minimum	-	9.4	15.0	34.3	36.1	50.0	45.8
Median	-	18.3	37.5	60.3	96.0	100.0	76.4
Maximum	-	33.3	101.5	142.5	159.1	137.5	100.0

P95: 95th percentile.
(a): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C4: Overview on 'Fish meat' consumption (g/day) in the consumers only by age class. Minimum, median and maximum values of the mean, 95th percentile values and percentage of consumers across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Percentage of consumers (%)[(a)]							
	7.1	24.3	34.6	39.7	48.0	50.3	49.1
Mean consumption in the consumers only (g/day)							
Minimum	17.2	12.6	13.0	12.6	18.1	23.5	27.1
Median	21.8	17.1	28.0	47.1	55.9	56.6	51.3
Maximum	26.5	95.0	53.5	69.6	79.1	74.7	69.0
P95 consumption in the consumers only (g/day)[(b)]							
Minimum	-	35.7	39.8	38.3	51.0	53.9	76.4
Median	-	63.3	76.7	107.0	139.6	134.4	123.2
Maximum	-	90.9	115.0	175.0	179.0	180.5	149.5

P95: 95th percentile.
(a): Based on average of percentages from all included surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

D. EXPOSURE

Table D1: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in toddlers in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	36	0.20	0.21	0.21	-(a)	-(a)	-(a)
Bulgaria	NUTRICHILD	428	0.25	0.27	0.28	1.51	1.53	1.58
Germany	DONALD 2006	92	0.31	0.31	0.31	2.11	2.13	2.15
Germany	DONALD 2007	85	0.18	0.19	0.19	0.85	0.86	0.87
Germany	DONALD_2008	84	0.26	0.27	0.27	1.63	1.65	1.66
Spain	enKid	17	1.32	1.42	1.51	-(a)	-(a)	-(a)
Finland	DIPP	497	0.58	0.59	0.60	2.70	2.72	2.74
Italy	INRAN SCAI 2005/06	36	1.49	1.57	1.65	-(a)	-(a)	-(a)
the Netherlands	VCP kids	322	0.09	0.09	0.09	0.66	0.68	0.70
Minimum			**0.09**	**0.09**	**0.09**	**0.66**	**0.68**	**0.70**
Median			**0.26**	**0.27**	**0.28**	**1.57**	**1.59**	**1.62**
Maximum			**1.49**	**1.57**	**1.65**	**2.70**	**2.72**	**2.74**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
Calculation of P95 not possible due to low number of participants.

Table D2: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in other children in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	625	0.28	0.29	0.29	1.59	1.60	1.62
Bulgaria	NUTRICHILD	433	0.21	0.22	0.23	1.40	1.43	1.49
Czech Republic	SISP04	389	0.50	0.50	0.51	3.32	3.35	3.38
Germany	DONALD 2006	211	0.22	0.23	0.23	1.15	1.16	1.17
Germany	DONALD 2007	226	0.20	0.20	0.20	1.11	1.12	1.13
Germany	DONALD_2008	223	0.24	0.24	0.24	1.52	1.53	1.55
Denmark	Danish Dietary Survey	490	0.37	0.38	0.39	1.20	1.21	1.24
Spain	enKid	156	1.05	1.09	1.14	4.47	4.69	4.90
Spain	NUT INK05	399	1.19	1.23	1.28	4.08	4.14	4.24
Finland	DIPP	933	0.49	0.49	0.50	2.33	2.36	2.38
Finland	STRIP	250	0.27	0.27	0.28	1.36	1.38	1.38
France	INCA2	482	0.61	0.63	0.64	1.88	1.97	1.99
Greece	Regional Crete	839	0.59	0.61	0.63	2.75	2.79	2.96
Italy	INRAN SCAI 2005/06	193	1.45	1.49	1.54	4.60	4.96	5.04
Latvia	EFSA TEST	189	0.20	0.20	0.21	1.61	1.63	1.64
the Netherlands	VCP kids	957	0.13	0.14	0.14	0.73	0.75	0.76
Sweden	NFA	1 473	0.31	0.32	0.32	1.28	1.31	1.33
Minimum			**0.13**	**0.14**	**0.14**	**0.73**	**0.75**	**0.76**
Median			**0.31**	**0.32**	**0.32**	**1.59**	**1.60**	**1.62**
Maximum			**1.45**	**1.49**	**1.54**	**4.60**	**4.96**	**5.04**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D3: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in adolescents in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	584	0.19	0.20	0.20	1.15	1.16	1.19
Cyprus	Childhealth	303	0.40	0.41	0.43	1.77	1.83	1.85
Czech Republic	SISP04	298	0.33	0.33	0.34	2.46	2.49	2.51
Germany	National Nutrition Survey II	1 011	0.08	0.08	0.09	0.41	0.42	0.42
Denmark	Danish Dietary Survey	479	0.23	0.23	0.24	0.78	0.79	0.80
Spain	AESAN FIAB	86	0.51	0.54	0.58	1.49	1.60	1.78
Spain	enKid	209	0.93	0.96	0.99	3.35	3.45	3.56
Spain	NUT INK05	651	0.74	0.77	0.80	2.70	2.80	2.85
France	INCA2	973	0.29	0.29	0.30	0.99	1.01	1.02
Italy	INRAN SCAI 2005/06	247	1.06	1.09	1.12	5.04	5.05	5.06
Latvia	EFSA TEST	470	0.07	0.08	0.08	0.62	0.64	0.65
Sweden	NFA	1 018	0.21	0.22	0.22	0.98	0.99	1.00
Minimum			**0.07**	**0.08**	**0.08**	**0.41**	**0.42**	**0.42**
Median			**0.31**	**0.31**	**0.32**	**1.32**	**1.38**	**1.48**
Maximum			**1.06**	**1.09**	**1.12**	**5.04**	**5.05**	**5.06**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D4: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in adults in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	1 304	0.24	0.24	0.25	1.34	1.35	1.38
Czech Republic	SISP04	1 666	0.20	0.20	0.20	1.50	1.52	1.53
Germany	National Nutrition Survey II	10 419	0.16	0.16	0.17	1.11	1.12	1.13
Denmark	Danish Dietary Survey	2 822	0.17	0.17	0.18	0.53	0.53	0.55
Spain	AESAN	410	0.89	0.92	0.95	2.91	2.98	3.08
Spain	AESAN FIAB	981	1.04	1.08	1.12	2.76	2.86	2.97
Finland	FINDIET 2007	1 575	0.36	0.36	0.37	2.01	2.03	2.05
France	INCA2	2 276	0.34	0.34	0.35	1.11	1.13	1.17
Great Britain	NDNS	1 724	0.30	0.30	0.31	1.01	1.02	1.03
Hungary	National Representative Survey	1 074	0.12	0.12	0.12	0.81	0.82	0.82
Ireland	NSIFCS	958	0.20	0.20	0.20	0.74	0.76	0.78
Italy	INRAN SCAI 2005/06	2 313	0.82	0.84	0.86	3.00	3.04	3.08
Latvia	EFSA TEST	1 306	0.20	0.20	0.20	1.26	1.28	1.29
the Netherlands	DNFCS 2003	750	0.07	0.07	0.07	0.50	0.51	0.53
Sweden	Riksmaten 1997/98	1 210	0.28	0.29	0.29	0.94	0.96	0.97
Minimum			**0.07**	**0.07**	**0.07**	**0.50**	**0.51**	**0.53**
Median			**0.24**	**0.24**	**0.25**	**1.11**	**1.13**	**1.14**
Maximum			**1.04**	**1.08**	**1.12**	**3.00**	**3.04**	**3.08**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D5: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	518	0.25	0.26	0.26	1.24	1.27	1.30
Germany	National Nutrition Survey II	2 006	0.19	0.19	0.19	1.23	1.24	1.26
Denmark	Danish Dietary Survey	309	0.18	0.18	0.19	0.50	0.51	0.52
Finland	FINDIET 2007	463	0.47	0.47	0.48	2.49	2.49	2.49
France	INCA2	264	0.41	0.42	0.43	1.11	1.13	1.14
Hungary	National Representative Survey	206	0.06	0.06	0.07	0.34	0.34	0.35
Italy	INRAN SCAI 2005/06	290	0.61	0.63	0.65	1.71	1.73	1.74
Minimum			**0.06**	**0.06**	**0.07**	**0.34**	**0.34**	**0.35**
Median			**0.25**	**0.26**	**0.26**	**1.23**	**1.24**	**1.26**
Maximum			**0.61**	**0.63**	**0.65**	**2.49**	**2.49**	**2.49**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D6: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in very elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	712	0.25	0.25	0.26	1.40	1.41	1.42
Germany	National Nutrition Survey II	490	0.21	0.21	0.21	1.38	1.42	1.42
Denmark	Danish Dietary Survey	20	0.23	0.24	0.24	-(a)	-(a)	-(a)
France	INCA2	84	0.37	0.38	0.39	1.08	1.11	1.13
Hungary	National Representative Survey	80	0.05	0.06	0.06	0.13	0.14	0.16
Italy	INRAN SCAI 2005/06	228	0.33	0.35	0.36	1.15	1.17	1.19
Minimum			**0.05**	**0.06**	**0.06**	**0.13**	**0.14**	**0.16**
Median			**0.24**	**0.25**	**0.25**	**1.15**	**1.17**	**1.19**
Maximum			**0.37**	**0.38**	**0.39**	**1.40**	**1.42**	**1.42**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Calculation of P95 not possible due to low number of participants.

