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EXECUTIVE SYNOPSIS

CHAPTER 1 - Introduction

1.   The United Nations Environment Programme (UNEP) Governing Council (GC), at its 22nd session requested UNEP, in cooperation and consultation with other appropriate organizations, to facilitate and conduct technical assistance and capacity building activities to support the efforts of countries to take action regarding mercury pollution. This request was reinforced by the UNEP GC at its 23rd session in February 2005. At that session, the GC also encouraged governments to promote and improve evaluation and risk communication methods, based on, *inter alia*, guidance from the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO), that will enable citizens to make health-protective dietary choices based on risk and benefit information.

2.   The UNEP GC at its 24th session in February 2007 recognized that a range of activities are still required to address the challenges posed by mercury, including substitution of products and technologies; technical assistance and capacity-building; development of national policy and regulation; data collection, research and information provision, bearing in mind the need to provide assistance to developing countries and countries with economies in transition.

3.   This "Guidance for Identifying Populations at Risk from Mercury Exposure" is intended to inform countries concerned about the potential health impacts of mercury pollution and, if necessary, to assist in identifying specific subpopulations that may be at risk. The document describes approaches that have been used to estimate exposure to mercury, including biomonitoring and methods that use data on fish consumption and mercury levels in fish. It also describes various environmental models that can be useful in predicting exposure to mercury. In addition, the document provides an overview of the assessment of mercury exposures for some specific exposure scenarios, including occupational and other "hot spot" exposures.

4.   This document can be used as a reference for conducting research or investigations regarding mercury exposure. Depending on the nature of the research, involvement of stakeholders in various stages of the research is important, especially for local communities. This includes the process of evaluating and addressing environmental issues. For research involving biomonitoring, consultation with the community and consideration of ethical and confidentiality issues are essential.

5.   Relevant reports of meetings and monographs prepared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) were taken into account in the development of this guidance document as part of international recommendations on mercury and methylmercury in fish and other food. This document is being issued jointly by UNEP and WHO in cooperation with FAO.

CHAPTER 2- Background and Overview of Health Risks

Risk analysis paradigm

6.   The risk analysis paradigm described by WHO/FAO consists of three components; risk assessment, risk management and risk communication. Risk assessment and management each consist of four steps (Figure 1). The overall process is carried out under the direction of the risk manager who has been delegated the primary responsibility for managing health risks on behalf of the society. Based on preliminary information, the risk manager uses the hazard identification as the basis for deciding whether to undertake a full risk assessment in the light of other risk priorities and available resources. In regard to food safety, risk managers should be aware that the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organizations requires that countries ensure that their food

safety measures are based on an assessment of risks to human health taking into account the risk assessment techniques developed by the relevant international organizations, in this case FAO and WHO.

Risk assessment

7.   A human health risk assessment for chemicals is generally a study to estimate the likelihood of adverse health effects occurring in an individual, subpopulation or population due to exposure to some chemical (such as mercury). Risk assessment consists of four main steps: 1) hazard identification; 2) hazard characterization, including dose-response assessment; 3) exposure assessment; and, 4) risk characterization. Hazard identification is the review of relevant toxicological, biological, and chemical information to identify the adverse health effects associated with a pollutant under various exposure scenarios. Epidemiologic and animal studies are some of the information examined. Hazard characterization usually includes a dose-response assessment, which defines the relationship between the degree of exposure (or amount of dose) observed in animal or human studies and the magnitude of the observed adverse health effects. This usually is expressed as a quantitative measure of adverse health effects for a range of doses.

8.   In an exposure assessment, the extent, duration, frequency and magnitude of exposures to a pollutant (or multiple pollutants) are estimated via various routes (ingestion, inhalation, dermal or transplacental/in utero exposure) for individuals or populations. Exposures can be estimated by measuring pollutant levels in various body tissues (such as hair, blood, urine, or nails) as biomarkers or by using various mathematical models along with input data (such as facility release information, fish mercury levels, dietary patterns, etc.). Risk characterization is the integration of the hazard identification, hazard characterization, especially dose-response, and exposure assessments to describe the nature and magnitude of the health risk in a given population. Once the risk characterization is completed, the results along with other information can then be used to develop priorities, strategies and programmes to protect those populations at risk.

9.   Although the scope of the document focuses on methylmercury in fish, the principles laid out can also be applied to other contaminants in fish (such as dioxins and polychlorinated biphenyls [PCBs]). In order to do an overall risk assessment of fish contaminated with other pollutants, guidance and information for assessing these pollutants would need to be obtained from other materials and sources.

Mercury in the environment

10.   Mercury (with the chemical symbol of Hg) is a naturally occurring element found in air, water, and soil. It is distributed throughout the environment by both natural and anthropogenic (human) processes. Mercury is found in various inorganic and organic forms and is persistent in the environment. The three predominant forms include: a) elemental mercury (with the chemical symbol of Hg^0; b) ionic mercury (also known as inorganic mercury with the chemical symbol of Hg (II) or Hg^{2+}) which in nature exists as Hg (II) mercuric compounds or complexes in solution; and c) organic mercury with methylmercury (with the chemical symbol of MeHg) being the most important.

11. In spite of its potential risks, mercury continues to be used in a variety of products and processes all over the world because of its unique properties. For example, it is the only metal that exists in liquid form at room temperature. Elemental mercury is used in artisanal and small-scale mining of gold and silver; chlor-alkali production; vinyl chloride monomer production, and in products (such as manometers for pressure measurement and control, thermometers, electrical switches, fluorescent lamp bulbs, and dental amalgam fillings). Mercury compounds are used in some batteries, pharmaceuticals, paints, and as laboratory reagents and industrial catalysts. Mercury can be released to air, water, and soils during production and uses or after disposal of the mercury-containing products and wastes. Mercury is also released during natural processes (such as volcanoes and leaching from certain soils).

12.   The UNEP 2006 report on the supply, trade, and demand of mercury reveals that demand or use of mercury is highest in small scale gold mining, followed by vinyl chloride monomer production, chlor-alkali production, and in products namely batteries, dental amalgams, measuring and control devices, lighting, electrical and electronic devices.

13.   As described in the UNEP 2002 Global Mercury Assessment, mercury is also released to the environment from various industrial sources that mobilize mercury impurities in input materials (such as fuels and feedstocks). Such sources include coal-fired power plants, non-ferrous metals smelters, and cement production plants, which are among the categories with the highest mercury emissions. These emissions lead to environmental contamination and human exposures. The degree of emissions and levels of exposures due to any one facility depends on various factors including the mercury levels in the fuel or feedstocks, emissions control devices present, stack heights, size of the operation and other factors.

Routes of exposure

14.   Mercury is a toxic, persistent pollutant that bioaccumulates and biomagnifies through food webs. People are exposed to methylmercury mainly through their diet, especially through the consumption of freshwater and marine fish and consumption of other animals that consume fish (such as marine mammals). People may be exposed to elemental or inorganic mercury through inhalation of ambient air during occupational activities, and from dental amalgams. Occupational exposures can occur where mercury or mercury compounds are produced, used in processes, or incorporated in products. Occupational exposures have been reported from (among others) chlor-alkali plants, mercury mines, mercury-based small-scale gold and silver mining, refineries, thermometer and sphygmomanometer factories, dental clinics with poor mercury handling practices, and production of mercury-based chemicals. Exposures to elemental mercury or inorganic mercury forms can also occur due to use of some skin-lightening creams and soaps, the presence of mercury in some traditional medicines, use of mercury in cultural practices, and due to various accidental mercury spills in homes, schools or other locations. Minor exposures to other forms of organic mercury may result from the use of thimerosal (ethylmercury thiosalicylate) as a preservative in some vaccines and other pharmaceuticals.

Health effects

15.   All humans are exposed to some low levels of mercury. The factors that determine the occurrence and severity of adverse health effects include: the chemical form of mercury; the dose; the age or developmental stage of the person exposed (the fetus is considered to be the most susceptible); the duration of exposure; and, the route of exposure (inhalation, ingestion, and dermal contact). Dietary patterns can increase exposure to a fish-eating population when fish and seafood are contaminated with mercury.

16.   The primary targets for toxicity of mercury and mercury compounds are the nervous system, the kidneys, and the cardiovascular system. It is generally accepted that developing organ systems (such as the fetal nervous system) are the most sensitive to toxic effects of mercury. Fetal brain mercury levels appear to be significantly higher than in maternal blood and the developing central nervous system of the fetus is currently regarded as the main system of concern as it demonstrates the greatest sensitivity. Other systems that may be affected include the respiratory, gastrointestinal, hematologic, immune, and reproductive systems.

17.   Effects on the nervous system (especially the developing nervous system) appear to be the most sensitive toxicological endpoint observed following exposure to elemental mercury and methylmercury, while damage to the kidneys is the key end-point in exposure to inorganic mercury compounds.

Susceptible populations

18.   Generally there are two susceptible subpopulations, namely, those who are more sensitive to the effects of mercury and those who are exposed to higher levels of mercury. The fetus, the newborn and children are especially susceptible to mercury exposure because of the sensitivity of the developing nervous system. In addition to *in utero* exposures, neonates can be further exposed by consuming contaminated breastmilk. Thus, new mothers, pregnant women, and women who might become pregnant

should be particularly aware of the potential danger of methylmercury. Individuals with diseases of the liver, kidney, nervous system, and lung are also at higher risk of suffering from the toxic effects of mercury.

19.   The other subpopulation that may be at greater risk to mercury toxicity are those exposed to higher levels of methylmercury due to fish and seafood consumption (such as recreational anglers and subsistence fishers, as well as those who regularly eat large amounts of fish and other seafood). Besides fish and shellfish, exposure can also be significant in populations consuming meat (muscle and organs) from marine mammals (such as seals and whales).

20.   Individuals with dental amalgams generally have greater exposure to elemental mercury than those who do not. Other populations with potential for higher than average exposure are workers with high occupational exposure, and individuals who use various consumer products that contain mercury (such as some skin lightening creams and soaps), traditional ethnic medicines containing mercury, or use mercury for cultural and religious purposes.

Reference levels

21.   Based on risk assessments and other considerations, several countries and international organizations have established reference levels for daily or weekly methylmercury or mercury intakes which, based on available data and research, are estimated to be safe (or without appreciable risk to health). The reference intake levels for methylmercury exposures range from 0.7 to 2 μg methylmercury per kilogram body weight (μg/kg body weight) per week. Reference levels have also been established to protect against inhalation of mercury metal and ingestion exposures to inorganic mercury compounds.

22.   The Joint FAO/WHO Expert Committee on Food Additives (JECFA), which also evaluates chemical contaminants in the food supply, has established provisional tolerable weekly intakes (PTWIs) for total mercury at 5 μg/kg body weight and for methylmercury at 1.6 μg/kg body weight. The PTWI is the amount of a substance that can be consumed weekly over an entire lifetime without appreciable risk to health and is an end-point used for food contaminants (such as heavy metals with cumulative properties). Its value represents permissible human weekly exposure, protecting the most susceptible part of the population, to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods. In the case of methylmercury, the developing fetus is considered to be the most sensitive subgroup, and neurodevelopment the most sensitive outcome.

23.   The US EPA has developed Reference Doses (RfDs) for mercuric chloride of 0.3 μg/kg body weight/day and methylmercury 0.1 μg/kg body weight/day and a Reference Concentration (RfC) for elemental mercury of 0.3 μg/cubic metre. An RfD (or RfC) 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 appreciable risk of deleterious non-cancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD (or RfC), the potential for adverse health effects increases.

24.   Because fish consumption dominates the pathway for exposure to methylmercury for most human populations, many governments provide recommendations or legal limits for the maximum allowable amount of mercury and/or methylmercury in fish to be sold on the market. For example, Codex Alimentarius guideline levels are 0.5 mg methylmercury/kg in non-predatory fish and 1 mg methylmercury/kg in predatory fish. The US FDA has set an action level of 1 mg methylmercury/kg in finfish and shellfish. The European Community allows 0.5 mg mercury/kg in fishery products (with some exceptions), and Japan allows up to 0.4 mg total mercury/kg (or 0.3 mg methylmercury/kg) in fish.

25.   Some governments and other organizations also provide dietary advice on the consumption of certain types and amounts of fish to help limit exposures based on consideration of both the benefits and risks of fish consumption. These advisories typically provide guidance on the amounts, types and frequency of fish consumption that is considered safe or potentially harmful for various groups (such as pregnant women and sport fishermen).

Risk characterization

26.   Risk characterization is the culminating step of the risk assessment process. It integrates information from the hazard identification, dose-response, and exposure assessments and synthesizes an overall description about the potential risks. The risk characterization is intended to inform risk managers and other audiences about the outcome of the risk assessment. It also presents the variability, uncertainties and limitations of the hazard characterization and exposure assessment. Risk characterization provides a summary of the risk assessment, which can be used along with other appropriate information to inform risk managers as they consider risk management options. The implications of risk characterization of methylmercury in fish are discussed further in Chapter 7 where guidance to risk managers is provided.

CHAPTER 3: Estimating Exposure Through Biomonitoring

27.   Approaches to estimate exposures to mercury include measuring mercury levels in hair, blood, and urine, which are considered forms of "biomonitoring". Measurements of mercury levels in these tissues can be excellent indicators of various types of mercury exposures, but the validity, usefulness, and meaning of such measurements depend on the form of mercury exposures, type of tissue measurement, and other factors.

28.   This chapter describes various protocol considerations, including sampling methods, questionnaires, health assessments, and tissue measurements (Annexes A,B,C,D,E,F). A study must be well designed to provide scientifically valid results. Selection of a representative sample is essential, and good histories (such as medical, occupational, family, dietary information) and health assessments (such as neurological tests) can be important components in a study of a population which is subject to mercury exposure. All sources of mercury exposure should be identified to the extent feasible. Various ethical issues also need to be taken into account.

Selecting a study population

29.   In order to select a representative sample, it is important to understand the socio-economic and demographic situation of the community. Obtaining a statistically representative sample of the community is usually the preferred approach. One important decision to consider is the number and type of individuals to be included in the study. The sample size chosen is likely to be based on various factors including costs, statistical power, staff, study facilities, and other factors. The sampling process can be random, judgmental, or possibly based on other approaches.

Biological markers

30.   Exposures can be estimated by measuring pollutant levels in various body tissues (such as hair, blood urine, or nails). These measurements of pollutants and/or their metabolites, also known as biological markers (or biomarkers), are useful as tools for human exposure assessment, and as surveillance tools for monitoring mercury exposure in individuals and populations. There is a well-established relationship between several biomarkers of mercury exposure and adverse health effects.

31.   In assessing the appropriateness of a particular biomarker of exposure, it is important to consider several factors: (1) how well the biomarker correlates with the dose (or external exposure) to various forms of mercury: (2) how well the biomarker correlates with the mercury concentration in the target tissue; (3) how well the variability over time in the biomarker correlates with changes in the effective dose at the target tissue over time; (4) what type of biomarker would be the most appropriate given the cultural characteristics of the population; (5) what kind of technology is available for collection of samples and mercury measurement; and, (6) invasiveness of the procedure in sample collection. The following biological media can be used as biomarkers for mercury exposure in humans: hair, blood, cord blood and cord tissue, urine, nails and human milk.

32.   Analysing mercury in biological samples is complicated by the different organic and inorganic forms of the metal that may be present. Therefore, all forms of mercury in the sample are usually reduced to their elemental state prior to analysis. Samples must be gathered using clean, proper equipment and

techniques to avoid contamination and sample loss. Some specific techniques are described for the various biological tissues.

33.   A number of analytical methods are available to determine mercury concentration, and the selection of a particular analytical method depends on various factors (such as analytical regulations and guidelines of each country, detection limits, laboratory skills, availability of analytical equipment, precision needed, and whether or not speciation of mercury forms is desired). Whatever analytical method will be used, it is important to practice careful quality control/quality assurance of the obtained data, including simultaneous determination of suitable certified reference materials.

34.   The presence of mercury in blood indicates recent or current exposure to mercury. There is a direct relationship between mercury concentrations in human blood and consumption of fish contaminated with methylmercury. Cord blood and cord tissue can also be considered as a biomarker sample that is worthwhile collecting if information on recent exposure is sought. The presence of mercury in urine generally represents exposure to inorganic and/or elemental mercury, and collection is non-invasive. Urine mercury levels are usually considered the best measure of recent exposures to inorganic mercury or elemental mercury vapour because urinary mercury is thought to indicate most closely the mercury levels present in the kidneys. Environmental studies have used human milk to evaluate maternal exposure to various chemicals and examine potential exposures for breast-feeding infants.

35.   Even though both blood and hair can be used to document methylmercury exposure, hair is generally the preferred choice as it provides a simple, integrative, and non-invasive sample. Once incorporated in the hair, mercury does not return to the blood, thus it provides a good long-term marker of exposure to methylmercury. Most mercury in hair is in the form methylmercury, especially among populations that consume fish. Hair incorporates methylmercury during its formation and shows a relatively direct relationship with blood mercury levels, providing an accurate and reliable method to measure methylmercury intake levels.

36.   Once mercury levels are measured in a body compartment (such as blood, hair, or urine), the approximate average daily dose (or exposure level) can be calculated by using various extrapolation or conversion factors. However, limitations, uncertainties and population variabilities in using these extrapolation factors should be kept in mind when doing such conversions. Nonetheless, the quantitative relationship between mercury levels in hair and blood and daily average dose (or intake) levels of mercury (especially methylmercury) are fairly well understood. For example, a daily average methylmercury intake of 0.1 microgram per kg body weight per day (0.1 μg /kg per day) by a pregnant woman is estimated to result in hair mercury concentrations of roughly about 1 μg /g, cord blood levels of about 5 to 6 μg /L and blood mercury concentrations of about 4 to 5 μg /L. This relationship is generally linear, or directly proportional.

Examples of biomonitoring studies

37.   Mercury exposures of numerous populations have been monitored by measuring mercury in blood, hair, and urine. Some of these exposure levels have been associated with human health effects and used to estimate tolerable daily intakes. Some of the most well known biomonitoring studies are in populations in Amazonian riparian communities, the Faroe Islands, and the Seychelles Islands. A number of other studies in various Arctic countries have measured mercury levels in body tissues in human populations. Mercury levels in environmental media (such as sediment, air, water, and fish) have also been measured in various studies.

38.   The table below provides information on various studies conducted showing biomarkers of exposure to mercury and methylmercury among various populations in different countries.

Table: Studies of biomarkers of exposure to mercury and methylmercury*

Country	Matrix	Population	Elevated intake of fish?	Concentration of total mercury	Reference
Brazil	hair	Indigenous children aged 7-12 years Indigenous women aged 14-44 years	Yes Yes	14.45 µg/g 15.7 µg/g	Oliviera Santos et al. (2002)
Canada	hair	Indigenous	Yes	4.4 µg/g	Muckle et al. (2001)
China	hair	Representative	No	0.42 µg/g	Feng et al. (1998)
Germany	urine	Representative	No	0.4-2.0 mg/l	Becker et al. (2003)
Japan	hair	Representative	Yes	1.76-3.37 µg/g	Yasutake et al. (2003)
Spain	hair,	Children	No	0.8 µg/g	Batista et al. (1996)
Spain	blood	Representative	Yes	11-22 ng/g	Sanzo et al. (2001)
Sweden	hair & blood	Pregnant women	Yes	0.35 µg/g (hair) 1.3 µg/l (cord blood)	Bjornberg et al. (2003)
UK	hair	Pregnant women	No	0.19 µg/g	Lindlow et al. (2003)
USA	hair	Representative	No	0.3 µg/g	Pelizzari et al. (1999)
USA	blood	Women aged 16-49 years	No	1.2 µg/l	Schober et al. (2003)
USA	hair	Women aged 15-45 years	No	0.4 µg/g	Smith et al. (1997)
USA	hair	Indigenous	Yes	0.83 µg/g	Gerstenberger et al. (1997)
USA	blood	Representative of high end fish consumers	Yes	14.5 µg/l	Hightower and Moore (2003)
USA	hair	Children (1-5 yrs) Women (16-49 yrs)	No	0.12 µg/g 0.20 µg/g	McDowell et al. (2004)

* Adapted from WHO, 2004

39.   Several biological sample collection and handling protocols are given in <u>Appendix C</u> of this document, along with sample documentation forms as examples.

CHAPTER 4: Exposure Assessment of Methylmercury in Fish

40.   Risk analysis consists of a process comprised of three distinct but interrelated components, namely, risk assessment, risk management and risk communication. In the case of methylmercury, all three components are important to achieve consumer protection and assure the benefits of fish consumption for consumers. Hazard characterization of mercury includes the establishment of a reference level, which describes the level of exposure that is likely to be without harm.

41.   In this chapter, exposure assessment is considered as this is perhaps the most important aspect for a national food safety authority. While reference levels are considered "portable" in that they generally apply to all populations, exposure of populations may be highly variable depending on their consumption patterns and on the levels of a particular chemical in food as consumed.

General approach

42.   Estimating exposure to methylmercury in fish can be used as a cost-effective tool by risk managers to assess the risk of methylmercury to susceptible populations, but broader health benefits, as well as the social, cultural and economic considerations of fish consumption, need to be kept in mind when considering risk management options.

43.   Mercury is an ubiquitous contaminant, even in the absence of local/regional point sources of contamination. As described in Chapter 2, the general population is primarily exposed to methylmercury through the diet, especially from fish. Levels of mercury are generally much higher in fish and marine mammals, (such as seals and some whales, than in other foods or drinking water). In predatory marine fish, about 90 % of the mercury exists in the methylated form (methylmercury), but the ratio is lower in freshwater fish.

44.   However, all fish consumers are exposed to some methylmercury. Both marine and freshwater fish, as well as marine mammals, accumulate methylmercury in their muscle tissue. Moreover, methylmercury biomagnifies through the food web, meaning that apical predators, that is carnivorous species feeding at the top of the food chain, tend to have higher levels of methylmercury. Also the larger (older) individuals tend to have higher contents. Methylmercury in fish is bound to tissue protein rather than in fatty deposits; therefore, trimming and skinning of mercury-contaminated fish does not reduce the mercury content of the fillet portion. In addition, the methylmercury level in fish is not reduced by cooking.

45.   Because most of the mercury in fish is methylmercury (at least for predatory marine fish) and most (greater than 95 %) of the methylmercury in fish ingested is readily absorbed into the body through the gastrointestinal tract, exposure to methylmercury (or intake) can be estimated if information is available on the following: a) types (that is, species) and amounts (such as frequency and serving size) of fish ingested per unit time (such as day or week); b) total mercury concentrations in the types of fish ingested; and, c) the body weight of persons consuming the fish.

46.   Using the above information, the methylmercury intake for individuals or populations can be calculated by the following basic equation:

$$\frac{\text{Amount of fish ingested per week (kg/week)} \; * \; \text{Mercury concentration in the fish ingested (µg/kg)}}{\text{Kilogram body weight (kg bw)}} = \text{Methylmercury intake per kilogram body weight per week (µg methylmercury per kg body weight per week)}$$

Screening methods

47.   In order to best use resources, risk managers may employ a tiered approach for assessing exposure. A tiered approach allows organizations to limit more detailed assessments to critical subpopulations that may have higher exposures or that might be more susceptible to lower levels of exposure, (such as pregnant women and children).

48.   Simple screening methods are used as an initial exposure estimate. These methods sometimes result in significant overestimates of the actual exposure, depending on the input data used and assumptions used in the assessment. Therefore, if an estimated intake of the chemical substance is below its reference level, there is generally no need for more refined assessments. However, if a screening assessment result exceeds the reference level, further investigation may be warranted.

49.   A screening assessment can also be used initially to estimate exposures among the general population and to help determine specific subgroups of the population considered most likely to be exposed to elevated levels of methylmercury. A process is presented in this chapter to perform increasingly refined assessments of exposures to by refining consumption estimates of fish and seafood and/or refining methylmercury concentration estimates.

Refinements to consumption estimates

50.   Refinements to estimating exposures for a specific population or subgroup follow the same general principles as screening-level exposure assessment, but are more complicated and require more data. In these cases, more detailed information is gathered and evaluated on the distribution of individual fish consumption patterns among the population, especially susceptible groups. Consumption data are then integrated with the data on mercury concentrations in fish commonly consumed to estimate the exposures in the subpopulations of concern. This can be best done through national dietary surveys of individuals, but purchase data and fish market sales can also be helpful.

Refinements to concentration estimates

51.   For most countries, the main source of human exposure to methylmercury is through the consumption of fish. However, levels of methylmercury vary among different fish species. For example, piscivorous fish (i.e., fish that eat other fish), also called predatory fish, are more likely to contain higher levels of methylmercury in their muscles and other tissues. Other factors that influence mercury levels in the fish include age, size, weight, and length of the fish. In addition, the environmental characteristics of the water body (such as local contamination, pH, reduction-oxidation potential, and other factors) can affect levels of mercury in the fish. Characterization of methylmercury levels in fish consumed by a population or subpopulation of interest can be obtained from existing databases in the country or region of interest. The use of surrogate data from an assemblage of the different data sets can also be used in preliminary estimates of exposures to mercury.

Exposure estimates of subpopulations

52.   Estimating exposure to mercury for target subpopulations potentially at risk may require gathering new data (such as the species of fish consumed by the subpopulations, including fish sourced from markets, and the determination of methylmercury levels in those fish). In a micro-scale assessment or a site-specific assessment, fish consumption rates among a surveyed population are combined with specific measurements of mercury concentrations in the local fish actually consumed to estimate the exposure levels for the population. Depending on the type of data collected, mercury exposures can sometimes be estimated for individuals and/or subgroups among the surveyed population.

CHAPTER 5: Environmental Exposure Models

53.   Mercury partitioning and movement in the environment is complex and depends on many environmental parameters. However, computer models can be used to predict the environmental fate and transport of emitted mercury and to estimate levels in various media and biota, and to estimate possible human exposures.

54.   The chapter does not aim to give a comprehensive list of models, but provides descriptions of some available models of relevance and a few model studies with appropriate references. Several organizations are working with exposure models (such as the USEPA Center for Exposure Assessment Modelling [CEAM]). As an example, a study performed by the EU EMECAP project, estimating the exposure of inhabitants around a chlor-alkali plant is presented. However, there is still a long way to go to have precise models for estimating human exposures to mercury.

55.   The use of models to estimate exposures can be a useful approach for assessing potential risks to human health. However, modelling relies on a number of assumptions with varying degrees of uncertainty, which is important to keep in mind when carrying out these types of exposure assessments.

CHAPTER 6: Assessment of Specific Exposure Scenarios

56.   Mercury "hot spots" are defined here as regions or locations where risks of higher contamination of the environment (air, soil, water or food sources) might occur following human (anthropogenic) activities, through either increased releases or increased methylation of mercury in the environment. The most common sources of anthropogenic mercury releases include industrial activities (such as artisanal and

small scale gold mining, energy production, chlor-alkali plants) and waste sites (domestic and industrial). Spills of mercury can lead to local pollution. Changes to the environment (such as deforestation or the building of reservoirs) may change the ecosystem, resulting in an increase of methylation of mercury in the environment.

57.   The additional exposures resulting from a mercury "hotspot" are generally assessed by considering the direct exposures (through inhalation, ingestion and dermal) to mercury and mercury compounds, and also the indirect exposures to mercury (especially, methylmercury) via food using the methods discussed previously in Chapter 4.

Assessment of occupational exposures

58.   A screening assessment should be carried out to address the likely sources of mercury exposure in the workplace. The screening assessment may include investigations of the workplace, monitoring of workplace mercury levels along with a health assessment, and, in many cases, it is also appropriate to collaborate with the local community. A workplace assessment may be done on a descriptive basis or may involve monitoring. Health assessments may determine whether signs of mercury toxicity are present, and, if warranted, may be extended to workers families and the community. Monitoring of actual exposures can be done utilizing the previously described biomonitoring tools. While workers are the primary focus of the assessment, it should be remembered that mercury contaminated clothing and other items may also result in contamination of the home environment. Following the assessment, a management plan should be developed if required to decrease occupational exposures to mercury.

Assessment of mercury "hot spots"

59.   One type of mining process for gold involves mixing wet ore with metallic mercury. The mercury chemically binds with the gold or silver in the mud. The remaining mud is washed away leaving a mercury-gold (or mercury-silver) amalgam, which is then heated to release the mercury, with mostly gold and/or silver remaining. Artisanal gold mining is a major source of income in many countries, with amalgamation being the preferred extraction method. However, the process can result in high mercury exposure levels for miners and their families, and also significant environment contamination, if proper control techniques are not used.

60.   Mercury is used directly in the manufacture of a number of products, and may also be released indirectly in a number of processes. Some important sources of mercury emissions are coal burning power plants, cement production, other mining activities producing mercury as a byproduct, chlor-alkali production and the manufacture of a number of products. Some of these sources may result in direct worker exposure and may also result in elevated mercury levels in the area immediately surrounding the release source, resulting in higher exposures to the population in that area.

61.   Mercury-containing wastes can be generated through industrial processes or domestic use. This waste can be discarded improperly, resulting in contamination of the local area and creation of a "mercury waste site." People who live near these waste sites can be exposed to elevated levels of mercury due to releases to the soil, air, and water. With the increased use of energy-efficient fluorescent bulbs, the disposal of such items posed a potentially serious source of mercury contamination. Although the amount of mercury used in each bulb is small, the cumulative impact of the disposal of millions of such bulbs in the future needs to be addressed by national and municipal governments.

62.   Another source of environmental contamination results from mining wastes, particularly historical tailing wastes where cyanide had been used in addition to mercury to extract gold. Releases from waste sites may contaminate local fish species, resulting in elevated levels of exposure to the local community.

Other exposure scenarios

63.   Mercury has traditionally been used in certain religious ceremonies resulting in high levels of ambient mercury. In addition, a number of skin lightening creams, popular in many parts of the world, contain mercury, as do some folk medicines, some of which may include the direct administration of mercury.

64.   Deforestation often leads to increased erosion. Deposition of soil in waterways can result in the release and methylation of mercury in these waters, leading to high levels in fish. Where forests are cleared by burning, elevated levels of mercury may be released into the environment. Populations living downstream of deforested areas may therefore be at risk from high levels of mercury in the fish.

65.   Dental amalgams containing mercury have been used for more than a century to repair dental caries. Low-level mercury exposure to the patient can arise from both inhalation and ingestion. Mercury exposure also occurs to dentists and dental workers. Mercury from dental amalgams can enter the environment through dental office wastes and from air emissions from crematoriums.

66.   Thimerosal is used as a preservative in multidose liquid presentations of vaccines. In the human body, thimerosal is converted to ethylmercury, which differs chemically from methylmercury. In particular, ethylmercury is very rapidly eliminated with a half life of less than a week.

67.   Reservoirs can have quite elevated levels of mercury following the initial flooding, which may result in very high levels in the local fish population. These elevated levels may be observed for up to 40 years following the initial flooding.

CHAPTER 7: Risk Management of Methylmercury in Fish

Risk manager's decision tree

68.   The chapter is intended to address potential risk of methylmercury posed by consumption of fish. Other dietary sources of methylmercury are not addressed, but are generally considered minor compared to fish. It should also be noted that inorganic mercury is a contaminant of food, but exposure is considered less important because of the lower toxicity of inorganic mercury compared to methylmercury. Therefore, inorganic mercury in food is not addressed. Some of the steps in the decision tree make use of techniques and methods described in Chapters 3 and 4. The seven steps presented here are part of a decision tree framework, which can guide risk managers in identifying populations at risk from methylmercury from fish consumption in a consistent and cost-effective manner. The approach uses increasingly detailed exposure assessments to better characterize the risk. Consequently, Chapter 7 of this document is intended to provide guidance to risk managers to better understand the risk posed by methylmercury in fish and to develop appropriate intervention strategies to minimize risk while maximizing the benefits of fish consumption.

69.   **Step 1** - In the management of potential risks posed by methylmercury in fish, the first step is the evaluation of the importance of fish as a source of protein and other nutrients for the local population. Because fish are the main pathways for human exposure to methylmercury, information on fish consumption by the population can be obtained from a number of sources. This initial phase can include a preliminary survey to identify frequency and type of fish consumed by different subgroups of the population. Note that if marine mammals are consumed, their potential contribution to mercury exposure should be included in the assessment.

70.   **Step 2** - Before implementing a comprehensive exposure assessment, a biomonitoring survey using human hair can be conducted to determine exposure levels to methylmercury. This will be most important for young children and women of child-bearing age consuming one or more meals per week containing fish with high mercury content and for high fish consumers. Exposure can be assessed by analysis of total mercury concentrations in composite hair samples. The use of hair is a non-invasive, relatively inexpensive and sufficiently accurate procedure for determining methylmercury exposure among fish-eating groups.

71.   **Step 3** - If average mercury concentrations in composite hair samples are much lower than reference levels, no further action is required. However, if average mercury concentrations in composite samples from any group exceed those considered hazardous, or if the margin of safety is relatively narrow, hair samples from each individual can be analysed. Evaluation of individual results will identify populations at risk from methylmercury and if levels of high percentile individuals warrant, further details on exposure can be obtained as below.

72.   **Step 4** - If biomonitoring results are high, exposure to total mercury due to fish consumption can be estimated for individuals of each potentially at-risk group taking into account dietary habits and total mercury levels in fish consumed. This can be conducted using a tiered approach with increasing refinement of the food consumption and concentration estimates. Consumption of fish by species, amount and frequency can be obtained through dietary consumption surveys of individuals, supplemented with other information. Determination of body mass of consumers can also be taken at that time. Average or mean total mercury levels for common types of fish consumed can be determined on composite samples or can be obtained from available data in other countries.

73.   **Step 5** - Based on the above data, total mercury exposure estimates can then be calculated on a weekly per kilogram of body weight basis, which can then be compared to the PTWI for methylmercury. If exposure is below the reference level, no further action is required in regard to fish, but investigation of other sources of mercury exposure may be warranted. If exposure to total mercury is calculated to exceed the reference levels for methylmercury, analysis of composite fish samples specifically for methylmercury can be considered.

74.   **Step 6** - Composite fish samples can be analysed specifically for methylmercury to refine the exposure assessment. Consideration should first be given to the type of fish normally consumed. The ratio of methylmercury to total mercury may be as low as 0.3 for freshwater non-predatory fish. However, for marine predatory fish, this step may be omitted because the ratio of methylmercury to total mercury is often around 0.9.

75.   **Step 7** - Once the methylmercury level in fish is determined, a refined calculation of methylmercury exposure from fish can be performed by multiplying the fish consumption data by average methylmercury content in fish. Intake values can then be expressed on a weekly basis and can be compared to the PTWI for methylmercury. If the PTWI is exceeded, risk management interventions can be considered as below.

Option selection

76.   In general, there are two strategies to reduce the public's exposure to methylmercury in fish. One makes use of public education to influence fish consumption among populations at risk, and the other uses regulatory measures to reduce levels of methylmercury in fish. Reduction of mercury in the environment by controlling emissions can also decrease exposure to methylmercury on a long-term basis.

77.   Public education strategies aimed at guiding fish consumption are important for the risk management for methylmercury exposure. The ultimate goal of these strategies is to change patterns of consumption so that people at risk can continue to eat fish and enjoy its health benefits, while also reducing their exposure to methylmercury. These strategies rely on effective risk communication, which is described in more detail below.

78.   Another risk management strategy is to reduce potential exposure to methylmercury through fish consists of setting maximum acceptable concentration limits. The FAO/WHO Codex Alimentarius Commission has set guideline levels for methylmercury at 1 mg/kg for large predatory fish (such as shark, swordfish, tuna and pike) and 0.5 mg/kg for non-predatory fish. Regulatory approaches, in the case of methylmercury in fish, have limitations in terms of cost and effectiveness and may not result in sufficient exposure reductions by themselves.

Risk communication

79.   Successful risk communication is a prerequisite for effective risk management. This is applicable to both public education and regulatory strategies. In regard to public education, the fundamental goal of risk communication is to provide meaningful, relevant and accurate information, in clear and understandable terms, targeted to a specific audience with regard to the risks and benefits of fish consumption and other routes of exposure to mercury.

80.   In early stages of the risk communication programme, once methylmercury in fish is identified as a problem, risk communicators need to define the goals to be achieved. The at-risk groups, or target audiences, must be clearly identified. A community can be segmented and different segments can receive

different messages, according to their specific needs and risks. For example, considering neurological risks to fetus, women of child bearing age, pregnant and breast-feeding women can be considered separately from other subpopulations.

81. The acceptability of the risk management measures is closely related to public perception of risk. Therefore, it is essential for risk communicators to ensure that the risk communication process reveals information about the general public's perception of the risk of mercury exposure associated with fish consumption. Experience demonstrates that, to be most effective, the strategy used for risk communication should be tailored to stakeholders' particular characteristics and concerns, for the appropriate audience, with cultural, social and economic factors considered.

82. Communication on the risk and benefits of fish consumption should involve a two-way dialogue. Risk communicators must provide external stakeholders with clear and timely information about methylmercury risks and measures to manage it. If appropriate, other pollutants (such as PCBs and dioxins) should also be addressed to the extent feasible in the risk assessment, risk management and risk communication process. Information on benefits of fish consumption must also be provided, as well as information on alternative foods, especially in regions where fish represent a main food source. This information should be communicated in a way that stakeholders can easily understand and using media that they can easily access.

Monitoring and review

83. Once implemented, the risk management option needs to be evaluated in order to determine whether it has achieved its goals. For public education, the indicator is the degree of responsiveness of the target audience to the key message. This review allows the identification of eventual adjustments or improvements that can be implemented. Risk communicators need to identify specific evaluation strategies to measure the effectiveness of their campaign.

1. INTRODUCTION

1.1 Background

84.   The United Nations Environment Programme (UNEP) Governing Council concluded, at its 22nd session in February 2003, after considering the key findings of the Global Mercury Assessment[1] report, that there is sufficient evidence of significant global adverse impacts from mercury to warrant further international action to reduce the risks to humans and wildlife from the release of mercury to the environment. The Governing Council decided that national, regional and global actions should be initiated as soon as possible and urged all countries to adopt goals and take actions, as appropriate, to identify populations at risk and to reduce human-generated releases.

85.   The Governing Council requested UNEP, in cooperation and consultation with other appropriate organizations, to facilitate and conduct technical assistance and capacity building activities to support the efforts of countries to take action regarding mercury pollution. This request was reinforced by the Governing Council at its 23rd session in February 2005. At that session, the Governing Council also encouraged governments to promote and improve evaluation and risk communication methods, based on, *inter alia*, guidance from the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO), that enable citizens to make health-protective dietary choices based on risk and benefit information concerning fish consumption.

86.   The Governing Council at its 24th session in February 2007 recognized that a range of activities are still required to address the challenges posed by mercury, including substitution of products and technologies; technical assistance and capacity building; development of national policy and regulation; data collection, research and information provision, bearing in mind the need to provide assistance to developing countries and countries with economies in transition.

87.   To support the efforts of countries to take action regarding mercury pollution, UNEP established a mercury programme within UNEP Chemicals, with the immediate objective to encourage all countries to adopt goals and take actions, as appropriate, to identify exposed populations, minimize exposures through outreach efforts, and reduce anthropogenic mercury releases. Among the priorities for the programme are to assist countries in assessing their own situation with regard to mercury pollution and identifying possible ways of dealing with any adverse impacts (such as developing tools and strategies to mitigate problems) increasing awareness and promotion of mercury-free products or responsible use of mercury, where appropriate, and developing strategies for enhanced communication to reach at-risk populations.

88.   An important part of the programme is to develop training materials, guidance documents and toolkits on a number of relevant topics that may be of use to Governments and others in their efforts to

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[1] The Global Mercury Assessment (UNEP, 2002), a comprehensive report covering most issues relevant to mercury pollution, including chemistry, toxicology, exposures and risk evaluations for humans, impacts on the environment, cycling in the global environment and possible prevention and control technologies for controlling releases and limiting use and exposure to mercury, can be accessed online at the UNEP Chemicals website (URL: http://www.chem.unep.ch/mercury/Report/Final%20Assessment%20report.htm). Hardcopies can be obtained by contacting UNEP Chemicals at the address given on the inside cover of this document.

evaluate and address mercury pollution. Governments will need to develop the knowledge base necessary for evaluating the risks posed by mercury and for taking appropriate action to reduce those risks.

89.   This "Guidance for Identifying Populations at Risk from Mercury Exposure" is intended to assist countries concerned about the potential impacts of mercury pollution on their population by identifying and characterizing populations (or subpopulations) that may be at risk. The document describes the exposure assessment methods and approaches that can be used in a decision tree framework to manage the possible health risk of mercury in a logical and cost-effective manner.

90.   This guidance document was initially developed by the Center for Environmental Analysis of the Research Triangle Institute (RTI International) in North Carolina, USA, especially Chapters 2, 3 and 5, and the Safe Consultants in Quebec, Montreal, especially Chapters 4 and 6. Finalization and technical editing was done by the UNEP Chemicals Mercury and Other Metals Team. Comments from members of the Global Mercury Assessment Working Group, Governments and other interested stakeholders were received and considered.

91.   The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has assessed the risks from mercury and methylmercury at several meetings. All relevant JECFA reports and monograph were taken into account in this guidance document as part of international recommendations on methylmercury in fish. The JECFA Secretariat made substantial contributions to this document, particularly for Chapters 2 and 3.