Table D8: Lower, middle and upper bound 95th percentile methylmercury exposure among fish meat consumers only by survey and age class in µg Hg/kg body weight per week.

Country	Survey	Age class	N	P95		
				LB	MB	UB
Spain	AESAN	Adults	279	3.03	3.08	3.20
Spain	AESAN FIAB	Adults	796	2.88	2.95	3.09
Cyprus	Childhealth	Adolescents	88	2.53	2.56	2.58
Denmark	Danish Dietary Survey	Other children	379	1.39	1.41	1.43
		Adolescents	394	0.80	0.80	0.81
		Adults	2.392	0.56	0.57	0.58
		Elderly	279	0.54	0.54	0.55
Belgium	National Diet 2004	Adolescents	128	2.38	2.40	2.42
		Adults	399	2.05	2.08	2.10
		Elderly	162	2.12	2.14	2.16
		Very elderly	201	2.29	2.31	2.33
Finland	DIPP	Toddlers	221	4.60	4.66	4.72
		Other children	443	2.89	2.90	2.92
the Netherlands	DNFCS 2003	Adults	87	1.65	1.66	1.67
Latvia	EFSA TEST	Adults	351	2.41	2.44	2.46
Spain	enKid	Other children	67	4.71	4.82	5.03
		Adolescents	101	4.86	5.09	5.22
Finland	FINDIET 2007	Adults	620	3.25	3.26	3.27
		Elderly	220	4.52	4.52	4.52
France	INCA2	Other children	336	1.96	2.00	2.02
		Adolescents	617	1.19	1.21	1.23
		Adults	1.716	1.21	1.22	1.23
		Elderly	224	1.08	1.11	1.15
		Very elderly	69	1.07	1.10	1.12
Italy	INRAN SCAI 2005/06	Other children	103	7.47	7.48	7.49
		Adolescents	140	7.22	7.25	7.29
		Adults	1.432	6.15	6.16	6.17
		Elderly	180	2.42	2.45	2.47
		Very elderly	118	1.30	1.31	1.32
Germany	National Nutrition Survey II	Adolescents	87	3.05	3.05	3.05
		Adults	2.304	2.02	2.04	2.07
		Elderly	565	1.95	1.95	1.95
		Very elderly	150	1.95	1.96	1.98
Hungary	National Represent. Survey	Adults	136	3.36	3.39	3.42
Great Britain	NDNS	Adults	1.136	1.22	1.24	1.25
Sweden	NFA	Other children	489	1.88	1.89	1.95
		Adolescents	290	1.30	1.32	1.33
Ireland	NSIFCS	Adults	609	0.84	0.85	0.86
Spain	NUT INK05	Other children	236	4.71	4.85	4.99
		Adolescents	370	3.11	3.14	3.25
Bulgaria	NUTRICHILD	Toddlers	62	4.87	5.10	5.32
		Other children	69	3.51	3.88	4.09
Greece	Regional Crete	Other children	252	5.86	5.86	5.86
Belgium	Regional Flanders	Other children	133	3.33	3.36	3.40
	Riksmaten 1997/98	Adults	725	1.04	1.05	1.06
Czech Republic	SISP04	Other children	95	5.13	5.18	5.23
		Adults	333	2.54	2.56	2.59
Finland	STRIP	Other children	94	2.30	2.32	2.34
the Netherlands	VCP kids	Other children	69	4.73	4.78	4.83

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D9: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in toddlers in µg Hg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	36	0.56	1.36	2.16	-(a)	-(a)	-(a)
Bulgaria	NUTRICHILD	428	0.41	1.13	1.84	0.86	1.99	3.26
Germany	DONALD 2006	92	0.31	0.82	1.33	0.88	1.52	2.36
Germany	DONALD 2007	85	0.27	0.79	1.31	0.67	1.35	2.18
Germany	DONALD_2008	84	0.28	0.83	1.38	0.72	1.55	2.39
Spain	enKid	17	0.51	1.16	1.80	-(a)	-(a)	-(a)
Finland	DIPP	497	0.37	0.94	1.51	1.07	2.30	3.54
Italy	INRAN SCAI 2005/06	36	0.59	1.15	1.71	-(a)	-(a)	-(a)
the Netherlands	VCP kids	322	0.35	1.16	1.98	0.82	2.24	4.06
Minimum			**0.27**	**0.79**	**1.31**	**0.67**	**1.35**	**2.18**
Median			**0.37**	**1.13**	**1.71**	**0.86**	**1.62**	**2.20**
Maximum			**0.59**	**1.36**	**2.16**	**1.07**	**2.30**	**4.06**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Calculation of P95 not possible due to low number of participants.

Table D10: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in other children in µg Hg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	625	0.39	0.99	1.60	0.82	1.69	2.66
Bulgaria	NUTRICHILD	433	0.35	0.92	1.50	0.74	1.62	2.56
Czech Republic	SISP04	389	0.29	0.59	0.89	0.87	1.27	1.66
Germany	DONALD 2006	211	0.25	0.70	1.14	0.59	1.22	2.06
Germany	DONALD 2007	226	0.24	0.67	1.10	0.51	1.23	2.05
Germany	DONALD_2008	223	0.25	0.66	1.08	0.67	1.23	1.93
Denmark	Danish Dietary Survey	490	0.26	0.71	1.17	0.50	1.12	1.81
Spain	enKid	156	0.43	0.84	1.26	1.14	1.73	2.35
Spain	NUT INK05	399	0.47	0.85	1.24	1.12	1.67	2.20
Finland	DIPP	933	0.38	1.06	1.75	0.86	1.99	3.37
Finland	STRIP	250	0.47	0.95	1.43	1.17	1.77	2.37
France	INCA2	482	0.35	0.78	1.21	0.74	1.38	2.16
Greece	Regional Crete	839	0.55	0.94	1.33	1.27	1.79	2.38
Italy	INRAN SCAI 2005/06	193	0.76	1.13	1.50	1.85	2.27	2.82
Latvia	EFSA TEST	189	0.44	0.69	0.94	0.98	1.36	1.78
the Netherlands	VCP kids	957	0.29	0.97	1.65	0.65	1.83	3.19
Sweden	NFA	1 473	0.42	0.81	1.21	0.88	1.41	2.01
Minimum			**0.24**	**0.59**	**0.89**	**0.50**	**1.12**	**1.66**
Median			**0.38**	**0.84**	**1.24**	**0.86**	**1.62**	**2.20**
Maximum			**0.76**	**1.13**	**1.75**	**1.85**	**2.27**	**3.37**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D11: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in adolescents in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	584	0.19	0.39	0.60	0.53	0.83	1.17
Cyprus	Childhealth	303	0.27	0.46	0.65	0.62	0.85	1.16
Czech Republic	SISP04	298	0.20	0.41	0.61	0.65	0.85	1.22
Germany	National Nutrition Survey II	1 011	0.17	0.42	0.67	0.48	0.91	1.42
Denmark	Danish Dietary Survey	479	0.16	0.42	0.68	0.31	0.71	1.16
Spain	AESAN FIAB	86	0.23	0.41	0.59	0.57	0.79	1.00
Spain	enKid	209	0.33	0.54	0.75	1.04	1.35	1.53
Spain	NUT INK05	651	0.29	0.51	0.74	0.70	0.99	1.33
France	INCA2	973	0.17	0.41	0.64	0.38	0.78	1.20
Italy	INRAN SCAI 2005/06	247	0.51	0.73	0.94	1.70	1.85	2.33
Latvia	EFSA TEST	470	0.34	0.52	0.70	0.76	1.02	1.30
Sweden	NFA	1 018	0.29	0.53	0.78	0.63	0.95	1.32
Minimum			**0.16**	**0.39**	**0.59**	**0.31**	**0.71**	**1.00**
Median			**0.25**	**0.44**	**0.68**	**0.62**	**0.88**	**1.26**
Maximum			**0.51**	**0.73**	**0.94**	**1.70**	**1.85**	**2.33**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D12: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in adults in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	1 304	0.19	0.35	0.51	0.52	0.72	1.01
Czech Republic	SISP04	1 666	0.14	0.26	0.38	0.42	0.55	0.72
Germany	National Nutrition Survey II	10 419	0.22	0.40	0.59	0.59	0.86	1.23
Denmark	Danish Dietary Survey	2 822	0.16	0.32	0.49	0.37	0.59	0.84
Spain	AESAN	410	0.30	0.46	0.61	0.79	1.03	1.25
Spain	AESAN FIAB	981	0.33	0.49	0.65	0.87	1.10	1.30
Finland	FINDIET 2007	1 575	0.20	0.36	0.52	0.63	0.81	1.02
France	INCA2	2 276	0.21	0.36	0.51	0.50	0.71	0.96
Great Britain	NDNS	1 724	0.27	0.41	0.55	0.59	0.77	0.97
Hungary	National Representative Survey	1 074	0.15	0.27	0.39	0.36	0.53	0.72
Ireland	NSIFCS	958	0.29	0.44	0.59	0.53	0.72	0.93
Italy	INRAN SCAI 2005/06	2 313	0.40	0.53	0.67	1.52	1.66	1.83
Latvia	EFSA TEST	1 306	0.30	0.41	0.53	0.70	0.86	1.07
the Netherlands	DNFCS 2003	750	0.23	0.42	0.61	0.56	0.78	1.06
Sweden	Riksmaten 1997/98	1 210	0.34	0.52	0.70	0.66	0.88	1.16
Minimum			**0.14**	**0.26**	**0.38**	**0.36**	**0.53**	**0.72**
Median			**0.23**	**0.41**	**0.55**	**0.59**	**0.78**	**1.02**
Maximum			**0.40**	**0.53**	**0.70**	**1.52**	**1.66**	**1.83**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D13: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	518	0.18	0.30	0.43	0.46	0.63	0.84
Germany	National Nutrition Survey II	2 006	0.22	0.37	0.52	0.56	0.75	1.01
Denmark	Danish Dietary Survey	309	0.17	0.32	0.47	0.39	0.58	0.86
Finland	FINDIET 2007	463	0.22	0.35	0.48	0.69	0.84	1.09
France	INCA2	264	0.23	0.37	0.50	0.54	0.72	0.92
Hungary	National Representative Survey	206	0.13	0.23	0.33	0.25	0.40	0.55
Italy	INRAN SCAI 2005/06	290	0.30	0.42	0.55	0.77	0.94	1.12
Minimum			**0.13**	**0.23**	**0.33**	**0.25**	**0.40**	**0.55**
Median			**0.22**	**0.35**	**0.48**	**0.54**	**0.72**	**0.92**
Maximum			**0.30**	**0.42**	**0.55**	**0.77**	**0.94**	**1.12**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D14: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in very elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	712	0.17	0.29	0.42	0.47	0.62	0.83
Germany	National Nutrition Survey II	490	0.24	0.38	0.52	0.61	0.78	1.01
Denmark	Danish Dietary Survey	20	0.19	0.34	0.49	-(a)	-(a)	-(a)
France	INCA2	84	0.19	0.31	0.44	0.34	0.54	0.78
Hungary	National Representative Survey	80	0.14	0.25	0.35	0.25	0.40	0.54
Italy	INRAN SCAI 2005/06	228	0.24	0.37	0.49	0.64	0.81	0.98
Minimum			**0.14**	**0.25**	**0.35**	**0.25**	**0.40**	**0.54**
Median			**0.19**	**0.33**	**0.47**	**0.47**	**0.62**	**0.82**
Maximum			**0.24**	**0.38**	**0.52**	**0.64**	**0.81**	**1.01**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a) Calculation of P95 not possible due to low number of surveys.

Table D15: Contribution (%) of the all food groups, FoodEx Level 1 to chronic dietary exposure to inorganic mercury using middle bound concentrations. Range of the average contribution is shown.

Food category	Lowest average contribution (%) – Highest average contribution (%)					
	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Fish and other seafood	1.6-29	2.9-32	3.0-38	3.7-53	5.6-35	4.5-26
Composite food	0.3-12	0-40	0-35	0-40	0-8.3	0-9.9
Non-alcoholic beverages	0-7.2	0.7-21	2.1-22	1.6-43	3.8-31	5.4-32
Vegetables and vegetable products	3.7-13	1.6-23	1.4-21	1.4-26	5.0-24	4.5-22
Fruit and vegetable juices	8.9-34	1.1-34	0.6-31	0.3-19	1.5-12	2.0-10
Grains and grain-based products	6.8-11	6.2-17	9.3-18	6.9-17	7.3-17	9.8-17
Milk and dairy products	16-29	6.5-22	5.4-16	4.8-14	5.4-13	6.6-12
Meat and meat products	2.3-6.8	2.6-9.4	4.1-11	2.6-13	4.2 - 12	3.7-12
Starchy roots and tubers	1.2-6.0	1.3-4.0	1.2- 4.3	1.1-5.9	1.4-4.9	1.7-5.3
Alcoholic beverages	0 – 0.0	0.0-0.1	0.0-0.7	0.6-5.8	0.5-3.8	0.7-3.7
Fruit and fruit products	2.4-8.2	2.0-8.2	2.3-6.8	2.1-5.5	4.6-7.3	5.1-7.6
Drinking water	0.6-3.8	0.0-3.1	0.0-3.3	0.3-5.0	0.5-2.5	0.3-3.0
Products for special nutritional use	0-0.1	0-1.6	0-6.9	0-3.8	0-1.1	0-5.7
Animal and vegetable fats and oils	0.2-1.7	0.3-2.2	0.2-2.5	0.2-2.6	0.7-2.6	0.8-3.0
Legumes, nuts and oilseeds	0.1-1.5	0.1-2.1	0.2-2.4	0.2-1.4	0.3-1.5	0.3-1.6
Herbs, spices and condiments	0.1-1.6	0.1-1.9	0.1-1.6	0.3-1.4	0.5-1.7	0.5-1.9
Sugar and confectionery	0.4-3.1	0.5-3.6	0.4-2.3	0.2-1.3	0.2-0.8	0.3-0.7
Eggs and egg products	0-0.7	0-0.9	0-0.9	0.1-1.1	0.2-1.1	0.2-1.0
Snacks, desserts, and other foods	0.1-6.0	0.4-6.0	0.4-1.1	0.1-0.9	0.1-0.5	0-0.6
Food for infants and small children	0.6-18	0-0.7	0-0.1	0	0	0

E. OVERVIEW OF REPORTED RATIOS OF BIOMARKERS

Table E1: Reported blood to hair ratios.