92.   Finally, this document, especially Chapters 4 and 7, incorporates in major sections of the unpublished document "Risk Managers Guide to Mercury in Fish", which is being prepared by the WHO Health Security and Environment (HSE), Department of Food Safety, Zoonoses and Foodborne Diseases in cooperation with the FAO. This document is being issued as a joint UNEP and WHO document in cooperation with FAO.

1.2   Purpose, scope and organization of this document

93.   For several decades the international scientific community has been aware of the issue of mercury contamination in the global environment. Governments of the industrialized countries invested considerable financial and human resources in order to better understand the biogeochemical behaviour and cycling of mercury and its impacts on the health of populations. Indeed, the general understanding of the sources and fate of this pollutant has greatly evolved since these early reports. Numerous protocols, technical documents, and epidemiological and clinical studies explaining ways to address mercury issues were published and are now available to extensively characterize the impacts of mercury on the environment and human health, guiding future research and interventions of scientists and policy makers.

94.   The environmental and health assessment approaches described in the literature yield quality information usable for fundamental research purposes. However, they are often costly and time-consuming to extract. In addition, it appears that general guidance on how to estimate exposure to mercury to identify populations at risk has not been previously developed or is not readily available.

Purpose

95.   The main purpose of this document is to provide guidance intended to help governments and other organizations identify populations potentially at risk due to exposures to mercury. To do this, the document focuses on the four steps of the risk assessment process, which includes hazard identification, hazard characterization (including dose-response assessment), exposure assessment and risk characterization. However, exposure assessment is given the most emphasis.

96.   This document was produced on the rationale that evaluating the potential risks due to exposures to mercury is possible even when financial and human resources are limited. The approaches presented in this document can be used by governments and other organizations to assess and describe particular national, regional, and local situations regarding mercury contamination, human exposures, and

identifying populations (or subpopulations) that may be at risk due to mercury exposures. The information generated from such assessments can help governments and other organizations determine priorities for possible interventions to decrease exposure for these populations.

Scope

97.   In order to best use resources, most experienced assessors will employ a tiered approach for assessing exposure. A tiered approach allows organizations to limit detailed assessments to critical sub-regions or subpopulations that may have high exposures or that might be more susceptible to lower levels of exposure. Simple screening methods are used initially to estimate exposures among the general population and to help determine priority locations or subpopulations considered most likely to be exposed to elevated levels of methylmercury. This can be followed by refinements to various aspects of the assessments (such as refinements to fish consumption estimates and estimates of mercury concentrations in fish).

98.   As described later in this document, the involvement of the community and other stakeholders may be important at various stages of research on environmental health impacts and during the process of evaluating and addressing environmental issues (such as mercury contamination and exposure). This participatory approach can be essential for such research to succeed and is especially important for local communities. At a minimum, consultation with community members may be necessary, and their consent obtained, before any such research proceeds. This involvement of the community is necessary to ensure participants are treated with dignity and respect and to help develop good relations between researchers/organizations, and community members.

99.   This guidance document follows a number of workshops for developing countries and countries with economies in transition, to raise awareness of the global issues related to mercury pollution and assist these countries in assessing their own situation with regard to mercury pollution and identifying possible ways of dealing with any adverse impacts. This document provides guidance to governments for risk management of methylmercury in light of the new JECFA provisional tolerable daily intake (PTWI).

100. While the incidents involving high exposures have resulted from man-made conditions, food safety authorities around the world continue to grapple with the question of the health implications of long-term low-level exposures to methylmercury, which is predominately through the consumption of fish. However, the risk also has to be seen in the context of the established nutritional benefits of fish consumption, which for many populations is the main source of protein. Consequently, Chapter 7 of this document is intended to provide guidance to risk managers to better understand the risk posed by methylmercury in fish and to develop appropriate intervention strategies to minimize risk while maximizing the benefits of fish consumption.

Organization

101. The risk analysis paradigm was used as a framework for the consideration of the risk of mercury and methylmercury. This paradigm is used in most developed countries and has been described by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in a series of expert consultation reports (FAO/WHO, 1995, 1997, 1998, 2006). The risk analysis paradigm has been adopted by the FAO/WHO Codex Alimentarius Commission as the basis for the establishment of international health and safety standards for food (Codex 2007).

102. Chapter 2 presents summary information on toxicity of mercury and mercury compounds available from existing assessments, including discussion of potential adverse health effects and exposure levels that may be considered to be "safe". In addition the document provides a summary of the process of risk characterization, whereby the information on mercury exposures is combined with information on toxicity to describe the potential risks to human populations.

103. Chapter 2 also presents background information, including a summary of the various forms of mercury, environmental fate and cycling of mercury in environmental media and biota, the primary routes of exposure, absorption, metabolism, toxicity, and risk characterization for mercury.

104. Chapters 3 describes approaches for estimating mercury exposures through biomonitoring, including details on measuring mercury in various body tissues (that is, blood, hair, urine, nails and human milk). This chapter includes a discussion of extrapolating levels measured in one tissue (such as hair) to estimate levels in another tissue (such as blood). Biomarkers of exposure should also correlate with actual exposure to mercury (such as the consumption of fish containing methylmercury).

105. Chapter 4 provides details on conducting exposure assessments of mercury through the collection and application of data on fish consumption patterns and mercury levels in fish. Various dietary survey methods and modelling techniques are described.

106. Chapter 5 describes models used to simulate environmental fate, uptake and exposures and Chapter 6 covers specific exposure scenarios, especially so-called "hot spots". Chapter 7 is devoted to presenting a decision tree approach based on increasingly more detailed estimates of exposures to methylmercury from fish for susceptible populations. Risk management options are presented along with a discussion of risk communication techniques that balance the risks and benefits of fish consumption.

107. UNEP and WHO encourage governments and other stakeholders to make use of the guidance when assessing possible risks from mercury exposure and invite all users of the guidance document to provide feedback on any aspect of this product. Researchers are also invited to submit the results of any exposure assessments to UNEP and WHO. A forum for exchange of information on countries' experiences, relevant new publications, and other information is planned. Further revised versions of the document might also be published and the most current version of this guidance document will at any time be available on the UNEP Chemicals mercury Website http://www.chem.unep.ch/mercury.

1.3   Sources of additional information

108. Several governments, international agencies, and other organizations have compiled extensive information on the sources, environmental fate and transport, potential health effects, exposure estimates, and potential risks of elemental mercury, inorganic mercury and methylmercury. Several useful resources are listed below with their full citations appearing in the reference list at the end of this document. Most can be obtained online.

- Global Mercury Assessment (UNEP Chemicals, 2002)

- Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects (WHO, 2003)

- Arctic Pollution 2002 (AMAP 2002)

- Human Health in the Arctic (AMAP, 2003)

- Canadian Arctic Contaminants Assessment Report II (CACAR II, 2003)

- Guide for Reducing Major Uses and Releases of Mercury (UNEP Chemicals, 2006)

- Mercury Study Reports to Congress (US EPA, 1997a, 1997b, 1997c, 1997d)

- Toxicological Profile for Mercury (Update) (US ATSDR, 1999)

- Protocols for Environmental and Health Assessment of Mercury Released by Artisanal and Small-Scale Gold Miners (UNIDO, 2003b)

- Summary of Supply, Trade, and Demand Information on Mercury (UNEP Chemicals, 2006)

- Toxicological Effects of Methylmercury (NRC, 2000)

- Toolkit for the Identification and Quantification of Mercury Releases (UNEP Chemicals, 2005)

- Mercury - Environmental Health Criteria Documents (WHO, 1976, 1989, 1990, 1991)

- Preventive Measures Against Environmental Mercury Pollution and Its Health Effects (JPHA, 2001)

- Mercury - A Priority for Action Important Community Messages (UNEP Chemicals, 2008)

- Advice on Fish Consumption: Benefits and Risks, Scientific Advisory Committee on Nutrition and Committee on Toxicity, Food Standards Agency and the Department of Health (TSO, 2004)

- Health implications of environmental contaminants in Arctic Canada: A review (Van Oostdam et al., 2005)

- Risks and benefits of fish consumption. A risk-benefit analysis based on the occurrence of dioxin/PCB, methylmercury, n-3 fatty acids and vitamin D in fish. (Swedish National Food Administration, Report 12, 2007 Available at: http://www.slv.se/upload/dokument/rapporter/mat_naring/2007_12_risks_and_benefits_of_fish_consumption.pdf?epslanguage=EN-GB)

- Opinion of the scientific panel on contaminants in the food chain on a request from the European Parliament related to the safety assessment of wild and farmed fish (European Food Safety Authority, EFSA Q-2004-22, 2005)

- A comprehensive assessment of fish and other seafood in the Norwegian diet. (Norwegian Scientific Committee for Food Safety, Oslo, 2007, ISBN 978-82-8082-207-9)

- Advice for Pregnant Women on Fish Consumption concerning Mercury Contamination (Japanese Joint Sub-Committees on Animal Origin Foods and Toxicology under the Food Sanitation Committee the Pharmaceutical Affairs and Food Sanitation Council, 2003. Available at: http://www.mhlw.go.jp/english/wp/other/councils/mercury/index.html)

- Mercury in Fish. (Food Standards Australia New Zealand, 2004. Available at: http://www.foodstandards.gov.au/newsroom/factsheets/factsheets2004/mercuryinfishfurther2394.cfm)

2. BACKGROUND AND OVERVIEW OF HEALTH RISKS

2.1 Risk analysis paradigm

109. The risk analysis paradigm described by WHO and FAO consists of three components; risk assessment, risk management and risk communication. Risk assessment and management are, in turn, each comprised of four steps (see Figure 1). The overall process is carried out under the direction of the risk manager to whom the primary responsibility for managing health risks on behalf of the society has been delegated. Based on preliminary information, the risk manager uses the hazard identification as the basis for deciding whether to undertake a full risk assessment in the light of other risk priorities and available resources. In regard to food safety, risk managers should be aware that the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organization requires that countries ensure that their food safety measures are based on an assessment of risks to human health, taking into account the risk assessment techniques developed by the relevant international organizations, in this case FAO and WHO.

110. For methylmercury in fish, national food safety authorities in many countries have concluded that the potential health risk posed by methylmercury warrants the completion of the risk assessment paradigm, namely hazard characterization and exposure assessment, leading to a risk characterization for their populations. At the international level, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) first performed a hazard characterization of methylmercury in 1972 and has continued to refine its evaluation as new data have become available. For JECFA the hazard characterization is expressed as the Provisional Weekly Tolerable Intake (PTWI) and is currently established at 1.6 µg of methylmercury per kg body weight (FAO/WHO, 1972, 1978, 1989, 2000, 2004, 2007). This value is based on the most sensitive toxicological endpoint, developmental neurotoxicity, in the most susceptible life-stage, the development in utero. JECFA noted in the report from the 67th meeting that other life-stages might be less sensitive to the adverse effects of methylmercury. In the case of adults, the Committee considered that intakes of up to about two times higher than the PTWI would not pose risks of neurotoxicity in adults, although in the case of women of childbearing age, the intake should not exceed the PTWI, in order to protect the embryo and fetus. For infants and children JECFA could not identify a level of intake higher than the PTWI that would not pose a risk of developmental toxicity for infants and children up to about 17 years of age, hence for this age group the PTWI of 1.6 µg/kg bodyweight applies.

111. JECFA has conducted an international evaluation of exposure based on the GEMS/Food Regional Diets and reviewed a number of national exposure assessments. Taken together, the hazard characterization and exposure assessment produced a risk characterization that suggested that most of the world's population was not at risk to the potential toxic effects of methylmercury. However, persons who are consuming large amounts of fish, especially if those fish contained high levels of methylmercury, can have exposures that exceed the PTWI. If those high exposure consumers are pregnant women or young children, the preparation of a risk evaluation by risk manager may be warranted.

2.2 Risk assessment principles

112. Risk assessment is a multidisciplinary evaluation of scientific information as a basis for estimating and evaluating the potential health effects that individuals or populations may experience as a result of exposure to hazardous substances. Risk assessments typically involve both qualitative and quantitative information. Risk assessments may include evaluations of cancer risk and the potential for development of adverse non-cancer health effects (such as neurological dysfunction). To derive statements of risk or the likelihood of adverse health effects, quantitative information on exposure is combined with information on toxicity.
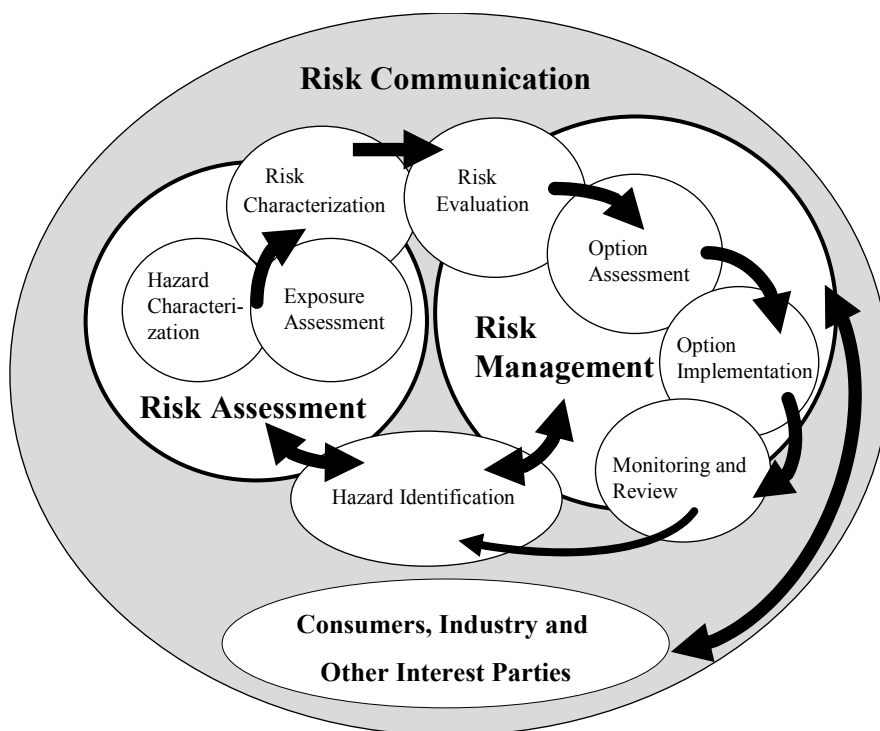
Figure 1 Risk analysis paradigm

113. In 1983, the US National Academy of Sciences (NAS) of the National Research Council (NRC) established a framework to guide risk assessments (NRC, 1983). Risk assessment has been broadly adopted by national and international agencies. At the international level, FAO and WHO have defined risk assessment as consisting of four steps (FAO/WHO, 1995):

    1)   Hazard identification;

    2)   Hazard characterization, including dose-response assessment;

    3)   Exposure assessment;

    4)   Risk characterization.

114. Hazard identification is the review of relevant toxicological, biological, and chemical information to identify the adverse health effects associated with a potential hazard under various exposure scenarios. Epidemiologic and animal studies are some of the information examined.

115. Hazard characterization, including dose-response assessment, defines the relationship between the degree of exposure (or amount of dose) observed in animal or human studies and the magnitude of the observed adverse health effects. This usually includes a quantitative measure of adverse health effects for a range of doses. For carcinogens, dose-response data are used to calculate quantitative estimates of the increased risk of developing cancer per unit of exposure. For chemicals that cause adverse health effects other than cancer (i.e., non-cancer effects), dose-response data are used to calculate "safe" levels (such as the Provisional Tolerable Weekly Intakes developed by the Joint FAO/WHO Expert Committees (WHO, 1987). The development of these values usually involves extensive review of available relevant data, the use of mathematical models, the application of uncertainty factors and dose conversions, and other considerations.

116. In an exposure assessment, the extent, duration, frequency and magnitude of exposures to a chemical are estimated via various routes (ingestion, inhalation, dermal, or in utero) for individuals or populations. Exposures can be estimated by measuring chemical levels in various body tissues (such as hair, blood, and

urine) as biomarkers or by using various mathematical models (US EPA, 1995a; WHO, 1997). Exposure assessments can be used for risk assessments, status and trends analyses, and epidemiology (US EPA, 1992).

117. Risk characterization is the integration of the hazard identification, hazard characterization, including dose-response, and exposure assessments to describe the nature and magnitude of the health risk in a given population. The risk characterization also includes a presentation of the uncertainties in the assessment, discussion of degree of confidence, data gaps, limitations, and other considerations to help describe the potential risks (US EPA, 1995a, FAO/WHO, 1995).

118. Once an exposure assessment and risk characterization are completed, the results of such risk assessments can then be used to help identify populations at risk, that is due to exposures to mercury, and to assist governments and other organizations with development of strategies and programmes to protect those populations from excessive risk.

2.3 Mercury in the environment

119. Mercury (with the chemical symbol of Hg) is a naturally occurring element found in air, water, and soil. It is distributed throughout the environment by both natural and anthropogenic (human) processes. Mercury is found in various inorganic and organic forms and is persistent in the environment. The three primary forms include: a) elemental mercury (with the chemical symbol of Hg^0); b) ionic mercury (also known as inorganic mercury with the chemical symbol of Hg (II) or Hg^{2+}) exists in nature as Hg (II) mercuric compounds or complexes in solution; and c) and organic mercury with methylmercury (with the chemical formula MeHg) being the most important.

120. As mercury moves through environmental media (in air, sediments, water), it undergoes complex transformations. Mercury cycles in the environment as a result of natural and human (anthropogenic) activities. Most of the mercury in the atmosphere is Hg^0 vapour, which circulates in the atmosphere for up to a year, and hence can be widely dispersed and transported thousands of miles from likely sources of emission. Most of the mercury in water, soil, sediments, or plants and animals is in the form of ionic mercury salts (such as mercuric chloride) or organic forms of mercury (methylmercury). Inorganic mercury, when either bound to airborne particles or in a gaseous form, is readily removed from the atmosphere by precipitation and is also dry deposited. As it cycles between the atmosphere, land, and water, mercury undergoes a series of complex chemical and physical transformations, many of which are not completely understood (US EPA, 1997c).

121. The air transport and deposition patterns of mercury emissions depend on various factors including the chemical form of mercury emitted, stack height, characteristics of the area surrounding the site, topography, and meteorology. The mercury emitted to the air from various types of sources (usually in elemental or divalent forms) transports through the atmosphere and eventually deposits onto land or water bodies. The chemical and physical properties of these different mercury forms determine their behaviour in the environment and the pattern of deposition. For example, divalent mercury is water soluble and relatively reactive and, therefore, is much more likely to deposit within a short distance from the emitting facility, especially if it is raining or snowing. On the other hand, elemental mercury tends to disperse long distances and may not deposit until it has travelled hundreds or thousands of kilometres.

122. Once deposited, the chemical form of mercury can be methylated in soils and sediments, largely through metabolism by bacteria. Methylmercury, which is the most toxic form of mercury, biomagnifies in food webs, especially the aquatic food web (such as in fish species higher in the food chain). Various studies indicate that anthropogenic releases of mercury from industrial and combustion sources contribute to the levels of methylmercury in fish, especially in freshwater and immediate coastal environments. However, also contributing to these fish methylmercury concentrations are existing background concentrations of mercury, which may consist of mercury from natural sources, as well as historic anthropogenic mercury which has been re-emitted from the oceans or soils (US EPA, 1997a, 1997c; UNEP, 2002). Methylmercury bioaccumulates (higher concentration than the surroundings) in marine and fresh water fish and mammals. The older the fish or mammal, the higher the methylmercury

concentration. It also biomagnifies, that is, the higher the organism is in the food chain, the higher its trophic level and the higher its methylmercury concentration (Watras et al., 1998). Therefore, bigger predatory fish are more likely to have higher levels of methylmercury (Storelli et al., 2002). High methylmercury concentration has also been observed in fish at lower levels in the food web, likely due to higher background levels of mercury in the environment.

123. In spite of its potential risks, mercury continues to be used in a variety of products and processes all over the world. Elemental mercury is used in artisanal and small-scale mining of gold and silver; chlor-alkali production; manometers for measurement and control; thermometers; electrical switches; fluorescent lamp bulbs; back lights of computers; and dental amalgam fillings. Mercury compounds are used in batteries; biocides in the paper industry, pharmaceuticals, paints, and on seed grain; and as laboratory reagents and industrial catalysts (ATSDR, 1999). Mercury can be released to air, water bodies, and soils during production (or other uses) or after disposal of the mercury-containing products and wastes.

124. Mercury is also present in various raw materials (such as coal, oil, wood, and various mining deposits) and can be released to the air or other media when these materials are burned, processed, or disposed. Among human activities, combustion of fossil fuels is the most important in terms of both volume and distribution. Moreover, large amounts of mercury that remain in mine tailings, landfills, sediments, and stockpiles present a threat of future release (UNEP, 2002).

125. In some areas, local and regional mercury depositions have affected mercury contamination levels over the years and countermeasures have been taken during the past decades to reduce national emissions. Mercury emissions can be, however, distributed over long distances in the atmosphere and oceans. Therefore, even countries with minimal mercury emissions, and other areas situated remotely from dense human activity, may be affected. For example, high mercury exposures have been observed in the Arctic, far from any significant sources of anthropogenic releases (ATSDR, 1999; UNEP, 2002; AMAP, 2002; AMAP, 2003, Van Oostdam et al., 2005).

2.4   Routes of exposure

126. Mercury is a toxic, persistent pollutant that bioaccumulates through food webs. Most people have some exposure to elemental, inorganic, or methylmercury as a result of normal daily activities. Almost all people have at least trace amounts of mercury (that is, methylmercury) in their tissues. Generally, these low exposures are not likely to cause adverse health effects. For example, human biological monitoring by the US Centers for Disease Control and Prevention (CDC) in 1999 and 2000 (Schober et al., 2003) shows that most subjects in a study representative of the general US population have blood mercury levels below a level associated with possible health effects. Also, more recent data from the US CDC, for years 1999 to 2002 support this general finding (US CDC, 2005).

127. People are exposed to methylmercury mainly through their diet, especially from fish and other marine species. People may be exposed to elemental or inorganic mercury through inhalation of ambient air during occupational activities and from dental amalgams. Inhalation is the primary route of exposure for elemental mercury. For example, mercury that is accidentally spilled from a mercury-containing thermometer is slightly vapourized at room temperature. Other possible routes of exposure to various forms of mercury include dermal exposure and breast-feeding (ATSDR, 1999; UNEP, 2002; US EPA, 1997a, 1997c, 1997d).

128. Fish are an important, beneficial and nutritious food. Fish are a good source of protein and other important nutrients (such as omega-3 fatty acids, and various vitamins and minerals). Nonetheless, consumption of fish (and marine mammals) is also generally the main pathway for human exposure to methylmercury. For certain fish, a large proportion of the accumulated mercury is in the form of methylmercury (NRC, 2000; US EPA, 1997c). Elevated methylmercury levels have been measured in numerous freshwater and marine fish species throughout the world. Because mercury biomagnifies in the aquatic food web, fish higher on the food web (or of higher trophic level) tend to have higher levels of mercury. The highest levels are found in fish that are apical predators of older age (such as king mackerel, pike, shark, swordfish, walleye, barracuda, large tuna, scabbard, and marlin) and fish-consuming

mammals (such as seals and toothed whales) (US EPA, 1997a, 1997c, 2003; UNEP, 2002). Because mercury is associated primarily with muscle tissue in the body of a fish, rather than with fatty deposits, trimming and skinning of mercury-contaminated fish does not reduce the mercury content of the fillet portion. Furthermore, cooking does not reduce the mercury content. The intake of mercury depends not only on the level of mercury in fish, but also the amount consumed and frequency. Moderate consumption of a variety of fish is not likely to result in exposures of concern. However, people who consume large amounts of contaminated fish or marine mammals may be highly exposed to methylmercury and therefore could be at risk (UNEP, 2002).

129. Mercury (primarily elemental or inorganic forms) in the working environment can lead to elevated exposures. Occupational exposures can occur where mercury or mercury compounds are produced, used in processes, or incorporated in products. Occupational exposures have been reported from (among others) chlor-alkali plants, mercury mines, mercury-based small-scale gold and silver mining, refineries, thermometer factories, dental clinics with poor mercury handling practices, and production of mercury-based chemicals (ATSDR, 1999; UNEP, 2002). In many countries, workers have become protected during the last few decades by the introduction of a range of workplace improvements including more closed manufacturing systems, better ventilation, safe handling procedures, personal protection equipment, and substituting mercury-based technologies with non-mercury alternatives. However, many workers may still be exposed to elevated mercury levels and therefore may be at risk (UNEP, 2002).

130. Small-scale or artisanal mining, using gold-mercury amalgamation to extract gold from ore, which is discussed further in Section 6.3.1, is a significant source of exposure for the workers and nearby populations (UNEP, 2002). Miners burn the gold-mercury amalgam to vapourize the mercury and recover the gold; thus the miners and local populations can have high exposure to mercury vapours. For example, mercury concentrations in air as high as 60 mg/m^3 have been associated with amalgam burning at a mining site. In addition, metallic mercury wastes are usually dumped into or near water courses. These discharges can lead to elevated methylmercury concentrations in the fish of these water bodies. Consumption of these contaminated fish by community residents can result in the intake of high levels of methylmercury (UNIDO, 2003a, 2003b).

131. Some fatalities and severe poisonings have been associated with acute exposures to elevated air levels resulting from heating metallic mercury and mercury-containing objects. Significant exposures to mercury vapours can also occur due to mercury spills in the home (such as due to children playing with mercury, broken thermostats, leaky gas meters, etc.) and in school laboratories as in the case of a mercury spill in a school in the Philippines. The use of mercuric compounds as fungicides in latex paint and to disinfect grain seeds can result in exposure to inorganic mercury, but such use has been discontinued in many countries. In addition, significant exposures can occur due to use of metallic mercury in religious, ethnic, or cultural practices (such as Voodoo, Santeria, and Espiritismo). A few of the activities reported include sprinkling elemental mercury in homes or cars, placing elemental mercury in an open container to rid the house of evil spirits, mixing mercury in bath water or perfume, or placing mercury in devotional candles. Any of these practices can liberate mercury vapour into the room air, exposing the occupants to elevated levels of mercury vapours (ATSDR, 1999; UNEP, 2002).

132. Dental fillings made with mercury amalgam can be a source of human exposure to elemental mercury vapours for many populations. Amalgam surfaces release mercury vapour into the mouth and lung, depending upon the number of amalgam fillings and other factors, the estimated average daily absorption of mercury vapour from dental fillings varies between 3 and 17 µg mercury (UNEP, 2002).

133. Exposures to elemental mercury or inorganic mercury forms can also occur due to use of some skin-lightening creams and soaps and the presence of mercury in some traditional medicines (such as certain traditional Asian or Chinese remedies). Exposures to organic mercury may result from the use of thimerosal (ethylmercury thiosalicylate) as a preservative in some vaccines and other pharmaceuticals (ATSDR, 1999; UNEP, 2002). However, the use of thimerosal in vaccines is being phased out, or significantly reduced, in many countries, especially in vaccines intended for children.

134. The UNEP 2006 report on the supply, trade, and demand of mercury reveals that demand or use of mercury is highest in small scale gold mining, followed by vinyl chloride monomer production, chlor

alkali production, and in products namely batteries, dental amalgams, measuring and control devices, lighting, electrical and electronic devices. Exposure to elemental and inorganic mercury will be mostly through occupational routes as well as mercury releases from mercury containing waste products.

2.5   Toxicokinetics

135. The toxicokinetics (absorption, distribution, metabolism, and excretion) of mercury is highly dependent on the form of mercury to which a person has been exposed. Below is a brief summary of the toxicokinetics information for the three forms of mercury.

2.5.1   Absorption and distribution of elemental mercury

136. In its metallic (liquid) form, elemental mercury (Hg^0) is not significantly absorbed or transformed by the human digestive system; when ingested in this form, it is almost completely excreted in the faeces with little toxic damage to the organism (Rowland et al., 1997). Similarly, skin contact with liquid elemental mercury results in relatively low absorption into the body, generally causing only mild symptoms (such as skin irritation, dermatitis, or cutaneous eruptions).

137. However, following inhalation exposure, the absorption of Hg^0 vapour occurs efficiently and rapidly through the lungs. About 80 % of inhaled vapours are absorbed by the lung tissues. Once absorbed, Hg^0 is readily distributed throughout the body; it crosses both placental and blood-brain barriers (ATSDR, 1999).

2.5.2   Absorption and distribution of inorganic mercury

138. Some limited information suggests that absorption occurs after inhalation of aerosols of mercuric (Hg^{2+}) chloride. For example, Clarkson (1989) reported absorption in dogs to be 40 % via inhalation. Absorption of Hg^{2+} through the gastrointestinal tract varies with the particular mercuric salt involved. Absorption decreases with decreasing solubility. Estimates of the percentage of Hg^{2+} that is absorbed vary; as much as 20 % may be absorbed. Increases in intestinal pH, a milk diet (relevant to neonates), and increases in pinocytotic activity in the gastrointestinal tract (as occurs in neonates) have all been associated with increased absorption of Hg^{2+}. There is also evidence that inorganic mercury can be absorbed through the skin (ATSDR 1999, MPP and NRDC, 2005). For example, studies suggest that the use of skin lightening soaps and creams, which contain mercuric iodine and ammoniated mercury, respectively can lead to elevated exposures to ionic mercury. Concentrations of mercury in hair from some women using mercury soaps were found to be especially high (MPP and NRDC, 2005). Inorganic mercury has a limited capacity for penetrating the blood-brain or placental barriers. Inorganic mercury accumulates in the kidneys.

2.5.3   Metabolism and excretion of elemental and inorganic mercury

139. Elemental mercury is oxidized to Hg^{2+} in most body tissues. However, there is also evidence that Hg^{2+} can be reduced by mammalian tissue back to the form Hg^0. Nonetheless, once Hg^0 crosses the blood-brain and placental barriers and is oxidized to mercuric ion, return to the general circulation is impeded. Thus, mercury can be retained in the ionic form for several weeks or months in various body tissues, especially the brain and the kidneys (Klaassen, 1996).

140. Because of the relatively poor absorption of orally administered Hg^{2+}, the majority of the ingested dose in humans is excreted through the faeces. However, the portion that is absorbed remains in the body for a considerable length of time. The reported half-life of inorganic mercury in blood is about 20 to 66 days. Ionic mercury is excreted primarily in the urine and faeces. However, ionic mercury can also be excreted via breast milk.

141. The elimination of Hg^0 occurs primarily via urine and faeces. Most of the mercury excreted in the urine occurs after the Hg^0 has been oxidized to ionic mercury. Thus, generally most mercury in urine is in

the ionic form. However, some of the Hg^0 can be excreted directly via urine and faeces before oxidation. Therefore, a small percentage of the mercury in urine can be in the elemental form. Some Hg^0 is also excreted directly via exhaled air. Nonetheless, the pattern of excretion is dependent on the extent to which Hg^0 has been oxidized to Hg^{2+}. There is also evidence that elemental and/or ionic mercury can be excreted to a lesser extent via other routes, including saliva, sweat, and bile (US EPA, 1997d; ATSDR, 1999).

2.5.4   Toxicokinetics of methylmercury

142. Following exposure via ingestion, methylmercury is rapidly and extensively absorbed (about 95 %) through the gastrointestinal tract. This form of mercury is distributed throughout the body and easily penetrates the blood-brain and placental barriers. Methylmercury distributed throughout the body combines with cysteine, which is an amino acid found in most protein and appears to be mediated by the formation of a methylmercury-cysteine conjugate, which is transported into cells via a neutral amino acid carrier protein. A methylmercury-cysteine conjugate can pass through not only the blood-brain barrier but also the placenta via an amino acid transporter. Methylmercury can enter the brain where it is oxidized and accumulated and eventually causes chronic exposure and, depending on the level of exposure, can lead to adverse human health effects (Kanai, 2003; Kerper, 1992; Mottet, 1985; Sakamoto, 2004).

143. Some methylmercury in the body is slowly converted to inorganic mercury. Methylmercury has a relatively long biological half-life in humans; estimates range from 44 to 80 days. Excretion of methylmercury occurs primarily via the faeces, in hair, with less than one-third of the total excretion occurring through the urine. Methylmercury is also excreted through human milk but at much lower levels (LaKind et al., 2005; WHO, 2004; US EPA, 1997d; ATSDR, 1999).

2.6   Health effects

144. All humans are exposed to low levels of mercury. As described above, almost all people have at least trace amounts of mercury in their tissues (that is, methylmercury in their hair). Generally, these low exposures are not likely to cause adverse health effects. However, mercury can cause significant adverse effects on human health if exposure levels exceed established safe levels.

145. The factors that determine the occurrence of adverse health effects and how severe the health effects include:

- chemical form of mercury;
- dose;
- age of the person exposed (developing systems are susceptible);
- duration of exposure;
- route of exposure (inhalation, ingestion or dermal contact); and,
- dietary patterns of fish and seafood consumption.

146. The primary targets for toxicity of mercury and mercury compounds are the nervous system, the kidneys and the cardiovascular system. It is generally accepted that developing organ systems (such as the fetal nervous system) are the most sensitive to toxic effects of mercury. Fetal brain methylmercury levels are higher than in maternal blood (SCAN, 2004), and the developing central nervous system of the fetus is currently regarded as the system of highest concern as it demonstrates the greatest sensitivity (WHO, 2004). It should be noted, however, that in humans the nervous system continues to develop through adolescence.

147. Other systems that may be affected include the respiratory, gastrointestinal, hematologic, immune, and reproductive systems. As described below, the health effects caused by elevated exposures to elemental mercury, inorganic mercury compounds, and organic mercury compounds (methylmercury) differ (ATSDR, 1999; UNEP, 2002; US EPA, 2005).

2.6.1   Elemental mercury

148. Effects on the nervous system appear to be the most sensitive toxicological end-point observed following exposure to Hg^0. Neurological and behavioural disorders in humans have been observed following inhalation of Hg^0 vapour. Symptoms include tremors, initially affecting the hands and sometimes spreading to other parts of the body; emotional lability (often referred to as "erethism" and characterized by irritability, excitation, excessive shyness, confidence loss, and nervousness); insomnia; neuromuscular changes (such as weakness, muscle atrophy, or muscle twitching); headaches; polyneuropathy (such as paresthesia, stocking-glove sensory loss, hyperactive tendon reflexes, slowed sensory and motor nerve conduction velocities); and memory loss and performance deficits in tests of cognitive function. At higher concentrations, adverse kidney and thyroid effects, pulmonary dysfunction, changes in vision and deafness may also be observed (ATSDR, 1999; US EPA, 1997d; UNEP, 2002). Short-term exposure to high concentrations of Hg^0 vapour damages the lining of the mouth, irritates lungs, cause tightness of chest, coughing, nausea, vomiting, diarrhea, and increased blood pressure (ATSDR, 1999).

149. A few studies suggest that Hg^0 may cause reproductive toxicity. However, most human studies indicate that long-term exposure to Hg^0 does not affect the ability to have children (ATSDR, 1999). Studies with rats suggest that Hg^0 exposure may result in behavioural developmental effects (US EPA, 1997d).

150. A number of epidemiological studies have been conducted that examined cancer among workers occupationally exposed to Hg^0. These studies, however, have limitations including small sample sizes, probable exposure to other carcinogens, failure to consider confounding factors (such as smoking, and/or failure to observe correlations between estimated exposure and the cancer incidence). Only one animal study was identified that examined cancer incidence in animals exposed (by injection) to. $Hg^{0.}$ While tumours were found at contact sites, the study was incompletely reported as to controls and statistics and, thus, considered inadequate for the purpose of risk assessment. Findings from genotoxicity assays are limited and do not provide supporting evidence for a carcinogenic effect of Hg^0 (US EPA, 1997d). Nonetheless, as noted above, noncancer effects on the nervous system appear to be the most sensitive effect.

2.6.2   Inorganic mercury

151. Damage to the kidneys is the key end-point in exposure to inorganic mercury compounds. The most sensitive adverse effect observed following exposure to Hg^{2+} is the formation of autoimmune glomerulonephritis (inflammation of kidney). Several studies in animals have evaluated the potential for developmental toxicity to occur following exposure to various inorganic salts. While the evidence suggests that developmental effects may occur, the studies had significant limitations. Accidental ingestion of mercuric chloride by children resulted in cardiac effects (increased heart rate and blood pressure) (ATSDR, 1999; US EPA, 1997d). Accidental drinking or ingestion of inorganic Hg can also cause considerable damage to the digestive tract and kidney even with the limited absorption rate. In addition, dermal exposures to ionic mercury can lead to adverse effects to the skin (such as dermatitis [ATSDR, 1999, MPP and NRDC, 2005]).

152. There are no human studies linking exposure to Hg^{2+} with carcinogenic effects. Data in animals are limited. Focal hyperplasia and squamous cell papillomas of the forestomach as well as thyroid follicular adenomas and carcinomas were observed in male rats gavaged with mercuric chloride. In the same study, evidence for an increased incidence of squamous cell forestomach papillomas in female rats and renal adenomas and carcinomas in male mice was considered equivocal. All increased tumour incidences were observed in excess of the maximum tolerated dose (MTD). In this context, the relevance of the tumours to humans has been questioned. Results from in vitro and in vivo tests for genotoxicity have been mixed and do not provide strong supporting data for carcinogenicity (US EPA, 1997d).

153. There are some data indicating that mercuric chloride may be a germ cell mutagen. Positive results have been obtained for chromosomal aberrations in multiple systems, and evidence suggests that mercuric chloride can reach female gonadal tissue (ATSDR, 1999; US EPA, 1997d). Nonetheless, as noted above, noncancer damage to the kidney is considered the most sensitive effect.

2.6.3   Methylmercury

154. The critical target for methylmercury toxicity is the nervous system, especially during its developmental stage. Neurotoxicity is the most sensitive endpoint. In humans, the indices of neurotoxicity include neurobehavioral deficits, neuronal loss, ataxia, visual disturbances, impaired hearing, paralysis and death (WHO, 2004). Because methylmercury-cysteine conjugate readily passes both the placental barrier and the blood-brain barrier and the developing fetus is especially sensitive to the toxic effects of methylmercury, exposures during pregnancy are of highest concern. Offspring born of women exposed to high levels of methylmercury during pregnancy have exhibited a variety of developmental neurological abnormalities similar to cerebral palsy, including the following: delayed onset of walking, delayed onset of talking, altered muscle tone and deep tendon reflexes, and reduced neurological test scores (ATSDR, 1999; NRC, 2000; US EPA, 1997d; UNEP, 2002).

155. A number of human studies exist for evaluating the potential systemic toxicity of methylmercury. This database is the result of studying two large-scale poisoning episodes in Japan and Iraq, as well as several epidemiological studies in populations that consume quantities of fish or seafood. Three epidemiological studies that have received significant attention are studies in the Faroe Islands (Grandjean, 1997), Seychelles (Myers, 1997) and New Zealand (Kjellstrom, 1986). (UNEP, 2002; NRC, 2000, WHO 2004). Additional epidemiological studies have studied other possible effects (such as potential reproductive toxicity, immunotoxicity, cardiotoxicity, and general medical status). In addition, much research on the toxicity of methylmercury has been conducted in animals including non-human primates (ATSDR, 1999; NRC, 2000; US EPA, 1997d, WHO 2004). These studies point to the possible effects of prenatal exposure to methylmercury on neurodevelopment. Developmental neurobehavioural deficits are considered to be the most sensitive health outcome and life in utero the most sensitive period of exposure (WHO, 2004).

156. From the methylmercury poisoning episodes in Japan and Iraq, it is known that severe effects take place in the development of the brain and nervous system of the unborn child (the fetus), but severe effects on adults were also observed. The most common clinical signs observed in adults were paraesthesia[2], ataxia[3], sensory disturbances, tremors[4], impairment of hearing, constriction of the visual field and difficulty in walking. Both the central and peripheral nervous systems show signs and damage (WHO, 2004; Eto et al., 2002). Deficits in acts of daily living were observed in Minamata Disease adult patients significantly increased and were further aggravated by aging (Kinjo et al. 1993). Neurological subjective complaints as well as nonspecific complaints in a population in a polluted area in Minamata could also be influenced by past methylmercury exposure (Fukuda et al. 1999). A few epidemiological studies (especially the Faroe Islands and New Zealand studies) have recently provided evidence that methylmercury in seafood consumed by pregnant women—even at low mercury concentrations (about 10–20 % of observed effect levels on adults)—appears to have subtle, persistent effects on children's mental development as observed at about age 4 to 7 (so-called cognitive deficits) (Grandjean, 1997; Kjellstrom, 1986).

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[2] Numbness and tingling (The International Programme on Chemical Safety (IPCS) -WHO, *Bibliography and Glossary.* Available (May 2005) at:
.http://www.who.int/ipcs/publications/training_poisons/basic_analytical_tox/en/index12.html
[3] Failure of muscular coordination. (The International Programme on Chemical Safety (IPCS) -WHO, *Bibliography and Glossary.* Available (May 2005) at:
.http://www.who.int/ipcs/publications/training_poisons/basic_analytical_tox/en/index12.html
[4] Shaking or quivering, especially in the hands. (The International Programme on Chemical Safety (IPCS) -WHO, *Bibliography and Glossary.* Available (May 2005) at:
.http://www.who.int/ipcs/publications/training_poisons/basic_analytical_tox/en/index12.html

157. The Faroe Islands population was exposed to methylmercury largely from contaminated pilot whale meat, which contained very high levels of about 2 mg methylmercury/kg. However, the Faroe Islands populations also eat significant amounts of fish. The study of about 900 Faroese children showed that prenatal exposure to methylmercury resulted in neuropsychological deficits at 7 years of age (Grandjean et al., 1997). The brain functions most vulnerable seem to be attention, memory, and language. Mercury concentration in cord blood appeared to be the best risk indicator for the adverse effects. Special concern was expressed on the impact of PCBs from whale blubber, which was present in the diet of the Faroese mothers. Several analyses showed that any potential effects of PCBs could be dissociated from those of methylmercury. Developmental delays were significantly associated with the methylmercury exposures, even excluding the children whose mothers had higher hair mercury levels (above 10 μg/g) (Grandjean et al., 1997). Within the low exposure range, each doubling of the prenatal methylmercury exposure level was associated with a developmental delay of 1-2 months (UNEP, 2002).