	Ratio	Additional information	Reference
THg blood / THg hair	1:250 (1:140 – 1:370)		FAO/WHO (2004)
THg blood / THg hair	median ratio 1:190; 5-95 % 1: 74 – 1:442 median ratio 1:370; 5-95 % 1:137 – 1:932 median ratio 1:264; 5-95 % 1: 67 – 1:632	Faroese children at birth (n = 993) 7 years of age (n = 665) 14 years of age (n = 780)	Budtz-Jorgensen et al. (2004)
THg blood / THg hair	mean ratio about 1:350	Japanese pregnant women (n = 115)	Sakamoto et al. (2007)
THg blood / THg hair	median ratio 1:254 (linear regression) THg blood/THg hair (calculated from mean values) 1:345 IHg blood/THg hair (calculated from mean values) 1:2 174 (OHg blood/THg hair (calculated from mean values) 1:416)* *OHg = THg-IHg	Swedish men (n = 5) and women (n = 23)	Berglund et al. (2005)
THg blood / THg hair	unadjusted medians 1:194 – 1:433 adjusted (for the lag from blood to hair on the scalp) medians 1:315 – 1:370 adjusted mean 1:344 (SD 54)	Healthy Japanese adults (n = 27), 29 weeks, 3.4 µg/kg b.w. per week methylmercury from the consumption of tuna/swordfish	Yaginuma-Sakurai et al. (2012)
THg blood / THg hair	1:250	42 male members of Faroese whaling society	Choi et al. (2009)

b.w.: body weight; THg: total mercury; IHg: inorganic mercury; OHg: organic mercury, SD: standard deviation.

Table E2: Reported ratios for cord blood to maternal biomarkers.

	Ratio	Additional information	Reference
THg cord blood / THg maternal blood	calculated unweighted ratio 1.48	review, 19 study populations	Murata et al. (2007)
THg cord blood / THg maternal blood	number-weighted ratio 1.51	review, meta analysis from 10 selected studies	Stern and Smith (2003)
MeHg cord blood / MeHg maternal blood	calculated unweighted ratio 1.72	Review, 9 study populations	Murata et al. (2007)
MeHg cord blood / MeHg maternal blood	number-weighted ratio 1.89	review, meta analysis from 10 selected studies	Stern and Smith (2003)
cord RBC / maternal RBC THg	1.6	Healthy pregnant Japanese women (n = 40) without any particular exposure to Hg	Sakamoto et al. (2008)
THg cord blood / THg maternal hair	1:190 (1:80 – 1:330)	585 pregnant women	Miklavčič et al. (2011b)
MeHg cord blood / THg hair	1:220 (1:110 – 1:390)	585 pregnant women	Miklavčič et al. (2011b)

THg: total mercury; MeHg: methylmercury.

Table E3: Reported blood to toenail ratios.

	Ratio	Additional information	Reference
THg blood / THg toenail	1:70 (calculated from mean values)	42 male members of Faroese whaling society	Choi et al. (2009)
THg blood / THg toenail	1:56 (calculated from mean values)	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)
MeHg blood / THg toenail	1:104	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)
IHg blood / THg toenail	1:122	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)

THg: total mercury; MeHg: methylmercury.

Table E4: Reported hair to toenail ratios.

	Ratio	Additional information	Reference
THg hair / THg toenail	3	42 male members of Faroese whaling society	Choi et al. (2009)
THg hair / THg toenail	2.56 (in the paper calculated from the mean values)	59 women (not occupationally exposed to Hg)	Ohno et al. (2007)
THg hair / THg toenail	2.38 (calculated from mean values) 1.41 (calculated from mean values)	161 non occupationally exposed individuals 155 dentists	Ritchie et al. (2002)
THg hair / THg toenail	2.39 (calculated from mean values) 1.65 (calculated from mean values)	155 non occupationally exposed individuals 161 dental workers (dentists, dental nurses)	Morton et al. (2004)

THg: total mercury.

F. OVERVIEW OF CONCENTRATIONS IN THE EUROPEAN POPULATION

Table F1: Overview of mercury concentrations in blood and hair samples from mother-child pairs.

Country	Additional information	Blood Hg (µg/L)[k]					Cord blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
FR												81	T:1.37 T:1.19[a]	T:0.94	T:1.2	T:0.54-2.90[d]	1
FR												144	0.67	0.5		0.33-0.81[e]	2
SE	Mothers	112 112			I:0.32 M:0.73	I:0.03-1.2[d] M:0.19-2.1[d]	98 98			I:0.34 M:1.4	I:0.09-0.79[d] M:0.26-3.8[d]						3
AT	Mothers	52			T:0.7	T:0.3-1.2[e]	43			T:1.1	T:0.4-1.9[e]	30			T:0.184	T:0.109-0.417[e]	4
FR	Mothers Children											691 87			0.52 0.38	0.30-0.82[e] 0.30-0.43[e]	5
SI	All mothers Mothers of which the THg in hair ≥ 1 mg/kg Mothers of which the THg in hair < 1 mg/kg						446 13 44	T:2.0[h] M:6.4[h] M:1.7[h]	M:2.3[h] M:1.5[h]	T:1.5[h] M:6.2[h] M:1.3[h]	T:0.5-4.2[c,h] M:3.3-9.9[c,h] M:0.3-4.0[c,h]	574 15	T:0.377 M:1.270	M:0.359	T:0.297 M:1.350	T:0.073-0.781[c] M:0.624-1.63[c]	6
SK	Mothers	99	0.79 0.67[a]		0.63	0.14-2.9[b]	99	0.86 0.74[a]		0.80	0.15-2.54[b]						7
IT	Mothers Children											242 208 203 116	T:1.33 M:0.96 T:1.22 M:0.86	T:1.22 M:0.84 T:1.22 M:0.76	T:0.93 M0.74 T:0.79 M0.56	T:1.56[f] M:1.13[f] T:1.53[f] M:1.11[f]	8
HR	Mothers											137	0.88	1.24		0.02-8.71[b]	9
PL	Mothers	231	0.55[a]		0.600		220	0.88[a]		0.850							10
PL		313	0.833	0.681	0.600		313	1.093	0.675	0.900							11
ES	• Valencia						554	T:13.1 T:9.5[a]		T:9.5	T:5.3-18.0[e] T:26.5[g]						12
	• Sabadell						460	T:8.2 T:6.3[a]		T:6.4	T:4.1-10.0[e] T:16.0[g]						
	• Asturias						340	T:13.9 T:10.8[a]		T:12.0	T:6.6-18.8[e] T:25.9[g]						
	• Gipuzkoa						529	T:9.3 T:7.5[a]		T:8.1	T:5.1-12.0[e] T:17.0[g]						
	• Total						1883	T:11.0 T:8.2[a]		T:8.5	T:5.0-14.0[e] T:22.0[g]						

Table F1: Continued.

Country	Additional information	Blood Hg (µg/L)[k]					Cord blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
SW	Mothers	20					20			M:0.99	M:0.52-3.8[b]						13
	• delivery				M:0.45 I:0.09	M:0.24-1.5[b] I:0.03-0.75[b]											
	• 13 weeks postpartum				M:0.60 I[i]	M:0.20-1.6[b] I[i]											
	Children	20															
	• 4 days				M:1.1 I:0.09	M:0.62-4.4[b] I:0.02-0.34[b]											
	• 13 weeks after birth				M:0.38 I:0.05	M:0.10-1.1[b] I:0-0.13[b]											
ES							1683	T:8.4[a]									14
GR	Mothers						391			T:5.8[h]	T:1.2-20[d,h] T:0.2-33[b,h]	454			T:1.12	T:0.242-3.84[d]	15
IT	Mothers	871			T:2.4[h]	T:0.05-40[b,h]	614			T:3.9[h]	T:0.1-33[b,h]	891			T:0.77	T:0.235-2.57[d]	
HR	Mothers	255			T:2.0[h]	T:0.6-21[b,h]	210			T:2.9[h]	T:0.3-32[b,h]	234			T:0.604	T:0.076-2.48[d]	

n: number of samples; µ: mean; SD: standard deviation; PX: Xth percentile; Ref.: reference; M: methylmercury; T: total mercury; I: inorganic mercury; FR: France; SE: Sweden; HR: Croatia; ES: Spain; AT: Austria; SI: Slovenia; SK: Slovakia; PL: Poland; GR: Greece.

1: Huel et al. (2008); 2: Abdelouahab et al. (2010); 3: Ask et al. (2002); 4: Gundacker et al. (2010a); 5: Drouillet-Pinard et al. (2010); 6: Miklavčič et al. (2011b); 7: Palkovicova et al. (2008); 8: Valent et al. (2011); 9: Cace et al. (2011); 10: Jedrychowski et al. (2006); 11: Jedrychowski et al. (2007b); 12: Ramon et al. (2011); 13: Björnberg et al. (2005); 14: Llop et al. (2012); 15: Miklavčič et al. (in press).