158. A study of brainstem auditory evoked potentials (BAEP) in the Faroese population exposed in utero showed an apparent effect of postnatal exposure in 14-year-old adolescents, and that this effect (a delay of the peak V latency) was independent of the prenatal exposure level. While this finding has not been reproduced in other studies, it suggests that susceptibility may last through adolescence (Murata et al., 2004).

159. Another prospective study is ongoing in the Seychelles Islands, where the methylmercury exposures are similar. The fish consumption of pregnant women in the Seychelles is high, typically 10-15 meals per week, while the mercury concentrations in the ocean fish consumed are lower than the mercury concentrations in the pilot whale meat consumed by the Faroe Islands population, with a mean of 0.2-0.3 mg/kg. The main longitudinal study was started in 1989-1990 and comprised about 700 mother-child pairs. Maternal hair and child hair, but not cord-blood levels, were used as markers of methylmercury exposure in this study. No effects on developmental tests up to 5.5 years of age were found to be associated with methylmercury exposure, as measured by hair mercury concentrations in the pregnant mothers (Myers, 1997). Further analyses of older children (9 years of age) from the Seychelles cohort lead to similar (or slightly lower) results than at the earlier age (van Wijngaarden et al., 2006); however, as for all epidemiological studies, there are a number of uncertainties involved in the dose-response assessments. Nevertheless, these studies provide a valid scientific basis for the derivation of health-based guidance values.

160. In addition, a study from New Zealand suggests an effect on the mental development of children at the age of 4 and 6-7 years. In a high-exposure group, the average maternal hair mercury concentration was about 9 μg/g; control groups were selected with lower exposure levels. About 200 children were examined at 6-7 years of age, and a negative association was found between maternal hair mercury concentrations and neuropsychological development of the children. Although carried out a decade earlier than the Seychelles and Faroe Islands studies (published as reports from the Swedish Environmental Protection Agency [Kjellström et al., 1986; 1989]), inclusion of the findings from this study was considered appropriate by the US EPA in its recent assessment (US EPA, 2001a) given the similarities in study design and endpoints considered and following a later analysis of data by Crump using a "benchmark dose" approach (UNEP, 2002). JECFA however decided not to include the New Zealand study in its evaluation because of methodological questions surrounding this study and one huge outlier (the maternal hair mercury concentration of one child was more than four times the next the highest concentration in the study sample and had a heavy impact on the benchmark dose lower confidence limits) that could not be interpreted.

161. In a study among Inuit children in Nunavik, Northern Quebec, Canada, it was found that exposure to methylmercury and PCBs resulting from fish and marine mammal consumption were associated with alterations of visual evoked potentials (VEP), especially for the latency of the N75 and P100 components. Significant associations were found with concentrations of neurotoxicants in blood samples collected at the time of testing, at the preschool age. The study suggests that the VEP can be a valuable tool to assess the developmental neurotoxicity of environmental contaminants of fish-eating populations (Saint-Amour et al., 2006).

162. Some cross-sectional studies using neuropsychological testing of older children in different settings (such as in the Amazonas and on Madeira Island) also found some associations between mercury exposure and adverse effects to the nervous system (for a review, see JECFA Monograph, WHO, 2004).

163. Various studies also suggest that exposures to methylmercury may cause adverse effects to the cardiovascular system, including increased risk of acute myocardial infarction and elevated blood pressure (Salonen et al., 2000, Rissanen et al., 2000, Guallar et al., 2002, Yoshizawa et al., 2002, Virtanen et al., 2005, Sorensen et al. 1999, Grandjean et al. 2004). These studies suggest that even small increases in methylmercury exposures may cause adverse effects on the cardiovascular system, thereby leading to increased mortality (UNEP 2002). WHO has concluded that the available evidence for the potential cardiotoxicity of methylmercury was, however, not conclusive, but noted that further studies were needed (WHO, 2004).

164. Three human studies that examined the relationship between methylmercury and cancer incidence were considered extremely limited because of study design or incomplete data reporting. Animal studies provide limited evidence of carcinogenicity. Male mice exposed orally to mercuric chloride were observed to have an increased incidence of renal adenomas, adenocarcinomas, and carcinomas (US EPA, 1997d). Renal epithelial cell hyperplasia and tumours, however, were observed only in the presence of profound nephrotoxicity suggesting that the tumours may be a consequence of reparative changes to the damaged kidneys (US EPA, 1997d). Methylmercury appears to be clastogenic but not a potent mutagen (ATSDR, 1999). Studies have also shown evidence that methylmercury may induce mammalian germ cell chromosome aberrations (ATSDR, 1999; US EPA, 1997d). Nonetheless, as noted above, adverse noncancer effects on the developing nervous system seem to be the most sensitive endpoint.

2.7   Susceptible subpopulations

165. There are two general types of susceptible subpopulations: those who are more sensitive to the effects of mercury and those who are exposed to higher levels of mercury. A sensitive population is a group that may experience more severe adverse effects at comparable exposure levels or adverse effects at lower exposure levels than the general population. For mercury, the most sensitive subpopulations are developing organisms, particularly the fetus. Studies have shown that methylmercury in pregnant women's diets can have subtle, persistent adverse effects on their children's development, even at levels at which no effects were observed in mothers (ATSDR, 1999; UNEP, 2002).

166. The fetus, the newborn and young children are especially susceptible to mercury exposure because of the sensitivity of the developing nervous system. In addition to in utero exposures, neonates can be further exposed by consuming contaminated breast milk (ATSDR, 1999). Thus, parents, pregnant women, and women who might become pregnant should be particularly aware of the potential harm of methylmercury. Methylmercury concentration in the blood of the fetus is about 1.5- to 2-fold higher than that of the mother because of the active transport of methylmercury to the fetus through the placenta (NRC, 2000; IPCS, 1990, Stern and Smith, 2003). Many governmental agencies where people eat fish and seafood (such as Japan, Canada, USA and others) have issued recommendations for limiting fish or shellfish consumption for women who might become pregnant, women who are pregnant, nursing mothers, and young children. However, recent evidence suggests that older children and adolescents may also be susceptible to adverse neurological effects as the human nervous system continues to develop post partum and into adolescence (Grandjean et al., 2004).

167. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its 67th meeting in 2006 noted that life-stages other than the embryo and fetus may be less sensitive to the adverse effects of methylmercury to the nervous system. In the case of adults, the Committee considered that intakes of up to about two times higher than the existing PTWI of 1.6 μg/kg bw would not pose any risk of neurotoxicity in adults, although in the case of women of child-bearing age, it should be borne in mind that intake should not exceed the PTWI in order to protect the embryo and fetus from the adverse effects. Concerning infants and children aged up to about 17 years, the data do not allow firm conclusions to be drawn regarding their sensitivity compared to that of adults. While it is clear that they are not more sensitive than the embryo or fetus, they may be more sensitive than adults because significant development of the brain continues in infancy and childhood. Therefore, the Committee could not identify a level of intake higher than the existing PTWI that would not pose a risk of developmental neurotoxicity for infants and children (FAO/WHO, 2007).

168. The PTWI is the amount of a substance that can be consumed weekly over an entire lifetime without appreciable risk to health and is an end-point used for food contaminants (such as heavy metals with cumulative properties). Its value represents permissible human weekly exposure, protecting the most susceptible part of the population, to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods. In the case of methylmercury, the developing fetus is considered to be the most sensitive subgroup, and neurodevelopment the most sensitive outcome.

169. Individuals with diseases of the liver, kidneys, nerves, and lungs are at higher risk of suffering from the toxic effects of mercury. Individuals with a dietary insufficiency of zinc, glutathione, antioxidants, or selenium and those who are malnourished may be more sensitive to the toxic effects of mercury poisoning because of the diminished ability of these substances to protect against mercury toxicity. There is also population variability in regard to elimination of methylmercury (NRC, 2000). Also, animal studies and limited human data indicate that some persons have a genetic predisposition to develop an autoimmune glomerulonephritis (a kidney effect) upon exposure to mercury (ATSDR, 1999).

170. Other subpopulations may be at greater risk of mercury toxicity because they could be exposed to higher levels of methylmercury due to fish and seafood consumption (such as people in some Asia/pacific countries bordering the sea who consume large amounts of fish or marine mammals compared to other regions). Indigenous populations and others who consume large amounts of fish or marine mammals may be exposed to elevated levels of methylmercury. Recreational anglers and subsistence fishers who frequently consume locally caught fish from mercury-contaminated water bodies or who consume long-lived predatory oceanic species (such as shark and swordfish) can be exposed to higher methylmercury than individuals who consume similar or lesser amounts of commercially marketed fish from a variety of sources. Methylmercury exposure will be higher among people who regularly eat fish and other seafood products compared to those who only occasionally or never eat fish or other seafood products. Subsistence hunters may be exposed to higher concentrations of mercury in marine mammals (such as seals, narwhal, walrus, and whales) or fish-feeding animals and birds (ATSDR, 1999).

171. Individuals with dental amalgams generally have greater exposure to elemental mercury than members of the general population who do not have dental amalgams (ATSDR, 1999; UNEP, 2002). For example, one study found that mercury levels in whole blood of people who had >6 amalgams but did not eat fish were higher (mean = 1.047 ppb), compared to people who had no amalgams and did not eat fish (mean = 0.2 ppb) (Schweinberg, 1994, as cited in ATSDR, 1999). Other populations with potential for higher than average exposures are some workers due to occupational exposure, individuals who use various consumer products that contain mercury (such as some skin lightening creams and soaps), traditional ethnic medicines containing mercury, or use mercury for cultural or religious purposes (ATSDR, 1999). Some of these exposure pathways are described further in Chapter 6 of this document.

2.8   Reference levels

172. Based on risk assessments and other considerations, several countries and international organizations have established levels of daily or weekly methylmercury or mercury intakes estimated to be safe (or without appreciable risk to health), based on available information. A few examples are discussed in this section.

173. The Joint FAO/WHO Expert Committee on Food Additives (JECFA), which also evaluates chemical contaminants in the food supply, has established provisional tolerable weekly intakes (PTWIs) for total mercury at 5 μg/kg body weight (WHO, 1978) and for methylmercury at 1.6 μg/kg body weight (WHO, 2004). The PTWI is the amount of a substance that can be consumed weekly over an entire lifetime without appreciable risk to health and is an end-point used for food contaminants, (such as heavy metals with cumulative properties). Its value represents permissible human weekly exposure, protecting the most susceptible part of the population, to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods. In the case of methylmercury, the human embryo and developing fetus are considered to be the most susceptible life-stage, and neurotoxicity the most sensitive toxicological enpoint. The PTWI for methylmercury of 1.6 μg/kg body weight was reconfirmed by JECFA at its 67th meeting in 2006 (WHO, 2007).

2.8.1   Elemental mercury

174. To assess possible risks due to inhalation exposures, the US EPA established an RfC for elemental mercury of 0.3 µg/m^3, based on a lowest-observed-adverse-effect-level (LOAEL) (adjusted for intermittent exposure) of 9.0 µg/m^3 and an uncertainty factor of 30 (to account for sensitive human subpopulations and database deficiencies). A human occupational study was used as the basis for the RfC. This study investigated neurological effects in humans exposed to elemental mercury in the workplace; hand tremors, increases in memory disturbances, and evidence of autonomic dysfunction were observed and were the basis for the LOAEL (US EPA, 1995b).

2.8.2   Inorganic mercury

175. The US EPA has developed Reference Doses (RfDs) for mercuric chloride of 0.3 µg/kg/day and methylmercury 0.1 µg/kg/day and an inhalation Reference Concentration (RfC) for elemental mercury of 0.3 µg / m^3 of air. An RfD (or RfC) 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 appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD (or RfC), the potential for adverse health effects increases (US EPA, 1995b, 1995c, 2001a). This was based on a consensus decision of a panel of mercury experts who used several LOAELs ranging from 0.23 to 0.63 mg/kg body weight/day and an uncertainty factor of 1,000 (to account for the use of a LOAEL, use of subchronic studies, extrapolating from animals to humans, and for sensitive human subpopulations). The LOAELs were derived from several rat feeding, gavage, and subcutaneous injection studies in which autoimmune glomerulonephritis were observed (US EPA, 1995c).

2.8.3   Methylmercury

176. A number of Governments and other organizations have estimated tolerable weekly intake /reference levels for methylmercury exposure that are intended to be protective against adverse effects (Table 1). Because the relationship between mercury concentrations found in maternal hair (as well as in umbilical cord blood) and methylmercury concentrations in human diet is relatively well described, it is possible to estimate corresponding levels of methylmercury doses in human diet deemed to be safe (UNEP, 2002, WHO 2004).   Variations among reference levels reflect the different risk assessment assumptions, data sets, and uncertainty factors employed (NRC, 2000). Consequently, the resulting reference levels for methylmercury can be considered relatively consistent.

Table 1   Reference levels for methylmercury

Country/Organization	Reference Level (μg MeHg/kg bw/ week)	Year Adopted
Canada[5]	1.4 [6][7]	1997
Japan[8]	2.0	2005
Netherlands[9]	0.7	2000
United States[10]	0.7 [7]	2001
JECFA[11]	1.6	2003

177. There are a number of uncertainties surrounding the determination of reference levels for methylmercury. The debate over which studies and which endpoints of concern to use as the basis for setting a protective level still continues among risk assessors. The apparently contradictory results from the Seychelles and Faroe Islands studies have made it difficult to determine a single best point of departure for risk assessment. Considering the amount of confounding factors, reference levels should not be interpreted as a sharp threshold separating safe from unsafe. Rather, there is a good deal of uncertainty about the degree of health risk when reference levels are exceeded. However, it may be said that any risk is likely to increase with the magnitude, frequency and duration of exceeding these reference levels, but quantification of impacts of incremental exposure above reference levels has not been done at this time (SACN, 2004).

178. The JECFA established a PTWI of 1.6 μg/kg body weight/week for methylmercury. The Committee based the PTWI on the evaluation of the Faroe Islands and Seychelles Islands studies and used the average from the two studies of the estimated maternal hair concentrations associated with the no-observed-effect-level/benchmark dose level (NOEL/BMDL) for neurotoxicity associated with in utero exposure. The Committee determined that a steady-state daily ingestion of methylmercury of 1.5 μg/kg body weight/day would result in the concentration in maternal blood estimated to be without appreciable adverse effects in the offspring in the Faroe and Seychelles Islands studies. This dose level was divided by a composite uncertainty factor of 6.4 (2 [the distribution of hair: blood mercury ratio on the overall average] × 3.2 [the pharmacokinetic ratio of methylmercury at the steady concentration of mercury]), which results in a daily dose of 0.23 μg/kg body weight/day. This daily dose was then multiplied by 7 to convert it to a weekly dose level, namely the PTWI of 1.6 μg/kg body weight/week (WHO 2004). In 2006, JECFA confirmed that the existing PTWI of 1.6 μg/kg body weight/week remained appropriate for protection of the most vulnerable life stages, the embryo and fetus (WHO 2007).

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[5] Bureau of Chemical Safety
[6] For pregnant women, women of childbearing age and young children. The reference level for the general population of 3.3 μg MeHg/kg bw was established in 1972.
[7] Originally expressed in terms of μg MeHg/kg bw/ day
[8] Food Safety Commission
[9] National Institute for Public Health and the Environment
[10] US Environmental Protection Agency
[11] Joint FAO/WHO Expert Committee on Food Additives

179. The US EPA developed an RfD of 0.1 µg/kg body weight per day for methylmercury. The current RfD was derived from a benchmark dose (BMD) divided by an uncertainty factor of 10. The BMD analysis used was based on the lower 95 % confidence limit for a 5 % effect level (above background), from several endpoints in the Faroe, New Zealand and Seychelles studies. A k power model with k=1 (essentially linear model) was used. Results from several neuropsychological tests were used, and an integrated analysis gave similar results for benchmark doses. The exposure metric was µg/ l blood, with cord blood levels assumed to be equal to maternal blood. In deriving the RfD, maternal blood levels were converted to maternal intakes using a one-compartment model. The RFD was based on a number of neurological endpoints and the weight of evidence from the Faroe Islands and the New Zealand studies, plus an integrated analysis of those two studies plus the Seychelles study. The US EPA applied an uncertainty factor of 10 to account for pharmacokinetic inter-individual variability, and pharmacodynamic uncertainty and variability (IRIS 2001). Additional areas of uncertainty discussed in US EPA, (2001a) included the relationship between cord and maternal blood mercury concentrations and lack of knowledge on possible long-term effects.

180. Because fish consumption dominates the pathway for exposure to methylmercury for most human populations, many governments provide dietary advice to limit consumption of fish where mercury levels are elevated. For example, as of December 2002, 48 US states issued 2,140 fish advisories for mercury. Nineteen of these states issued advisories for all freshwater bodies (such as lakes, rivers) in their state, and 11 states issued state-wide advisories for their coastal waters (US EPA, 2003).

181. The Codex Alimentarius Commission has adopted a recommendation on guideline levels of 0.5 mg methylmercury/kg in non-predatory fish and 1 mg methylmercury/kg in predatory fish. The US FDA has set an action level of 1 mg methylmercury/kg in finfish and shellfish. The European Community allows 0.5 mg total mercury/kg in fishery products (with some exceptions). Japan allows up to 0.4 mg total mercury/kg (or 0.3 mg methylmercury/kg) in fish (UNEP, 2002). In addition, the US EPA has established a water quality criterion for methylmercury in fish of 0.3 mg/kg (US EPA 2001c).

2.9   Risk characterization

182. As described earlier in this section, risk characterization is the culminating step of the risk assessment process (NRC, 1983; US EPA, 1997e; FAO/WHO, 1995). It integrates information from the hazard identification, hazard characterization, and exposure assessment and synthesizes an overall description about the potential risks. The risk characterization is intended to inform risk managers and other audiences about the outcome of the risk assessment (NRC, 1983; US EPA, 1995a). It also presents the variability, uncertainties and limitations of the risk assessment (US EPA, 1995a). Risk characterization provides a summary of the risk assessment, which can be used along with other appropriate information, to inform risk managers as they consider risk management options.

183. To determine the likelihood of an adverse non-cancer effect in an exposed population resulting from the long-term ingestion of mercury-contaminated foods, the estimated oral dose (that is, mg mercury/kg body weight/week) is divided by an oral reference level (such as the PTWI) to calculate a hazard index. For inhalation exposures, mainly occupational, the air concentration (that is, mg mercury/m3) is divided by an inhalation reference level (such as the RfC). The available reference levels vary slightly but they are indicators of the potential for adverse effects when consistently exceeded. For example, if the hazard index is less than 1, the mercury exposure could be regarded as unlikely to lead to adverse health effects. On the other hand, a hazard index greater than 1 is an indication that there may be a risk for adverse health effects. As exposures increase above the reference level, either by magnitude or by time, the likelihood of adverse effects also increases. Generally, if the hazard index is greater than 1, more evaluation is warranted, including determining the degree and frequency of exposures above the reference level, uncertainties in the assessment, data gaps and other factors, to determine the overall concern for adverse effects. Nonetheless, a statement of risk can be partly based on this ratio (US EPA, 1995a; NRC, 1983).

184. A risk characterization conveys the risk assessor's judgment as to the nature and existence of (or lack of) human health risks (NRC, 1983; US EPA, 1995a). A risk characterization might include information

about human subpopulations that may be at elevated risk from mercury exposures, the potential extent of the exposures and risks, assessment of exposures from various environmental media, and description of the limitations, uncertainties and variability in the assessment.

3. ESTIMATING EXPOSURE THROUGH BIOMONITORING

3.1 Introduction

185. This chapter describes potential approaches to estimate exposures to mercury by measuring mercury levels in human tissues (such as hair, blood, nails, milk and urine), which are considered forms of biomonitoring. As described below, measurements of mercury levels in these tissues can be excellent indicators of various types of mercury exposures. However, the validity, usefulness, and meaning of such measurements depend on the form of mercury exposures, type of tissue measurement, and other factors.

186. To conduct an appropriate study, an investigator must consider some fundamental questions in the early design stages, as follows:

- Study group: What population (or subpopulation) is the target of the study? How many people (study subjects) from this population can be included in the study? How should we identify the study subjects (individuals) to be included in the study? Should we aim to identify a "representative" sample? If so, how do we select a "representative" sample?

- What actions and protocols are needed to ensure that the study is done in an ethical manner? How will the investigators consult with community members, and request and obtain consent of the participants? What procedures will be used to ensure the security and privacy of personal information?

- Questionnaire: What information should we try to obtain about each study subject? What are the appropriate questions that can be used to obtain such information? Are there other methods to obtain such information (such as medical records, birth data, etc.)?

- Health assessment: Will the study include a medical exam for each subject? If so, what medical tests will be conducted? How? Who will conduct such tests?

- Tissue measurements: What body tissues should be sampled (hair, blood, urine)? How will the samples be taken and preserved? What analytical methods will be used? What laboratory will do the analyses? What measures will be taken to ensure the safety and health of the participants (for example, sterile needles, proper training of medical team, etc.)?

187. Experience has made clear that it is very important to consult with community members and other stakeholders during all stages of the assessment to ensure that participants are treated with dignity and respect and to develop good relations between researchers/organizations and community members. Consent must be obtained by participants, and appropriate communication and participation should be encouraged throughout the assessment. Without the support and cooperation of communities, success of the assessments may be threatened (CACAR II, 2003).

3.2 Selecting a study population

188. In order to select a representative sample of the population of interest, it is important to understand the socio-economic-demographic conditions of the community. Obtaining a statistically representative sample of the community is usually the preferred approach. One important decision to consider is the number and type of individuals to be included in the study. The sample size chosen is likely to be based on various factors including costs, statistical power, staff, study facilities, and other factors. The sampling process can be random, judgmental, or possibly other approaches. Randomization is a more expensive

and time-consuming process but provides a broader picture of the mercury exposures among the population compared to a selective sampling process. Using a judgmental approach, only the individuals at higher risk of being exposed to mercury are selected for study (UNIDO, 2003b; Veiga and Baker, 2004).

3.3   Information on socio-economic conditions and demographics

189. Once a sample group is gathered, basic information should be collected about each study subject, including:

- Age, gender, and pregnancy status of individual and family [or other household] members,

- Housing location (such as town/village, and globe positioning system [GPS] coordinates for mapping),

- Education, occupation, and income(s) of individual and family members,

- Hygiene and sanitation practices, and

- Access to mercury.

190. These data can aid in identifying the most susceptible and/or sensitive groups of people in a community, as well as groups who can serve as controls. An example of a socio-economic-demographic questionnaire obtained from the Protocols for Environmental and Health Assessment (UNIDO, 2003b; Veiga and Baker, 2004) is shown in Appendix A.

3.4   Health questionnaire and assessment

191. A health assessment study can provide important information about the health status of the study subjects and the population and help determine whether or not there is an association between some health conditions and mercury exposures. A health assessment can also provide valuable insights for developing site-appropriate interventions (behavioural, medical, environmental, and/or economic). A medical exam can be performed that includes the health history of each individual, a physical examination, and a neurological examination. A health assessment questionnaire (including a dietary survey) can also be used to gather information about possible exposures to mercury and other health information. An excellent example of such a health assessment questionnaire and the content to be covered in a medical exam cited in the Protocols for Environmental and Health Assessment (UNIDO, 2003b, Veiga and Baker 2004) is shown in Appendix B. The questionnaire covers the following data:

- Personal data (such as age, gender, address, etc);
- General questions related to:
    - o Work exposure to mercury;
    - o Other exposure to mercury (use of traditional medicines, use of mercury for ritualistic or religious purposes, known spills such as a broken thermometer) presence of dental amalgam;
    - o Diet issues (frequency and types of food, particularly fish);
    - o Health problems (based on symptoms described by the patient);
    - o Alcohol consumption habits (frequency, amount, and type);
    - o Other possible confounding factors (use of drugs; smoking; malaria; handling of gasoline, kerosene, pesticides; number of dental amalgam fillings; exposure to selenium);
- Specific health questions related to mercurialism (metallic taste, salivation, loss of weight, etc.);

- Physical examination (blood pressure, signs of gingivitis[12], tremors, reflexes, number of dental fillings, etc.);

- Specific neuropsychological tests (memory, coordination, etc.);

- Sampling human tissues (urine, blood, hair), which is described further in the next section.

192. As described in Chapter 2, exposures to elemental, inorganic, or methylmercury, depending on their magnitude, can result in a continuum of health effects by severity from subtle responses to very frank adverse outcomes. Subjective symptoms include numbness, dizziness, trembling, motor disturbance, irritability, loss of memory, insomnia, and metallic taste. Objective symptoms include gingivitis, bluish discolouration of gums, sensory disturbance, disturbance in balance, abnormal gait, altered reflexes, disturbance in coordination, tremor, and dysarthria[13]. If mercury intoxication is apparent, the volunteer should be informed about ways to reduce further exposure (UNIDO, 2003b; Veiga and Baker, 2004).

193. A series of specific neurophysiologic tests (digit span test, match box test, Frostig score, pencil tapping, etc.) can be used to detect the effects of mercury poisoning. These tests are simple, but local health care professionals need to be trained to administer them. These tests do not demand special equipment and, when associated with analysis of human tissues (such as urine, blood, cord blood, hair, human milk) that reflect the extent of exposure, can provide information on potential effects of mercury exposure (UNIDO, 2003b; Veiga and Baker, 2004).

194. Confounding factors should be investigated to exclude from the statistical analysis other explanations for any symptom found. Many factors can cause symptoms (such as fatigue, dizziness, and tremors) and can introduce false diagnosis to the clinical examination and neuropsychological tests (UNIDO, 2003b; Veiga and Baker, 2004).

195. Volunteers must be fully informed by the interviewers about the project and how the data generated by the study can help them and their community. Brochures can be useful to provide this preliminary background information to volunteers, and can also include some basic information about the hazards related to mercury exposure and a simplified diet advisory (UNIDO, 2003b; Veiga and Baker, 2004).

196. It is important to identify dietary sources of mercury exposure. Inclusion of fish in the diet varies with geographic location, season of the year, ethnicity, economics, and personal food preferences. Approaches to evaluate the diet, including dietary surveys, are described in the next chapter.

197. It is also important to try to identify non-dietary exposures to mercury, including occupational (artisanal gold mining and processing, dentistry, etc.), nearby industrial releases, use of traditional medicines, ritualistic purposes, spills, etc. Exposures to various contaminated environmental media should be quantified when possible (WHO IPCS, 2000).

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[12] Inflammation of the gums (Sinclair, J.M. 1995. *Collins English Dictionary and Thesaurus*, HaperCollins Publishers, Glasgow, 1995 p. 478.)

[13] A defect in the articulation of the speech (Noncommunicable Diseases and Mental Health. *STEP-Stroke Manual(Version 1.4).* WHO. Available (May 2005) at:
(http://www.who.int/ncd_surveillance/steps/stroke/en/steps_stroke_manual(v1.4).pdf)

3.5   Biological markers

198. Exposures can be estimated by measuring pollutant levels in various body tissues (such as hair, blood, cord, urine, human milk and nails). These measurements, also known as biological markers (or biomarkers), are useful tools for human exposure assessment. They are sensitive indices of an individual's exposure to mercury, providing a measure of the internal dose, which can be used to evaluate the likelihood of adverse health effects and improve clinical diagnoses (IPCS, 2000). These biomarkers are useful as surveillance tools for monitoring mercury exposure in individuals and populations. There is a well-established relationship between several biomarkers of mercury exposure and adverse health effects.

199. In assessing the appropriateness of a particular biomarker of exposure, it is important to consider several factors: (1) how well the biomarker correlates with the dose (or external exposure) to various forms of mercury; (2) how well the biomarker correlates with the mercury concentration in the target tissue; (3) how well the variability over time in the biomarker correlates with changes in the effective dose at the target tissue over time; (4) what type of biomarker would be the most appropriate given the cultural characteristics of the population; and (5) what kind of technology is available. The validity and validation of these media as biomarkers needs to be confirmed (IPCS 2001, EHC 222). The following biological media can be used as biomarkers for mercury exposure in humans:

- Blood;
- Cord blood and cord tissue;
- Hair;
- Urine;
- Human milk; and
- Toenails.

200. Most of these biological media can be collected non-invasively (except blood), and samples can be stored easily. Samples may need to be transported to a local (or distant) laboratory. However, some in situ analyses of total mercury (such as using LUMEX or colourimetric procedures) are available and can be very useful for a preliminary screening and rapid diagnosis (UNIDO, 2003b; Veiga and Baker, 2004).

201. Analysing mercury in biological samples is complicated by the different organic and inorganic forms of the metal that may be present. Therefore, all the mercury in the sample is usually reduced to its elemental state prior to analysis, but this is not appropriate when information about the individual mercury species is needed. In addition, some methods require pre-digestion of the sample prior to reduction. Mercury is also relatively volatile and, therefore, easily lost during sample preparation and analysis. In spite of these complications, several methods have been developed for determining trace amounts of mercury in biological samples (ATSDR, 1999). Samples must be gathered using clean, proper equipment and techniques to avoid contamination and sample loss. Some specific techniques are described for the various biological tissues in the following sections. Most of the methods available to determine mercury levels in blood, urine, tissues, and hair use atomic absorption spectrometry (AAS), atomic emission spectrometry (AES), atomic fluorescence spectrometry (AFS), neutron activation analysis (NAA), mass spectrometry (MS), or anodic stripping voltametry (ASV). Cold vapour AAS (or CVAAS) is the most widely used. Table 2 presents details of selected methods used to determine mercury in biological samples (ATSDR, 1999), and some of the specific methods for blood, urine, and hair are described in more detail in the following sections.

Table 2   Methods to determine mercury in biological samples

Sample Matrix (mercury form)	Preparation Method	Analytical Method	Sample Detection Limit	Percent Recovery	Reference
Blood, hair, and urine (total)	Pre-concentration using a column followed by treatment with $SnCl_2$.	CV-ICP-AES	0.01 μg/L	No data	Anthemidis *et al.*, 2004
Hair (total)	Inter-laboratory comparison study.	CVAAS CVAFS ICP-MS			Gill *et al.*, 2002
Blood and hair (total)	Digestion with HNO_3 followed by treatment with $SnCl_2$.	CVAAS	1.0 nmol/L (blood); 1.0 nmol/g (hair)	No data	Muckle *et al.*, 2001
Hair (total)	Digestion of samples with nitric and sulphuric acids for 6-8hrs, followed by treatment with bromine monochloride, and hydroxylamine hydrochloride.	CVAFS	0.012 ng/g	91-113%	Pellizzari *et al.*, 1999
Blood, breast milk (total, inorganic)	Digestion of sample with nitric/perchloric acid overnight for total, and with H_2SO_4 overnight for inorganic; reduction and purging.	CVAAS	0.1 ng/g (blood); 0.04 ng/g (milk)	97%	Oskarsson *et al.*, 1996
Blood and erythrocytes (inorganic, total)	Digestion of sample with H_2SO_4 (mixture of nitric and perchloric acid for total) overnight, reduction with $SnCl_2$, purging onto gold wire to form amalgam (pre-concentration) followed by thermal release of elemental mercury.	CVAAS	0.06 ng/g (0.06 ppb) for total; 0.04 ng/g for inorganic.	75–114%	Bergdahl *et al.*, 1995
Blood (total)	Irradiation of sample followed by treatment with permanganate, sulfuric acid, distilled water, ammonia, and hydroxylamine hydrochloride; treatment with ion exchange.	NAA	0.3 ng/mL	100%	Fung *et al.*, 1995
Blood, urine, hair, fish (total and MeHg)	Total: digestion of sample with nitric, perchloric, and sulphuric acids; methylmercury in hair: digestion with HCl and extraction into benzene. Methylmercury in blood, fish, and urine: digestion with KOH and extraction into dithizone solution, cleaned up via extractions.	Total: CVAAS, methyl mercury: GC/ECD	0.1 ng	99-104%	Akagi *et al.*, 1991,1995
Urine (total)	Addition of HCl to sample followed by bromate/bromide solution and equilibration for 15 minutes; decomposition of excess bromine by addition of hydroxylamine hydrochloride.	AFS	1 ng/L	95-98% (methyl mercury, phenyl mercury)	Corns *et al.*, 1994
Blood (total)	Treatment of sample with dilute hydrochloric acid; addition of a pH buffer and a complexing agent (diethyldithiocarbamate); extraction of mercury species into toluene.	ETAAS	2 μg/dm^3	>94%	Emteborg *et al.*, 1992

Sample Matrix (mercury form)	Preparation Method	Analytical Method	Sample Detection Limit	Percent Recovery	Reference
Blood (total and MeHg)	Cleavage of both organic and inorganic mercury from blood protein thiol groups using hydrochloric acid, extraction of mercury species into toluene as their diethyldithiocarbamate (DDTC) complexes; addition of Grignard reagent to toluene phase to form butyl derivatives of the mercury species.	GC/MPD	0.4 µg/L	>100%	Bulska *et al.*, 1992
Blood and urine	Dilution of sample in ammonia buffer; reduction with sodium borohydride.	ICPAES	0.5 µg/L	100	Buneaux *et al.*, 1992
Blood and urine	Total mercury: precipitation-extraction with 50% volume/volume hydrochloric acid containing EDTA and cysteine; centrifugation; filtration through screening column. Methylmercury: extraction of the methylmercury into benzene or toluene; back extract into aqueous cysteine solution.	ICP-MS	0.2 µg/L	91.6–110.2	Kalamegham and Ash, 1992
Blood, plasma, urine (total)	Digestion of blood and plasma samples overnight in a mixture of nitric acid and perchloric acid.	CVAAS	5 nmol/L	93.4–103	Vesterberg, 1991
Urine, tissue, hair (total)	Digestion of sample with HNO_3 in closed vessel in microwave; cooling and dilution with water; reduction with $SnCl_2$; purging to detector.	AFS	0.9 ng/L	94–102	Vermeir *et al.*, 1991a, 1991b
Blood, urine, tissues (inorganic)	Dilution of blood or urine sample with water; homogenization of tissue samples with water; reduction of mercury with $SnCl_2$ followed by purging to detector.	CVAAS	`6 µg/L	77–110	Friese *et al.*, 1990
Urine (total)	Digestion with $HNO_3/HClO_3$ and heat; evapouration; addition of NH_4Cl/ ammonium solution; dilution with water.	ASV	NR	100–105	Liu *et al.*, 1990
Hair (total)	Washing of samples with acetone and water; digestion with HNO_3 and heat; oxidation with permanganate solution and heat; cooling and addition of hydroxylamine hydrochloride; reduction of mercury with $SnCl_2$; purging to detector.	CVAAS	NR	100–101	Pineau *et al.*, 1990

Sample Matrix (mercury form)	Preparation Method	Analytical Method	Sample Detection Limit	Percent Recovery	Reference
Tissue, hair (total)	Washing of hair sample with acetone and water; homogenisation of hair or tissue sample in micro dismembrator; irradiation; addition of carriers; digestion with concentrated HNO_3/ H_2SO_4 solution and heat in a closed Teflon bomb; extraction of digest with $CHCl_3$ to remove bromide ion, extraction of aqueous phase with Zn-$(DDC)_2$/$CHCl_3$; counting of ^{197}Hg in organic phase.	NAA	0.36 ng/g (tissue) 3.6 ng/g (hair)	85–110	Zhuang *et al.*, 1989

Key:

AFS = atomic fluorescence spectrometry;
$CHCl_3$ = trichloromethane;
CVAFS = cold-vapour atomic fluorescence spectrometry;

DDTC = diethyldithiocarbamate;
ECD = electron capture detection;
ETAAS = electrothermal atomic absorption spectrometry;
GFAAS = graphite furnace atomic absorption spectrometry;
$HClO_3$ = perchlorous acid;
H_2SO_4 = sulphuric acid;

ICP-MS = inductively coupled plasma mass spectrometry;
MPD = microwave-induced plasma emission;
NH_4Cl = ammonium chloride;
Zn-$(DCC)_2$ = zinc diethyldithiocarbamate.

ASV = anodic stripping voltametry;
CVAAS = cold vapour atomic absorption spectrometry;
CV-ICP-AES = cold vapour-inductively coupled plasma-atomic emission;

DMPS = dimercaptopropane sulfonate;
EDTA = ethylenediamine tetraacetic acid;
GC = gas chromatography;
HCl = hydrochloric acid;
HNO_3 = nitric acid;
ICPAES = inductively coupled plasma atomic emission spectroscopy;
KOH = potassium hydroxide;
NAA = neutron-activation analysis;
$SnCl_2$ = tin(II) chloride;

202. A number of analytical methods are available to determine mercury concentration, and an analytical method depends on various factors (such as an analytical regulation of each country), laboratory skills, analytical equipment, etc. Whatever analytical method will be used, it is important to practice careful quality control/quality assurance of the obtained data, including simultaneous determination of suitable certified reference materials (CRMs). Currently, the CRMs prepared for the quality control/quality assurance of analytical values for mercury as well as methylmercury in various biological and environmental matrices are commercially available from several organizations, including the IAEA (International Atomic Energy Agency), NIST (National Institute of Standards and Technology, Office of Standard Reference Materials, USA), NRCC (National Research Council of Canada), and NIES (National Institute for Environmental Studies, Japan) (Japan Ministry of the Environment 2004).

3.5.1   Blood

203. The presence of mercury in blood indicates recent or current exposure to mercury. There is a direct relationship between mercury concentrations in human blood and consumption of fish contaminated with methylmercury. As described previously, methylmercury in the diet is readily absorbed through the gastrointestinal tract and distributed throughout the body by the blood. Usually blood methylmercury concentration reaches a maximum within 4 to 14 hours and undergoes clearance from the blood to other body tissues after 20 to 30 hours. WHO considers the normal mean concentration of total mercury in blood to be between 5 to 10 µg/L in individuals with no consumption of contaminated fish (UNIDO, 2003b). The NRC identifies 2 µg/L as the normal mean concentration for populations with little or no fish consumption in the US (NRC, 2000). Collection, storage, and shipping of blood samples can be resource-intensive. Also, blood sampling is invasive to the subject (usually drawn from a vein) and requires proper sterile equipment and requires a trained phlebotomist or other medical professional to assure the samples are collected safely and properly (IPCS, 2000), and necessitates subject consent. In addition, various

cultural and/or ethical issues or other societal factors may need to be considered. For example, some societies may be opposed to providing blood samples because of cultural or ethical beliefs, or other reasons.

204. The standard metric for mercury in blood is for whole blood (Stern, 2003). The sample should be stored in the refrigerator temperature immediately after collection. If the sample is stored for a long period, it should be frozen (Ministry of the Environment, Japan, 2004). Amount of sample available for analysis can be highly variable depending on the age and physical condition of the study participant. Measuring blood methylmercury levels among a representative sample of a population appears to be adequate for characterizing population distributions of methylmercury exposures. However, blood mercury levels do not provide information regarding historical exposure and seasonal (or other peak) variations.

205. Blood mercury concentrations can be determined by a variety of analytical techniques. Often blood samples are digested with high purity mineral acids and oxidants prior to instrumental analysis. Sample preparation and digestion procedures play an important role in blood sample analysis as the sample matrix can interfere with analysis and lead to inaccurate results. Cold vapour atomic absorption spectrometry (CVAAS) is widely used for determination of mercury in blood (Oskarsson et al., 1996; Bergdahl et al., 1995). CVAAS has adequate sensitivity to measure total mercury in blood at low parts-per-billion (ppb) levels, and the method is relatively easy to perform in a standard laboratory. Inductively coupled plasma optical emission spectrometry (ICP-OES) and inductively coupled plasma mass spectrometry (ICP-MS) with or without cold vapour generation can also be used for measurement of mercury in blood at low ppb levels (Buneaux et al., 1992; Kalamegham and Ash, 1992). Cold vapour atomic fluorescence spectrometry (CVAFS) is one of the most sensitive methods available with detection limits ranging down to sub parts-per-trillion levels (ppt) (Pellizzari et al., 1999). The method is also very specific and less prone to matrix-related interferences. The increased sensitivity of the method can be highly advantageous in situations where sample amount is very limited. In comparison, inductively coupled plasma atomic emission spectrometry (ICP-AES) and ICP-MS methods involve expensive instrumentation and higher per-sample costs.