(a): geometric mean;
(b): minimum-maximum;
(c): P10-P90;
(d): P5-P95;
(e): P25-P75;
(f): P75;
(g): P90;
(h): µg/kg;
(i): about the same level as at delivery;
(j): maternal blood samples were collected at gestational week 36;
(k): maternal blood unless specified differently in the population.

Table F2: Overview of mercury concentrations in the European population in blood and hair.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Sweden	Fishermen[(o)]	189	M:2.9	M:2.4	M:2.3	M:0.5-6.9[(d)]						1
Finland	Fishermen and family members	299	M:3.6		M:2.7	M:<0.15-22[(b)] M:8.0[(h)]						2
Norway	Pregnant women	119	1.88	1.21	1.67	0.32-4.30[(d)]						3
France	Women of childbearing age (18-44 years old)	133	M:2.68	M:1.99		M:5.58 [(f)]						4
France	Pregnant women at 12 weeks of pregnancy Pregnant women at 32 weeks of pregnancy						161 137	0.82 0.79		0.67 0.65	1.89[(f)] 1.95[(f)]	5
Croatia	Women 25-45 years old						12				T:0.03-3.4[(b)]	6
Greece	Pregnant women and mothers of children of under 5 years						246 238	T:1.36[(a)] M:1.07[(a)]			T:0.046-17.5[(b)] M:0.031-16.2[(b)]	7
Norway	Women											8
	• 2nd trimester of pregnancy	211	1.5 1.2[(a)]	1.1		0.1-6.6[(b)]						
	• 3 days postpartum	211	1.2 1.0[(a)]	0.7		0.2-3.7[(b)]						
	• 6 weeks postpartum	211	1.8 1.5[(a)]	1.0		0.2-6.4[(b)]						
Italy	Pregnant women											9
	• Syracusan industrial area						100	1.45	0.96	1.15	0.09-4.98[(b)]	
	• Augusta						100	1.14	0.77	0.87	0.18-4.18[(b)]	
Czech Republic	Schoolchildren (13-14 years) from Kasperské Hory (a non-polluted control area) Schoolchildren (13-14 years) from Stary Plzenec (located close to the heavily industrialised zone of city Plzen) Schoolchildren (13-14 years) from Benesov (a predominantly agricultural area)									T:0.28 M:0.13 I: 0.17 T:0.38 M:0.17 I:0.22 T:0.46 M:0.12 I:0.36	T:0.14-0.42[(c)] M:0.07-0.19[(c)] I:0.08-0.34[(c)] T:0.25-0.53[(c)] M:0.11-0.23[(c)] I:0.14-0.32[(c)] T:0.25-0.85[(c)] M:0.07-0.21[(c)] I:0.19-0.72[(c)]	10
Spain	Preschool children Menorca						65	T:0.706 M:0.490	T:0.665 M:0.638		T:0.225-3.826[(b)] M:0.110-3.644[(b)]	11
	Preschool children Ribera d'Ebre						71	T:1.093 M:0.914	T:1.016 M:1.107		T:0.189-5.627[(b)] M:0.081-6.992[(b)]	
	Newborns Madrid						57	T:1.417	T:0.901		T:0.126-5.095[(b)]	
	Newborns Sabadell						25	T:1.999	T:1.925		T:0.132-8.426[(b)]	
	Total						218	T:1.416 M:0.973	T:1.387 M:1.104		T:0.126-8.426[(b)] M:0.081-6.992[(b)]	
Germany	Children	1240	0.24[(a)]		0.3	1.0[(f)]						12

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Poland	Children 3-4 years of age						38	0.23[a]				13
	Children 7-9 years of age						37	0.14[a]				
Denmark	Children (3-14 years)	1552	0.33 0.23[g]		0.2	<0.2-0.7						14
Croatia	Children (7-14 years)	52	0.44[a]			0.14-1.9[b]						15
Czech Republic		21	0.21[a]			<0.07-0.75[b]						
Poland		30	0.12[a]			<0.07-1.4[b]						
Slovakia		57	0.52[a]			0.12-2.3[b]						
Slovenia		45	0.94[a]			0.36-3.0[b]						
Sweden		41	0.43[a]			0.10-1.4[b]						
Czech Republic	Children											16
	• 1996	380			0.57	1.98[f]	412			0.23	0.54[f]	
	• 1997						372			0.20	0.54[f]	
	• 1998	384			0.39	1.25[f]	359			0.16	0.30[f]	
	• 1999	362			0.38	1.38[f]	360			0.16	0.37[f]	
	• 2000						343			0.26	0.84[f]	
	• 2001	354			0.42	1.48[f]	325			0.20	0.72[f]	
	• 2002						319			0.20	0.50[f]	
	• 2003						292			0.14	0.50[f]	
	• 2006	382			0.45	1.39[f]	372			0.13	0.28[f]	
	• 2008	198			0.35	1.32[f]	316			0.18	0.61[f]	
Spain	Boys (48-57 months)						72 23	T:0.96[a] M:1.81[a]		T:1.04		17
France	Adult males (18-64 years old)	93	M:3.41	M:2.25		M:7.17[f]						4
	Adult females (18-64 years old)	254	M:3.67	M:4.26		M:8.63[f]						
	Elderly (65 years old and over)	38	M:4.85	M:3.15		M:10.7[f]						
Ukraine	Residents of Horlivka (geological and industrial sources of environmental mercury)	29	1.31		1.01	0.17-7.72[b]	31	0.22		0.14	0.00-1.15[b]	18
	Residents of Artemivsk (city outside the mercury-enriched area)	29	0.96		0.92	0.25-1.93[b]	30	0.64		0.42	0.08-5.82[b]	
	Total	58	1.13		0.95	0.17-7.72[b]	61	0.42		0.24	0.00-5.82[b]	
Norway	Deceased adults, elderly and very elderly (47-91 years of age)	30	T:5	T:5.3	T:3.3	T:1.4-12.5[c]						19
		30	I:2.3	I:4.2	I:1.0	I:0.2-5.2[c]						
		30	M:2.7	M:2.3	M:2.2	M:0.9-6.2[c]						
Austria	Men, women and children						104			M:0.017	M:0.340[e]	20

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Italy	General population of Umbria	288	0.78[(m)] 0.79[(a,m)]	0.02[(m,n)]	0.75 [(m)]	0.29-1.43[(m,d)]						21
	General population of Calabria	215	0.65[(m)] 0.57[(a,m)]	0.02[(m,n)]	0.58 [(m)]	0.24-1.37[(m,d)]						
Austria	Adults (18 to 65 years)	152	T:2.38	T:1.55		T:0.34-9.97[(b)]						22
United Kingdom	Staff of the University of Glasgow						161	0.43[(a)]			0.04-3.86[(b)]	23
Czech Republic	Men											16
	• 1996	284			0.79	2.01[(f)]						
	• 1997	291			0.84	3.86[(f)]						
	• 1998	314			0.53	2.22[(f)]						
	• 1999	297			0.78	2.29[(f)]						
	• 2000	300			1.31	3.34[(f)]						
	• 2001	286			0.81	2.84[(f)]						
	• 2002	290			0.80	3.1[(f)]						
	• 2003	290			0.95	2.87[(f)]						
	• 2005	233			0.91	2.66[(f)]						
	• 2007	248			0.85	2.56[(f)]						
	Women											
	• 1996	134			0.83	2.04[(f)]						
	• 1997	103			0.93	3.35[(f)]						
	• 1998	81			0.81	3.50[(f)]						
	• 1999	101			0.94	2.66[(f)]						
	• 2000	98			1.33	4.37[(f)]						
	• 2001	114			0.93	3.60[(f)]						
	• 2002	107			0.92	4.15[(f)]						
	• 2003	105			0.99	3.51[(f)]						
	• 2005	172			1.16	3.46[(f)]						
	• 2007	163			0.89	2.94[(f)]						
Portugal	Adults – <5 km from an incineration facility (Lisbon)											24
	• T0	138	1.0	0.7	0.8	0.2-4.6[(b)]						
	• T1	75	0.5	0.4	0.4	0.1-1.8[(b)]						
	• T2	75	0.3	0.2	0.2	0.1-1.1[(b)]						
	Adults – > 5 km from the incineration facility (Lisbon)											
	• T0	29	1.5	0.6	1.4	0.7-4.2[(b)]						
	• T1	75	0.6	0.5	0.4	0.1-2.1[(b)]						
	• T2	75	0.3	0.3	0.3	0.1-1.2[(b)]						