3.5.2   Cord blood and cord tissue

206. Cord tissue can also be considered as a biomarker sample that is worthwhile collecting (Grandjean et al., 2005; Akagi, et al., 1998; Harada, 1977; Daniels et al., 2004). It has been used in the original studies in Minamata and in at least two cohort studies. A validation study has shown that cord blood concentrations were better in characterizing children's prenatal methylmercury exposures than maternal hair levels. This sample is easy to collect, provided the birth is a medical setting. In a prospective study in the Faroe Islands, the main exposure biomarkers were the mercury concentrations in cord blood and maternal hair obtained at parturition. These exposure biomarkers have now been supplemented with mercury analyses of umbilical cord tissue from 447 births. In particular, when expressed in relation to the dry weight of the tissue, the cord mercury concentration correlated very well with that of cord blood. Structural equation model analysis showed that these two biomarkers have an average total imprecision of about 30%, which is much higher than the laboratory error. The imprecision of the dry-weight-based concentration was lower than that of the wet-weight-based parameter, and it was intermediate between those of the cord blood and the hair biomarkers. In agreement with this finding, regression analyses showed that the dry-weight cord mercury concentration was almost as good a predictor of methylmercury-associated neuropsychological deficits at 7 years of age as was the cord-blood mercury concentration. A recent analysis of studies using the umbilical cord as a biomarker for exposure assessment revealed that umbilical cord mercury concentration appears to be a direct biomarker of the fetus. Moreover, the increased cord mercury concentration was associated with some neurobehavioral and neurophysiological deficits in the child. (Murata, K. et al, 2007). Cord mercury analysis can therefore be used as a valid measure of prenatal methylmercury exposure, but appropriate adjustment for the imprecision should be considered.

3.5.3   Hair

207. Hair sequesters methylmercury during its formation and shows a direct relationship with blood mercury levels, providing an accurate and reliable method to measure methylmercury levels in the body. Blood can be used to document methylmercury short-term exposure and provides different information

than hair. Hair is the preferred choice for many studies as it provides a simple, integrative, and non-invasive sample for estimating long-term average exposure. Once incorporated in the hair, mercury does not return to the blood, thus it provides a good long-term marker of exposure to methylmercury. Hair structure depends on ethnicity and age, and this may affect the incorporation of mercury. If a hair mercury concentration is used as a dose parameter, then such factors should be taken into account. Hair colour also seems to play a role and permanent wave treatment removes mercury from the hair (Yamaguchi et al., 1975; Yamamoto et al., 1978; Sakamoto et al., 2004; Grandjean et al., 2002). Total mercury in hair is about 250 to 300 times higher than the blood mercury concentration at the moment hair is formed. The normal level of mercury in hair is 1-2 ppm (or 1-2 μg/g), but people who consume fish one or more times per day may have mercury levels in hair exceeding 10 ppm. The USEPA reference dose corresponds to approximately 1ppm mercury in hair for people who have low fish consumption. Methylmercury usually constitutes at least 80 % of the total mercury analysed in hair among fish consumers (McDowell et al., 2004). Therefore, hair mercury is a very good biomarker for methylmercury, and is often used to characterize methylmercury exposures. Hair is not as good an indicator of mercury vapour exposure as urine is (IPCS, 2000; UNIDO, 2003b). Measurements of mercury levels in hair allow sequential analysis, and help in the identification of peak exposures (such as due to seasonal consumption variations). Peak exposures, in a chronic exposure setting, have been identified in some studies as an important contributing factor to adverse health effects (McDowell et al., 2004). Hair grows approximately 1 cm per month and can be evaluated along the shaft to provide a profile of exposure over time; previous exposures remain unchanged for up to 11 years (IPCS, 2000; UNIDO, 2003b; Suzuki, 1991).

208. Hair sample collection usually involves cutting a bundle of hair, approximately 100-150 strands (which is a bundle approximately 0.75-1.0 centimetre in diameter) about 3 cm in length, from the occipital region of the head. It is very important to cut the bundle as close to the scalp as possible and retain the orientation of the hair strands whenever possible as the distance from the scalp is directly proportional to duration of time since exposure. Caution must be exercised to avoid contamination during sample collection. Blunt-tipped, clean stainless steel scissors can be used for cutting the hair and a cleaning step involving rinsing the hair with 70 % isopropyl alcohol is recommended prior to sample collection. Once cut, the hair bundle is wrapped closed to the scalp end with a small Post-it note or a clean piece of paper (approximately 3.5 cm x 5 cm) and held together with a plastic clip. A clean, sealable bag (such as zip closable bag) can be used to store the collected samples. However, some authors (Trace elements laboratory, 2005) discourage the use of plastic bags because the generation of static electricity that makes the handling of hair very difficult and their weight unreliable, therefore, they recommend to place the hair sample in a marked paper envelope. If the hair is too short to be cut and clipped together, hair can be cut directly into the storage bag (or envelope) using scissors or thinning shears. Collected samples can be stored in properly labelled zip-closable bags (or envelopes) and shipped to the analysis laboratory at ambient temperature.

209. Numerous analytical methods are available for analysis of hair for total mercury. CVAAS is one of the most widely used analytical methods for hair mercury analysis. CVAAS has adequate sensitivity to measure mercury at sub-ppm levels and has a low per- sample cost compared to some newly developed methods. Neutron activation analysis (NAA) can also be used to measure mercury in hair samples; however, the detection limits are not as good as cold vapour generation methods. CVAAS is one of the most sensitive methods available, with detection limits ranging down to sub-ppt levels. The method is also very specific and less prone to matrix interferences. The high sensitivity of this method has greatly reduced the sample requirements to as low as a few strands (mg sample sizes) of hair and resulted in very high response rate from study participants as only a very few hair strands are needed. ICP-MS with or without cold vapour generation can also be used to measure mercury in hair at ppb to ppt levels. In comparison, CVAAS and ICP-MS methods involve expensive instrumentation and higher per-sample costs (Levine et al., 2002).

210. Cold vapour atomic fluorescence spectrometry, inductively coupled plasma mass spectrometry, and cold vapour atomic absorption spectrometry, as mentioned above are the most common methods to measure total mercury in hair. One drawback of these methods is that they require 5-10 mg of hair for analysis. To obtain spatial resolution of centimetres (for biomonitoring purposes), 100-150 hair strands need to be collected. This large sample may be intrusive to participants, which can lead to low donor rates. In addition, manipulating such samples can be difficult.

211. Even though quality assurance and quality control of data can be achieved by using certified reference materials (CRMs) during analyses and by participating in interlaboratory calibration programmes, more efficient analytical techniques which require less material (and therefore less number of strands) would facilitate assessment, particularly in large monitoring programmes.

212. Direct solid introduction techniques have been shown to minimize the above weaknesses. Because no sample pretreatment is required, very little chemical waste is produced and the potential for contamination is lowered. In addition, the number of hair strands required for analysis can be reduced to single hair strands, and therefore the throughput is increased.

213. Commercial instruments capable of measuring Hg directly in solid and liquid matrices have recently become available. The principle combines combustion, Hg collection with gold amalgamation and detection with atomic absorption spectrometry (C-GA-AAS). Legrand et al. (2005) validated this technique to measure mercury in a single hair strand with detection suited to assess typical levels.

214. A 1:1 relationship was observed between C-GA-AAS and the established cold vapour atomic absorption spectrometry for analysis of 1-cm segment from a bundle of hair. For individual hair variability, the average relative standard deviation of mercury between hair strands was $6.5 \pm 2.8\%$, thus justifying the use of a single hair strand for biomonitoring. With a 0.1 ng mercury quantification limit and a 0.05 mg average weight of a 1-cm segment hair strand, one hair strand can be used to determine yearly exposure if the mercury concentration in hair is equal or above 0.2 mg/kg and monthly exposure if the hair mercury concentration is equal or above 3 mg/kg. To screen for exposure using the USEPA guideline of 1 mg/kg as a cut-off, one hair strand is required for annual exposure estimation and three hair strands are required for monthly exposure estimation. C-GA-AAS presents clear advantages for hair mercury analysis as significantly less number of hair strands and no chemical pretreatment are required while maintaining an adequate detection limit. With an autosampler, it takes 7 minutes per analysis and the associated cost per sample is about five US dollars. This technique facilitates routine biomonitoring and provides the high throughput required for large health surveillance purpose (Legrand et al., 2005).

3.5.4   Urine

215. The presence of mercury in urine generally represents exposure to inorganic and/or elemental mercury, and collection is non-invasive (IPCS, 2000). Urine mercury levels are usually considered the best measure of recent exposures to inorganic mercury or elemental mercury vapours because urinary mercury is thought to indicate most closely the mercury levels present in the kidneys (Clarkson et al., 1988). However, as previously explained, inorganic mercury accumulates in the kidney and is slowly excreted through the urine. Therefore urine mercury levels can also represent exposures to elemental mercury and/or inorganic mercury that occurred some time in the past.

216. Since the concentration of waste products in urine can vary significantly due to amount of dilution with water, tests for contaminants in urine are often expressed in units of µg contaminant per gram creatinine. Creatinine is a breakdown product of creatine, which is an important part of muscle. Over time, the creatine molecule gradually degrades to creatinine. Creatinine is a waste product, that is, it cannot be used by cells for any constructive purpose. The daily production of creatine, and subsequently creatinine, depends on muscle mass, which fluctuates little in most normal people over long periods of time. Creatinine is excreted from the body entirely by the kidneys. With normal kidney function, the serum (blood) creatinine level should remain relatively constant and in the normal range (MedlinePlus online, Medical Encyclopedia, 2005). Therefore, measuring µg mercury per gram creatinine is a useful measure of mercury levels in urine.

217. A strong correlation between elemental mercury levels in inhaled air and urine levels at medium and high concentrations has been reported. The maximum urine mercury concentration set by WHO (1991) is 50 µg/g creatinine. Mercury urine levels rarely exceed 5 µg/g creatinine in persons who are not occupationally exposed to mercury (UNIDO, 2003b).

218. The preference is to collect the 50-100 ml urine sample in the morning (first-morning void). This can be easily achieved by providing each participant with an instruction sheet describing how to collect

and store the sample until pick-up. However, spontaneous urine collection does not dramatically affect results. In general, new, sterile plastic containers (100 or 150 ml size) are used for collection of samples, and the containers are kept closed until ready for analysis. It is important that participants wash their hands before collection, open the container just before collection and close it immediately after collection, avoid touching inside the container or cap. The sample must be placed inside a secondary container such as a sealable bag to avoid potential contamination. Steps must be taken to ensure that microorganisms do not proliferate, as they may cause inorganic mercury to reduce to mercury vapour, which will be lost (Ministry of the Environment, Japan, 2004).

219. The sample should be frozen shortly after collection and kept frozen during transportation to the laboratory (Pellizzari et al., 1995). Acidifying the urine sample has been suggested as a means of stabilization prior to storage in a frozen condition. Drinking large amounts of water a few hours before sample collection should be avoided because this dilutes the urine samples. Once the samples are received at the laboratory, an aliquot should be transferred into a clean, sealed glass container as a precaution to avoid any potential vapour phase contamination of mercury (UNIDO, 2003b; Veiga and Baker, 2004).

220. A variety of analytical techniques are available for urinary mercury analysis. Usually samples are prepared by treating with mineral acids and oxidants or just diluted with an appropriate solvent prior to analysis. CVAAS is often used for determination of mercury in urine. CVAAS has adequate sensitivity to measure mercury in urine at low ppb levels, and the method is relatively low-cost. ICP-MS with or without cold vapour generation can be used for measurement of mercury in urine at ppb and ppt levels. Sample carry over and sample cross-contamination can cause problems and lead to inaccurate results due to the complexity of the urine matrix, especially for methods involving simple dilution rather than digestion with mineral acids and oxidants. In comparison, ICP-AES and ICP-MS methods involve expensive instrumentation and higher per-sample costs.

3.5.5 Human milk

221. Environmental studies have used human milk to evaluate past maternal exposure to various chemicals and examine potential exposures for breast-feeding infants. Human milk represents a major route of excretion of lipophilic substances. However, most forms of mercury are not lipophilic. Mercury concentrations in human milk are a function of age, body mass, time of sampling, nutritional status, lactation period, and fat content of milk (WHO IPCS, 2000). Mercury in hair is significantly affected by maternal methylmercury ingestion during pregnancy but not during the postnatal breast-feeding period, and the mercury levels in milk do not correlate with mothers or infants hair (UNIDO, 2003b).

3.6 Converting biomonitoring levels to exposure levels

222. The mercury levels are measured in a body tissue (such as blood, hair, or urine) can be converted to an approximate average daily dose (or exposure level) by using various conversion factors. However, there are limitations, uncertainties and variability in using these conversion factors that should be considered. Exposures to different forms of mercury (such as inorganic mercury from dental amalgams, or methylmercury from fish consumption) will result in different outcomes with regard to tissue levels and clearance. Therefore, exposures to different forms of mercury should be considered. Also, as described in previous sections of this document, there is a time lag between the intake of various mercury forms (such as methylmercury) and the mercury levels found in the various body tissues. More information on conversions can be obtained from, among others, the following references: US ATSDR, 1999; NRC, 2000; US EPA 2001a, US EPA, 1997c and US EPA, 1997d, WHO 2004.

223. Nonetheless, the quantitative relationship between mercury levels in hair and blood and daily average dose (or intake) levels of mercury (especially methylmercury) are fairly well understood. Therefore, such dose conversions can often be made with reasonable confidence if enough information is known about the various mercury forms and other factors. Population variability should, however, be noted in dose conversion (Stern, 2005b). For example, a daily average methylmercury intake of 0.1 microgram per kg body weight per day (0.1 µg/kg per day) by an adult woman is estimated to result in

hair mercury concentrations of about 1 µg/g, cord blood levels of about 5 to 6 µg/L and blood mercury concentrations of about 4 to 5 µg/L. This relationship is generally directly proportional. If information is available indicating that methylmercury is the primary form of mercury for which a population is exposed to, and data are available on measured levels in blood or hair, then the estimated daily dose (or intake) can thus be calculated.

224. Table 3 provides an example of measured levels in blood converted to estimated hair levels and intake levels. Blood concentrations were measured in population of 1709 women of child-bearing age in the USA (from NHANES 1999-2000) and the corresponding levels in hair and intake (dose) level of methylmercury were estimated. Based on information on dose conversions described above, it is assumed that a methylmercury intake of 0.02 µg /kg day corresponds with blood levels of about 1 µg/L and hair levels of about 0.2 µg/g. Therefore, the dose levels in the table were calculated by multiplying blood level (in µg/L) by 0.02, and hair levels (in µg/g) were calculated by multiplying blood levels (in µg/L) by 0.2. Blood levels change over time after methylmercury intake, with peak blood levels occurring about 4 to 14 hours after exposure, with clearance occurring after this peak (UNIDO 2003). Therefore, these calculations rely on the assumption that intake is, on average, relatively constant over a period of many days. Actual blood levels will go up and down among members of the population depending on pattern of intake and other factors. However, the average ratios between intake (µg/kg day) and blood levels (µg/L) and hair levels among a population, overtime, are expected to be generally consistent with the ratios presented in the table.   .

Table 3   Correlation of blood, hair and dietary intake levels of methylmercury

	Geometric mean	25th%	50th%	75th%	90th %	95th %
Measured mercury concentration in whole blood (µg /L)	1.02	0.4	0.9	2.0	4.9	7.1
Estimated corresponding level in hair (µg/g)	0.2	0.08	0.18	0.4	1.0	1.4
Estimated corresponding dose level (µg/kg day)	0.02	0.008	0.018	0.04	0.1	0.14

3.7   Ethical and cultural considerations

225. Sampling biological materials is an important component of studies that estimate human exposures. For investigators, it is essential to collect biological specimens and obtain associated clinical information from informed and willing study participants. In accordance with the Declaration of Helsinki, participants in medical research studies must give their explicit informed consent and in the case of minors, this consent must be given by the legal guardians (World Medical Association, 2004).

226. The data must be kept safe and secure. Personal information must be handled and maintained confidential. Scientists and study administrators must ensure that those who participate in their exposure assessment studies are adequately protected from unwarranted harms resulting from the inadvertent release of important personal information (NBAC, 1999). In recent years, policymakers and public advocacy groups have helped raise awareness about the need to protect individuals' health information. As a result, various laws and regulations have been enacted at the local and federal government levels limiting the access of patient medical records and protecting the information pertaining to biological specimens. These policies and regulations may differ from one country to another.

227. Various cultural and religious aspects must also be taken into consideration when designing an exposure assessment study. The acceptability of sampling blood and hair can vary. For example, as mentioned previously, there may be variable degrees of acceptance within and among some societies in Africa and Latin America with regard to the use of hair (UNIDO, 2003b; Veiga and Baker, 2004).

3.8   Examples of biomonitoring studies

228. Population exposure to mercury has been monitored by measuring mercury in blood, hair, and urine. These exposure levels have been used to estimate acceptable daily intakes. Some of the most well known biomonitoring studies are of Amazonian riparian communities, the Faroe Islands, and the Seychelles Islands. Mercury levels in environmental media (sediment, air, water, and fish) have also been measured.

229. Table 4 provides a summary of data for Canada on levels of mercury and methylmercury in maternal blood (AMAP, 2003). Similar data from Russia, Alaska, Finland, Greenland and Faroe Islands are available in the AMAP reports. In addition, more than 8,000 tissue samples (hair, blood, urine, fish), sediment, and water have been collected in the State of Para, Brazil by research institutes from around the world (UNIDO, 2003b; Veiga and Baker, 2004).

Table 4   Mercury and methylmercury in maternal blood in Canada

Country/Ethnic Group/Region	Number of Individuals sampled	Total Mercury Mean (µg /L)	Total Mercury Range (µg /L)	Methylmercury Mean (µg /L)	Methylmercury Range (µg /L)
Canada					
Caucasian[1] (1994-99)	134	0.9	nd-4.2	0.69	nd-3.6
Metis/Dene (1994-99)	92	1.4	nd-6.0	0.8	nd-4.0
Other (1995)	13	1.3	0.2-3.4	1.2	nd-3.0
Inuit					
Baffin[1] (1996)	31	6.7	nd-34	6.0	nd-29
Inuvik[1] (1998-99)	31	2.1	0.6-24	1.8	nd-21
Kitikmeot[1] (1994-95)	63	3.4	nd-13	2.9	nd-11
Kivalliq[1] (1996-97)	17	3.7	0.6-12	2.7	0.4-9.7
Nunavik[2] (1995-2000)	162	9.8	1.6-44	na	na

nd = not detected; na = not available
[1]Walker *et al*. (2001); [2]Muckle *et al*. (2001b)

230. Table 5 provides information on various studies conducted using biomarkers of exposure to mercury and methylmercury among various populations in different countries.

Table 5   Studies of biomarkers of exposure to mercury and methylmercury (adapted from WHO, 2004)

Country	Matrix	Population	Elevated intake of fish?	Concentration of total mercury	Reference
Brazil	hair	Indigenous children aged 7-12 years Indigenous women aged 14-44 years	Yes Yes	14.45 µg/g 15.7 µg/g	Oliviera Santos et al., 2002
Canada	hair	Indigenous	Yes	4.4 µg/g	Muckle et al., 2001
China	hair	Representative	No	0.42 µg/g	Feng et al., 1998
Germany	urine	Representative	No	0.4-2.0 mg/l	Becker et al., 2003
Japan	hair	Representative	Yes	1.76-3.37 µg/g	Yasutake et al., 2003
Spain	hair	Children	No	0.8 µg/g	Batista et al., 1996
Spain	blood	Representative	Yes	11-22 ng/g	Sanzo et al., 2001
Sweden	hair & blood	Pregnant women	Yes	0.35 µg/g (hair) 1.3 µg/l (cord blood)	Bjornberg et al., 2003
UK	hair	Pregnant women	No	0.19 µg/g	Lindlow et al., 2003

USA	hair	Representative	No	0.3 µg/g	Pelizzari et al., 1999
USA	blood	Women aged 16-49 yrs	No	1.2 µg/l	Schober et al., 2003
USA	hair	Women aged 15-45 yrs	No	0.4 µg/g	Smith et al. (1997)
USA	hair	Indigenous	Yes	0.83 µg/g	Gerstenberger et al., 1997
USA	blood	Representative of high end fish consumers	Yes	14.5 µg/l	Hightower and Moore, 2003
USA	hair	Children (1-5 yrs) Women (16-49 yrs)	No	0.12 µg/g 0.20 µg/g	McDowell et al., 2004

* Adapted from WHO, 2004

231. Mercury levels exceeding 20 µg/L urine have been found in urine samples from miners who frequently burn gold-mercury amalgams in open pans. Very high mercury concentrations in urine (as high as 1,168 µg/L) were reported in workers of gold shops in Amazonian villages. The gold shop workers (who work in confined environments) had higher concentrations of mercury in urine than miners burning amalgam outdoors. In Alta Floresta, Mato Grosso, Brazil, the urine of employees in gold shops (where gold was melted in fume hoods with no filters) was analysed; the results showed mercury urine levels greater than 20 µg/L for at least 13 of 17 workers sampled (UNIDO, 2003b; Veiga and Baker, 2004).

232. Mercury levels in human hair and fish were investigated in communities where fish is extensively consumed but which were not impacted by gold mining activities. Mean mercury levels in hair ranged from 3.98 to 8.58 µg/g at various locations. Mean mercury concentrations in fish tissue from those locations ranged from 0.01 to 2.53 µg/g for carnivorous species and 0.001 to 0.87 µg/g for noncarnivorous species (UNIDO, 2003b; Veiga and Baker, 2004).

233. The National Human Exposure Assessment Survey (NHEXAS) is a probability-based population study conducted in US EPA Region V (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) designed to document exposure to various metals, pesticides, and other organic chemicals and use that to characterize the exposure distribution for the general population. As part of this study, hair samples were collected from 182 study subjects to examine the mercury levels. During the study, food diary information and 4-day duplicate diet samples were collected from all the participants and were available for data analysis along with the total mercury analysis results.   Out of 182 participants, 39 (21 %) reported eating a fish meal at least once during the 4-day survey period. The mean hair level for all fish consumers was 0.42 µg/g, whereas the mean for people not eating fish during the survey period was about 0.3 µg/g. For women of child-bearing age (16 to 49 years), the mean level was 0.42 µg/g among fish consumers and 0.33 µg/g for those not eating fish. Among children ages 9 years and younger, the mean hair mercury level was 0.12 µg/g; none of them reported eating fish during the survey period (Pellizzari et al., 1999).

234. The National Health and Nutrition Examination Survey (NHANES) is another large-scale study that is designed to produce descriptive statistics that can be used to measure and monitor the health and nutritional status of the general population. The NHANES is conducted once per year. It includes a representative sample of about 5,000 people in the United States. The sample is chosen using a stratified, multistage selection process. The study includes medical exam, health and dietary survey, and blood measurements for many chemicals and metabolites. In 1999-2001, hair and blood mercury measurements were taken for women of child-bearing age and young children. The NHANES uses standardized methods and regular reporting (US CDC, 2001).

235. The NHANES study for years 1999-2000, which included 1,709 women (ages 16 to 49 years) and 705 children (ages 1 to 5 years) in the US found that about 8 % of the women had mercury concentrations in blood exceeding the levels corresponding to the US EPA's reference dose (an estimate of a safe dose) (Schober et al., 2003). Also, more recent data from the US CDC, for years 1999-2002, showed similar exposure levels (US CDC 2005). Other examples of exposure assessments are discussed in the UNEP 2002 Global Mercury Assessment and in other references.

236. Several biological sample collection and handling protocols are given in Appendix C, along with sample documentation forms as examples.

4. EXPOSURE ASSESSMENT OF METHYLMERCURY IN FISH

237. Risk analysis consists of a process comprised of three distinct but interrelated components, namely, risk assessment, risk management and risk communication. In the case of methylmercury, all three components are important to achieve consumer protection and assure the benefits of fish consumption for consumers. In Chapter 2, hazard characterization of mercury was presented, including the establishment of reference levels, which describe a level of exposure that is likely to be without harm. In this chapter, exposure assessment is considered as this is perhaps the most important aspect for a national food safety authority. While reference levels are considered "portable" in that they generally apply to all populations, exposure of populations may be highly variable depending on their consumption patterns and on the levels of a particular chemical in the food as consumed.

4.1   General approach

238. Because much of the mercury in fish is methylmercury and most (greater than 95 %) of the methylmercury in fish ingested is readily absorbed into the body through the gastrointestinal tract, individual exposures to methylmercury (or intake) can be estimated if information is available on:

- Types (such as species) and amounts (such as frequency and serving size) of fish ingested per unit time (such as day, week or month);
- Concentration of mercury in the types of fish ingested; and,
- Body weight of person consuming the fish.

239. With this information, the methylmercury intake for an individual can be calculated by the following basic equation:

$$\frac{\text{Amount of fish ingested per week (g/week)}}{\text{Kilogram body weight (kg bw)}} * \text{Mercury concentrations in the fish ingested (µg/g or ppm)} = \text{Methylmercury intake per kilogram body weight per week (µg methylmercury per kg body weight per week)}$$

240. Estimating exposures for a population (or subpopulation) follows the same general principles as for an individual, but requires more data. For example, information is needed on the distribution of the fish consumption rates and patterns among the population. This information may be gathered for a representative sample of the population through a dietary survey or other data on food consumption among the population. Information is also needed on the mercury concentrations in the types of fish consumed. Information on consumption must then be integrated with the data on mercury concentrations in fish to estimate the exposure distribution across the population.

241. In order to best use resources, most experienced assessors will employ a tiered approach for assessing exposure. A tiered approach allows managers (or organizations) to limit detailed assessments to critical sub-regions or subpopulations that may have high exposures or that might be more susceptible to lower levels of exposure. Subgroups of particular concern for high exposure include sport anglers, different ethnic groups, indigenous communities, and economically subsistent fishing communities. Starting with simple highly conservative screening methods, the need for a further detailed exposure assessment is avoided if the exposure for a chemical does not exceed its corresponding reference level. If the reference level is approached or exceeded, however, this does not necessarily mean that the chemical is a risk to health. Rather, this signals that there may be a need for more detailed and accurate data to refine the exposure assessment. The refined exposure assessment can employ better and more detailed

food consumption and chemical concentration data. Nevertheless, a tiered approach should be used where possible to make best use of resources.

4.2   Screening methods

242. Simple screening methods are used to obtain initial estimates of exposures. These methods usually result in overestimates of the actual exposure, but if such methods show that intake of a chemical well below the reference level, this is a good indication that there is no need for more refined assessments. A screening level assessment may also be used to estimate exposures among the general population to help determine specific locations or subgroups of the population considered most likely to be exposed to elevated levels. While screening assessments are usually designed to overestimate exposure by using conservative default assumptions, sometimes a screening assessment may underestimate exposure, particularly for the high-percentile consumers. In this regard, average or mean intakes in a population are not necessarily a good basis for consumption advisories. Rather, it is the upper percentiles of intake that are often the drivers and these cannot be accurately estimated from the average (mean).

243. One screening approach uses information already available through JECFA and GEMS/Food Consumption Cluster Diets. Mean exposure levels for the general population can readily be calculated from average daily consumption levels and average mercury levels in fish. This will yield an average intake of mercury for a population in units of micrograms of methylmercury per day. This dose can then be divided by an average body weight for the general population and multiplied by 7 days to give an exposure estimate expressed in units of micrograms of methylmercury per kg body weight per week. This value can then be compared to the PTWI to determine whether a more detailed assessment is warranted.

244. Using average total consumption rates of all fish and shellfish from the 5 GEMS/Food Regional Diets, JECFA performed a screening assessment by matching these consumption data with mean concentration of mercury in tuna reported by Australia and the United States of America. This screening assessment provided exposure estimates that ranged from 0.3 to 1.1 μg/kg body weight per week based on a 60 kg adult (FAO/WHO, 2000). This assessment was updated by JECFA, adding intake information from France, Japan, New Zealand and Slovakia and using biomarkers of exposure to methylmercury. In addition, published information on concentrations of mercury and methylmercury in various fish species, as well as analyses of methylmercury intake by populations consuming large amounts of fish (>100g per person per day) were included in the evaluation. The result of the updated assessment confirmed the previous results, in the range of 0.3 to 1.5 μg/kg body weight per week for the five regional diets and from 0.1 to 2.0 μg/kg body weight per week for numerous national diets (WHO, 2004).

245. Using FAO Food Balance Sheet data for a specific country, which is accessible through the Internet, improvements can readily be made in this screening assessment[14]. However, it should be noted that both GEMS/Food Consumption Cluster Diets (which have now replaced the Regional Diets) and FAO Food Balance Sheets provide only per capita estimates of consumption and do not give any indication of the differences that may exist in the diet consumed by different population groups (such as age and gender) as well as different socioeconomic groups, ecological zones and geographical areas within a country; neither do they provide information on seasonal variations in consumption.

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[14] http://faostat.fao.org/faostat

246. Another type of screening assessment available at the national level is total diet studies (TDS). TDS are considered to be the most cost-effective methods for assessing exposure of the population and subgroups to a full range of common contaminants in the diets (WHO, 2005). In many countries, TDS are the primary sources of information on the levels of various chemical contaminants and nutrients in the diet. They can provide general assurance that the food supply is safe from chemical hazards and/or to develop priorities for possible risk management intervention. In addition, TDS results can be an indicator of environmental contamination by chemicals. TDS can also be used to assess the effectiveness of measures to reduce exposure of the population to chemical hazards. TDS, in general, offer a complete estimate of exposures for a country as they explicitly take into account all foods in the diet as prepared for final consumption.

247. In some cases, the results of the screening level assessment may indicate that no further action is needed. In other words, the exposure at current consumption levels and patterns is not likely to cause adverse health effects. On the other hand, if the exposure exceeds or corresponds to a significant portion of the reference level, a more refined exposure assessment may be needed. For example, many screening methods only provide mean exposures. Based on data from individual dietary surveys, the high percentile exposure related to the consumption of a single food (such as fish) is about three times the mean. Furthermore, exposure by children is about two to three times the exposure of the general population when consumption is expressed on a body weight basis (WHO, 1985).

248. Using relatively inexpensive screening techniques, this strategy can be used to determine whether a population's exposure to methylmercury in fish warrants further detailed study. This approach allows the manager to limit detailed assessment to specific situations that lead to excessive exposure of vulnerable groups (such as pregnant women and children). This chapter describes the assemblage of the different data sets and other information on fish consumption patterns and fish contamination levels that can be used to assess exposure to methylmercury by a population.

4.3   Refinements to consumption estimates

249. Refinements for estimating exposure can be achieved by using more detailed information on the distribution of individual fish consumption rates among the population, especially vulnerable groups. Such refinements can improve the reliability of exposure estimates for high percentile consumers.

4.3.1   National dietary surveys

250. If national dietary data on fish consumption are unavailable, or insufficient to adequately determine fish consumption patterns, this information may need to be collected via an appropriate dietary survey tool. Fairly simple, concisely designed surveys can provide very useful information on fish consumption amounts and types of fish at relatively low cost. Depending on the level of detail required, individual consumption, including the amount and frequency for each fish species, can be obtained.

251. National dietary survey data can be used to characterize fish consumption rates and patterns among a population. Various governments and other organizations have conducted such surveys. For example, the National Health and Nutrition Examination Survey (NHANES) conducted by the US Centers for Disease Control and Prevention and the Continuing Surveys of Food Intake by Individuals (CSFII, 1995) conducted by the United States Department of Agriculture (USDA) are two good examples of survey data available in the US. Also, the European Community has initiated national surveys based on the European Food Consumption Survey Method (EFCOSUM, 2000). These survey questionnaires include simple, specific questions that are intended to gather appropriate information on fish consumption, without being overly complicated or burdensome for the participant. These surveys are usually based on 1-, 2-, 3- or 7-day recall questionnaires or diaries.

252. Examples of fish consumption survey questions are provided in Table 6 and Table 7. It should be noted, however, that surveys using self-reporting, especially if open ended or involving a long-term recall, such as 12 months, are subject to significant uncertainties (Xue et al., 2007).

253. Food consumption surveys can provide very useful information to generate estimates of fish consumption rates and patterns, but care must be taken in the design of the questionnaire. The CSFII example above would have been enhanced by adding a question about canned fish, such as "During the past 7 days have you eaten any canned fish such as tuna, salmon, or other types of canned fish?"

254. In recent NHANES, women of child-bearing age were asked about fish consumed during the past 30 days following the basic format shown in the following table. More information can be obtained through the US CDC website: http://www.cdc.gov/nchs/about/major/nhanes.

Table 6   Examples of fish consumption surveys (NHANES III, 1994; CSFII, 1995)

NHANES III 1994: Main dishes, meat, fish, chicken, and eggs	Times consumed per				
	Day	Week	Month	Never	Do not know
Shrimps, clams, oysters, crabs, and lobster					
Fish, including fillets, fish sticks, fish sandwiches, and tuna fish					

CSFII 1995		
During the past 12 months since (NAME OF MONTH), have you/has (NAME) eaten any (FOOD) in any form?	**Yes**	**No**
Shellfish	1	2
Fish, other than shellfish or canned fish	1	2
If yes, was any of the fish you ate caught by you or someone you know?	1	2
If yes, did any of the fish come from a freshwater lake or river?	1	2
If yes, did any of the fish come from the ocean?	1	2
If yes, did any of the fish come from a bay, sound, or estuary?	1	2

255. Table 7 presents an excerpt from a questionnaire based on form used in NHANES (1999-2001) that was intended to collection information on fish type and consumption frequency.

Table 7   Sample fish type consumption questionnaire (adapted from NHANES, 1999-2001)

Question for participant:				
Please look at the list of fish. During the past 30 days, which of the following types of fish did you eat and how many times did you eat them?				
Fish Type	*Number of times eaten in past 30 days*	*Fish Type*	*Number of times eaten in past 30 days*
Breaded fish products		Porgy	
Tuna canned or fresh		Salmon	
Bass		Sardines	
Catfish		Sea Bass	
Cod		Shark	
Flatfish		Swordfish	
Haddock		Trout	

Mackerel		Walleye	
Perch		Other types of fish	
Pike		Unknown types of fish	
Pollack			

256. To conduct an exposure assessment in a particular country or region, an investigator should try to determine if such dietary survey data exist for the country or region under study. Often data may exist, but be difficult to locate. Sometimes such data is in the private sector and needs to be purchased. If data are not available or insufficient to adequately determine dietary patterns of fish consumption, then the investigator may consider conducting such a survey. The survey should include a limited number of questions that are simple and clear, and that yield appropriate information. If the survey is too long, or questions are not clear, then response rate and accuracy will be low. On the other hand, if the survey is too simple, sufficient data may not be collected.

257. The surveys described above generate estimates of consumption frequency of fish per day, week, or month. Depending on the level of details available in these surveys, an average consumption frequency by fish species can be obtained. Estimates of the distribution of the consumption rates among the population, or various percentiles (10%, 25%, 75%, 90%) can sometimes be estimated using data on typical portion size. Volume IV of the US EPA Mercury Study Report to Congress (US EPA, 1997c) provides a good example of how to use this approach.

258. However, information gathered through these surveys generally does not provide adequate data on fish consumption patterns throughout the year, which can be different given seasonal availability of fish species, unless the surveys are repeated multiple times during the year for each individual (such as one time per season).

259. Also, these surveys generally do not provide sufficient information to generate reliable estimates of fish consumption rates and patterns for an individual. Rather, if the surveys are conducted on a representative sample of the population, they can provide good estimates of the consumption rates and patterns for a given population. To estimate average consumption rates for subpopulations (such as anglers or indigenous communities), specific information (such as age, gender, occupation, fishing practices, and other appropriate information) must be gathered to obtain cross-tabulated data for these particular subpopulations. Cross-tabulation allows a more precise characterization of subpopulations. For instance, if a national dietary survey conducted in a country established that 50 % of the populations surveyed were fish consumers, it would be useful to analyse the proportion of fish eaters among men and women, given that women can constitute a targeted population. Breaking down the percentage of fish eaters by gender (or other subgroups) is cross-tabulating the data.

Table 8   Example of a population surveyed on fish consumption

	Yes	No	Total
Fish eaters total	5,000	5,000	10,000
	Men	**Women**	**Total**
Fish eaters by gender	2,000	3,000	5,000

260. In this example (Table 8), 50 % of the population surveyed (10,000 individuals, half men and half women) are fish consumers, but there is a gender difference: 2,000/5,000 (40 %) surveyed men compared to 3,000/5,000 (60 %) surveyed women are fish eaters. The data can be cross-tabulated with information such as age groups or other relevant information (percent of anglers, different ethnic groups, indigenous communities, and economically subsistent fishers, etc.), leading to more precise information regarding targeted subpopulations.

4.3.2   National purchase data and national fish market sales

261. National purchase data as well as national fish market sales can also be used to generate a per capita or per user consumption rate and profile. However, for the latter, information on the percentage of consumers must be available. Also, to generate a per capita consumption rate, basic demographic data such as the total population must be available. A per capita or a per user consumption rate and profile will not provide information regarding consumption rates for subgroups (women, children, subsistence fisher subpopulations, recreational anglers, etc.). Information also will not be available for subpopulations living in various areas (coastal communities, river fishing villages, etc.), unless the data were gathered for specific areas or regions within the country.

262. National purchase data and national fish market sales surveys were used in the United States to estimate fish consumption patterns (Johnson and Associates, 1997). Descriptions of long-term trends in fish and shellfish consumption in the United States and information regarding current market trends in the seafood industry were used to give rough estimates of frequency of fish intake for populations or subpopulations. Similar data for other countries may be available as well, or such data could be collected through various programmes.

263. Other information regarding average portions (by weight) as well as average human body weight will be necessary to be able to generate mean estimates of human methylmercury intake in various populations or subpopulations (Section 4.2.3). These data may be available from national dietary surveys.

264. In the absence of national surveys, traditional and demographic knowledge of behaviours regarding fish consumption (such as, fish is a traditional food, or fish is an essential a protein source) can generate useful qualitative information. However, such qualitative information will only give a likelihood of exposure to methylmercury.

4.4   Refinements to concentration estimates

265. Mercury is a ubiquitous contaminant, even in the absence of local/regional point sources of contamination. The general population is primarily exposed to methylmercury through the diet, especially from fish. Levels of mercury (primarily in the form methylmercury) are generally much higher in fish and marine mammals (such as seals and some whales) than in other foods or drinking water (WHO, 2003; Dabeka et al., 2003). In fish, up to 90 % of the mercury in fish exists as methylmercury, (NRC, 2000; WHO, 2003).

266. All fish consumers are exposed to some level of methylmercury. Both marine and freshwater fish, as well as marine mammals, accumulate methylmercury in their muscle tissue (WHO, 2003; Dabeka et al., 2003; FAO and WHO, 2003; UNEP, 2002; US EPA, 1997c; ATSDR, 1999). Moreover, methylmercury biomagnifies up the food web, meaning that apical predators, that is carnivorous species feeding at the top of the food chain, tend to have higher levels of methylmercury (WHO, 2003; Grieb et al., 1990; Bloom, 1992; Francesconi and Lenanton, 1992; Wiener et al., 2004). Also the larger (older) individuals tend to have higher contents. In addition, other foods (such as some land animal meats and certain plant foods) can occasionally have elevated mercury levels due to local contamination or other factors. These other foods may also be considered in specific exposure scenario assessments, as appropriate, as a possible source of mercury exposure. However, this section will focus refinement of methylmercury concentration levels in fish.

267. Methylmercury in fish is bound to tissue protein rather than with fatty deposits, therefore trimming and skinning of mercury-contaminated fish does not reduce the mercury content of the fillet portion. Moreover, the methylmercury level in fish is not changed when cooked. However, because some moisture is usually lost during cooking, methylmercury concentrations are often slightly higher in cooked fish than 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 methylmercury (WHO, 2003). However, the total amount of methylmercury in fish remains relatively unchanged after cooking, and the

slight changes in methylmercury concentrations due to cooking methods are relatively insignificant and generally do not need to be considered when estimating exposures.

4.4.1   Available data on mercury in fish

268. Levels of methylmercury vary widely among different fish species and between the same species from different geographical areas. Some examples are shown in Table 9. Piscivorous (carnivorous) fish (i.e., fish that eat other fish), called predatory fish elsewhere in this document, are more likely to contain higher levels of methylmercury in their muscles and other tissues. Other factors that influence mercury levels in the fish include age (indicated by girth, weight, or length), and characteristics of the water body (such as local contamination, pH, reduction-oxidation potential, and other factors). Because mercury biomagnifies in the aquatic food web, fish higher on the food web (or of higher trophic level) tend to have higher levels of mercury. Hence, apical predators, such as king mackerel, pike, shark, swordfish, walleye, barracuda, large tuna, scabbard, and marlin, as well as some marine mammals, such as seals and toothed whales, contain the highest concentrations (Grieb et al., 1990, Storelli et al., 2003).

Table 9   Total mercury concentrations in fish from several regions

Seafood sample	Species	Region	n	Mean length (cm)	Mean weight (kg)	Range Hg concentration (mg/kg)	Mean Hg ± SD (mg/kg)	Reference
Albacore tuna	*Thunus alalunga*	Fiji Islands	31	72.7	21.3	0.03 - 1.01	0.34 ± 0.22	Kumar et al. (*in press*[a])
Yellowfin tuna	*Thunus albacore*	Fiji Islands	24	71.3	15.2	< 0.02 - 0.40	0.11 ± 0.11	Kumar et al. (*in press*[a])
Skipjack tuna	*Katsuwanas pelamis*	Fiji Islands	12	45.7	2.4	< 0.02 - 0.16	0.06 ± 0.04	Kumar et al. (*in press*[a])
Marlin	*Tetrapturus audax/ Mokaira mazara*	Fiji Islands	5	167.6	67.4	0.45 - 5.60	1.76 ± 1.94	Kumar et al. (*in press*[a])
Reef fish		Fiji Islands	5	17.2	0.1	< 0.02 - 0.04	0.04 ± 0.01	Kumar et al. (*in press*[a])
Barracuda	*Sphyraena sp*	Fiji Islands	4	61.3	1.3	0.18 - 0.38	0.26 ± 0.07	Kumar et al. (*in press*[a])
Bokkem	*Trachurus trachurus*	Adriatic sea	100	32.7	0.36	ND - 1.87	0.23 ± 0.47	Storelli et al. 2003
Gilt sardine	*Sardinella aurita*	Adriatic sea	150	18.8	0.03	ND - 0.30	0.09 ± 0.07	Storelli et al. 2003
Pilchard	*Sardina pilchardus*	Adriatic sea	300	15.9	0.03	ND - 0.40	0.13 ± 0.14	Storelli et al. 2003
Sprat	*Sprattus sprattus*	Adriatic sea	70	12.9	0.03	ND - 0.14	0.06 ± 0.05	Storelli et al. 2003
Pandora	*Pagellus erythinus*	Adriatic sea	170	14.9	0.06	ND - 0.70	0.22 ± 0.19	Storelli et al. 2003
Four spotted megrim	*Lepidorhombus bosci*	Adriatic sea	180	24.9	0.11	0.14 - 0.69	0.35 ± 0.19	Storelli et al. 2003
Megrim	*L. whifjagonis*	Adriatic sea	150	29.6	0.12	0.09 - 1.17	0.39 ± 0.45	Storelli et al. 2003
Red fish	*Helicolenus dactylopterus*	Adriatic sea	220	21.8	0.10	0.11 - 0.84	0.42 ± 0.20	Storelli et al. 2003
Striped mullet	*Mullus barbatus*	Adriatic sea	270	16.5	0.07	ND - 1.74	0.39 ± 0.47	Storelli et al. 2003
Skate	*Starry ray*	Adriatic sea	120	44.0	0.41	0.09 - 1.78	0.73 ± 0.54	Storelli et al. 2003
Forkbeard	*Phycis blennoides*	Adriatic sea	330	18.9	0.05	0.16 - 0.57	0.36 ± 0.14	Storelli et al. 2003
Goldline	*Sarpa salpa*	Adriatic sea	140	26.7	0.31	0.06 - 0.16	0.08 ± 0.05	Storelli et al. 2003
Frost fish	*Lepidopus caudatus*	Adriatic sea	300	70.2	0.37	0.09 - 1.61	0.61 ± 0.38	Storelli et al. 2003
Angler fish	*Lophius budegassa*	Adriatic sea	200	57.0	0.87	0.19 - 1.77	0.76 ± 0.46	Storelli et al. 2003
Picarel	*Spicara flexuosa*	Adriatic sea	180	15.9	0.02	0.09 - 0.60	0.20 ± 0.13	Storelli et al. 2003
Tuna	*Thunnus thynnus*	Japanese markets	58			0.36 - 5.25	1.11	Nakagawa et al. 1997
Bonito	*katsuwonus pelamis*	Japanese markets	18	NA	NA	0.12 - 0.41	0.25	Nakagawa et al. 1997
Yellow tail	*Seriola dorsalis*	Japanese markets	8	NA	NA	0.06 - 0.76	0.26	Nakagawa et al. 1997
Seabass	*Seriola purpuraseens*	Japanese markets	6	NA	NA	0.04 - 0.37	0.20	Nakagawa et al. 1997
Anchovies		USA markets	40	NA	NA	ND - 0.34	0.04	US FDA 2006
Butterfish	*Pampus argenteus*	USA markets	89	NA	NA	ND - 0.36	0.06	US FDA 2006
Catfish	*Ictalurus sp*	USA markets	23	NA	NA	ND - 0.31	0.05 ± 0.08	US FDA 2006
Cod	*Gadus morhua*	USA markets	39	NA	NA	ND - 0.42	0.10 ± 0.09	US FDA 2006
Croaker Atlantic	*Micropogonias undulates*	USA markets	35	NA	NA	0.01 - 0.15	0.07 ± 0.04	US FDA 2006
Herring	*Alosa sapidissima*	USA markets	38	NA	NA	ND - 0.14	0.04	US FDA 2006
Mackerel Atlantic	*Scomber scombrus*	USA markets	80	NA	NA	0.02 - 0.16	0.05	US FDA 2006
Mackerel chub	*Scomber japonicus*	USA markets	30	NA	NA	0.03 - 0.19	0.09	US FDA 2006
Mackerel King	*Scomberomorous cavalla*	USA markets	213	NA	NA	0.23 - 1.67	0.73	US FDA 2006
Mackerel Spanish	*Scomberomorus sierra*	USA markets	109	NA	NA	0.05 - 1.56	0.32	US FDA 2006

Marlin	*Makaira nigricans/ Tetrapturus audrax*	USA markets	16	NA	NA	0.10 - 0.92	0.49 + 0.24	US FDA 2006
Mullet	*Mugil sp*	USA markets	191	NA	NA	ND - 0.13	0.05	US FDA 2006
Pollack	*Pollachius virens*	USA markets	62	NA	NA	ND - 0.78	0.04 + 0.10	US FDA 2006
Salmon*	Several species	USA markets	34	NA	NA	ND - 0.19	0.01 + 0.04	US FDA 2006
Sardine		USA markets	29	NA	NA	0.004 - 0.04	0.02 + 0.01	US FDA 2006
Shark	*Carcharhinus limbatus*	USA markets	351		NA	NA	ND - 4.54	0.99 + 0.63	US FDA 2006
Swordfish	*Xiphias gladius*	USA markets	618	NA	NA	ND - 3.22	0.98 + 0.51	US FDA 2006
Tilefish	*Caulolatilus princeps*	USA markets	60		NA	NA	0.65 - 3.73	1.45	US FDA 2006
Trout (freshwater)	*Oncorhynchus mykiss*	USA markets	34		NA	NA	ND - 0.68	0.07 + 0.14	US FDA 2006
Tuna (canned, light skipjack)	*Katsuwonus pelamis*	USA markets	347		NA	NA	ND - 0.85	0.12 + 0.12	US FDA 2006
Tuna (canned, albacore)	*Thunnus alalunga*	USA markets	399		NA	NA	ND - 0.85	0.35 + 0.13	US FDA 2006
Tuna (fresh/frozen)	Several species	USA markets	228		NA	NA	ND - 1.30	0.38 + 0.27	US FDA 2006

Notes: * Only methylmercury was analysed; n = number of samples; ND = mercury concentration below detection level; NA- data not available

269. Because mercury bioaccumulates with age older apical predators fish exhibit higher mercury levels than fish that are younger and/or lower in the food-chain (Figure 2). About 90 % of the total mercury in these predatory fish species is assumed to be methylmercury. However, the percentage of methylmercury to total mercury may be quite variable, and can be as low as 30 % in certain non-predatory freshwater fish Concentrations of methylmercury within each fish species also vary, generally increasing with fish length or weight, which are correlated with age, and trophic level). Therefore, estimates of fish consumption rates and patterns for the general population and various subgroups should include as detailed information as possible regarding fish species that are consumed (Garcia and Carignan, 2005).
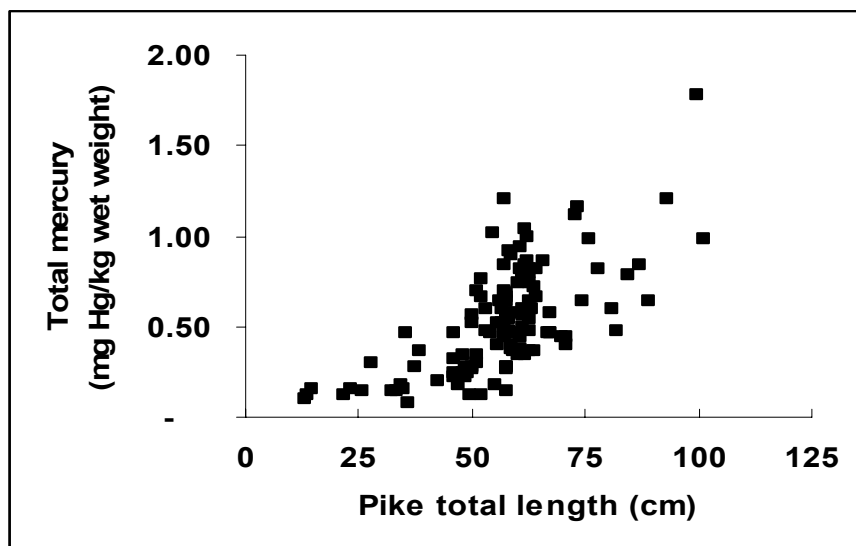
Figure 2   Mercury concentrations and length of Northern pike[15]

270. Mercury levels are also higher in fish from highly contaminated areas than from less contaminated areas (SACN, 2004). This variability, coupled with study sample size, makes it difficult to compare different studies looking at a relationship between geographical location and mercury levels. In farmed fish, particularly salmon and trout, mercury levels tend to be relatively low (FSA, 2002). These lower concentrations can be attributed to lower mercury levels in the diet and also to the fact that farmed fish are usually harvested at a young age. In addition, the chemical characteristics of pond aquaculture (high pH and high content of suspended organic compounds) reduce methylmercury bioavailability (FAO/NACA/WHO, 1999).

271. Besides fish, marine mammals and shellfish, particularly bivalve molluscs, may also represent a source of mercury. Exposure can be significant in populations consuming meat (muscle and organs) from marine mammals, such as seals and whales ([Table 10]). The kidney and liver of marine mammals in particular can have extremely high levels of mercury. Regarding crustacean shellfish, relatively low levels of mercury have generally been reported (Burger et al., 2005; SACN, 2004), and methylmercury represents in general less than 60% of total mercury present. In the United Kingdom, for example, dietary intakes of mercury did not represent any known health risk even to high-level shellfish consumers (SACN, 2004). However, mercury concentration in shellfish collected from polluted areas can be elevated, and diets combining high shellfish and fish consumption can lead to high methylmercury exposure.

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[15] From seven pristine lakes in Quebec, Canada (Garcia and Carignan, 2005)

Table 10 Total mercury concentrations in marine mammals

Common name	Origin	Muscle* (mg/kg)	Liver* (mg/kg)	Kidney* (mg/kg)	Muktuk* (mg/kg)	Reference
Beluga whale	Canadian Arctic	0.13 - 8.35 (305)	4.10 - 43.8	0.16 - 20.7 (535)	0.19 - 1.92 (176)	Lockhart et al. (2005)
Narwhal	Canadian Arctic	0.51 - 1.20 (20)			0.32 - 0.85 (20)	Wagemann & Kozlowska (2005)
Harp seal	Greenland Sea	0.04 - 0.31 (25)	0.08 - 3.3 (25)	0.14 - 0.68 (25)		Brunborg et al. (2006)
Hooded seal	Greenland Sea	0.08 - 0.31 (25)	0.004 - 0.13 (25)	1.00 - 4.40 (25)		Brunborg et al. (2006)
Pilot whale	Faroe Islands	3.3				
Pilot whale	Japan coast	5.38 - 13.8 (4)	390 - 422 (2)			Endo et al. (2004)
Risso's dolphin	Japan coast	9.09 - 9.21 (2)	30.2 - 645 (7)	7.30 - 28.8 (4)		Endo et al. (2004)
Striped/Bottlenose/Common dolphins	Japan coast	1.43 - 63.4 (12)	7.6 - 1980 (11)	7.85 - 153 (10)		Endo et al. (2004)
Baird's beaked whale	Japan coast	1.71 - 5.30 (4)				Endo et al. (2004)
Minke whale	Japan coast	0.03 - 0.12	0.12 (1)	0.01 (1)		Endo et al. (2004)

* Figure given in parentheses is the number of samples

272. The GEMS/Food databases[16] on chemicals in food and the total diet have a large number of records for mercury in food. Although data from every region and country are not currently available, much information has been collected through monitoring and surveillance activities. Mercury levels in commonly consumed marine and freshwater fish, canned fish and other seafood have been published in many scientific papers. Summaries of such data are available from various sources (FDA, 2006; NIFES, 2006; UNEP, 2002; USEPA, 2001b). If data on mercury levels for fish species consumed in the area are not available, data on mercury levels for these species from other areas could be adequate for estimating exposure by the population of interest. Given the cost and time needed for the analysis of methylmercury, data on total mercury is often used for exposure assessment purposes. However, the ratio of methylmercury to total mercury can be quite low in non-predatory species and fish produced by aquaculture as noted above.

4.4.2   Using available data on mercury in fish

273. The first step in using data on methylmercury levels in a fish species consumed by a given population is to make an inventory of existing data. Consideration should be given to the quantity and quality of the data. After a suitable database is assembled on methylmercury and/or total mercury levels

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[16] http://www.who.int/foodsafety/chem/gems/en/index.html

in fish, rough estimates of potential fish contamination levels can be calculated for each fish species. Information yielded by these databases may provide preliminary estimates of the methylmercury levels in the fish, and may help to identify locations where in-depth field measurement may be needed. These preliminary data may also help identify other data needs, such as additional mercury measurements for actual marketed fish or locally caught fish.

274. In pursuing this approach, the following points should be considered. Even if many international/ national/regional/tribal entities have environmental monitoring programmes, variations in methods used (such as sampling procedures and laboratory procedures) can make comparisons difficult (ECACAN, 2001). Sampling and analysis protocols often are not reported or are simply absent, which can hinder judgment on the validity and accuracy of the data.

275. Accumulation of methylmercury in fish species can greatly differ according to the particular characteristics of various ecosystems. Many factors, other than the loading of mercury from atmospheric deposition (or from other releases), can strongly influence the concentrations of mercury in aquatic biota. Striking examples exist, such as in Nova Scotia (Canada) and elsewhere (EC, 1998; Simoneau et al., 2004), where nearby lakes exhibit levels of mercury in the same fish species that vary by as much as a factor of 10 (or one order of magnitude). In fact, the capacity of a lake ecosystem to transform mercury loadings into methylmercury determines the extent to which it is actually incorporated in the food web and biomagnified by fish species. Environmental factors such as the presence of riparian wetlands, high organic carbon loadings, high biological activity, and elevated ratio of drainage basin area versus lake area are favourable for methylmercury production and, therefore, water bodies with these characteristics tend to have fish with higher levels of methylmercury.

276. Bigger fish are usually older and exhibit higher methylmercury levels than smaller and younger specimens of the same species. If available, information on the size (weight, length, girth and/or age) of fish should be taken into account when establishing mean methylmercury levels. Then, if feasible, calculations of arithmetic average concentration should be performed on size classes comparable to the ones actually eaten by the population of interest.

277. In the absence of geological or anthropogenic point sources of mercury (that is, local contamination attributable to human activities), the global atmospheric pool represents the primary mercury input to lake ecosystems (Fitzgerald et al., 1998; Johansson et al., 1991; Monteiro and Furness, 1997; Downs et al., 1998; Lin et al., 2001; Bindler et al., 2001; Wiener et al., 1990). Following the adoption of strong mercury control programmes in some countries, many indicators point to a decrease in atmospheric mercury loadings in some locations (Benoit et al., 1998; Shotyk et al., 2003). Thus, the amount of mercury brought to lakes can vary yearly. Information older than three years might not fully reflect the current situation of fish contamination (Wiener et al., 2004).

4.4.3   Use of surrogate data

278. The availability of pertinent measurements greatly varies from country to county. In the absence of such information, surrogate data might still be of use as indicators of the potential mercury levels in fish in the region/country/area. Well-identified trends do exist regarding mercury accumulation in food webs, and can be used as clues when trying to extrapolate available information. For example, it is expected that, for all locations, piscivorous (predatory) fish accumulate more mercury than herbivorous fish species that feed on aquatic vegetation (algae, plankton). Greater local fish diversity (characteristic of the presence of complex food webs featuring many herbivorous and predator species) might be an indication of enhanced accumulation of mercury in apical predators.

279. However, the use of surrogate data should be approached with caution. There are always uncertainties and limitations in use of surrogate data, which need to be considered in the exposure assessment. The degree of uncertainties and limitations will vary depending on how well the surrogate data represent the actual fish consumed by the population. The following guidelines could be considered:

280. **Surrogate data from the region of interest.** In some situations, mercury levels in regional fish species not consumed by populations might be available, but data for those species consumed by the

population are missing. Such data can still be used to predict on first approximation the mercury levels in the regional species of interest. For example, in North America, it was established that the concentrations of total mercury in 1- or 2-year-old yellow perch are strongly and positively correlated with concentrations in co-existing piscivorous fish, including walleye, black bass, and northern pike (Cope et al., 1990; Suns et al., 1987). This relationship enables the generation of rough estimates of mercury levels of these other species. Caution should then be exerted to consider the respective ranks of the species in the food web, in order to apply correction factors that take into account the progressive accumulation of mercury from herbivorous to first-level predators to higher predators. Proper expertise should be sought to examine the feasibility of such estimation.

281. **Surrogate data from other regions.** Considering the complexity of the biogeochemical cycle of mercury, the best source of data regarding mercury levels in fish is recent field measurements in the site of interest. However, in regions where the global atmospheric pool represents the primary source of mercury loadings (that is, in the absence of local mercury point sources), and in the scope of the macro-scale screening assessments, surrogate data gathered in other areas than the one of interest can be useful to provide initial rough estimates of the potential methylmercury levels in the fish, providing that:

- Identical fish species, or similar species, that are part of similar food web structures and trophic levels, are compared.

- Similar environmental settings and eco-zones are compared, preferably in regions in the vicinity of the one under study. The environmental characteristics of lakes should be considered and reference lakes chosen to closely fit to the ecosystem where information is needed.

282. In addition to being a major factor in methylation processes, the environmental setting of a lake greatly influences growth rates of fish, which, according to recent findings (Simoneau et al., 2004), could in turn influence methylmercury levels in fish tissues. In fact, fish growing faster in response to either lower competition for food or enhanced food abundance (higher productivity of a local environment) will be younger for a given length and tend to have lower methylmercury levels in their tissues. Surprisingly, the situation of lower competition for food is encountered in lakes where exploitation of fish resources has removed a significant part of the predatory fish biomass; therefore, sustained fishing activities might lower the levels of methylmercury in certain fish species. This criterion should also be kept in mind when extrapolating from other data sources.

283. Many environmental monitoring programmes limit their mercury monitoring to target fish species that are considered good indicators of the overall levels of mercury in the fish resource, in order to determine temporal trends in mercury levels. There are distinct characteristics (migration behaviour, dietary habits, wide geographic distribution) that make certain fish species good bioindicators of the levels of local mercury contamination (Wiener et al., 2004; US EPA, 2000). For example, black piranhas (Serrasalmus rhombeus) living in the Amazon are an ideal bioindicator (UNIDO, 2003b) because 80 % of their diet is fish based, their diet does not change seasonally, they do not make long migrations, and they mainly live in quiet waters (Goulding, 1980). Elsewhere, other species, such as the Eurasian perch (Europe and Northern Asia) (Thorpe, 1977), the walleye and the yellow perch (North America) (Scott and Crossman, 1973; Becker, 1983) also fit this description. These species might be of greater significance in the context of the use of surrogate data, again providing that compared species originate from similar environments.

284. **Marine fish species**. A significant part of the mercury entering marine environments is removed from the biological cycle and trapped in sediments through the formation of particles with sulphur-based molecules. However, marine environments are characterized by complex food webs featuring numerous trophic levels and favouring the bioaccumulation of mercury in top predator species, even if mercury levels in the lower compartments of the food web remain fairly low. In the absence of local mercury point sources, many marine fish species tend to have relatively low levels of methylmercury. However, other fish species, especially large predatory species, such as shark, large tuna, king mackerel, and swordfish tend to have higher methylmercury levels. If data on methylmercury levels for predatory marine fish species consumed in the area are not available, data on methylmercury levels for these species from other areas could be adequate for estimating mercury levels in fish consumed by the population of interest. Examples of available data on methylmercury levels in marine fish are presented in various reports, including UNEP (2002), US EPA (1997), and others.

285. **Canned products**. Most commercially canned fish products are subjected to various national quality regulations and oversight, including some testing of methylmercury levels. Also, some organizations have tested levels of methylmercury in canned products as part of various studies. These sources of data can be useful for determining potential levels of methylmercury in canned fish products and for estimating mercury exposures for those populations that consume these products. Among canned fish species, tuna has been identified as sometimes containing relatively high levels of mercury. There are six species of tuna intensively fished around the world: skipjack, northern bluefin, southern bluefin, big eye, yellow fin, and albacore. Smaller species such as skipjack are usually destined for canning (FDA, 1994).

286. If data on the canned tuna products that are sold are unavailable for a given country or region, surrogate data from similar products in other countries (Dabeka et al., 2003; US EPA, 1997c) could be used as estimates of the methylmercury levels in canned tuna consumed in the country under study. However, as both the raw material and the canned products are widely traded the country of origin will not necessarily reflect where the tuna was actually caught.

4.4.4   Calculation of exposure estimates

287. As described earlier in this document, the estimated exposure to methylmercury due to fish consumption can be calculated by multiplying the amount of consumption of fish by the estimated methylmercury levels in that fish (ppm, or mg mercury per kg fish). When several species are consumed, the quantity of each fish species consumed per unit of time (that is, kg fish per day) (multiplied by the estimated mercury levels in those fish species) must be added to estimate the total mercury intake.

288. Exposure estimates may be made for the mean or average population or for some high percentile fish consumers. These so-called "point estimates" are simple and easy to calculate. In contrast, calculations that use the full distribution of consumption and/or mercury concentrations provide a more complete picture of exposures in a population. These so-called "probabilistic estimates", however, require much more data and computer software. As both methods are equally accurate in estimating exposure, only "point estimates" are presented in this document. Further information on distributional methods is available elsewhere (WHO, 2008).

289. If average daily consumption rates and average methylmercury levels are used in the calculations, then the result is an estimated average dose of methylmercury for a population, usually expressed in units of milligrams or micrograms methylmercury per day (mg or μg Hg per day). If this dose is divided by an average body weight (kg bw) for the population, a dose in units of milligrams or micrograms of methylmercury per kg body weight per day (mg or μg Hg per kg bw per day). The dose is also often expressed in terms of dose per week (mg of Hg per kg body weight per week), which can be derived by multiplying the daily dose (mg/kg bw per day) by 7 (days/week). The average body weight is usually country specific and may be derived through national surveys of body mass index.

290. Average mercury intake generated by these data sets for different subpopulations will provide initial estimates of exposures, allow a ranking scheme, and help prioritize interventions. A detailed assessment, based on specific information regarding local dietary habits and mercury levels found in fish consumed by local populations, might then be the next step for more precise characterization of the mercury intake in particular subpopulations.

4.5   Exposure estimates of subpopulations

291. Once the mercury exposure has been estimated using existing national databases or surrogate information, more refined exposure assessments may be necessary for certain subpopulations. Specific information for the subpopulation (such as site-specific information, ethnic/cultural information, etc.) can be important because consumption patterns vary considerably between subgroups. National surveys often provide only average rates for a whole population and/or for only certain subgroups (depending on the design of the survey, particular data gathered, survey questions used, etc). Moreover, fish that are

consumed in a specific area can contain methylmercury levels quite different from fish sampled in other parts of the country.

292. This section describes an approach to estimate exposures to mercury for target subpopulations potentially at risk. In this section guidance is presented for gathering new data, such as methods/approaches to gather samples of the species of fish consumed by the population (or subpopulations), including market-based fish (canned, fresh, frozen, and/or locally caught fish), and the chemical testing/analyses (methods, options, etc.) to determine methylmercury levels in those fish. In a micro-scale assessment or a site-specific assessment, fish consumption rates among a surveyed population are combined with specific measurements of mercury concentrations in the local fish actually consumed to estimate the exposure levels for the population. Depending on the type of data collected, sometimes mercury exposures can be estimated for individuals and/or subgroups among the surveyed population.

293. Acceptance of local intervention by (and with the collaboration of) the population is the basis of any successful subpopulation assessment. The assessment could also include a comprehensive evaluation of all sources of mercury exposure (exposures due to fish consumption and other pathways) to obtain an estimate of total exposure to mercury.

294. As described in Chapter 3, methylmercury intake from fish consumption can be directly estimated using human biological markers (or biomarkers). Potential biomarkers, such as total mercury levels in hair, can be useful to estimate exposure of subpopulations.

4.5.1 Consideration of local dietary habits

295. Fish consumption rates and patterns are an important component of a subpopulation exposure assessment. Ideally, fish consumption information will include descriptive information on the consumption of locally caught fish and other fish (such as market-based fish imported to the area). For locally caught fish and market-based fish (such as canned, fresh, and frozen fish species shipped to the area from other parts of the country or from other countries), the questionnaire should record species, frequency of the meals (over the short and long term), and portion sizes, as well as information regarding temporal patterns of consumption throughout the year (to the extent feasible). For locally caught fish, additional information should be collected, including the size and location of the fishing population using specific water bodies. In general, fish consumption studies describe individual frequency of consumption of different fish species throughout the year as well as the average portion consumed. Different tools are available to gather information on fish consumption rates and patterns, such as the following retrospective survey methods:

- Food frequency questionnaires based on one-year recall. The 1-year period is usually separated by season, allowing information to be gathered more precisely and seasonal consumption patterns to emerge. For example, in North America a year comprises four seasons, but in Brazil a year will be split into dry and rainy seasons;

- 24-hour recall questionnaires; and,

- Three- to thirty-day recall questionnaires.

296. These retrospective dietary-assessment methods are simpler and less expensive than prospective methods such as daily diaries and duplicate-diet methods and are therefore used more often as a basis of dietary exposure assessments. Food frequency studies take the form of participants identifying their typical fish consumption (such as, "How many times per week/month do you usually eat fish A?"). Diet histories involve recollection of specific meals over a specific time (such as, 24-hour or 1-week periods). They also provide information regarding the usual portion that is eaten. Some examples of questionnaires were presented in Section 4.3. Other examples of questionnaires used to characterize local dietary habits are given in Appendices D and E. However, these questionnaires need to be adapted to local fish consumption situations.

297. Basic socio-demographic data, such as gender, age and geographic location of the respondent, should also be collected in order to provide cross-tabulated data as described earlier. Cross-tabulated data are

useful for determining exposures among different subgroups, such as men vs. women, children vs. adults and seaside villages vs. inland communities.

298. Time constraints and human resources usually do not allow for gathering dietary data for a whole population or for all subpopulations. Therefore, it is common to gather data for a sample of the population (and/or various subpopulations) to provide estimates of the consumption rates and patterns for the population (and/or subpopulations). These sample(s), to be most useful, should be representative of the population (or subpopulation) from which it is drawn and to which conclusions regarding dietary patterns and mercury intake will be extrapolated. Valid samples are the basis for valid inferences to be made at the population and subpopulation levels.

299. Different strategies exist to assure representative samples. A random sample of a population or subpopulation can provide a good estimate of existing patterns in the subpopulation. For example, in the NHANES study, the US Centers for Disease Control and Prevention (CDC) surveys a random representative sample (a stratified, multistage random sample) of far less than 1 % of the population, and the results produce data that are useful for characterizing general dietary patterns among the United States population. However, NHANES data are not useful for determining high-end consumption patterns.

300. Moreover, when trying to characterize local communities or smaller subpopulations, 1 % of the population could be too small a sample. In some cases (depending on the level of precision desired in the study and the total number of people in the population) sampling efforts must be enhanced, reaching as much as 10 % of the population. Such sampling efforts were necessary in Canadian studies of populations composed of about 1,500 persons; in this example, collecting a sample of less than 1 % would have led to invalid information (de Grosbois et al., 2004).

301. Also, in some cases, random sampling is not feasible and the sample can be constituted based on local participation, or other factors. However, the constitution of this type of "convenient" sample should be based on a gender-weighted, age-specific structure of the subpopulation from which it was drawn and, once again, might need to include as much as 10 % or more of the subpopulation. In any case, information, such as basic census of the subpopulation, should be available.

4.5.2   Estimating mercury in locally consumed fish

302. This section presents methodologies that can be used to gather new data on methylmercury levels in fish consumed on a local scale. Information yielded by fish consumption questionnaires may be the basis for identifying types of fish for which data are needed on methylmercury levels, including fish from markets, local harvests, and canned products. Many parts of the guidance summarized here are inspired by a guidance document prepared by US EPA (2000).

4.5.2.1   *Summary of sampling strategies*

303. Species targeted by sampling and analyses programmes should be the ones identified by the food frequency questionnaires, including locally harvested fish, marketed fish, and canned products. The approach described here involves sampling a number of sites to: (1) characterize methylmercury levels in fish tissue; (2) identify locations where these levels could represent a threat to consumers' health; and, (3) produce enough information to later characterize mercury intake attributable to fish consumption. Sites selected for this type of study should be limited to locations used by sports, subsistence and commercial fishers. Thus, site selection should be guided by local knowledge.

304. Prior to field collection, fish to be sampled should be divided in three size categories (from small to large specimens) that, depending on the edible species, match the consumption patterns. In order to minimize analytical costs, the investigator can use composite samples defined here as a single homogeneous mixture of a certain number (two or more, preferably 3–10) of fish fillets. Ideally, fish of comparable size are used to construct composite samples in order to minimize artefacts caused by important differences between mercury levels of specimens forming the composite. The total weight of the composite sample should be about 200 g (US EPA, 2000).

305. Based on available resources and other factors, sample collection can be adjusted to one of the three following strategies:

- Minimally collecting a single composite sample for each of the three size classes of each target species;

- If resources permit, collecting replicate composite samples for one of the size classes for each target species; and,

- If resources permit, collecting replicate composite samples for each of the three size classes of each target species.

306. In addition, in order to maximize information yielded given available resources for field sampling, the investigator could seek the help of sports/subsistence/commercial fishers (or other volunteers) to gather fish samples, if feasible. Otherwise, the choice of capture devices, ranging from active (electro-shocking units, seines, trawls, angling equipment) to passive techniques (gill nets, fyke nets, trammel nets, hoop bets, pound nets, d-traps) depends on the species to be caught and on the environmental setting of the water body to be sampled. Active collection is usually more efficient in shallow waters and enables coverage of larger number of sites. Passive collection is more convenient in deep water and yields larger catches. It might be of interest, in a given cultural context, to consider the use of non-destructive sampling equipment such as biopsy needles to puncture aliquots of fish flesh without damaging the whole fillet or possibly without even killing the animal (Cizdziel et al., 2002; Buhl and Hamilton, 2000; Baker et al., 2004).

307. A number of additional field measurements should be performed, if feasible, in order to better interpret data on mercury levels, including total length, total weight, age, and sex of individual fish. Age is determined either by counting the number of rings that compose the otholites (small calcareous concretions on the head of fish), or by examining scales. Details on these techniques are presented elsewhere (DeVries and Frie, 1996; Casselman and Scott, 1989).

308. **Intensive fish collection strategy and analyses of locally caught fish**. Intensive studies enable an in-depth evaluation of the extent of contamination in fish species, including detailed size classes. Intensive studies are usually costly and should only be envisaged when adequate resources are available. The protocol presented here differs from a similar approach elaborated by US EPA (2000), calling for a larger number of specimens to be collected at each site. If resources for sampling operations are sufficient, sample collection is planned in order to gather enough information for each species to calculate accurate standardized mean mercury concentrations. Otherwise, average methylmercury levels can be used as a proper estimation. An assessment of trophic level status of the fish, either through food web characterization or analysis of stable isotopes could be informative to the detailed assessment strategy.

309. **Use of standardized mean methylmercury concentrations**. It is widely recognized that there is a positive correlation between fish size (length and weight) and methylmercury concentration in muscle tissue (Wiener et al., 2004). Therefore, the mean methylmercury concentration of fish tissues for a random assemblage of specimens depends on the size distribution of fish being analysed. Thus, individual methylmercury concentrations should be measured over a wide range of sizes (within the range consumed by the population) to eliminate the bias associated with differences in fish size among the samples collected.

310. Then, appropriate statistical procedures can be used to determine the mean methylmercury concentration for a specific fish size. Usually, the fish size representative of that most frequently captured by consumers is chosen for this purpose. This is called the size adjusted or "standardized" mean mercury concentration (SMMC). Data gathered through food frequency and 24-hour recall questionnaires can be used to indicate consumption of the different fish species and on the usual portion of the meals. However, in many cases, little information is available on the actual length (or size) of fish consumed, although this information can sometimes be gathered by interviewing fishermen or reviewing catch size (length or weight) regulations. Nonetheless, SMMCs provide the best estimate of the amount of methylmercury associated with different fish meals. SMMCs also represent a valid base for inter-regional comparisons of the levels of methylmercury in various fish species.

311. One widely used approach to calculate SMMC is to sample specimens of a particular population across a range of lengths and to apply linear regression between methylmercury levels and fish length to estimate the methylmercury concentration in a fish of some standardized length (Parks and Hamilton, 1987; Johnston et al., 2003). Strange and Bodaly (1999) established a protocol that describes the sample size and size range of fish needed to derive a good statistical relationship between methylmercury concentration and fish size. Optimally, tissues from 25–35 fish are gathered from each species in size categories ranging from small to large (see also Exponent, 2003). A more complex approach to calculate SMMC involves polynomial regression with indicator variables (Tremblay et al., 1998). This procedure allows rigorous statistical comparison of Hg-to-length relations among years and is superior to simple linear regression and analysis of covariance for analysis of data on Hg-length relations in fish.

312. **Sampling strategy for fish from the market**. Considering that ancillary data (age, length, weight, sex) on fish sold at the market are often impossible to gather, the assemblage of composite samples and the calculation of arithmetic mean methylmercury concentrations are probably the best approach for characterizing methylmercury levels in market fish consumed by a given population. Fish samples can be collected through participation of the local population, sharing of small portions of fish meals, collaboration with local fishermen, market sampling, etc.

313. Canned products. If data on canned fish products consumed by the local population are unavailable, replicate composite samples of individual packages sold at local markets can be gathered and analysed to calculate arithmetic mean methylmercury concentrations.

4.5.2.2   *Sample preparation*

314. Once collected, fish are sealed in plastic bags and either cooled on wet ice (preservation up to 24 hours) or dry ice, or frozen until further processing (US EPA, 2000). However, it is preferable to slice fillets prior to freezing in order to prevent rupture of internal organs, which can then result in cross-contamination between tissues. When working with the collaboration of local fishers or sampling at the market, a small portion of fillets (50 g) can be cut and preserved likewise. Once properly cooled and packed, the fish sample can then be shipped to a laboratory for treatment and analysis. Shipment must be arranged and achieved with minimal delay to preserve the integrity of the sample. In addition, investigators may choose to archive some samples. Proper long-term archiving of tissue samples might be useful and informative for future analyses.

315. Once at the laboratory, fillets are sliced from whole specimens, cut in small cubes, and homogenized using high-speed blenders. If relevant, composite samples are then prepared by precisely weighing aliquot parts and combining them in equal quantities. All equipment used to process the samples must be carefully cleaned and free of contamination. Quartz, PTFE, ceramic, polypropylene, and polyethylene-based equipment, as well as stainless-steel devices, are suitable for mercury analyses. Protocols for cleaning the laboratory wares usually involve soaking in acid solutions and rinsing with treated water.

316. It is acceptable and generally easier to express mercury concentrations in fish tissue on a wet-weight basis. Thus, pre-drying or lyophilisation (freeze-drying) of tissues is not necessary. The inclusion or removal of fish skin from the sample to be analysed should mimic local cooking habits and traditions. Details for all parts of the procedure are available in US EPA (2000).

4.5.2.3   *Laboratory analyses*

317. Analyses that measure total mercury are much simpler and less expensive compared to analyses that measure methylmercury. Considering that about 90 % of total mercury found in fish muscle is usually in the form of methylmercury, total mercury measurements can be used in most cases to adequately represent approximate methylmercury concentrations (Grieb et al., 1990; Bloom, 1992; Francesconi and Lenanton, 1992; Hill et al., 1996; Hammerschmidt et al., 1999; Bodaly and Fudge, 1999).

318. Fish homogenates are decomposed using a heated mixture of strong acids (US EPA, 1979). A reducing agent (usually stannous chloride) is added to the resulting solution, which causes the release of mercury from the mixture in the form of elemental mercury (designated as cold vapours). Gaseous

elemental mercury is then carried to the detection cell by an inert gas (usually argon). Mercury detection is based on the property of mercury atoms to absorb or emit light when excited by specific light sources. Two techniques are commonly used to measure mercury, atomic adsorption and atomic fluorescence, the latter being the most sensitive.

319. Here, mercury atoms submitted to 256 nm light accumulate energy and, in response, re-emit light at a different wavelength. The amount of light emitted is proportional to the amount of mercury going through the detection cell (US EPA, 1998b). This technique is generally used for high-sensitivity (low mercury concentrations) measurements in samples such as water. Since the late 1960s, cold vapour atomic adsorption (CVAA) has been the most commonly used technique for analysing mercury levels in fish samples. With CVAA, the amount of light adsorbed by mercury atoms present in the sample solution (containing the dissolved fish tissue and the acid mixture) is measured by the device and compared to a standardized sample of known mercury concentration (Brown et al., 2003).

320. The ability of local laboratories to properly perform mercury analyses is usually tested using reference material such as homogenized fish tissue containing known levels of mercury. These reference materials are available through agencies such as the International Atomic Energy Agency, the National Research Council of Canada, the National Institute for Standards and Technology of the US, Marine Environment Laboratory, the National Institute for Environmental Studies of Japan, and other organizations. Analytical standard solutions prepared with precise amounts of mercury chloride salts are used to calibrate concentrations measured for sample solutions.

5. ENVIRONMENTAL EXPOSURE MODELS

5.1   Fate, transport and exposure models

321. Mercury partitioning and movement through environmental compartments is complex and depends on many environmental parameters. However, computer models can be used to predict the environmental fate and transport of emitted mercury and to estimate levels in various media and biota, and estimate possible human exposures (US EPA, 1997a).

322. Numerous models have been developed by governmental agencies and private companies to model elemental, divalent, and methylmercury emissions into the environment; fate, transport, and deposition in aquatic and terrestrial media (that is, air, water, soil, sediments); uptake by plants and animals; biotransformations; and multi pathway exposures of humans and ecological receptors. Most of these models are complex, data-intensive, site-specific, and often resource-intensive (such as time, money, computer requirements, and expertise). If resources are constrained, risk assessors may want to consider using less-refined screening model analyses (using conservative assumptions, with less site-specific data required) or look-up table analyses.

323. Several fate and transport models and associated data are presented in the Mercury Study Report to Congress (US EPA, 1997b). The models described include a long-range atmospheric transport model (Regional Lagrangian Model of Air Pollution [RELMAP]), a local scale atmospheric transport model (Industrial Source Code air dispersion model [ISC3]), and aquatic and terrestrial fate, transport, and exposure models, such as the Indirect Exposure Model – version 2 for Mercury (IEM-2M). The RELMAP model uses site-specific emission source data and predicts mean, annual atmospheric mercury concentrations, and wet and dry deposition rates across a geographic region. The ISC3 model predicts (on a local scale) the annual average atmospheric concentrations and deposition rates within 50 km of anthropogenic emission sources (such as coal combustion units).

324. The major input data used to conduct such modelling include, among others: mercury emissions estimates (that is, kilograms per year), preferably for each form of mercury emitted (gaseous elemental, gaseous divalent, or particulate-bound mercury); stack release height and exit velocity; stack gas temperature; location of facilities (such as longitude and latitude); meteorological data, including precipitation (amount and timescale of rain, snow, sleet, etc), wind direction and velocities, etc; and terrain information (flat, complex, etc.). Several dispersion models (including ISC3) and related information can be obtained from the US EPA's Support Center for Regulatory Air Models (SCRAM) website (found at http://www.epa.gov/scram001/).

325. The IEM-2M predicts environmental mercury concentrations based on air concentrations and deposition rates to watershed soils and water bodies (lakes). The IEM-2M simulates the fate of elemental, divalent, and methylmercury using mass balance equations. The mass balances are performed for each mercury species, with internal transformation rates linking the three species. Sources include wetfall and dryfall loadings and diffusion of atmospheric mercury vapour to watershed soils and the water body. Sinks include leaching from watershed soils, burial from lake sediments, volatilisation from the soil and water column, and advection out of the lake. Methylmercury concentrations in fish are estimated from water concentrations based on bioaccumulation factors (BAFs). Much data that are required by these models are provided in the Mercury Study Report to Congress (US EPA, 1997b), including atmospheric modelling parameters, watershed and water body modelling parameters, and BAFs; however, site-specific data are often required as well.

326. The Community Multiscale Air Quality Modelling System for Atmospheric Mercury (CMAQ-Hg) simulates the emission, transport, chemical and physical transformation, and wet and dry deposition of atmospheric mercury. Other (long-range) air dispersion models include CALPUFF, AERMOD, and EDMS.

327. Within the UN-ECE Convention on long-range transboundary air pollution, modelling of transboundary transport of mercury is performed by the Meteorological Synthesizing Center - East (www.msceast.org). Modelling tools include atmospheric models with geographical coverage of Europe (EMEP region) and the Northern Hemisphere. Specific modelling of ecosystem cycling or human exposure is not performed within the convention but methods for calculating critical loads and critical concentrations in precipitation, to ecosystems have been developed and applied. (http://www.unece.org/env/wge/mapping.htm).