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Portugal (continued)	Adults –total (Lisbon)											
	• T0	167	1.1	0.7	0.9	0.2-4.6[(b)]						
	• T1	150	0.5	0.4	0.4	0.1-2.1[(b)]						
	• T2	150	0.3	0.3	0.3	0.1-1.2[(b)]						
	Adults – <5 km from the incineration facility (Madeira)											
	• T0	55	0.9	1.0	0.5	0.1-4.4[(b)]						
	• T1	55	0.2	0.2	0.1	0.1-0.8[(b)]						
	Adults – >5 km from the incineration facility (Madeira)											
	• T0	55	0.7	0.5	0.7	0.1-1.8[(b)]						
	• T1	55	0.3	0.3	0.3	0.1-1.3[(b)]						
	Adults –total (Madeira)											
	• T0	110	0.8	0.8	0.5	0.1-4.4[(b)]						
	• T1	110	0.3	0.2	0.2	0.1-1.3[(b)]						
United Kingdom	Staff of the University of Glasgow						161	0.57	0.48	0.47	0.04-3.86[(b)]	25
Poland	Men[(p)] drinking water from steel pipelines						22	0.224	0.192			26
	Men[(p)] drinking water from copper pipelines						7	0.167	0.114			
	Men[(p)] drinking water from plastic pipelines						12	0.230	0.203			
	Women[(p)] drinking water from steel pipelines						35	0.176	0.122			
	Women[(p)] drinking water from copper pipelines						18	0.195	0.159			
	Women[(p)] drinking water from plastic pipelines						23	0.252	0.168			
	Total population										0.03-0.8[(b)]	
Germany	Office workers in a harbour (administrative work)	84			2.2	0.3-9.4[(b)]						27
Italy	Habitual consumers of fresh tuna	10			T:44.0 O:41.5	T:15-93[(b)] O:13-85[(b)]	8			9.6	1.4-34.5[(b)]	28
	Controls	6			T:3.9 O:2.6	T:1.2-5.4[(b)] O:0.8-4.0[(b)]						
Germany	Patients with health complaints and amalgam fillings	27			T:1.28[(k)] I:0.37[(k)] O:0.91[(k)] T:0.49[(j)] I:0.38[(j)] O:0.11[(j)]	T:0.82-2.18[(g,k)] I:0.17-0.50[(g,k)] O:0.53-1.43[(g,k)] T:0.30-0.81[(g,j)] I:0.19-0.59[(g,j)] O:0.08-0.16[(g,j)]						29

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Germany (continued)	Healthy amalgam bearers	27			T:1.19 [k] I:0.35 [k] O:0.81 [k] T:0.51 [j] I:0.36 [j] O:0.12 [j]	T:0.69-2.07 [g,k] I:0.19-0.49 [g,k] O:0.28-1.43 [g,k] T:0.36-0.78 [g,j] I:0.26-0.47 [g,j] O:0.05-0.20 [g,j]						
	Healthy amalgam-free patients	27			T:0.96 [k] I:0.08 [k] O:0.88 [k] T:0.16 [j] I:0.08 [j] O:0.10 [j]	T:0.58-1.87 [g,k] I:0.06-0.13 [g,k] O:0.53-1.71 [g,k] T:0.10-0.31 [g,j] I:0.04-0.11 [g,j] O:0.06-0.21 [g,j]						
Greenland Denmark	Adults				16.2 2.2							30
Germany	Adults (20-29 years)											31
	2010	457	0.9 0.8 [a]	0.7	0.8	0.2-2.1 [d]						
	2001-1010	4353	1.24 0.96 [a]	0.94	1.01	0.25-2.98 [d]						
United Kingdom	Adults (16-64 years)	1216	1.13 [a]			0.26-4.45 [b]						32
Sweden	Adults (28-60 years)	28	T:2.2 I:0.35 O:1.8 T:0.65 [j] I:0.39 [j] O:0.26 [j] T:4.1 [k] I:0.29 [k] O:3.8 [k]	T:1.4 I:0.23 O:1.3 T:0.30 [j] I:0.26 [j] O:0.16 [j] T:2.6 [k] I:0.18 [k] O:2.5 [k]	T:2.0 I:0.35 O:1.6 T:0.63 [j] I:0.37 [j] O:0.22 [j] T:4.0 [k] I:0.26 [k] O:3.6 [k]	T:0.34-7.3 [b] I:0-0.94 [b] O:0.26-6. 9 [b] T:0.07-1.3 [b,j] I:0-1.1 [b,j] O:0.05-0.70 [b,j] T:0.40-14 [b,k] I:0-0.70 [b,k] O:0.25-13 [b,k]	28	T:0.76 I:0.062 O:0.69	T:0.40 I:0.030 O:0.37	T:0.71 I:0.060 O:0.66	T:0.08-2.0 [b] I:0.010-0.12 [b] O:0.072-1.9 [b]	33

n: number of samples; µ: mean; SD: standard deviation; PX: X[th] percentile; Ref.: reference; M: methylmercury; T: total mercury; I: inorganic mercury; O: organic mercury; T0: baseline; T1: observation 1; T2: observation 2.

1: Rignell-Hydbom et al. (2007); 2: Airaksinen et al. (2010); 3: Brantsæter et al. (2010); 4: Sirot et al. (2008); 5: Pouzaud et al. (2010); 6: Holcer and Vitale (2009); 7: Gibičar et al. (2006); 8:Hansen et al. (2011); 9: Madeddu and Sciacca (2008); 10: Čejchanova et al. (2008); 11: Diéz et al. (2009); 12: Schulz et al. (2007); 13: Majewska et al. (2010); 14: Becker et al. (2008); 15: Hrubá et al. (2012); 16: Puklová et al. (2010); 17: Freire et al. (2010); 18: Gibb et al. (2011); 19: Björkman et al. (2007); 20: Hohenblum et al. (2012); 21: Bocca et al. (2010); 22: Gundacker et al. (2006); 23: Morton et al. (2004); 24: Reis et al. (2007); 25: Ritchie et al. (2004); 26: Chojnacka et al. (2011); 27: Wegner et al. (2004); 28: Carta et al. (2003); 29: Melchart et al. (2008); 30: Pedersen et al. (2005); 31: Karch et al. (2011); 32: Bates et al. (2007); 33: Berglund et al. (2005).

(a): geometric mean;

(b): minimum-maximum;

(c): P10-P90;
(d): P5-P95;
(e): maximum;
(f): P95;
(g): P25-P75;
(h): P90;
(i): P33-P67;
(j): concentration in plasma (µg/L);
(k): concentration in erythrocytes (µg/L);
(l): concentration in erythrocytes (ng/g);
(m): concentration in serum (µg/L);
(n): standard error;
(o): concentrations calculated as the difference between total Hg and inorganic Hg;
(p): students.

Table F3: Overview of mercury concentrations in the European population in nails.

Country	Additional information	Fingernails Hg (mg/kg)					Toenails Hg (mg/kg)					Reference
		n	μ	SD	P50	Variation (specified by footnotes)	n	μ	SD	P50	Variation (specified by footnotes)	
Ukraine	Residents of Horlivka (geological and industrial sources of environmental mercury)	31	0.41		0.31	0.01-2.63[(b)]	31	0.35		0.31	0.00-1.14[(b)]	Gibb et al. (2011)
Ukraine	Residents of Artemivsk (city outside the mercury-enriched area)	28	0.18		0.09	0.00-1.18[(b)]	26	0.12		0.11	0.00-0.58[(b)]	
Ukraine	Total	59	0.3		0.2	0.00-2.63[(b)]	57	0.25		0.18	0.00-1.14[(b)]	
Norway	Deceased adults, elderly and very elderly (47-91 years of age)						29	0.28	0.214	0.236	0.067-0.624[(c)]	Björkman et al. (2007)
United Kingdom	Staff of the University of Glasgow	155	0.24[(a)]			0.02-2.49[(b)]	155	0.18[(a)]			0.02-1.22[(b)]	Morton et al. (2004)
United Kingdom	Staff of the University of Glasgow	155	0.32	0.30	0.23	0.02-2.49[(b)]	155	0.24	0.19	0.18	0.02-1.22[(b)]	Ritchie et al. (2004)
France	Healthy volunteers	130			0.29	0.06-0.83[(d)]						Goullé et al. (2009)
		50			0.20	0.09-0.56[(d)]	50			0.16	0.07-0.38[(d)]	

n: number of samples; μ: mean; SD: standard deviation; PX: X^{th} percentile.
(a): geometric mean;
(b): minimum-maximum;
(c): P10-P90;
(d): P5-P95.