328. Models that can be used to estimate emissions from waste management units include US EPA's Industrial Waste Air Model (IWAIR) and Industrial Waste Management Evaluation Model (IWEM). IWAIR can be used to estimate the release and dispersion of chemicals (including mercury) from waste management units and determine ambient air concentrations at specified human receptor locations. IWEM can be used to estimate leachate concentrations and impacts on groundwater.

329. US EPA is currently developing the Multimedia, Multipathway, and Multireceptor Risk Assessment (3MRA) modelling system and the Total Risk Integrated Methodology (TRIM) fate and exposure modules, which could be used to model mercury exposures and potential risks. The 3MRA modelling system will be used to conduct screening-level risk-based assessment of potential human and ecological health risks resulting from long-term (chronic) exposure to various chemicals (including mercury) released from land-based waste management units.

330. Mercury Maps is a geographical information system (GIS)-based tool that relates changes in mercury air deposition rates to changes in mercury fish tissue concentrations. When used in conjunction with air deposition modelling results, Mercury Maps can be used to help quantify the benefits of air emission reductions. Alternatively, Mercury Maps can be used to estimate the percent reductions in air deposition required to reduce fish mercury levels to levels considered safe for consumption. The Regional Mercury Regression Model is a GIS-based regression model to predict mercury levels in fish tissue.

331. US EPA's Center for Exposure Assessment Modelling (CEAM) provides exposure assessment methodologies and models for aquatic, terrestrial, and multimedia pathways for metals and organic chemicals. These models and other information can be obtained at the following website: http://www.epa.gov/ceampubl/. This website also includes models for groundwater, surface water (CORMIX, EXAMS, HSCTMD2, HSPF, PLUMES, PRZM3, QUAL2EU, SED3D, SMPTOX3, SWMM, TMDL USLE, Visual Plumes, WASP), food chain (FGETS, LC50), and multimedia assessments (3MRA, MINTEQA2, MMSOILS, MULTIMED).

332. Exposure of inhabitants around the chlor-alkali plant was estimated under the framework of the EU EMECAP project (Gibicar et al., 2007). The Atmospheric Pollution Model' (TAPM) from CSIRO in Australia was used for meteorological calculations and an off-line dispersion chemistry model EPISODE has been adapted to include a mercury-chlorine chemistry scheme in modelling process and to calculate deposition and concentration fields of gaseous elemental mercury, reactive gaseous mercury and total particulate mercury. A mercury/chlorine/ozone chemistry scheme was developed to describe chemistry in the plume as well as in the factory itself. For the local scale modelling the development and testing of a suitable dispersion modelling system to describe local scale mercury dispersion and chemistry was performed. The model was validated against observed concentration and emission data, collected during the measurement campaigns. The dispersion and deposition of mercury emitted from the Mercury chlor-alkali plant was simulated for the year 2002 for two different plants (Italy and Sweden) and local concentration and deposition fields were calculated (Denby and Pacyna, 2004).

333. The appropriate approach for simulating the transport and transformations of Hg in the water compartment requires the use of a hydrodynamic model with additional modules for transport-dispersion and biogeochemistry. In the framework of the EU project MERCYMS the model PCFLOW3D has been upgraded with a biogeochemical module and used for simulations of mercury transport and transformation processes in the Mediterranean (Rajar et al., 2004, Yagar et al., 2006). The circulation for the four seasons due to wind, thermohaline forcing and inflow momentum of the main rivers and through the straits has been calculated. The upgraded biogeochemical module deals with different mercury species: gaseous elemental (Hg^0), divalent (Hg^{2+}), and mono-methyl mercury in dissolved form and bound to particulate

matter and plankton. Exchange of mercury at the boundaries (bottom sediment/water and water/atmosphere) and transformation processes such as methylation, demethylation, reduction and oxidation were taken into account. The modelling framework was attempted for the simulation of mercury in fish.

5.2   Data requirements and potential sources of information

334. Risk assessments can range from generic screening analyses to complex site-specific risk analyses. The data required to support such risk assessments also vary. The data are used to describe site characterization scenarios and as inputs to fate and transport modelling, human exposure assessments, and risk analyses. Some data are site-specific (such as land-use data, watershed and water body layout, soil/vadose zone, human receptor type and location), some are regional (such as meteorological, surface water, and aquifer data), and others are national (such as reference levels, human exposure factors, waste management unit characteristics, farm food-chain and aquatic food web data). National census data are useful to characterize and locate populations. In addition, chemical-specific data (i.e., chemical properties such as molecular weight, vapour pressure, bio-uptake, and bioaccumulation factors) are fixed. These chemical-specific data identified by WHO, US EPA, and other organizations are appropriate for all governmental agencies to use (for more information please see IPCS, 1976, 1989, 1990, 1991, 2000; WHO, 2003; US EPA, 1997b, 1997f, 1998c, 1999; ATSDR, 1999).

335. In order to perform human exposure assessments, data for some or all of the following exposure parameters may be required:

- body weight;
- consumption rates of various foods (fish in particular);
- drinking water ingestion rates;
- inhalation rates;
- soil ingestion rates;
- exposure duration.

336. Subpopulation-specific (such as subsistence fisher, recreational angler) and age-specific (such as child vs. adult) data are preferable and will reduce uncertainty in the analysis. Some exposure parameters have default data available (such as inhalation rate, body weight). More information on exposure factors, input data, default values, and other relevant information can be obtained in the US EPA Exposure Factors Handbook (1997g) and other sources.

337. However, much data are specific to a particular nation. For example, the Solar and Meteorological Surface Observation Network (SAMSON) contains meteorological data for 218 meteorological facilities throughout the United States; however, these data are only useful for modelling the fate and transport of mercury within the United States. Also, US EPA geographic information system (GIS) data on watershed and water body delineations and US Bureau of the Census data on population size and location can only be used in the United States.

338. Information on food (such as fish) consumption rates can be obtained from various studies and surveys. Some examples from the US, which are described in greater detail in chapter 4, include the Continuing Surveys of Food Intake by Individuals (CSFII) and the National Health and Nutrition Examination Survey (NHANES) (US EPA, 1997c, 1997g, 1998a). Similar data may be available for other nations. Nonetheless, additional information on this topic can be obtained from, among others, UNIDO 2003b.

5.3   Uncertainties and limitations

339. The use of models to simulate the fate and transport of mercury in the environment, and to estimate exposures, can be a useful approach for assessing potential risks to human health. The results of such exposure assessments can inform risk managers about the potential concern for public health, and potential need for some mitigation measures. Nonetheless, these assessments always have some uncertainty. Sometimes these uncertainties are quite significant. Data are not available for all aspects of the assessment, and those data that are available may be of questionable or unknown quality. Typically, these exposure assessments, which are based on modelling, rely on some number of assumptions with varying degrees of uncertainty (US EPA, 1992).There are three types of uncertainty in these exposure assessments:

- Scenario uncertainty (uncertainty resulting from incomplete information needed to characterize the exposure and dose);
- Parameter uncertainty; and
- Model uncertainty.

340. Uncertainties should be evaluated and characterized in these exposure assessments. The evaluation of uncertainties should include qualitative (characterized in a narrative) and/or quantitative analyses (such as ranges or sensitivity analysis). The extent and degree of uncertainty will vary depending on a number of factors. Some considerations regarding the degree and extent of uncertainty in the exposure assessment include how accurate the data are, how well the data represent (or are applicable to) the specific situation being assessed, the age of the data, the use of default data when specific data are not available, and data gaps. Monitoring levels of mercury in media (such as surface water, air) and biota (such as in fish, humans) can substantially reduce uncertainty compared to modelling these concentrations; however, uncertainty can also be present in these data due to biases, limitations of the sampling protocol, and other factors.

6. ASSESSMENT OF SPECIFIC EXPOSURE SCENARIOS

6.1   General considerations

341. Mercury "hot spots" are defined here as regions/locations where risks of higher contamination of the environment (air, soil, water or food sources) might occur following human (anthropogenic) activities, through either increased mercury loadings including the workplace or enhancement of the ecosystem's capability to methylate mercury species.

342. This chapter briefly addresses some of the most common sources of anthropogenic mercury releases: industrial activities (such as artisanal and small scale gold mining, energy production, chlor-alkali plants) and waste sites (domestic and industrial). The extent of regional contamination attributable to various sources greatly depends on the form of mercury emitted into the environment and other factors.

343. Direct spills into aquatic environments can cause significant local contamination that can lead to elevated population exposures and are therefore likely to be of greater local concern compared to contamination solely due to atmospheric mercury emissions, such as those occurring following the burning of coal. In the latter case, a smaller portion of mercury released is deposited locally, and the remainder reaches the global atmospheric pool and is transported over greater distances.

344. This chapter also discusses exposures that may occur through direct exposure to mercury following its use in dental amalgams and cultural or religious practices. Finally, human intervention such as reservoir impoundments and deforestation can disrupt the natural equilibrium of ecosystems and create conditions favourable for mercury methylation. These situations, where the productivity of aquatic environments and their methylation capacity are artificially boosted by excess loadings of external nutrients, are briefly discussed in Section 6.3.4

345. For the purpose of this document, distinction is made between two patterns of exposure to mercury related to the presence of "hot spots":

- Populations/subpopulations/groups living in areas impacted by anthropogenic aquatic mercury loading may be exposed to elevated levels of mercury primarily through fish consumption; therefore, exposures for these populations may be evaluated using the approaches presented in previous chapters;

- Workers in a contaminated worksite may be at risk of high mercury exposure through direct contact and/or the breathing of mercury vapours. These populations could be assessed following the approaches described in this chapter.

6.2   Occupational exposures

346. Mercury exposures can occur in various occupations where mercury is used in a production process (such as in chlor-alkali manufacturing and artisanal gold mining) or where mercury-containing products are made (such as in factories that make batteries, thermostats, thermometers, sphygmomanometers, other pressure gauges or measuring devices, or electric switches). Workers exposed to mercury are the primary focus of an occupational exposure assessment. However, workers can sometimes bring mercury into the home through contaminated clothing and shoes; therefore, exposures can also be experienced by the worker's families and neighbours. Hence, assessments of occupational exposure to mercury should take into account these other subpopulations as appropriate and feasible.

347. As a first step, a general screening workplace assessment can provide useful information regarding the potential exposures encountered in a particular workplace. Screening assessments help identify potential problems and priorities so that limited resources can be used efficiently. Using this approach, detailed risk analyses, which require greater resources, can be focused on areas, situations, or subpopulations where higher exposures are more likely to occur.

348. The screening assessment could include investigation about possible sources of exposure in the workplace (such as presence of elemental mercury or mercury compounds, handling of mercury, open containers of mercury, etc). The screening assessment could also include air monitoring using portable instruments (such as the LUMEX, Jerome, Nippon, and Genesis), which can detect elevated levels of mercury vapour in the workplace or other settings (Veiga and Baker, 2004).

349. The screening assessments can provide information regarding exposure, with and without technological devices. Such screenings could also include a health assessment, looking for the presence of acute and chronic symptoms, if appropriate and feasible.

350. Good general workplace assessments as well as individual assessments should be conducted in acceptance with (and collaboration with) the local population (workers, families, neighbours). Local knowledge adds important information to the assessment and constitutes a first step in the educational process regarding mercury issues. Such collaboration with local populations (or communities) can be formalized through the establishment of joint committees in the workplace and in the community. Such experiences exist in some countries of Latin and North America (Sass, 1993; Messing and de Grosbois, 2001).

6.2.1 Establishment of joint assessment committees

351. Occupational joint committees allow the discussion of aspects related to the work organization that may lead to elevated mercury exposures. Important issues for such committees may include ventilation, clean-up procedures, mercury storage containers and techniques, work shifts, rotation on the different tasks performed by the workers (some tasks being more at risk of exposure), personal protective equipment, and education related to mercury vapour exposure. Communal joint committees allow the discussion of aspects related to mercury exposure experienced by the community.

6.2.2 Workplace assessment

6.2.2.1 Exposure assessment

352. An initial characterization phase, using a data collection sheet such as the example provided in Appendix F, can provide qualitative information about the potential for exposure of workers to mercury vapour through inhalation, or other types of mercury exposures (such as through dermal contact or accidental ingestion). This example data collection sheet may be appropriate for some assessments. However, depending on the type of occupation, processes and other factors, an investigator could choose a different data collection sheet, as appropriate, to collect useful information about potential exposures. Data to collect could include, among others, general information on the workforce, workplace, tasks performed, number of workers performing these tasks, toxic substances used (frequency, quantities, etc.), ventilation, and safety procedures. Descriptive workplace assessments may provide evidence of potential high mercury exposure for the workers, their families, and the neighbourhood. Also, air sampling using appropriate automatic or manual devices can be used to estimate levels of mercury vapours in the workplace. Sampling and analyses of workers may be performed by collection of mercury with a three-section solid phase sampler, followed by analysis with an atomic adsorption spectrophotometer (NIOSH, 1980) or possibly by using other techniques.

6.2.2.2 Health assessment

353. Several symptoms reflecting an acute high exposure to mercury vapour as well as symptoms reflecting a chronic, usually lower, exposure could be recorded and monitored as part of a general exposure assessment profile (Pranjic et al., 2003; Urban et al., 2003; Lucchini et al., 2003; Gobba and Cavalleri, 2003; Veiga and Baker, 2004). Exposure and health assessments can be extended, with some

slight modifications, to workers' families and neighbours, to encompass the reality of the community. The potential for exposure, given the proximity, would be assessed instead of the tasks performed. As mentioned above, while families and neighbours do not necessarily work with mercury, they are potentially exposed given that they live with the workers or live nearby the source.

6.2.3   Worker assessment

6.2.3.1   Exposure assessment

354. As discussed in Chapter 3, blood and urine are the usual biomarkers of exposures to metallic mercury in the workplace or through other exposure scenarios. Blood mercury can be a good indicator of recent exposure to metallic mercury. However, blood mercury also reflects methylmercury exposure through dietary fish intake. Therefore, urine mercury level is a better biomarker of metallic mercury exposure.

6.2.3.2   Health assessment

355. Individual health assessments can be conducted. Health assessment questionnaires are discussed in Chapter 3 and an example is provided in Appendix B. Given the neurotoxic properties of mercury (Lucchini et al., 2003; Iregren et al., 2002; Veiga and Baker, 2004), this type of assessment should include neuro-functional impairments. However, it is important to keep in mind that elevated Hg in urine or other body tissues does not always correlate with findings of neurological tests. For example, adverse neurological symptoms could be present in an individual due to many other factors (viral diseases, head injury, etc).

6.2.4   Interventions to decrease occupational exposures

356. Conducting an exposure assessment in the workplace usually leads to increased awareness of possible health impacts to workers and other individuals due to occupational exposures to mercury. This increased awareness is the first step towards intervention plans to decrease occupational exposures (such as improved work practices to reduce the use and releases of mercury, better ventilation, better waste management, or use of respiratory protective equipment).

6.3   Examples of mercury "hot spots"

6.3.1   Artisanal gold mining

357. This section discusses mercury exposures due to artisanal gold mining and some considerations for assessing exposures for these communities. The discussion is largely based on information in reports by the United Nations Industrial Development Organization (Veiga and Baker, 2004), except where noted otherwise. More details and additional information on this topic can be obtained from these documents.

6.3.1.1   Overview of the mining process and potential exposures to mercury

358. For centuries, the capacity exhibited by mercury to form amalgamates with gold has led people to use mercury to extract the precious metal. Most modern large-scale commercial mining operations have adopted the cyanide leaching process to capture gold from raw ores. For this reason, this section will focus on mercury exposures due to artisanal small scale mining (ASM) and similar small-scale mining operations, where mercury is still used to form amalgams. Generally, this mining process involves the following: the wet ore (or mud or ore concentrate) is mixed with metallic (liquid) mercury; the mercury chemically binds with the gold or silver in the mud; the remaining mud is washed away leaving a mercury-gold (or mercury-silver) amalgam and contaminated tailings. The amalgam is then heated in various stages to release the mercury, with increasing levels of purity of the gold or silver.

359. ASM provides an important source of livelihood in rural regions of many developing countries. Although mercury use is illegal in many countries, amalgamation is the preferred method employed by

artisanal gold miners to ensure successful gold collection, but also results in widespread mercury pollution. UNIDO has estimated that the number of artisanal miners in 1998 was around 15 million workers in 55 countries and rising (UNEP Trade Report, 2006). This suggests that 80 to 100 million people worldwide have depended on this activity for their livelihood.

360. Artisanal miners are generally the most directly exposed, either through direct handling or by breathing the mercury vapours generated during the burning of the gold-mercury amalgam. However in many cases, heat separation of gold is performed in houses, or in other locations close to family members and other people, exposing these other people to elevated levels of gaseous mercury.

361. Vapour inhalation is generally the most important and dangerous pathway of exposure to metallic mercury for artisanal gold miners and their families. This is also true for gold dealers (and the people inhabiting in the vicinity of "gold shops"), who generally operate their business in more urban areas, purchasing amalgams from artisanal miners and/or refining gold pellets still containing appreciable amounts of mercury, often in closed rooms without proper ventilation.

362. Mercury releases by ASM occur as liquid mercury lost to aquatic environments during the amalgamation process or in waste discharges and vapours entering the atmosphere. It is difficult, even locally, to evaluate the amount of mercury emitted due to ASM. Mercury losses during ASM operations largely depend on the amalgamation technique used and on the way gold is separated from the amalgam, either through the use of nitric acid, retorting or burning in open pans. If retorts are not used with the heating process, the greatest part of the mercury introduced in the amalgamation process is released to the atmosphere. The most environmentally damaging approach to creating amalgamates is to place mercury on sluice boxes or spread it on the ground to be mixed with the raw ground ore to "attract" the gold, while losing a significant portion of this metallic mercury to rivers and lakes. A cleaner and more efficient approach consists of amalgamating only gravity concentrates, enabling extraction of up to 90 % of the initial gold content. Such amalgams have mercury contents of 20–40 %. Excess mercury can then be removed through centrifuging or using a piece of fabric (Hinton et al., 2003).

363. Mercury emissions from informal gold mining operations represent a serious environmental problem in developing countries. In the Amazon, from 70 to 170 t of Hg are discharged annually. The extent of biota contamination is also more widespread. Mercury must be rendered soluble and then converted into methylmercury in order to accumulate in the food-chain. Generally, it is considered that oxidation of mercury must occur to produce significant dissolution. Some authors (Meech et al., 1998) have examined the stability of mercury in the unoxidized aqueous elemental mercury in aquatic environments. Although methylation of these soluble species is not fully-understood, formation of such complexes in darkwater rivers must contribute to increased bioavailability.

364. Many of the available estimates on environmental mercury releases attributable to ASM are based on regional mercury sales, but these numbers do not take into account recycled mercury or mercury bought on alternative markets. Even given the uncertainties related to these estimates, ASM represents one of the most important sources of mercury emissions to the global environment attributable to human activities. Although disagreement exists on the regional scope of the environmental contamination attributable to ASM, local increases in the mercury levels in fish tissues have been reported in various studies on this topic. These increased mercury levels in the fish can lead to additional mercury exposures through fish consumption for people involved in ASM activities, as well as for other people who live in the vicinity of the ASM activities (Van Straaten, 2000a, 2000b; Yallouz et al., 2002; Limbong et al., 2003; Kambey et al., 2001; IDRC, 1999).

6.3.1.2   Assessment of workers' exposure

365. Given the way artisanal mining is conducted, exposures can be experienced by the workers and also by their families and neighbours. Therefore, assessment of exposure should take into account these subpopulations. As a first step, occupational and communal joint committees can be established. Exposures to workers and people in the community can be measured using biomonitoring approaches described in Chapter 3 of this document, or possibly by other approaches described in the UNIDO reports.

6.3.1.3   *Environmental considerations*

366. All mercury entering the environment from ASM is not necessarily incorporated in the food web of aquatic ecosystems. Metallic mercury is rather stable, nearly insoluble in water, and does not accumulate in aquatic biota unless it is first transformed, under certain environmental conditions, into a chemical form by living organisms (mercury methylation). The natural characteristics of regional environments might also arm the ecosystems against the intrusion of mercury pollution. For example, in Poconé (State of Mato Grosso), Brazil, a region impacted by ASM, lateritic soils, rich in hydrous ferric oxides, act as sponges adsorbing many mercury chemical species and reducing its availability to the biota (Veiga and Fernandes, 1990; Veiga, 1997). For such reasons, measurement of mercury levels in fish tissues (especially top predators) remains the best, easiest, and most integrative way to evaluate the real local impact of mercury contamination on the biota and to determine potential higher exposures of communities living in ASM areas.

367. Amalgam burning transforms some of the mercury-bound molecules into volatile elemental (reduced) mercury or reactive (oxidized) forms of mercury that are carried in the air, partially reaching the global atmospheric pool (long-range atmospheric transport). But part of this mercury might redeposit after short-range atmospheric transport and be readily available for methylation and bioaccumulation.

368. Metallic mercury is heavy and not easily transported through watersheds, but it becomes more mobile following its association to small particles or the formation of organic mercury species. The extent of regional transport of mercury will depend on local topography and hydrology and other factors (Meech et al., 1998).

6.3.2   Other industrial activities

369. Mercury is used in various manufacturing processes (measuring and control equipment such as thermometers and blood pressure measuring devices, batteries, lamps, switches, paint production, and the chlor-alkali industry). It is also indirectly emitted as by-products of other industrial activities such as metal refining and coal burning for heat and electricity generation. In the latter case, exposure of populations to residual mercury is diffuse and can be assessed using approaches such as those presented in Chapters 3, 4 and 5 of this document. Some important sources of anthropogenic releases of mercury include:

- Coal-fired power and heat production (largest single source to atmospheric emissions);
- Energy production from other carbon fossil fuels;
- Cement production (mercury in lime);
- Mining and other metallurgic activities involving the extraction and processing of virgin and recycled mineral materials, including production of gold, iron and steel, ferromanganese, zinc and other nonferrous metals.

370. Industrial use of mercury can result in different patterns of human exposures, including:

- Occupational exposure of workers in direct contact with either forms of mercury in their workplace. In these cases, assessment of workers' exposure to mercury can be addressed following the guidelines described earlier;
- Exposure of populations living near industrial settlements and impacted by releases to air or water and disposal of wastes (effluents, refuses, and landfills). For example, exposures can occur due to mercury releases from mercury-cell chlor-alkali plants. Such releases can lead to elevated mercury exposures for local communities. Therefore, local in-depth assessment could be considered a priority and evaluated following the guidelines described in this document.

6.3.3   Waste sites

371. Mercury-containing wastes generated through either industrial processes (pharmaceutical and car equipment plants, abandoned chlor-alkali plants, closed mining operations, etc.) or domestic use can be

discarded improperly, resulting in contamination of the local area and creation of a "mercury waste site". People who live near these waste sites can be exposed to elevated levels of mercury due to releases to the soil, air, and water bodies.

372. Mercury is present in a vast array of domestic products. In some cases, recycling programmes to retrieve these products before they are discarded with other refuse are cost-prohibitive, inefficient, or simply nonexistent in many communities. Many of these products are discarded to landfills or other disposal sites. Rain percolating through these dump piles can carry mercury residues into groundwater or downstream to rivers and lakes, resulting in contamination of water, sediments, and fish.

373. Sometimes significant releases can occur due to historical industrial or mining wastes. For example, in many parts of Latin America, thousands of tons of mercury are still present in the environment, due to past gold mining operations. Ancient stories of Spanish galleons carrying tons of gold looted from the natives of Central and South America back to Spain are well known. Mercury that left Spain for the "New World" is a less well-known story. The Spanish conquistadors used mercury to process gold before shipping it back to Spain. Parts of Mexico are still heavily contaminated from mercury that was brought from Spain in the 400-year period of Spanish rule (Pollution Probe, 2003). In other types of mining operations, mercury present in tailing piles as impurities can be leached by water infiltration to nearby watersheds. Similar situations also occur in gold mining operations using cyanide-leaching techniques instead of gold amalgamation. Here, dissolved cyanide reacts with traces of mercury in the tailing and acts as a carrier downstream (Boyle and Smith, 1994).

374. Populations consuming fish from the water bodies impacted by the presence of waste sites could be at risk of higher mercury exposure. Therefore, these populations may be a priority for local in-depth assessment.

375. UNEP Chemicals in collaboration with the Secretariat of the Basel Convention is in the process of developing a set of technical guidelines on the environmentally sound management of mercury waste. The guidelines will cover minimum standards on mercury waste minimization, collection, long term storage, treatment and disposal (SBC, 2007).

6.3.4   Other exposure scenarios

6.3.4.1   Dental amalgams

376. For more than a century, an inexpensive alloy of silver, copper, tin, and mercury has been used in dental practice as the preferred tooth-filling material; mercury constitutes 50 % of this material. Mercury released from amalgam fillings can take several forms: elemental mercury vapour, metallic ions, and/or fine particles. Of the mercury vapour, some is exhaled before it further penetrates the respiratory tract, some is inhaled into the lungs and absorbed into the blood, some is retained in the vapour form in the saliva and swallowed together with amalgam particles, and some is oxidized to an ionic form and spat from the mouth or swallowed. Of that portion swallowed, only a small fraction is expected to be absorbed through the gastrointestinal tract. Results from human studies and experiments in laboratory animals are controversial regarding contribution to mercury body burden in humans who have amalgam fillings (WHO, 2003; Wiener and Nylander, 1995; Yip et al., 2003). According to Barregard et al. (1995), several factors can explain individual variation in mercury intake from dental amalgams. Gum chewing habits and bruxism (a rhythmic or spasmodic grinding of the teeth other than chewing and typically occurring during sleep) are among the most important factors to explain individual differences. Average daily absorption of mercury ranges between 3 and 17 μg, depending on the number of amalgam surfaces in a person's mouth (UNEP, 2002).

377. Dental amalgams are the primary source of exposure to inorganic mercury for most people who have mercury-containing dental fillings. Moreover, many workers in dental offices (such as dentists, dental hygienists) are exposed to mercury through the production and use of mercury fillings. There is clear evidence in the scientific literature of elevated body burden of mercury in dentists and dental hygienists (Kostyniak, 1998). In fact, in a recent study Ritchie et al. (2002) showed that dentists had, on average, urinary mercury concentrations over four times that of control subjects. Exposures for dental workers can be assessed following the approach described in Chapter 3.

6.3.4.2   *Cultural/Religious/medical use of mercury*

378. Historic records suggest signs of mercury use by ancient Chinese and Hindu civilizations. Archaeologists found traces of mercury in an Egyptian tomb dating from 1500 BC. The Egyptians and Chinese may have used mercury ore as pigments in paints, and many civilizations had beliefs about mystical properties attributed to mercury. Alchemists tried for ages to transmute base metals into gold through the action of mercury. Today, elemental and inorganic (oxidized) mercury are still used in some populations for cultural, religious, or ritualistic purposes, in cosmetics, or as folk medicine (UNEP, 2002).

379. **Cosmetic treatments**. Examining 38 different skin-lightening creams, Al-Sahel and Al-Doush (1997) found that 45 % contained mercury levels above the US Food and Drug Administration (US FDA) limit of 1 mg/kg; two of the products had mercury concentrations over 900 mg/kg. Such uses have resulted in reports of toxicity in a number of cases (Kang-Yum and Oransky, 1992; Dyall-Smith and Scurry, 1990). Most of these skin lightening creams are being sold in West Africa and in Asia (Mercury Policy Project, 2007).

380. **Folk medicine and Ayurvedic Medicine**. Mercury is thought to exhibit healing properties and is sometimes used as an antiseptic, in herbal remedies, or even as a treatment for diseases such as syphilis. Mercuric chloride, mercuric oxide, mercuric iodide, mercurous acetate, and mercurous chloride also are or have been used for their antiseptic, bactericidal, fungicidal, diuretic, and/or cathartic properties.

381. Commercially produced herbal ball preparations used in traditional Chinese medicine can contain mercury. Adult dosage for traditional Chinese medicine is two balls daily, resulting in daily intake levels of up to 1.2 g of mercury (Kang-Yum and Oransky, 1992).

382. **Cultural/religious practices**. In some cultures, mercury is believed to chase away evil spirits when placed on the walls of houses. Elsewhere, it is thought that mercury-based talismans can bring good luck. Obscure religious practices involving the use of mercury are known, but the topic remains poorly documented (US EPA, 2002).

383. Metallic mercury is sold, in some regions, under the name "azogue" (sometimes called botanicas). Some of the uses of this "azogue" include, among others, mixing the mercury in bath water or perfume, wearing it in vials as jewellery, placing it in devotional candles, sprinkling it on floors of houses or automobiles, applying it directly to the skin or in some cases injecting it. This mercury is also seen as a "good humour" product, bringing smoothness of movement to merengue dancers in the Caribbean.

384. Even though scientific evaluations of the different medical/ritualistic/traditional uses of mercury are limited, it is undoubted that such practices may lead to elevated mercury exposures for some subpopulations. Difficulties could be expected while trying to assemble representative samples within these subpopulations, considering the relative secrecy surrounding many of these practices. If feasible, such samples should be constructed and health assessments conducted. However, assessment of exposure may then only be accurately estimated through human tissue measurements (such as hair, urine, and blood) using approaches described in Chapter 3.

6.3.4.3   *Deforestation*

385. The impacts of large-scale deforestation on ecosystems are numerous. In tropical environments, the organic-rich layer of soils, naturally held in place by tree roots, is often eroded during seasonal rains. Mercury accumulated in these soils due to atmospheric deposition is also flushed to rivers and lakes. According to some authors (Roulet et al., 2000; Carmouze et al., 2001), this source of mercury loading to aquatic ecosystems might be of greater importance in some regions than ASM activities. For example, studies in the Brazilian Amazon identified situations of high mercury exposure through fish consumption for some populations living far from gold mining areas in the Tapajos River drainage basin.

386. Trees and other vegetation contain mercury. For example, in investigations in the USA, the mercury content of litter and green vegetation from seven locations in the USA ranged from 0.01 – 0.07 mg Hg/kg dry weight (Friedly et al., 2001). This mercury in vegetation originates from both naturally present mercury and mercury deposited from anthropogenic emissions (COWI, 2002). Trees (especially needles and leaves) absorb

mercury from the atmosphere over time (Friedly et al., 2001). Fire is the most primitive method of deforestation. It is also used to control agricultural pests. Forest fires mobilize Hg contained in biomass and redistribute it into the atmosphere, either as vapour or attached to particulates. Currently, with the high rate of deforestation by fire in developing countries, mercury emissions derived from wood combustion are significant.

387. The amount of mercury emitted annually by deforestation in the Amazon has been estimated at between 0.78 kg/km² and 1.76 kg/km² (Lacerda, 1995; Veiga et al, 1994). Estimates depend on vegetation biomass, the area burned and mercury levels in plants and organic matter (ranging from 0.02–0.3 mg/kg). Regardless of differences in emission estimates, the significance of the forest fire as a vector for mercury emissions in the Amazon region is indisputable. Concentrations up to 1 g of Hg per kg were measured in smoke particles smaller than 2.5 μm in a forest fire in Amazon (Kaufman et al, 1992). Through analysis of aerosol particles, Artaxo et al. (2000) estimated that about 30% of the mercury in atmospheric particles in the Amazon region might be associated with biomass burning and 63% from gold mining (Veiga and Baker, 2004). Populations consuming fish from water bodies impacted by deforestation could be at risk of higher mercury exposures. Therefore, these populations could be a priority for local in-depth assessments.

6.3.4.4   *Vaccines*

388. Thimerosal is used as a preservative in vaccines (such as DTP, hepatitis B, and Hib), mostly in developing countries, to protect against bacterial contamination; this preservative contains nearly 50 % ethylmercury. Thimerosal has been used since the 1930s in the manufacture of some vaccines and other medical products (WHO, July 2006).

389. Once in the body, thimerosal is metabolized to ethylmercury and thiosalicylate. Half life of ethyl mercury is only 6 days (95% CI: 3-10 days) compared with 40-50 days for methylmercury. It is actively excreted into the intestinal tract and not accumulated in the body. It rapidly converts to inorganic mercury (that is less toxic to the brain than ethyl or methylmercury). The United States and other industrialized countries have decreased or eliminated the use of thimerosal from many vaccines. However, thimerosal still exists in some vaccines used in various parts of the world, in particular in settings where accessibility and cost require the availability of multidose vials of vaccines, such as in developing countries. Therefore, when assessing exposures to mercury for a population or subpopulation, this possible source of exposure should be considered (WHO, 2003; UNEP, 2002).

390. Upon review of the current epidemiological evidence and pharmacokinetic profile of thimerosal, the Global Advisory Committee on Vaccine Safety concluded that there is currently no evidence of mercury toxicity in infants, children, or adults exposed to thimerosal in vaccines. It also concluded that there is no reason to change current immunization practices with thiomersal-containing vaccines on the grounds of safety. The safety of thimerosal-containing vaccines is reviewed at regular intervals. In the meantime, the available evidence warrants the recommendation that current WHO immunization policy with respect to thiomersal-containing vaccines should not be changed (WHO, August 2008).

6.3.4.5   *Reservoirs*

391. Most studies dealing with the environmental impacts of reservoir creation focus on the fact that flooding terrestrial ecosystems leads to increased mercury levels in fish species living in the newly created reservoirs (Lucotte et al., 1999; Verdon et al., 1991; Rogers et al., 1995; Morrison and Therien, 1995; Kehrig et al., 1998; Park and Curtis, 1997; Porvari, 1998; Bermudez et al., 1999). In many cases, these increases result in mercury levels in fish that may be unsafe for regular human consumption. The creation of reservoirs favours the recycling of the mercury burden accumulated for years in soils prior to flooding. Reservoirs also act as efficient incubators for mercury methylation. Nutrients and particles leached from soils through the flooding process increase the biological productivity of these artificial aquatic ecosystems, including higher activities of bacterial consortiums involved in the transformation of mercury into bioavailable methylmercury. Furthermore, drawdown zones, periodically flooded and dried out, typically represent environments where efficient mercury methylation can occur. Depending on the type of environment impacted by flooding and on the fish species considered, increased mercury levels in fish tissues are observed for 15–40 years following the initial flooding episode. Populations regularly consuming fish from young reservoirs could be exposed to elevated levels of mercury and could therefore be priority for further assessment.

7. RISK MANAGEMENT OF METHYLMERCURY IN FISH

392. This chapter, sourced from WHO, is intended to provide risk managers with a cost-effective approach for identifying populations at risk to methylmercury in fish. Risk managers have the responsibility to reduce methylmercury exposures while maintaining the health and nutritional benefits associated with fish consumption. Fish play an important role in the diets of most of the world's population. In addition, the risk manager needs to keep the risk of methylmercury in the perspective of broader social, cultural and economic considerations.

393. A decision-tree approach has been developed to assist risk managers in the identification of specific populations and conditions that may lead to unacceptable exposure to methylmercury. Using both biomonitoring (Chapter 3) and tiered exposure assessments (Chapter 4), the decision tree is a risk management tool that provides a rational and cost-effective approach for characterizing risk for susceptible populations. Other factors normally associated with risk evaluation are also discussed. Finally, possible management options are presented for instances where the need to reduce exposure to methylmercury has been established. In particular, the role of risk communication in public education is emphasized.

7.1   Risk manager's decision tree

394. This decision tree has been designed to provide a simple road map for risk managers in order to assess whether or not methylmercury in fish poses an unacceptable risk to their population. Before entering the decision tree, the risk manager should undertake preliminary hazard identification. Clearly, if fish are consumed in very low quantities, there is no need to proceed. However, it there is a perceived risk, the risk manager should initiate a risk assessment using the decision tree as guidance (Figure 3 - Risk manager's decision tree - Hazard identification and risk assessment).
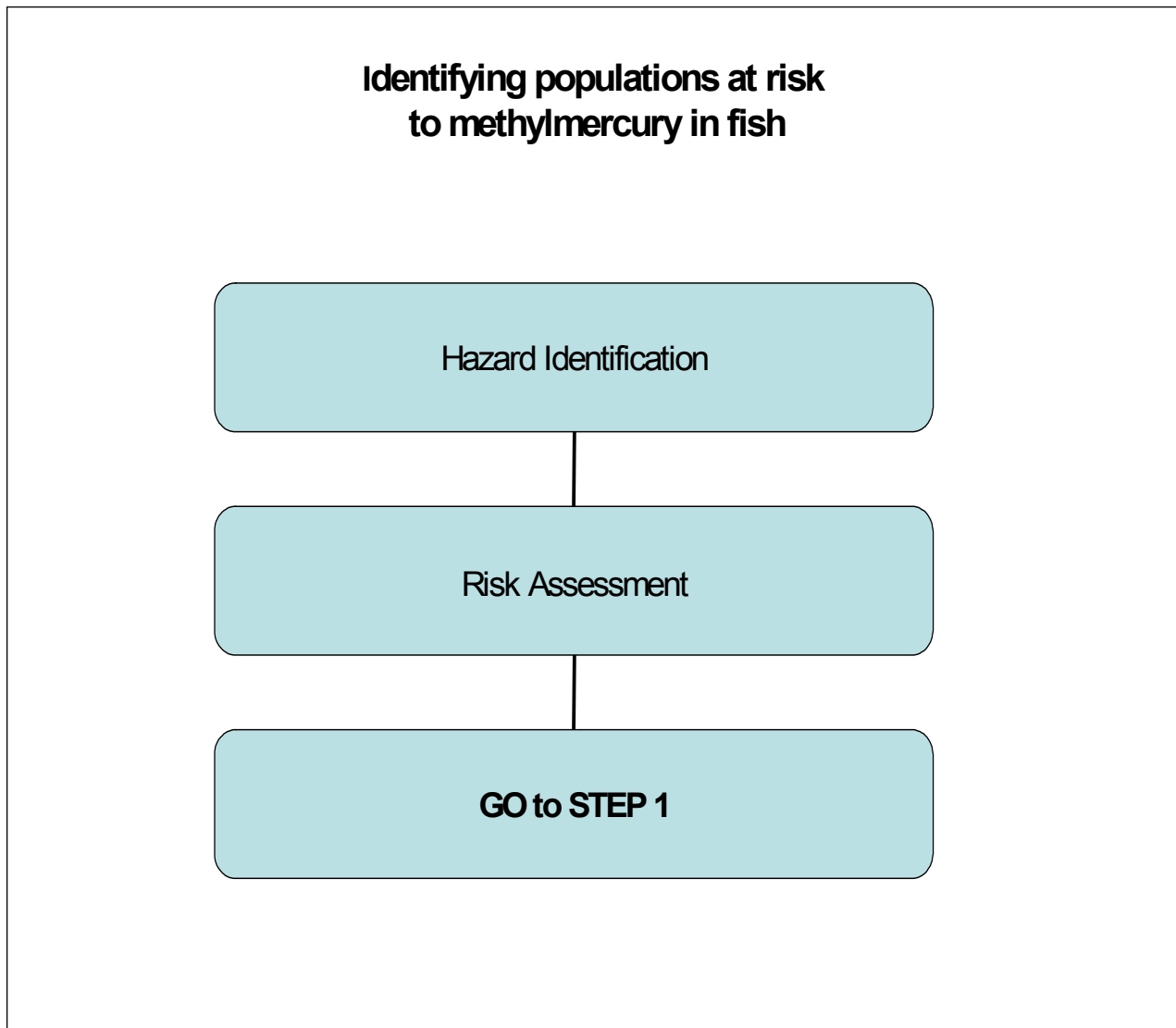
Figure 3   Risk Manager's Decision Tree: Hazard identification and risk assessment

395. It is recognized that in developing countries, resources for risk assessment are limited. Consequently, the decision tree is structured to use the most cost-effective approach to answer the basic safety question. When an exposure estimate is below the reference level, the risk manager is instructed that "No further action is required". If not, a more refined estimate of exposure should be obtained by proceeding to the next step. As conditions in countries vary dramatically, this decision tree should be viewed only as providing guidance. Risk managers may exit this process at any time they feel a satisfactory solution has been achieved.

396. **Step 1** - In the management of risk from methylmercury in fish, the first step is the evaluation of the importance of fish in the diet (Figure 4 - Risk manager's decision tree: Step 1 - Determine importance of fish in the diet). This may also include other seafood, particularly marine mammals, if these are consumed by the target population. Because fish are the main pathways for human exposure to methylmercury, two susceptible groups should be considered at risk in terms of fish consumption: those who are more sensitive to effects of methylmercury and those who are exposed to higher levels of methylmercury. The first group includes the fetus and young children, due to the sensitivity of the developing nervous system. This implicitly also includes women of child-bearing age. The second group consists of high fish consumers,

particularly of predatory species. This latter group may need to be assessed using methods described in Chapter 4.
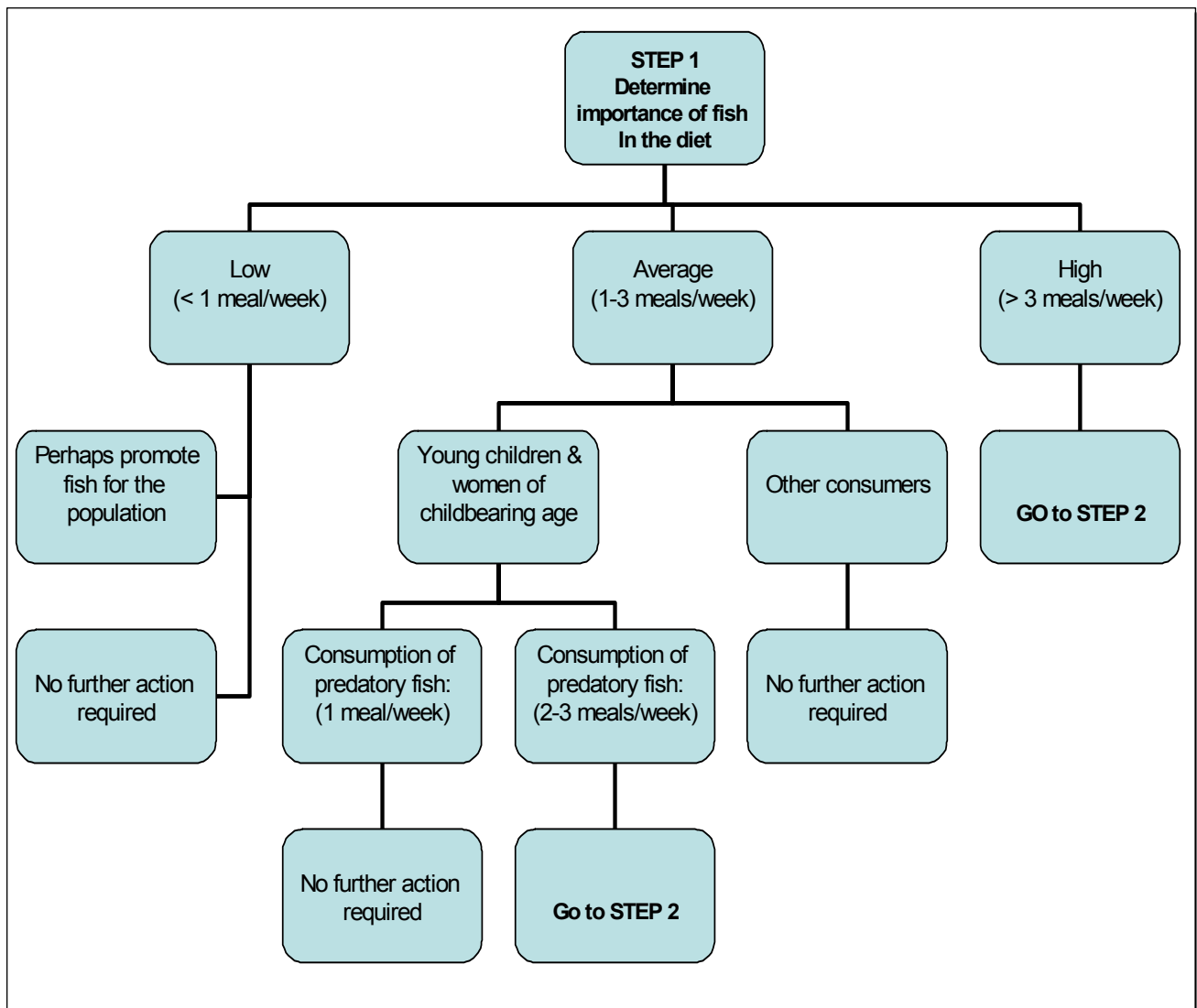
Figure 4   Risk Manager's Decision Tree:
Step 1- Determine importance of fish in the diet

397. At the initial phase, a survey should be conducted in order to identify weekly frequency of fish consumption among different subgroups of the population. A representative number of individuals of both sexes and of different ages should be included among the participants. From the results of this survey, the population could be then divided into three groups: low (less than one meal per week), average (between 1 and 3 meals per week) and high fish and seafood consumers (more than 3 meals per week). For consumers of less than one fish meal per week, no further action regarding exposure to methylmercury is required, and risk managers could even consider the promotion of fish consumption for this group. Average fish consumers are unlikely to be at risk regarding exposure to methylmercury provided that their consumption of fish identified as having a high mercury content is lower than one meal per week. However, an exposure assessment should be considered for average fish consumers, especially young children and women of child-bearing age, if at least one of their weekly meals consists of such fish (or particularly, a marine mammal). Exposure assessment should also be conducted for all groups consuming a high number of fish meals (> 3 meals /week).

398. **Step 2** - Before undertaking a comprehensive exposure assessment, a relatively simple biomonitoring survey can be used to estimate exposure levels to methylmercury (Figure 5 - Risk manager's decision tree: Step 2 - Determine mercury levels in composite hair samples).   This should be targeted at young children and women of child-bearing age consuming one or more meals containing high mercury fish per week, as well as likely high fish consumers. Exposure can be assessed by analysis of total mercury concentrations in hair, which is a non-invasive, relatively inexpensive and accurate procedure for determining methylmercury in fish-eating groups. When financial resources are limited, composite samples consisting of hair of several individuals from each of the above three groups could be initially used instead of individual samples. Average mercury concentrations in composite hair samples from each group should be compared with reference values, such as 2µg/g (WHO/IPCS, 1990) or national references values. Chapter 3 provides guidance in the collection and analysis of hair samples.
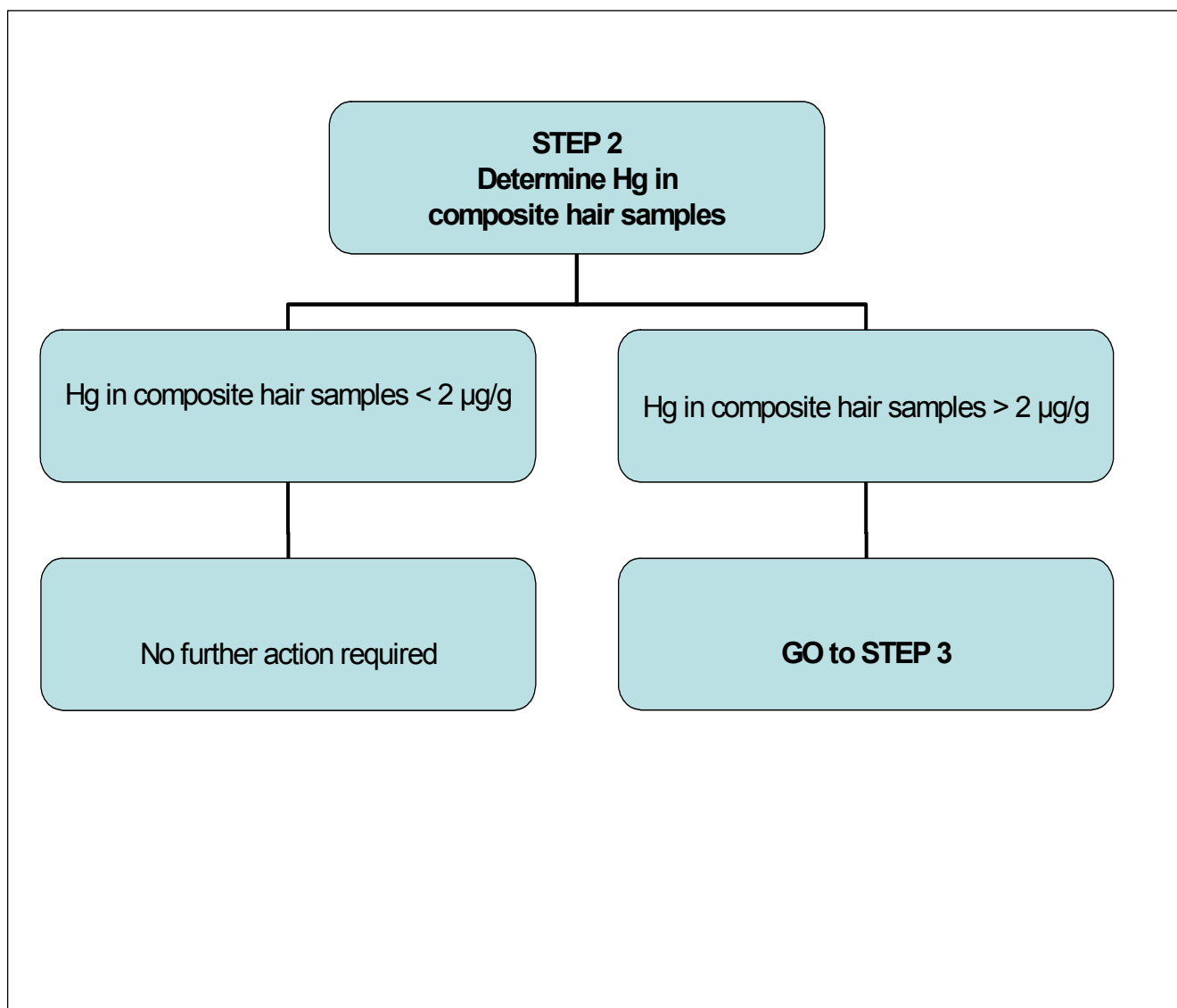
Figure 5   Risk Manager's Decision Tree:
Step 2 - Determine mercury level in composite hair samples

399. **Step 3** - If average mercury concentrations in composite hair samples are much lower than reference values, no further action is required. However, if average mercury concentrations in composite samples from one or more groups exceeds the reference levels (such as 2µg/g) for total mercury or if the margin of

safety is relatively narrow, it may be appropriate to analyse hair samples from each individual to gain a better understanding of the distribution of exposures (Figure 6- Risk manager's decision tree: Step 3 - Determine mercury levels in individual hair samples).
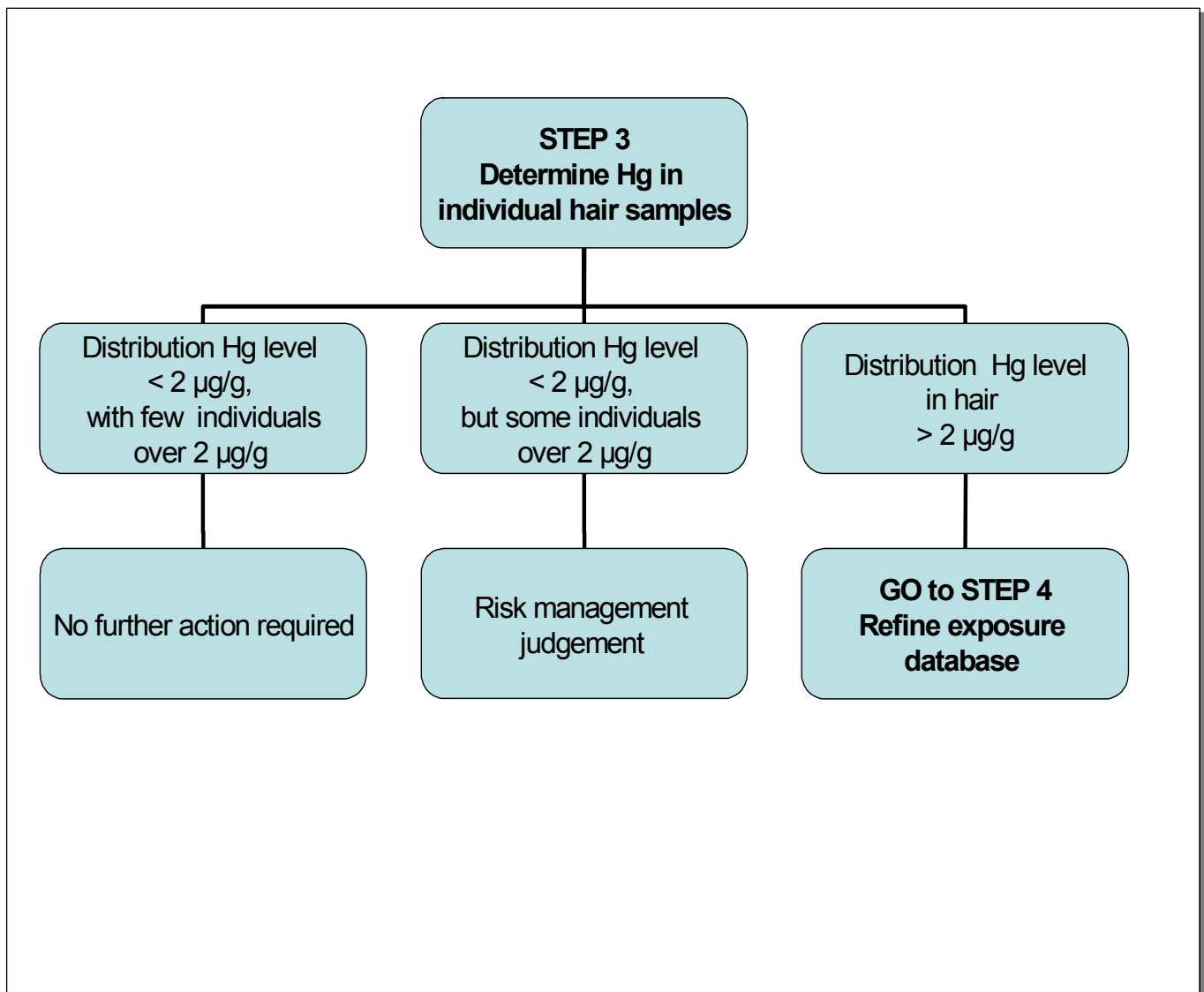
Figure 6   Risk Manager's Decision Tree:
        Step 3 - Determine mercury levels in individual hair samples

400. From the values of total mercury in individual hair samples, a histogram of the frequency of distribution of total mercury levels in hair of young children and women of child-bearing age consuming one or more meals containing fish with high contents of mercury per week, and of high fish consumers can be built. If the frequency of distribution of total mercury in hair in a given group shows a significant proportion of individuals above the reference value, this is an indication that this group or an important fraction of it is potentially at-risk. In this case, further information may be needed on consumption patterns for the potentially at-risk group in order to develop more precise risk management interventions.

401. **Step 4** - Using a tiered approach, exposure to methylmercury due to fish consumption can be estimated for individuals of each potentially at-risk group taking into account dietary habits and methylmercury levels in fish consumed (Figure 7 - Risk manager's decision tree: Step 4 - Refine exposure

databases). The characterization of consumption habits should include species, frequency of the meals and the average portion of each species consumed during a given time. For locally caught fish, additional information on fish size and site of collection should be provided.   Consumers' body weight should also be noted to allow a comparison of their estimated exposures to methylmercury to the reference level (such as the JECFA PTWI).   Detailed guidance for developing tiered approaches for estimating exposure is given in Chapter 4. Because of the cost and time of conducting new studies, however, making the best use of available data is emphasized.
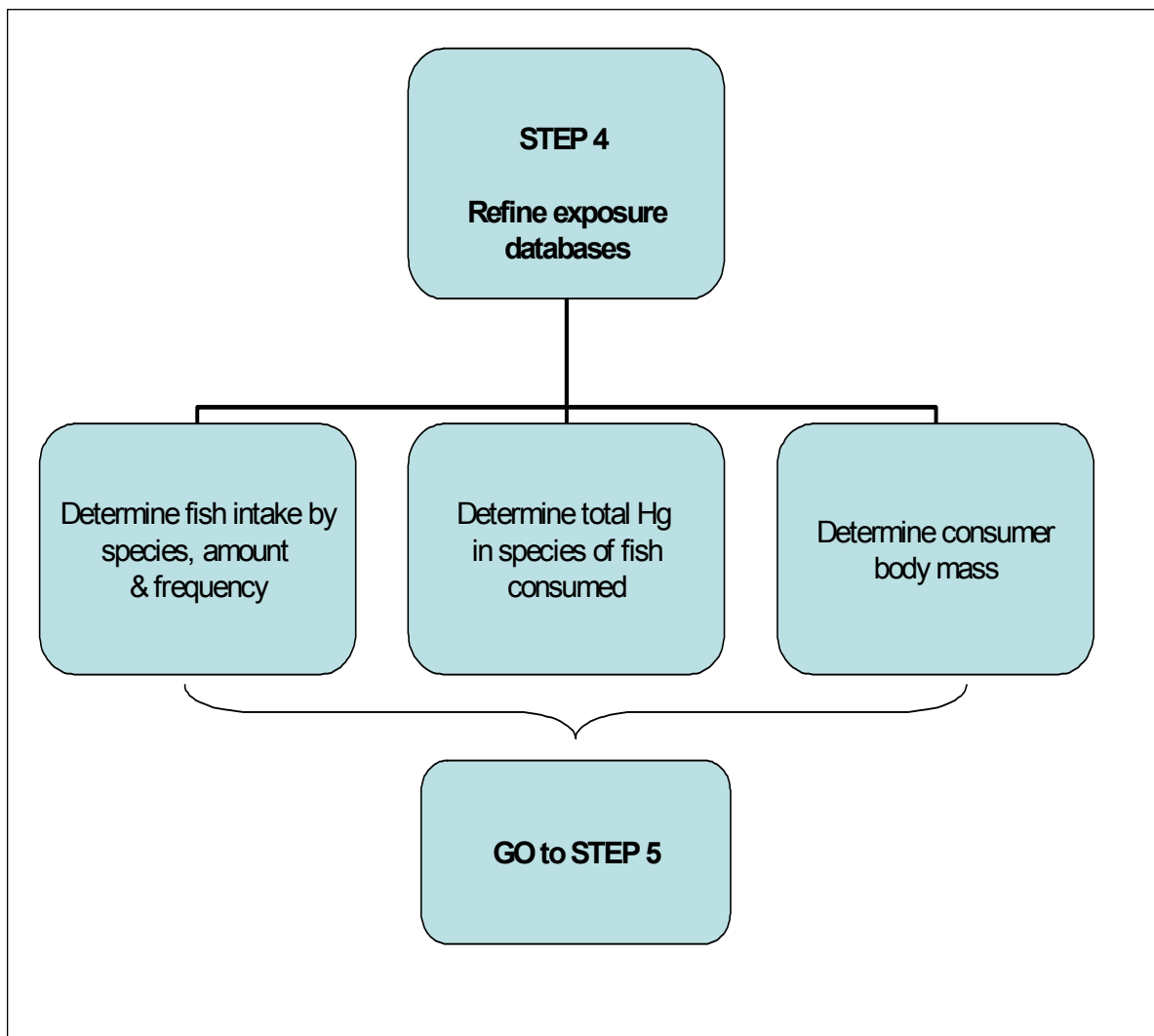
Figure 7   Risk Manager's Decision Tree:
Step 4 - Refine exposure databases

402. Mercury levels should be determined in fish identified in the dietary habits survey, including locally harvested, market and canned fish. As a practical matter, total mercury should be analysed instead of methylmercury. Low-cost semi-quantitative methods are available (Yallouz et al., 2000) and could be used at this stage for a general screening of total mercury levels in fish. Additionally, composite samples of muscle of fish of comparable size and from a same species could be used to reduce the number of samples. Analyses should be performed in composite samples of three size classes (small, medium and large individuals), defined according to consumption patterns, for each target species of fish.