Table F4: Overview of mercury concentrations in the European population in urine.

Country	Population	Urine Hg (µg/L)					Reference
		n	µ	SD	P50	Variation (specified by footnotes)	
Poland	Healthy children	20	2.1	1.0	2.0	0.25-4.8[(b)]	Kałuzna-Czaplińska et al. (2011)
Spain	Male adults	35	0.96[(a,g)]				Castaño et al. (2012)
	Female adults	130	1.31[(a,g)]				
	Total	165	1.23[(a,g)]		1.19[(g)]	0.45-3.30[(g,d)] 0.56-2.72[(g,c)]	
Czech Republic	Children						Puklová et al. (2010)
	• 1996	435			0.25[(g)]	2.54[(g,f)]	
	• 1997	397			0.38[(g)]	2.56[(g,f)]	
	• 1998	399			0.27[(g)]	4.22[(g,f)]	
	• 1999	393			0.28[(g)]	2.40[(g,f)]	
	• 2000	384			0.35[(g)]	3.15[(g,f)]	
	• 2002	349			0.43[(g)]	3.94[(g,f)]	
	• 2003	270			0.28[(g)]	4.46[(g,f)]	
	• 2006	364			0.26[(g)]	2.19[(g,f)]	
	• 2008	312			0.16[(g)]	1.01[(g,f)]	
Germany	Children	1354	0.10[(a)]		<0.1	0.52[(f)]	Schulz et al. (2007)
Germany	Children (age 9-11 years)	510			<0.2	1.2[(f)]	Wilhelm et al. (2006)
Germany	Children (3-14 years)	1734	0.19 <0.1[(a)]		<0.1	<0.1-0.3	Becker et al. (2008)
Germany	Children (9-11 years)						Link et al. (2012)
	• 1996/1997	1324	0.78	1.98	0.25	<0.2-3.1[(d)]	
	• 1998/1999	1255	0.59	1.43	0.20	<0.2-2.3[(d)]	
	• 2000/2001	1276	0.57	4.01	<0.2	<0.2-1.6[(d)]	
	• 2002/2003	510	0.31	0.62	<0.2	<0.2-1.2[(d)]	
	• 2004/2005	448	0.24	0.47	<0.2	<0.2-0.8[(d)]	
	• 2008/2009	1294	0.13	0.24	<0.2	<0.2-<0.2[(d)]	
Ukraine	Residents of Horlivka (geological and industrial sources of environmental Hg)	31	0.18[(g)]		0.15[(g)]	0-0.51[(g,b)]	Gibb et al. (2011)
	Residents of Artemivsk (city outside the mercury-enriched area)	30	0.37[(g)]		0.26[(g)]	0.09-1.28[(g,b)]	
	Total	61	0.27[(g)]		0.21[(g)]	0-1.28[(g,b)]	
United Kingdom[(a)]	Adults	78	1.12[(g)]		0.55[(g)]	<LOD-13.47[(g,b)]	Levy et al. (2007)
United Kingdom	Staff of the University of Glasgow	163	0.67[(a,g)]			0.05-7.45[(b,g)]	Morton et al. (2004)
Czech Republic	Men						Puklová et al. (2010)
	• 1996	247			0.61[(g)]	2.79[(g,f)]	
	• 1998	294			0.51[(g)]	2.70[(g,f)]	
	• 2000	275			0.63[(g)]	5.23[(g,f)]	
	• 2002	251			0.44[(g)]	5.39[(g,f)]	
	• 2003	246			0.63[(g)]	4.93[(g,f)]	

Table F4: Continued.

Country	Population	Urine Hg (µg/L) n	µ	SD	P50	Variation (specified by footnotes)	Reference
Czech Republic (continued)	• 2005	165			0.84[g]	5.13[g,f]	Puklová et al. (2010)
	• 2007	170			0.90[g]	4.72[g,f]	
	Women						
	• 1996	114			1.29[g]	4.66[g,f]	
	• 1998	73			0.99[g]	13.27[g,f]	
	• 2000	84			0.90[g]	7.07[g,f]	
	• 2002	84			1.05[g]	11.81[g,f]	
	• 2003	76			1.09[g]	10.52[g,f]	
	• 2005	113			2.18[g]	10.37[g,f]	
	• 2007	109			1.57[g]	8.55[g,f]	
United Kingdom	Staff of the University of Glasgow	163	1.19[g]	1.21[g]	0.89[g]	<0.02-7.45[b,g]	Ritchie et al. (2004)
Germany	Office workers in a harbour (administrative work)	84			0.7[g]	0.1-4.2[b,g]	Wegner et al. (2004)
Italy	Habitual consumers of fresh tuna	22			6.5[g]	1.8-21.5[b,g]	Carta et al. (2003)
	Controls	22			1.5[g]	0.5-5.3[b,g]	
Italy	General population[n]	203	1.2[g]			<LOD-16.2[b,g]	Jarosińska et al. (2008)
Poland		160	0.22[g]			<LOD-19.3[b,g]	
Sweden		215	0.21[g]			<LOD-9.6[b,g]	
Germany	Residents living on a highly contaminated grounds	28	0.08[a]		<0.05	<0.05-0.4[b]	Ewers et al. (2004)
	Controls	22	0.2[a]		0.2	<0.05-1.4[b]	
Germany	Patients with health complaints and amalgam fillings	27			0.40	0.25-0.85[d]	Melchart et al. (2008)
	Healthy amalgam bearers	27			0.73	0.20-0.94 [d]	
	Healthy amalgam-free patients	27			0.16	0.11-0.25 [d]	
Germany	Adults (20-29 years)						Karch et al. (2011)
	2010	461	0.2 0.1[a]	0.42	0.1	0.1-1.0[d]	
	1997-2010	5810	0.4 0.2[a]	0.65	0.18	0.03-1.49[d]	
Sweden	Adults (28-60 years)	28	T:1.9[g] I:1.9[g] O:0.013[g]	T:2.0[g] I:2.1[g] O:0.12[g]	T:1.3[g] I:1.2[g] O:0.018[g]	T:0.12-10[b,g] I:0.12-11[b,g] O:0-0.23[b,g]	Berglund et al. (2005)

n: number of samples; µ: mean; SD: standard deviation; PX: Xth percentile.
(a): geometric mean
(b): minimum-maximum
(c): P10-P90
(d): P5-P95
(e): maximum
(f): P95

GLOSSARY AND ABBREVIATIONS

GLOSSARY OF FISH SPECIES

English name	Latin name
Anchovy	*Engraulis* Cuvier spp.
Barbel	*Barbus* Cuvier spp.
Barracuda	*Sphyraenidae*
Bass	*Morone* Mitchill spp.
Bonito	*Sarda sarda* Bloch
Bream	*Diplodus* Rafinesque spp. (old name *Charax* Scopoli spp.)
Capelin	*Mallotus villosus* Müller
Carp	*Cyprinus* L. spp.
Char	*Salvelinus* L. spp.
Cod and whiting	*Gadus* L. spp.
Dentex	*Dentex* Cuvier spp.
Dories, John Dory	*Zeiformes* (order), *Zeomorphi*
Eels	*Anguillidae*
Flounder	*Platichthys flesus* L.
Garfish	*Belone belone* L. and *Belone acus* Risso
Grey mullet	*Mugil* L. spp.
Grenadiers	*Coryphaenoides* spp.
Grouper	*Acanthistius* Gill. spp., *Ephinephelus* Bloch spp., *Mycteroperca* Gill spp., *Myctoperca* Gill spp. and *Serranus* Cuvier spp.
Gurnard	*Triglidae*
Hake	*Merluccius* Rafinesque spp.
Halibut	*Hippoglossus* Cuvier spp.
Herring	*Clupea* L. spp.
Lizardfish	*Saurida* Valenciennes spp. and *Synodus* L. spp.
Lophiiformes (syn. Anglerfish)	*Lophiiformes* Garman (order)
Luvarus	*Luvarus imperialis* Rafinesque
Mackerel	*Scomber* spp.
Mackerel and Jack Mackerel (except Scomber)	*Carangidae*
Meagre	*Sciaena* L. spp.
Perch	*Perca* spp.
Pike	*Esox* L. spp
Plaice	*Pleuronectes* L. spp.
Rays	*Rajiformes* (syn. *Hypotremata)* (order)
Redfish	*Centroberyx* Gill spp. and *Centroberyx affinis* Günther
Roach	*Rutilus* Rafinesque spp.
Salmon and trout	*Salmo* L. spp.
Sardine and pilchard	*Sardina* Antipa spp.
Scorpion fish	*Scorpaenidae*
Sea bass	*Morone labrax* L.; *Dicentrarchus labrax* L. and *Morone saxatilus* Walbaum
Sea catfish and wolf-fish	*Anarhichas* L. spp.
Selachoidei or sharks	*Pleurotremata* (syn. *Euselachii) (superorder)*
Shad	*Alosa* Linck spp., *Hilsa* Regan spp. and *Ethmalosa fimbriata* Bowdich
Smelt	*Osmerus* L. spp.
Sole	*Limanda* Gottsc spp., *Solea* Quensel spp.

English name	Latin name
Sprat	*Sprattus sprattus* L.
Sturgeons	*Acipenseriformes* Berg (order)
Swordfish	*Xiphiidae*
Tuna	*Thunnus* South spp.
Turbot	*Scophthalmidae*
Weever	*Trachinidae*
Whitefish	*Coregonus* spp.
Wrasse	*Labridae* Cuvier

ABBREVIATIONS

μ	Mean
AA	Arachidonic acid
AAS	Atomic absorption spectrometry
ADHD	Attention Deficit Hyperactivity Disorder
AFS	Atomic fluorescence spectrometry
ALA	alpha-linolenic acid
ALA-D	δ-aminolevulinate dehydratase
AMI	Acute myocardial infarction
ANA	Antinuclear antibodies
AT	Austria
ATSDR	Agency for Toxic Substances and Disease Registry
BAEPs	Brainstem auditory evoked potentials
BMD	Benchmark dose
BMDL	The 95 % benchmark dose lower confidence limit
BMI	Body mass index
BMR	Benchmark response
BP	Blood pressure
BSID-II	Bayley's scale of infant development-II
b.w.	Body weight
CE	Coronary event
CEN	European Committee for Standardization
CHD	Coronary heart disease
CI	Confidence interval
CONTAM Panel	EFSA Scientific Panel on Contaminants in the Food Chain
CPT	Continuous Performance Test
CPT-HRT	Continuous Performance Test-Hit Reaction Time latencies
CRM	Certified reference material
CSF	Cerebrospinal fluid
CV	Cold vapour
CV-AAS	Cold vapour atomic absorption spectrometry
CV-AFS	Cold vapour atomic fluorescence spectrometry
CVD	Cardiovascular disease
CY	Cyprus
CZ	Czech Republic
DBP	Diastolic blood pressure
DCM Unit	EFSA Dietary and Chemical Monitoring Unit (former DATEX)
DDST	Denver Development Screening Test
DE	Germany
DHA	Docosahexaenoic acid
DK	Denmark
DPA	Docosapentaenoic acid
d.w.	Dry weight
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic acid
ERP	Event-related potential
ES	Spain
ET-AAS	Electrothermal atomic absorption spectrometry
EU	European Union
FAPAS	Food Analysis Performance Assessment Scheme
Fe	Iron
FI	Finland
FR	France

FTII	Fagan infantest
GC	Gas chromatography
GC-ICP-MS	Gas chromatography inductively coupled plasma mass spectrometry
GC-MS	Gas chromatography coupled with mass spectrometry
GC-pyro-AFS	Gas chromatography - pyrolysis atomic fluorescence
GM	Geometric mean
GR	Greece
GST	Glutathione S-transferase
HDL	High-density lipoprotein
HF	High frequency
Hg	Mercury
Hg^0	Elemental or metallic mercury
Hg_2^{2+}	Mercurous cation
Hg^{2+}	Mercuric cation
$HgCl_2$	Mercuric chloride
HgO	Mercuric oxide
HgS	mercuric sulphide
HOME	Home Observation for Measurement of the Environment
HPLC	High-performance liquid chromatography
HR	Hazard ratio
HRT	Hit Reaction Time latencies
HRV	Heart-rate variability
IAEA	International Atomic Energy Agency
ICP-AES	Inductively coupled plasma atomic emission spectroscopy
ICP-MS	Inductively coupled plasma mass spectrometry
I/IHg	Inorganic mercury
Ig	Immunoglobulin
IGGE	Institute of Geophysical Exploration
IQ	Intelligence quotient
IQR	Interquartile range
IRMM	Institute for Reference Materials and Measurements
IT	Italy
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LA	Linoleic acid
LB	Lower bound
LC	Left-censored
LCD	Liquid crystal displays
LCPUFA	Long-chain polyunsaturated fatty acids
LDL	Low-density lipoprotein
LF	Low frequency
LOAEL	Lowest-observed-adverse-effect level
LOD	Limit of detection
LOQ	Limit of quantification
LU	Luxembourg
LV	Latvia
M/MeHg	Methylmercury
MB	Middle bound
MCDI	MacArthur Communicative Development Inventory
MDI	Mental Developmental Index
MeHgCys	Methylmercury L-cysteine complex
MI	Myocardial infarction
ML	Maximum level
MRL	Maximum residue level
MS	Mass spectrometry
MT	Malta

N	Number of samples/results/participants/surveys
n/a	Not available/not applicable
n.r.	not reported
n-3 LCPUFA	n-3 long-chain polyunsaturated fatty acids
n-6 LCPUFA	n-6 long-chain polyunsaturated fatty acids
$NaBEt_4$	Sodium tetraethylborate
$NaBPr_4$	Sodium tetrapropylborate
NAS	National Academy of Sciences
NADPH	Nicotinamide adenine dinucleotide phosphate
NBAS	Neonatal behaviour assessment scale
NBNA	Neonatal behavioural neurological assessment
ND	Not detected
NHANES	National Health and Nutrition Examinations Survey
NIST	National Institute of Standards and Technology (USA)
NL	the Netherlands
NO	Norway
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect-level
NRC	National Research Council
NRCC	National Research Council of Canada
NRL	National Reference Laboratory
O/OHg	Organic mercury
OR	Odds ratio
Pb	Lead
PCB	Polychlorinated biphenyls
PDI	Psychomotor Developmental Index
PND	postnatal day
PT	Portugal
PTFE	Polytetrafluoroethylene
PTWI	Provisional tolerable weekly intake
PX	X^{th} percentile
RfD	Reference dose
RO	Romania
RONS	Reactive oxygen and nitrogen species
RR	Relative risk
r_s	Spearman correlation coefficient
SACMEQ	Southern and Eastern Africa Consortium for Monitoring Educational Quality
SBP	Systolic blood pressure
s.c.	subcutaneous
SCDNS	Seychelles Child Development Nutrition Study
SCDS	Seychelles Child Development Study
SD	Standard deviation
SDANN	Standard deviation of the average R-R intervals calculated over 5-minute periods
Se	Selenium
SE	Sweden/Standard error
SES	Socio-economic status
SI	Slovenia
SK	Slovakia
SRM	Standard reference material
TDS	Total diet study
T/THg	Total mercury
TSH	Thyroid stimulating hormone
TWI	Tolerable weekly intake
UB	Upper bound

UBA	Umweltbundesamt
UK	United Kingdom
US-EPA	United States Environmental Protection Agency
USA	United States of America
VLF	Very low frequency
VRM	Visual recognition memory
w.w.	Wet weight