403. **Step 5** - Estimates of mercury exposure from fish can be calculated by multiplying the fish consumption data by average mercury content in fish ([Figure](#)8 - Risk manager's decision tree - Step 5 Calculate mercury exposure). Intake values can then be calculated on a weekly basis and per kilogram of body weight, and can be compared to the PTWI of 1.6 µg/kg bw/week for children up to about 17 years of age and women of child-bearing age, or up to approximately twice this value for other adults. If distributions of consumption and/or concentration levels are available, computer programmes are available that can produce so-called "probabilistic" assessments of exposure. While no more accurate that point calculations, (such the mean or the 97.5th percentile), distribution of exposures can provide a more complete picture of the exposed population.


```
                    ┌─────────────────────────┐
                    │         STEP 5          │
                    │   Calculate Hg exposure │
                    └─────────────────────────┘

  ┌──────────────────────┐              ┌──────────────────────┐
  │      Hg intake       │              │      Hg intake       │
  │                      │              │                      │
  │  < 1.6 µg/kg bw/week*│              │  > 1.6 µg/kg bw/week*│
  │  < 3.2 µg/kg bw/week**│             │  > 3.2 µg/kg bw/week**│
  └──────────────────────┘              └──────────────────────┘

  ┌──────────────────────┐              ┌──────────────────────┐
  │                      │              │        STEP 6        │
  │ No further action    │              │  Determine MeHg in   │
  │ required             │              │ composite fish samples│
  └──────────────────────┘              └──────────────────────┘

                                        ┌──────────────────────┐
                                        │                      │
                                        │     GO to STEP 7     │
                                        │                      │
                                        └──────────────────────┘

  *  Valid for women of childbearing
  age and young children

  ** Valid for other adults
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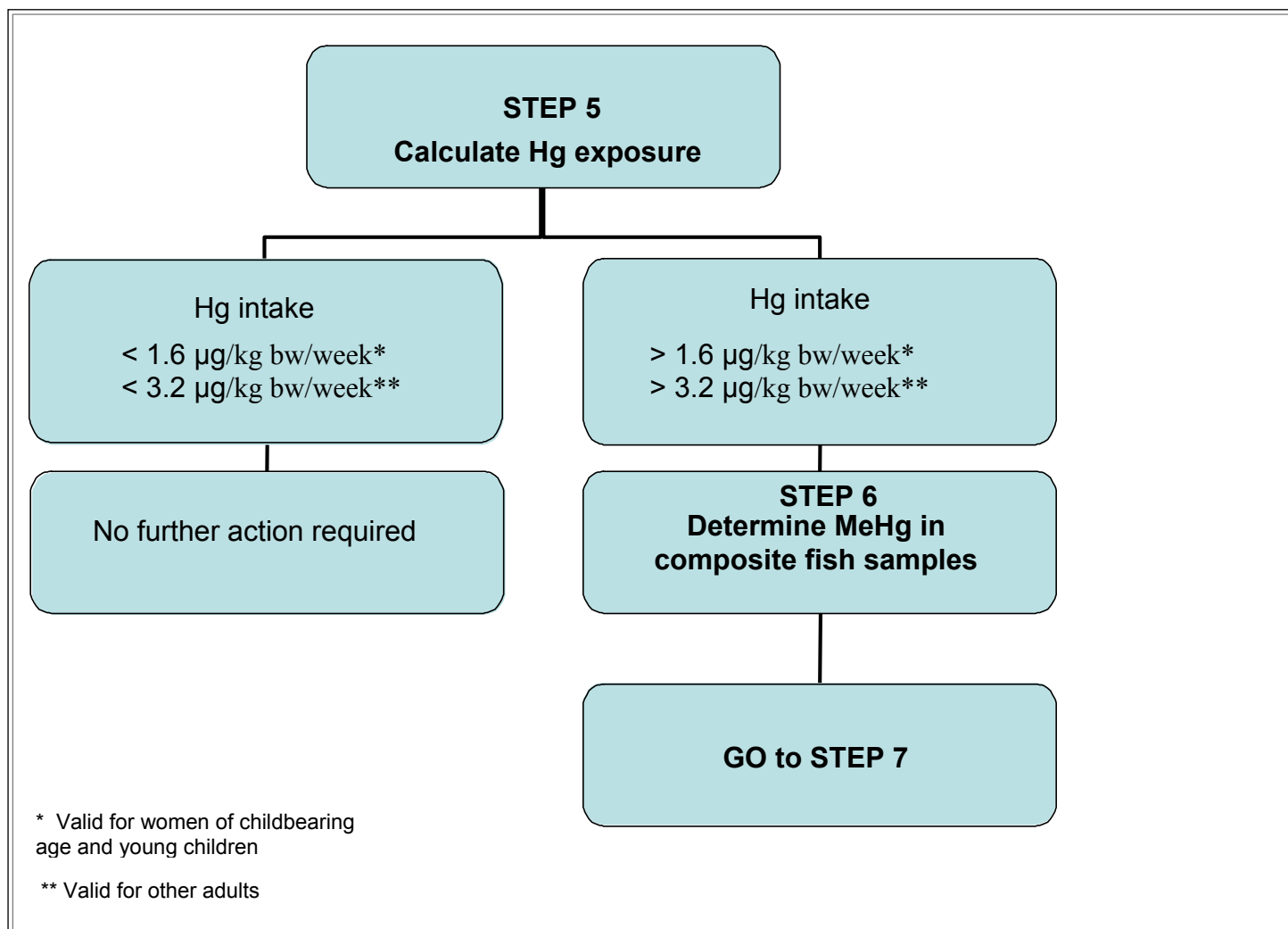
Figure 8   Risk Manager's Decision Tree:
         Step 5 - Calculate mercury exposure and
         Step 6 - Determine methylmercury in composite fish samples

404. If the average methylmercury intake is lower than the PTWI, and if the proportion of individuals exceeding the PTWI is relatively small, no further action is required. Otherwise, the population is actually at-risk and risk management interventions should be considered. However, if the consumption consists of non-predatory, freshwater or aquacultured fish that have been raised in polluted waters, a more refined estimation of methylmercury exposure can be useful.

405. **Step 6** - Measuring the actual ratio of methylmercury to total mercury in some fish can improve exposure estimates in certain cases (Figure 8 - Risk manager's decision tree: Step 6 - Determine methylmercury levels in composite fish samples). Given that the proportion of methylmercury to total mercury in some fish species can be lower than 30%, assuming that all mercury in all species of fish is in the methylated form may be too conservative. This is more true for some freshwater fish, non-predatory fish and aquaculture fish, but less so for predatory marine fish. Therefore, composite samples of the fish species consumed can be analysed to determine the ratio of methylmercury to total mercury.

406. **Step 7** - Using the ratio of methylmercury to total mercury from above, the best estimate of methylmercury exposure can be calculated (Figure 9- Risk manager's decision tree: Step 7 - Calculate methylmercury exposure). If the average methylmercury intake is still higher than the PTWI, or if the proportion of individuals exceeding the PTWI is still relatively high, the methylmercury must now be considered a risk management issue.
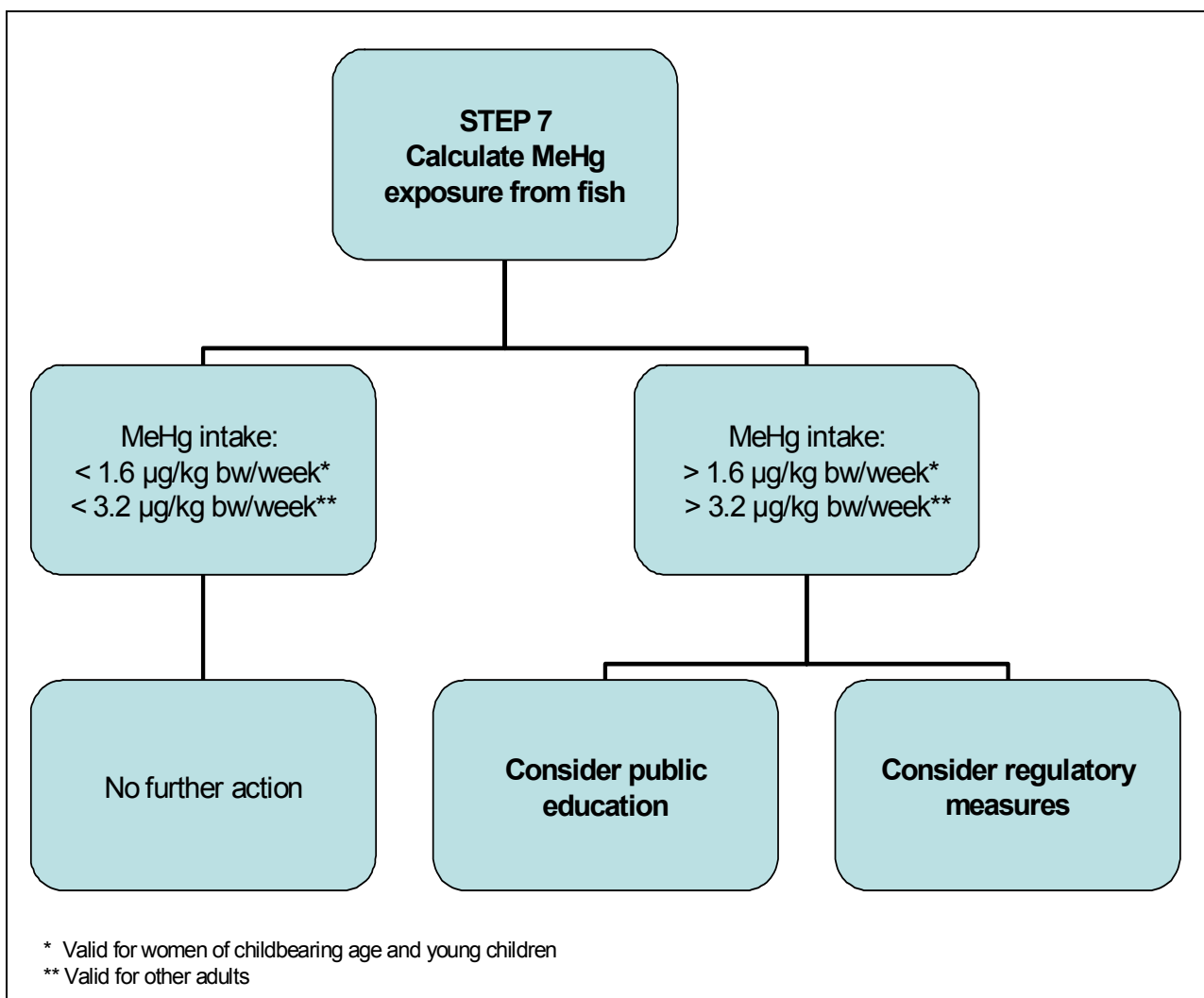

Figure 9   *Risk Manager's Decision Tree:*
                   Step 7- Calculate methylmercury exposure from fish

7.2   Risk evaluation

407. If methylmercury is a risk management issue, the risk manager needs to place the risk in a societal context. For mercury in fish, this includes consideration of several factors, including subpopulation at risk, nutritional benefits of fish consumption, available replacement foods and socio-economic impacts. In completing the decision tree, essential information on the subgroups at risk can be obtained to facilitate risk management. For example, fish consumption patterns by women who are pregnant or of child-bearing age is an essential piece of information for public education. Also information on other at-risk groups, such as ethnic groups, subsistence fishers and other groups with frequent or high consumption of mercury-containing fish, should be available. However, one of the most important considerations is the contribution of fish to health and nutrition.

7.2.1   Health and nutritional benefits of fish consumption

408. Fish have provided humanity with an essential food source since time immemorial and the vigour and growth of coastal populations around the world is a testimony to the value and wholesomeness of fish as a human food. Scientific studies have confirmed the superiority of fish as a protein source. Indices of the amino acid profile and ability to support growth are higher for fish proteins than for beef, pork, chicken and milk proteins (TERA and USEPA, 1999). The fatty acid profile of fish also differs significantly from other protein sources. Approximately 50% of the fatty acids in lean fish and 25% in fatty fish are polyunsaturated fatty acids (PUFAs). The proportion of saturated fatty acids, at about 25%, tends to be relatively constant across fish species. In contrast, in beef only 4-10% of fatty acids are polyunsaturated and 40-45% are saturated. Fish are a good source of niacin and vitamin B12, and, in general, are better sources of vitamins D and A than beef, pork or chicken (TERA and USEPA, 1999). Fish also provide dietary sources for calcium and a range of micronutrients, including selenium, iodine, taurine, fluorine, copper and zinc.

409. Fish are a particularly rich source of long-chain polyunsaturated omega-3 fatty acids (n-3 PUFAs), specifically docosahexaenoic acid (DHA) and eicosahexanoic acid (EPA). EPA and DHA found in the lipids from fish and other seafood are ten to 100 times more concentrated than in fats of terrestrial origin. These n-3 PUFAs may protect against several adverse health effects. There is increasing evidence, for example, that DHA and EPA long-chain fatty acids have cardiovascular health benefits. DHA is also a major component of the retina. In addition, DHA and arachidonic acid (AA), an omega-6 PUFA found in plants, eggs or the dietary fats from grain-fed animals, are essential for the development of the central nervous system in mammals (SACN, 2004; TERA and USEPA, 1999). During the last trimester of pregnancy, fetal requirements for DHA and AA are very high because of the rapid synthesis of brain tissue, and the main source of the DHA and AA that accumulates in the brain is drawn from the maternal circulation. Human breast milk, in turn, supplies DHA to newborn infants. In pre-term and low-birth-weight babies, DHA deficiency has been associated with visual impairment and delayed cognitive development. There is some evidence that increased maternal intake of omega-3 fatty acids, via consumption of fish or fish oil supplements, may prolong gestation in populations where shorter gestation periods and lower birth weights are observed, possibly due to lower background intake of omega-3 and fish (SACN, 2004; Olsen et al., 1986).

410. Overall, a number of studies offer strong evidence to support the hypothesis that fish or fish oil consumption reduces all-cause mortality and various cardiovascular disease outcomes (Wang et al., 2004). Collectively, the data on cardiovascular disease support the recommendation for consumption of at least two servings of fish per week (particularly fatty fish), but a significantly lower risk of death from coronary heart disease can be observed with a single weekly intake (Kris-Etherton et al., 2002; Hu et al., 2002). The Scientific Advisory Committee on Nutrition (SACN) of the United Kingdom and the US Dietary Guidelines Advisory Committee (DGAC) Report endorse the general recommendation to eat at least two portions of fish per week, of which one should be fatty, and agree that this recommendation should also apply to pregnant women (SACN, 2004; DGAC, 2005). Consuming even small quantities of fish can reduce chances of myocardial infarction and coronary heart disease mortality risk (Konig et al., 2005). Depending on the type of fish consumed, 227 grams (170 g cooked weight) per week will provide an omega-3 intake of EPA and DHA of about 200-500 mg/day; the amount recommended by the DGAC (2005).

411. Fish play an important role in contributing to the health and nutrition of most of the world's population. Fish are economically important at the local, national and international levels. Consequently, the risk manager needs to keep the risk of methylmercury (and other contaminants) in the perspective of broader health benefits, social, cultural and economic considerations. The place for bringing these elements together is the risk evaluation.

7.2.2   Other risk evaluation considerations

412. The risk manager needs to characterize the role of fish in the population of concern. Fish may play a large role in the cultural and socioe-conomic fabric of the country or region. The risk manager needs to evaluate whether there are alternative foods that are readily available, affordable and of equal nutritional benefit. There may be other risks associated with alternative fish or foods that should be identified and evaluated. In addition to methylmercury, there may also be pathogens (such as *Vibrio parahaemolyticus* and *Listeria spp.*), parasites (such as trematodes and nematodes) and toxins (e.g. histamine, ciguatera) that can pose localized risk to the population or subgroups (WHO, 1999). Fish are also known to contain variable levels of other chemical contaminants (such as pesticide residues and lead). Available data indicate that levels of lead also increase with the age and size of the fish (JECFA, 2000). Persistent organic pollutants (POPs), such as, dioxins and dioxin-like polychlorinated biphenyls (PCBs), may pose risks to the developing fetus because of their ability to bind to hormone receptors (JECFA, 2000). Similarly to methylmercury, POPs can biomagnify up the food-chain; however POPs are lipophilic and tend to accumulate in the adipose tissue. Thus, whereas methylmercury does not specifically accumulate in fatty fish, higher levels of POPs may be found in fatty fish, such as salmon, mackerel and herring. These inter-species differences in accumulation, together with temporal and geographical variations in methylmercury and POPs bioavailability, further complicate a comparison and joint evaluation of risk of these contaminants in fish. The management options for these potential hazards will require specific control measures, according to their nature. There is currently no established methodology for conducting a comprehensive analysis of the health risks and benefits of fish consumption (SACN, 2004). The general approach taken by most countries is to develop guidelines for fish consumption advice for the general population and/or sensitive subgroups that, if at risk, allow them to minimize exposure to contaminants while ensuring health and nutritional benefits.

7.3   Option selection

413. In general, there are two options to reduce the public's exposure to methylmercury in fish. One makes use of communication tools to influence fish consumption (Figure 10 Options for regulatory measures) and the other makes use of regulatory policies and measures to reduce levels of methylmercury (Figure 11 Options for public education). Reduction in environmental emissions can decrease exposure to methylmercury on a long term basis, and these are addressed in other UNEP documents.
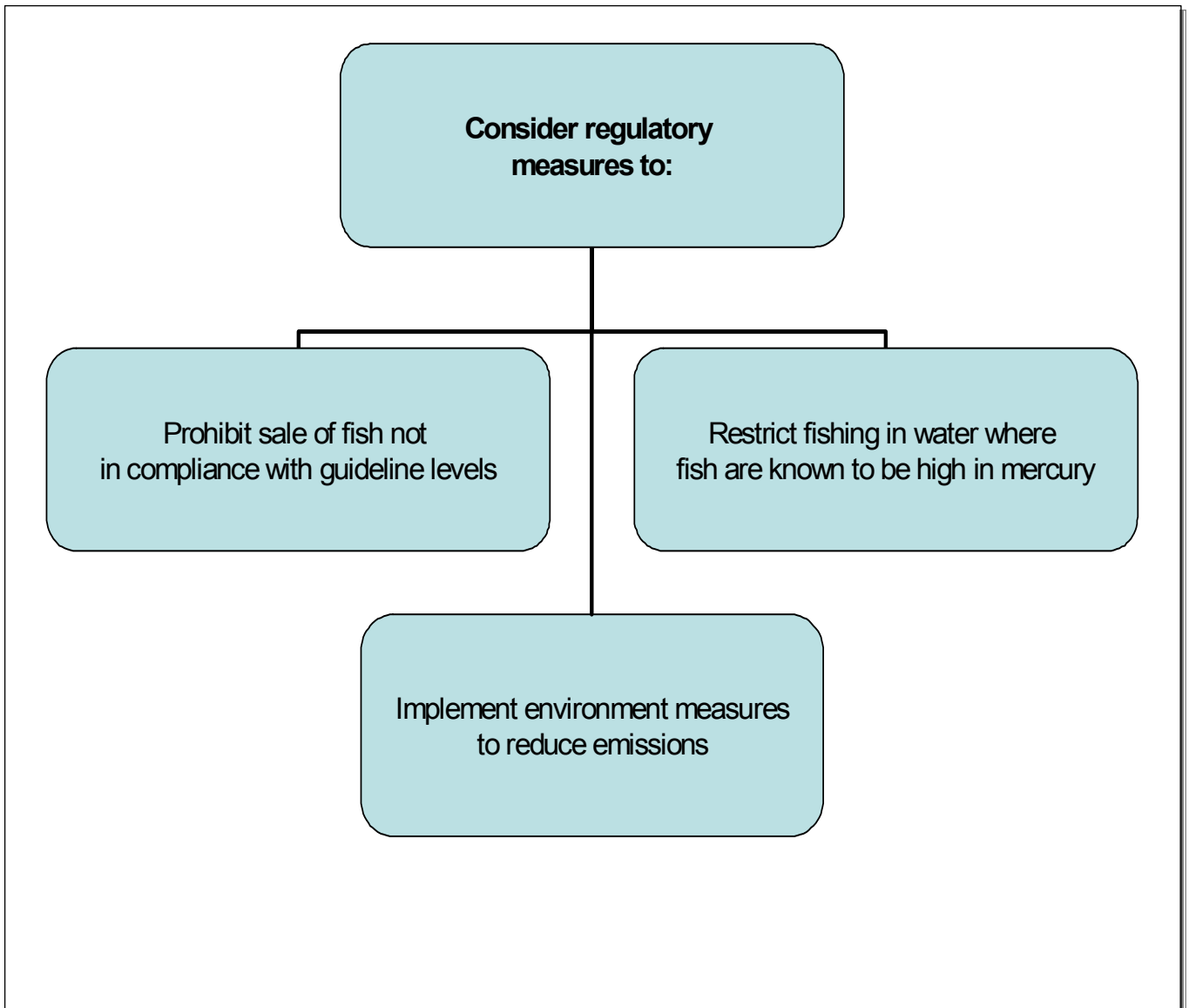
Figure 10 Options for regulatory measures
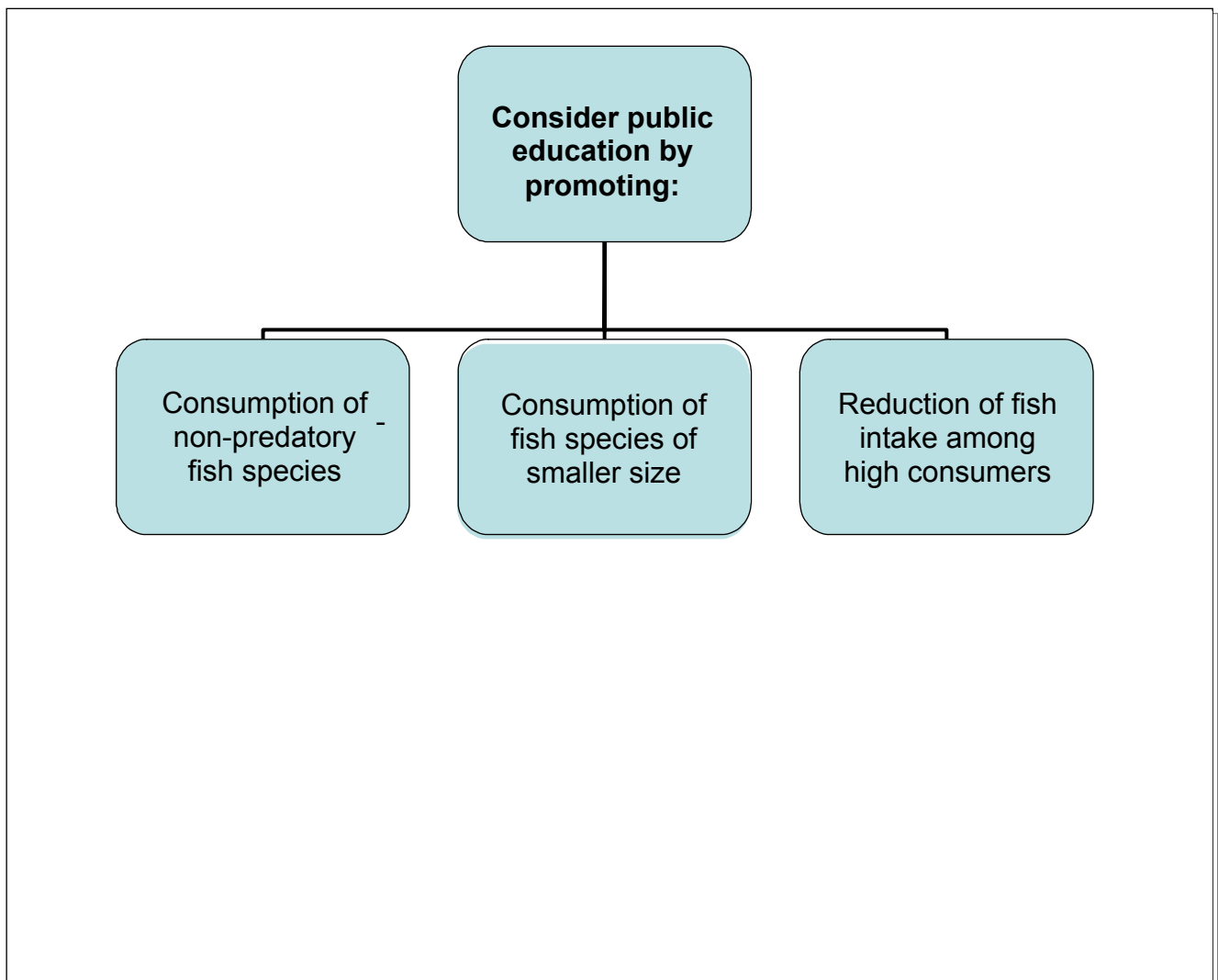
Figure 11 Options for public education

414. Regulatory approaches in the case of methylmercury have limitations in terms of cost and effectiveness. In addition, these approaches are not specifically targeted at populations at greatest risk. Given the health and nutritional benefits of fish consumption, many risk management options will involve influencing consumption patterns through informing consumers about the ways for reducing their exposure.

7.3.1   Information approaches

415. Information approaches vary from country to country, according to variations in amount and type of commonly consumed fish, and in levels of mercury in these species. For example, Australia, Canada, Japan, Norway, Sweden, the United Kingdom and the United States of America have issued fish advisories to consumers containing recommendations on how to reduce exposure to mercury through consumption of fish. Often, at-risk groups, such as pregnant women and women of child-bearing age, are targets of such advisories.

416. The US Food and Drug Administration has advised women of child-bearing age to limit their consumption of shark, swordfish, tilefish and king mackerel based on their high methylmercury content. At the same time, it advises consumers to eat up to 12 ounces or 340 grams (2 average meals) a week of a variety of fish and shellfish that are lower in mercury, and check local advisories about the safety of fish caught in local lakes and water courses. If no advice is available, fish from local waters may be eaten up to 6 ounces or 170 grams (one average meal) per week, but other fish may not be consumed during that week.

417. The authorities in Sweden recommend pregnant or breast-feeding women and women planning to have children soon, not to consume species, such as pike, perch, turbot and eel, because of risk of increased methylmercury exposure. Another example is the Food Standards Agency in United Kingdom, which advised that pregnant women, women who intend to become pregnant, infants and children under 16 years of age should avoid eating shark, swordfish and marlin. According to the Finnish National Nutrition Council, children, young people and women of child-bearing age should not eat more than one or two portions a month of pike, Baltic salmon or Baltic herring longer than 17 cm. Pregnant and breast-feeding women are advised not to eat pike at all. Australia has developed a strategy that involves fish retailers in advising pregnant women about low-mercury containing fish.

418. The Japanese authorities have issued advice relating to fish intake for pregnant women or women who would be pregnant. Based upon the currently available data, it is advisable to limit the consumption of;

- Meat of bottlenose dolphin, in 60 to 80 grams per serving size, to once per two months or less,
- Meat of Baird beaked whale, short-finned pilot whale, sperm whale and various kinds of sharks (muscle meat only), in 60 to 80 grams per serving size, to once a week or less,
- Meat of swordfish and alfonsino, in 60 to 80 grams per serving size to twice a week or less.

419. Food Standards Australia New Zealand (FSANZ) has also issued advice for Australia, which provides information on the safety of eating fish. This advice states that it is safe for all population groups to eat 2-3 servings (i.e. 150 g) of fish per week. However, pregnant women, women planning to have children and young children should limit their intake of shark swordfish, broadbill, marlin and shark to no more than one serving per 14 days with no other fish intake dutring that time. For orange roughy and catfish, the advice is to consume no more than one serving per week, with no other fish being consumed that week.

420. Health Canada advises consumer to limit consumption of shark, swordfish and fresh or frozen tuna to a maximum of no more than one meal per week. This excludes canned tuna, because these shipments are regularly tested and usually found to be well below the Health Canada guideline of 0.5 ppm. For children, pregnant women and women of child-bearing age, consumption of these fish should be limited to no more than one meal per month. For fish caught in local waters, consumers should be aware of any fish advisories. However, consumers are also encouraged to consider the significant beneficial health effects of including fish in their diet, and take a best-balanced approach to possible exposure to methyl mercury and fish consumption.

421. The national risk manager should consider implementing similar approaches, tailored to their own specific circumstances. In addition to listing fish with high mercury levels, listing fish varieties shown to generally contain low levels of methylmercury also can be important. A negative list alone could result in consumers taking precautionary action and avoiding all fish. This can result in the loss of an important source of nutrients in the diet.

422. In designing guidance on fish consumption, it is important to understand how and why people make food choices, including the consumption of fish. In general, patterns of food consumption are often very resistant to change (TERA and USEPA, 1999). One of the greatest challenges for developing messages on mercury involves addressing the trade-offs between the beneficial health and other effects of fish consumption and the health risks associated with exposure to mercury. Risk managers should adopt a participatory approach with a broad public health context that incorporates social and cultural factors in communities or among specific subgroups (TERA and USEPA, 1999; Egeland and Middaugh, 1997; Smith and Sayhoun, 2005). Public health workers, community opinion leaders, and members of affected groups should be included in the process (TERA and USEPA, 1999; Smith and Sayhoun, 2005).

7.3.2   Regulatory approaches

423. Another risk management approach to reduce potential exposure to methylmercury through fish consists in setting maximum acceptable concentration limits. The FAO/WHO Codex Alimentarius Commission has adopted recommendations on guideline levels for methylmercury at 1 mg/kg for large predatory fish, such as shark, swordfish, tuna and pike, and 0.5 mg/kg for non-predatory fish. The guidelines levels are intended for methylmercury in fresh or processed fish and fish products moving in

international trade. Lots should be considered in being in compliance with the guideline levels if the methylmercury concentration in the analytical sample, derived from the composite bulk sample, does not exceed the above levels. Where these guideline levels are exceeded, governments should decide whether and under what circumstances the food should be distributed within their territory and jurisdiction and what recommendations, if any, should be given as regards restrictions on consumption, especially by vulnerable groups such as pregnant women.

424. In countries where no specific guidelines have been established, management options could include routine monitoring of commonly consumed fish for levels of mercury for comparison. Using international standards, compliance monitoring can be used to keep highly contaminated products out of the food supply. However, risk managers should consider the impact of exclusion of samples in order to decrease the average methylmercury levels in fish supply.

425. For example, a typical log-normal distribution for mercury in fish is shown in Figure 12 below. If an authority sets a limit for methylmercury concentration of 1.0 mg/kg and effective enforcement is able to remove all fish above 1.4 ppm, the average level of methylmercury will shift to the left. In practice, the removal of highly contaminated fish at the extreme right of the distribution can result in significant reduction in the mean level. For the most part, these fish are the ones that are longer, heavier and with wider girth and can be identified by their size. However, to make further progress in reducing the mean mercury concentration, a sizable chop in the tail of the distribution is required to move the mean substantially downward. The rejection of such large numbers of fish may be unacceptable considering the potential health gain achieved by such a minor improvement in mercury levels.
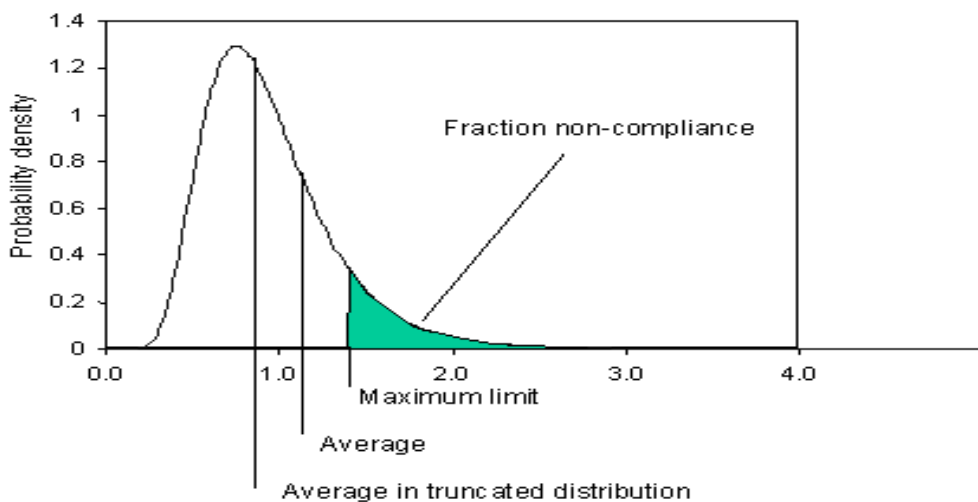

Figure 12 Reduction of mean mercury concentration in a fish-lot following exclusion of non-compliant specimens

7.3.3   Environmental measures

426. It is important to establish long-term goals at the national and international levels to reduce the environmental burden of mercury, which ultimately contributes to methylmercury in the food supply. As mandated by the UNEP Governing Council, a UNEP mercury programme to reduce environmental emissions of mercury is in place. Global reductions in environmental emissions of mercury would help to lower the background levels of mercury in water systems, thereby lowering the levels of mercury available to accumulate in fish.

7.4   Option Implementation

427. Effective option implementation, whether through public education or regulations, depends on risk communication that can break through traditional boundaries within government sectors, between governmental and non-governmental organizations, and between government and public and private sectors. Cooperation is essential and this requires the creation of partnerships between the different sectors at all levels. Communication efforts to reach the segments of the population of particular concern (such as women of child-bearing age and high fish consumers) are needed. Greater collaboration between government agencies, communication specialists and target group representatives would reduce the cost by producing effective communications and by ensuring that acceptable and relevant recommendations are designed so that people can effectively use them (Tilden et al., 1997). Indeed, public participation during decision making about risks can lead to more widely accepted risk policies (Arvai, 2003). This approach leads to higher quality decisions that are a product of more widely accepted decision processes. Consequently, risk communication is presented in detail in this document.

7.5   Risk communication of methylmercury

428. Risk communication is a tool for creating that understanding, closing the gap between lay people and experts, and helping people make more informed and healthier choices. Sometimes information about the adverse effects to human health and the environment strongly impresses people to overreact against an environmental issue even if a pollution level is much lower than a regulation or standard. In order to avoid misunderstanding about environmental issues, it is important to provide information about safe levels of mercury exposure in the ambient environment as well as any accidental mercury exposure, particularly to at-risk populations.

7.5.1   Goals of risk communication

429. Risk communication is an integral part of risk analysis together with risk management and risk assessment. Risk communication provides timely, relevant and accurate information to members of the risk analysis team, as well as external stakeholders, in order to improve knowledge about the nature and effects of a specific food safety risk. Successful risk communication is a prerequisite for effective risk management and risk assessment. The fundamental goal of risk communication is to provide meaningful, relevant and accurate information, in clear and understandable terms, targeted to a specific audience. Risk communication does not occur automatically during risk assessment and risk management. Risk communication must be carefully planned, implemented and managed to ensure effective results. Risk communication can be a powerful tool in helping people makes more informed choices about risks of mercury exposure and benefits of fish consumption.

430. In early stages of the risk communication programme, once methylmercury in fish is identified as a problem, risk communicators need to define the goals to be achieved. At this step, risk communicators should consider what information is crucial to convey in initial messages in order to prompt appropriate

public responses, and what the obstacles to effective communications are and how they can be minimized. A step by step guide for risk communication of mercury in fish is given in Annex G.

7.5.2   Tailoring the message for the audience

431. The at-risk groups, or target audiences, must be clearly identified. A community can be segmented and different segments can receive different messages, according to their specific needs. For example, considering neurological risks to fetus, women of child-bearing age, pregnant and breast-feeding women can be considered separately from other segments. Information about age, gender, ethnic, health and socioeconomic factors, as well as typical diet and fish consumption (type, amount and source) is essential to the development of the risk communication plan.

432. The acceptability of the appropriateness of risk management measures is closely related to public perception of risk. Therefore, it is essential for risk communicators to ensure that the risk communication process reveals information about the general public's perception of the risk of mercury exposure associated to fish consumption. Experience demonstrates that, to be most effective, the strategy used for risk communication should be tailored to stakeholders' particular characteristics and concerns, for the appropriate audience, with cultural, social and economic factors considered. Success of the communication can be directly attributed to community involvement, reinforcing the participatory approach in developing advisory material. For example, in the James Bay region of Northern Quebec, Canada, extensive hydroelectric development brought methylmercury contamination of fish with direct impact on the local communities subsisting on these resources. Community leaders, community health representatives, medical staff, and others were consulted to identify community needs with regards to methylmercury. Noel et al. (1998) reported that this extensive consultation led to the preparation of a brochure on methylmercury in a question and answer format, as well as to the creation of posters that were published in French, English and Cree and distributed to each community. Messages on exposure to methylmercury and practices for reducing risk must not only reach the people who fish and eat fish but also the people who influence fishing behaviour and consumption. In the absence of knowledge, it has been shown that people (lay public) rely on social trust in complex situations requiring judgment (Siegrist and Cvetkovich, 2000). Thus, it is important for health professionals (such as doctors, midwives, nurses, dieticians, and health care workers) and fish handlers (such as the fishing industry, sellers at markets or at wharfs, and recreational anglers) to understand mercury and its related issues as they are key individuals who are continually approached with questions regarding fish, particularly following media releases.

433. Risk communication on the risks and benefits of fish consumption should involve a two-way dialogue. Risk communicators must provide external stakeholders with clear and timely information about methylmercury risks and measures to manage it. Information on benefits of fish consumption must also be provided, as well as information on alternative food, especially in regions where fish represent the main food source. In these circumstances regulations designed to exclude from the food supply those fish that present a risk may be the preferred option. The information should be communicated in a way that stakeholders can easily understand and using a media that they can easily access. Opinion leaders/influencers, for example, are aware of specific community concerns and can help in the development and communication of key messages. The involvement of community representatives can help risk managers to gain the trust and support of the community. In addition, it is essential for risk communicators to solicit feedback from external stakeholders and listen to their opinions in order to refine the key message communicated and to fully and adequately address stakeholder concerns.

434. In order to effectively reach the target audiences, it is also important to identify their educational level and potential sources of information: television, newspaper, internet, health professionals, teachers, community organizations, local leaders etc. This is basic information for choosing support materials that will be distributed to target groups, and for the implementation of the campaign.

435.   Once implemented, the risk communication programme needs to be evaluated in order to determine the degree of responsiveness of the target audience to the key message. This step allows the identification of eventual adjustments or improvements to be affected. Risk communicators need to identify specific evaluation strategies to measure the effectiveness of their campaign.

7.5.3   Risk communication for other mercury exposure scenarios

436. Risk communication may also be needed to protect humans from excessive exposures to mercury and mercury compounds for other exposure scenarios as discussed in Chapter 6 of this document. This chapter will not include in-depth discussion of risk communication for these other exposure scenarios. However, the reader is referred to sources of additional information listed at the end of Chapter 1 of this document.

7.6   Monitoring and Review

437. Risk managers are responsible for verifying that the risk prevention and mitigation measures are achieving the intended results and that their performance is robust and can be sustained in the longer-term. Risk management decisions should be reviewed periodically on the basis of new scientific information or insights, as well as of data gathered during monitoring. This will enable the revision, as needed, of risk management decisions and of the public health goals of risk management. During monitoring, risk managers may measure the concentration of mercury in commonly consumed fish. Data from mercury in hair from groups at risk should be gathered and analysed on an ongoing basis to ensure that food safety goals are being achieved.

438. The capacity of the risk management option to reduce the risk to the desired levels among the population should also be monitored and verified. Epidemiological data and incident investigation data may be necessary for this purpose. Where nonexistent, the development of infrastructure for this kind of monitoring and review should be considered so the effectiveness of the measures can be verified.

439. In some cases, monitoring might result in a revision of the risk assessment to reduce previous uncertainties or update the analysis with new or additional information. The revised risk assessment results could lead to another iteration of the risk management process with a possible impact on the goals of the risk analysis and the risk management option chosen. Changes in public health goals, changing values, or technological innovations are all reasons to revisit the risk management option and possibly update the risk analysis.

GLOSSARY, ACRONYMS AND ABBREVIATIONS

The terms, acronyms and abbreviations below may appear in this document.

< - less than;

> - greater than;

µg – microgram (10^{-6} gram);

µg/kg body weight per day – micrograms per kilogram body weight per day; units used for describing intakes (or doses) of mercury such as intakes that are considered safe for humans. In some cases the time unit weeks is also used;

% – percentage;

3MRA – Multireceptor Risk Assessment;

AAS – atomic absorption spectrometry;

AERMOD – modelling system created by the AERMIC (American Meteorological Society/Environmental Protection Agency Regulatory Model Improvement Committee), which introduced state-of-the-art modelling concepts into the EPA's local-scale air quality models;

AES – Atomic Emission Spectrometry;

AFS – Atomic Fluorescence Spectrometry;

AGM – Artisanal Gold Mining

ATSDR – USA Agency for Toxic Substances and Disease Registry;

ASM – Artisanal and Small-Scale Gold Miners;

ASV – Anodic Stripping Voltametry;

BAF – Bioaccumulation Factor;

BAT – Biologischer Arbeitsstoff-Toleranzwert;

BAEP –Brainstem Auditory Brain Potentials;

BEI – Biological Exposure Indices;

BMD – Benchmark Dose;

bw - body weight;

CALPUFF – advanced non-steady-state meteorological and air quality modelling system developed and distributed by Earth Tech, Inc. The model has been adopted by the US Environmental Protection Agency (US EPA);

CDC – Centers for Disease Control and Prevention (in the USA);

CEAM – Center for Exposure Assessment Modelling (of the US EPA). The centre provides exposure assessment methodologies and models for groundwater, surface water, food chain, and multimedia assessment, as mentioned in Section 5.1;

cm – centimetres;

CMAQ-Hg – Community Multiscale Air Quality Modelling System for Atmospheric Mercury;

Creatinine – is a compound present in the muscles and blood that is passed in the urine. When creatinine levels rise in the blood, it can be a sign that the kidneys are not functioning well. Sometimes, creatinine is measured in the blood and in the urine, as part of a Creatinine Clearance test, which is a diagnostic test for kidney function;

CSFII - Continuing Surveys of Food Intake by Individuals (of the USDA);

CVAAS – Cold Vapour Atomic Absorption Spectrometry;

CVAFS – Cold Vapour Atomic Fluorescence Spectrometry;

DTP – Vaccine for Diphtheria-Tetanus-Pertussis;

EC – Environment Canada;

ECACAN – Environmental Council of States and Clean Air Network;

EDMS – Emission and Dispersion Modelling System;

EFCOSUM – European Food Consumption Survey Method;

FAO – Food and Agriculture Organization of the United Nations;

FDA – Food and Drug Administration (in the USA);

g – gram;

GEMS/Food – Global Environment Monitoring System / Food Contamination Monitoring and Assessment Programme;

GPS – Global Positioning System;

HBM - Human Bio-Monitoring;

hepB – vaccine hepatitis B;

Hg – mercury;

Hg⁰ - elemental mercury;

Hg(II) or Hg2or Hg^{2+} - divalent mercury - the dominating mercury form in organic and inorganic mercury compounds. In the atmosphere, mercury species with divalent mercury are more easily washed out of the air with precipitation and deposited than elemental mercury;

Hib – vaccine Haemophilus influenza type b;

HIV/AIDS - Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome;

ICP-AES – Inductively Coupled Plasma Atomic Emission Spectrometry;

ICP-OES – Inductively Coupled Plasma Optical Emission Spectrometry;

ICP-MS – Inductively Coupled Plasma Mass Spectrometry;

ID - identity document;

IDRC – International Development Research Centre;

IEM-2M – Indirect Exposure Model - version 2 for mercury-. It is an aquatic and terrestrial fate, transport, and exposure model;

ILO - International Labour Organization;

IOMC – Inter-organization Programme for the Sound Management of Chemicals;

IPCS – International Programme on Chemical Safety;

ISC3 – Industrial Source Code air dispersion model. It is a local scale atmospheric transport model;

IWAIR – Industrial Waste Air Model (developed by US EPA);

IWEM – Industrial Waste Management Evaluation Model (developed by US EPA);

JECFA – Joint FAO/WHO Expert Committee on Food Additives;

kg – kilogram;

l or L – litre;

Lao PDR - Lao People's Democratic Republic

LC50 - Lethal Concentration, 50%; concentration of toxic substance in a medium (for example water) at which 50% of the individuals in the toxicity test sample die; a unit used to describe the level of toxicity of a substance to a specific species, for example fish;

LOAEL – Lowest Observed Adverse Effect Level -see LOEL-;

LOEL - Lowest Observed Effect Level (also called LOAEL – lowest observed adverse effect level); for toxic or other effects imposed on organisms or experienced by humans;

m – metre;

MD - Medicinæ Doctor, Doctor of Medicine;

M Kip – thousand kip. The kip (LAK) is Lao PDR's currency;

mg – milligram (10^{-3} gram);

MeHg – Methylmercury;

MS – Mass Spectrometry;

MOT – Management of Technology Program;

MPS – Meals Per Season;

MPW – Meals Per Week in a season;

MRL – Minimum Risk Level; term used in evaluation of risk of toxic effects from various chemicals (such as methylmercury) on humans; the MRL is defined by US ATSDR as an estimate of the level of human exposure to a chemical that does not entail appreciable risk of adverse non-cancer health effects;

MTD – Maximum Tolerated Dose;

NAA – Neutron Activation Analysis;

NAS – National Academy of Sciences (in the USA);

ng – nanogram (10^{-9} gram);

NBAC - National Bioethics Advisory Commission;

NHANES – National Health and Nutrition Examination Survey (in the USA);

NHEXAS – National Human Exposure Assessment Survey (in the USA);

NAA – Neutron Activation Analysis;

NIOSH - National Institute for Occupational Safety and Health (in the USA);

NOEL - No Observed Effect Level (also called NOAEL – no observed adverse effect level); for toxic or other effects imposed on organisms or experienced by humans;

NOEL/BMDL – No Observed Effect Level/Benchmark Dose Level;

NRC – National Research Council of the United States of America;

OECD - Organization for Economic Cooperation and Development;

PCB – Polychlorinated Biphenyls;

pH – An expression of both acidity and alkalinity on a scale of 0 to 14, with 7 representing neutrality; numbers less than 7 indicate increasing acidity and numbers greater than 7 indicate increasing alkalinity;

ppb – parts per billion;

ppm - parts per million;

ppt - parts per trillion;

PTFE – polytetrafluoroethylene. Commonly known with its synonym as Teflon®;

PTWI – Provisional Tolerable Weekly Intake. The PTWI is an endpoint used for food contaminants such as heavy metals with cumulative properties. Its value represents permissible human weekly exposure to those contaminants unavoidably associated with the consumption of otherwise wholesome and nutritious foods;

QC – Quality Control;

RELMAP – Regional Lagrangian Model of Air Pollution. It is a long-range atmospheric transport model;

RfC – Reference Concentration;

RfD – Reference Dose; term used in evaluation of risk of toxic effects various chemicals (such as methylmercury) on humans; the RfD (or RfC) is defined by US EPA as 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;

SAICM – Strategic Approach to International Chemicals Management;

SAMSON – Solar and Meteorological Surface Observation Network;

SBC – Secretariat of the Basel Convention

SCRAM – Support Center for Regulatory Air Models (in the United States);

SMMC – "Standardized" Mean Mercury Concentration. It is also called size adjusted;

SP – sample person;

TRIM – Total Risk Integrated Methodology;

UN - United Nations;

UNCED - United Nations Conference on Environment and Development;

UNEP - United Nations Environment Programme;

UNIDO - United Nations Industrial Development Organization;

UNITAR - United Nations Institute for Training and Research;

US – United States of America;

USDA – United States Department of Agriculture;

US EPA – Environmental Protection Agency of the United States of America;

USA – United States of America;

WHO - World Health Organization.

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ANNEX A
EXAMPLE OF A SOCIO-ECONOMIC-DEMOGRAPHIC QUESTIONNAIRE

**This socio-economic-demographic questionnaire was developed by
Earth System Lao, Vientiane, Lao PDR[17].**

INTRODUCTION

The purpose of this Study is to conduct a survey of mining practices along the Nam Khong and Nam Ou rivers. This will involve a village and household level survey to gather baseline socio-economic data and to describe the mining methods being used.

Request to speak to the person who knows best about the livelihood activities of the household. In most cases this is likely to be the head of the household. Where possible request that the interview is conducted with both the male and female head of the household.

Request the consent of the household to be interviewed.

Questionnaire ID No.: _____

Household ID No.:   _____

Village Name: _____

District Name: _____

Date of survey: _____

Name of Principal Surveyor: _____

Name of Enumerator 1:   _____

Name of Enumerator 2:   _____

Respondent (male):	**First Name:** _____	**Family Name:** _____
Respondent (female):	**First Name:** _____	**Family Name:** _____

---

[17] Source: UNIDO 2003b

1.   PERSONAL INFORMATION

For all persons

1	2	3	4	5	6	7	8	9	10
Who is a member of this house-hold?	**What is rela-tionship to head of household?** *1 Head* *2 Spouse* *3 Son/Daughter* *4 Parent* *5 Other rela-tive* *6 Not related*	**Is male or fe-male?** *1 Male* *2 Female*	**How old?**	**Number of years living in this vil-lage?**	**What is citizen-ship?**	**What is eth-nic origin?**	**What is marital status?** *1 Never married* *2 Married* *3 Divorced/ separated* *4 Widowed*	**What is religion?**	**Major sick-ness in the last 2 years?** *1 No* *2 Malaria* *3 ARI[18]* *4 Diarrhea* *5 Abdominal pain* *6 Other*

For persons aged 6 years and above			For persons aged 10 years and above	
11	**12**	**13**	**14**	**15**
Can read and write? *1 Yes* *2 No*	**Has ever attended school?** *1 Never* *2 At school* *3 Left school*	**What is highest level of education completed?**	**What was main activity the last 12 months?**	**What was main occupation during the last 12 months?**

2.   SOCIO-ECONOMIC INFORMATION

16. What is the approximate average annual income of your household?

___ 0 - 2M Kip
___ 2M Kip to 5M Kip
___ 5M - 10M Kip
___ > 10M Kip

17. Who in your household manages the income?

___ Head

---

[18] Acute Respiratory Illness

___ Spouse of head
___ Son / Daughter of head
___ Other

18. Who in your family manages the expenditure?

___ Head
___ Spouse of head
___ Son/Daughter of head
___ Other

---

3. HOUSING CHARACTERISTICS

19. What is the tenure status of the household?

___ Owner / purchaser
___ Lodger
___ Tenant
___ Other

20. Type of dwelling unit?

___ Concrete
___ Timber
___ Bamboo
___ Other (specify): _____

21. Is the dwelling unit electrified?

___ No
___ Yes (own meter)
___ Yes (share meter)
___ Yes (own generator)
___ Yes (car battery)

22. What is the households main source of energy for cooking?

___ Electricity
___ Paraffin
___ Charcoal
___ Gas
___ Wood
___ Coal
___ Sawdust
___ Other

23. What is the living area of the dwelling unit? ___ m^2

<Mark the location of the dwelling on the village map - include Household ID No.>

4.   WATER FOR DRINKING AND COOKING

24. What is the household's main source of water for drinking and cooking?

___   Piped water in/outside
___   Well/borehole
___   River/stream/dam
___   Rainwater from tank/jar
___   Other (specify): _____

25. Distance from house to the main source of water for drinking and cooking? ___ m

<Mark the location of the water source on the village map>

26. Is drinking water treated before use?

___   Yes
___   No

If so, how?
___   Boiled
___   Filtered
___   Other (specify): _____

27. Are you satisfied with the quality of your drinking water?

___   Yes
___   No
If no, why not? _____

28. Who most commonly collects the drinking / cooking water in your household?

___   Head
___   Spouse of head
___   Son / Daughter of head
___   Other

5.   SOURCES OF FOOD

29. For each of the following food groups identify:

(i) The number of meals over the past 7 days when this food group has been eaten;
(ii) The source of the food.

Food Group	No. Times	Source (tick the appropriate boxes)

Red meat			Market		Family livestock		Forest
Chicken / duck			Market		Family livestock		Forest
Eggs			Market		Family livestock		Forest
Vegetables			Market		Garden		Swidden	Forest
Fruits			Market		Garden		Forest
Rice			Market		Paddy field		Swidden	Forest
Fish			Market		Fishpond		River
Other aquatic food			Market		Fishpond		River
Other			Market		Family livestock		Forest

6. DEATHS IN THE HOUSEHOLD AND HYGIENE

30. Did any death occur in the household in the last 12 months? (*also children at birth*)

___ Yes
___ No

If Yes:

#	Was the deceased male or female? ___ *Male* ___ *Female*	How old was the deceased? *Age in years* _____	*For woman aged 15 to 49 years:* Did she die while pregnant, while giving birth or within 42 days after giving birth? ___ *Yes* ___ *No*
1			
2			
3			
4			

31. What type of toilet facility is mainly used by the household?

___ Flush toilet
___ Dry toilet
___ Other
___ None

Has anyone in your family been engaged in mining activities? (Either currently or previously)

If yes, continue to Part B of the questionnaire.

If no, thank the respondent for their cooperation, and ask the respondent whether they would be prepared to participate in a follow-up health survey at a later date?

□ **YES** □ **NO**

Additional observations of the Surveyor:

_____
_____
_____
_____
_____

ANNEX B
EXAMPLE OF A HEALTH ASSESSMENT QUESTIONNAIRE

Example of a Health Assessment Questionnaire[19]

This health assessment questionnaire was developed for a United Nations Industrial Development Organization (UNIDO) project on artisanal gold mining by Dr. Stephan Boese O'Reilly, Prof. Dr. Gustav Drasch, Stefan Maydl, and Dr. Milan Vosko of the Institute for Forensic Medicine, Ludwig-Maximilians University, Munich, Germany; and Dr. Claude Casellas, and Dr. André Rambaud of the Dept. Sciences de l'Environment et Santé Publique, Faculté de Pharmacie, Université de Montpellier, France.

Name: _____

I hereby declare that I want to take part in the UNIDO project. I will be questioned about my living circumstances and health problems related to mercury. I will be medically examined including neurological examination. Blood, urine and a small amount of hair will be taken. The _____ will inform me after the laboratory analysis about my personal results. The UNIDO and the _____ will get the results in a form where my name can not be identified. The assessment is done respecting the "Recommendation for Conduct of Clinical Research" (World Health Organization Declaration of Helsinki).

>>translation<<

Local and Date: _____   _____
                                                        Signature
                                          (*in case of children signature of parents/guardian*)

Witnesses (if needed):
_____ and _____
(Name):   (Name):

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[19] Source: UNIDO 2003b; Veiga and Baker, 2004

1.   PERSONAL DATA

Participant ID Number: _____

Family Name: _____

First Name: _____

Date of Birth: _____ Age: _____(years)

Gender: ____ Female ____ Male

Address: _____

_____

Any telephone for contact: _____

2.   GENERAL QUESTIONNAIRE

Date of interview: _____

Name of the interviewer: _____ Code of the interviewer _____

2.1.   Work Exposure

How long have you been living in this area? _____ year(s)

Occupation (Detailed description of the job)

____ Miner

____ Mineral processor (in charge of amalgamation)

____ Gold smelter (gold buyer)

____ Worker at a cyanidation plant

____ Farmer

____ Office Job

____ Driver

____ School child (not working)

____ Other job _____

Have you ever worked in the _____ area?

____ No

____ Yes

If yes, for how many _____ year(s)?

Have you ever worked as a miner with direct contact with mercury?

____ No

____ Yes

If yes, from when to when: _____

Have you ever worked burning amalgam in open pans or melting gold in inadequate fume hoods?

____ No

____ Yes

If yes, from when to when: _____

Have you ever used a retort?

____ Yes, when_____ and which type _____

____ No

Have you stored mercury containers or flasks?

____ Never

____ At work

____ At home

Have you kept your dirty working clothes at your home?
_____ No
_____ Yes

For how many years have you been working with mercury?
_____ not applicable (have not working directly with mercury)
_____ year(s)

2.2. Diet Issues

How frequently do you eat fish?
_____ Never
_____ At least once a **month**
_____ At least once a **week**
_____ At least once a **day**

The interviewer should ask about the size of the portion of fish consumed. Based on the portion in the meal the interviewer estimate the approximate mass of fish consumed:

_____ grams (___ per day or _____ per week).

Name the fish you consume regularly (if possible indicate if the fish **species** is **c**=carnivorous, **o**=omnivorous, **d**=detritivorous, **h**=herbivorous). If possible, list from the most to the least consumed species (*try to obtain a % of each species consumed in each season*)

Fish name	Species	% (dry season)	% (wet season)
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

Do you know where the fish come from?
_____ don't know the origin of the fish (buy in the market)
_____ from areas distant from mining
_____ from areas impacted by mining

Can you name the river and area where you catch most fish you have consumed?
_____ No
_____ Yes, the river (or lake or pool) is _____

Has this river (or water body) dark water (Coca-cola colour)?
_____ don't know the origin of the fish (buy in the market)
_____ Yes, mild
_____ Yes, very dark
Name the place where you obtain drinking water: _____

Do you consume from local production chicken, ducks or eggs?

____ Never
____ At least once a **month**
____ At least once a **week**
____ At least once a **day**

Do you consume from local production meat (>>beef, pork, etc.<<)?
____ Never
____ At least once a **mont**h
____ At least once a **week**
____ At least once a **day**

Do you consume from local production vegetables, fruits?
____ Never
____ At least once a **month**
____ At least once a **week**
____ At least once a **day**

2.3. Confounders

Have you ever had any neurological disorders (epilepsy, stroke, Parkinson, etc.) or mental disorders (schizophrenia, bi-polar disorder, etc.)?
____ No
____ Yes

Which disease (problem)? _____

Have you ever had malaria?
____ No
____ Yes
If yes, how many time ago you had your last malaria? _____ (days or months or weeks)

Do you have fever at the moment?
____ No
____ Yes

Have you been constantly handling gasoline and kerosene? (this can develop tremors)
____ No
____ Yes
If yes, how many years you have been doing this? _____ (years)

Have you been constantly handling insecticides or pesticides?
____ No
____ Yes
If yes, how many years you have been doing this? _____ (years)

Do you smoke?
____ Never
____ Rarely (0-10 cigarettes per day)
____ Medium (10-20 cigarettes per day)
____ Lots (more then 20 cigarettes per day)

Do you drink alcohol?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

Do you have HIV /AIDS?
____ No
____ Yes
When did this happen? _____ (days or weeks or months or years) ago

Do you or did you suffer from Leprosy?
____ No
____ Yes

Have you been using whitening soap (for lightening the skin)?
____ No
____ Yes

Have you ever had hepatitis or any other hepatic disorder?
____ No
____ Yes

Which disease (problem)? _____

Did you ever have tuberculosis?
____ No
____ Yes
When did this happen? _____ (days or weeks or months or years) ago

Have you ever had any other major infectious disease?
____ No
____ Yes
Which disease (problem)? _____

Did you have any serious accidents (did you have to go to hospital)?
____ No
____ Yes, but not severe
____ Yes, and it was severe (more then 1 hour unconsciousness)
When did this happen? _____ (days or weeks or months or years) ago

How is your current financial situation?
____ above average
____ average
____ below average

How is your current social life? (friends, family, hobby activities, etc.)
____ OK
____ medium
____ bad

Exclusion criteria from statistical evaluation
Severe neurological disease such as Parkinson, stroke, severe accident (brain injury), birth trauma, tetanus, polio, hyperthyroidism, epilepsy, malaria or any acute severe disease, etc. may introduce too many factors that confound with Hg intoxication symptoms.

To be filled in by project doctor.

*Based on the confounders, should this individual be **excluded** from the Health Assessment?*

____ No
____ Yes

Why this individual should be excluded from the assessment:

_____
_____
_____

3. HEALTH QUESTIONNAIRE

Date of interview: _____
Name of the interviewer: _____ Code of the interviewer _____

Do you feel a kind of a metallic taste?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

Do you suffer from excessive salivation?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

How is your appetite?
____ OK
____ medium
____ bad

Did you loose weight within the last year?
____ No
____ Yes

Did you loose hair within the last year?
____ No or only rarely
____ Yes, slight to moderate
____ Yes, marked to sever

Have you been coughing within the last year for more then for 3 month?
____ No
____ Yes

Have you ever had kidney disease except urinary tract infection?
____ No
____ Yes
Which disease (problem)? _____

Have you ever had severe respiratory problems (asthma, pneumonia)?
____ No
____ Yes
Which disease (problem)? _____

Are you healthy now?

____ Yes

____ No

Why not? _____

Has the actual or former health problem worsened since exposure to mercury occurred?

____ No mercury exposure

____ Mercury exposure, but no worsening effects

____ Yes, mercury exposure **and** worsening

TREMORS

Have you had any problems with tremor (shaking)?

(Clinical Tremor Rating Scale)

____ I have no tremor or tremor does not interfere with my job

____ I am able to work, but I need to be more careful than the average person

____ I am able to do everything, but with errors; poorer than usual performance because of tremor

____ I am unable to do a regular job, I may have changed to a different job due to tremor; it limits some housework, such as ironing

____ I am unable to do any outside job; housework very limited

SLEEP DISTURBANCES

How do you feel after a usual night of sleep?

____ OK

____ medium

____ bad

FATIGUE

Score to estimate the state of fatigue (Wessely S, Powell R: Fatigue syndrome)

Have you got tired easily?

____ Same as usual

____ Worse then usual

____ Much worse than usual

Do you need to rest more?

____ Same as usual

____ Worse then usual

____ Much worse than usual

Do you feel sleepy or drowsy?

____ Same as usual

____ Worse then usual

____ Much worse than usual

Can you no longer start anything?

____ Same as usual

____ Worse then usual

____ Much worse than usual

Do you always lack energy?

____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you have less muscle strength?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you feel weak?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Can you start things without difficulties, but get weak as you go on?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Physical fatigue sum: _____ score sum

MENTAL FATIGUE

Do you have problems concentrating?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you have problems thinking clearly?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you have problems to find correct words when you speak?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you have problems with eyestrain?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Do you have problems with memory?
____ Same as usual
____ Worse then usual
____ Much worse than usual

Mental fatigue sum: _____ score sum

WELL BEING

Do you feel nervous?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a d**ay**

Do you feel sad?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

How is your current sexual life? (for men)
____ OK
____ average
____ bad

Do you have palpitations?
Feeling the heart beating
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

Do you have a headache?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

Do you have nausea?
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

Do you feel numbness, prickling, aching at any location of your body?
Mainly perioral dysesthesia and sensory impairment of the glove and-stocking type
____ Never
____ at least once a **month**
____ at least once a **week**
____ at least once a **day**

4.   CLINICAL-NEUROLOGICAL EXAMINATION

Date of neurological examination: _____
Name of the neurological examiner: _____ Code _____
Weight and Height
Weight: _____ Kg
Height:_____ cm
Blood pressure:_____/_____ mmHg

MOUTH AND TEETH CONDITIONS

Clinical signs of stomatitis
____ No
____ Yes

Clinical signs of gingivitis
____ No
____ Yes

Bluish discolouration of the gums
____ No
____ Slight
____ Yes, obvious

How many teeth with dental fillings (Amalgam)?
____ None

____ One or more → how many _____

Examination of the eyes:
_____ No changes
_____ Bluish coloured iris ring
_____ Kayser-Fleischer ring

WALKING

Person is asked to walk up and down, first with eyes open, then with eyes closed.

Ataxia of gait (walking)
Examiner is watching for signs of ataxia (Klockgether Score)
___ Absent
___ Slight (ataxia only visible when walking on tandem or without visual feedback)
___ Moderate (ataxia visible in normal walking; difficulties, when walking on tandem)
___ Marked (broad-based, staggering gait; unable to walk on tandem)
___ Severe (unable to walk without support; wheelchair bound)
___ Most severe (bedridden)

Rigidity of gait (walking)
Examiner is watching the gait, the swing of the arms, general posture and rates
____ Normal
____ Mild diminution in swing while the patient is walking
____ Obvious diminution in swing suggesting shoulder rigidity
____ Stiff gait with little or no arm swinging noticeable
____ Rigid gait with arms slightly pronated; this would also include stopped-shuffling gait with propulsion and retropulsion

STANDING

Tremor - finger to nose test
Person is asked to stand still, legs together– arms outstretched. Eyes closed. Finger tip should touch the nose. Examiner is watching and rates the **tremor** (*modified Clinical Tremor Rating Scale*)

____ None
____ Slight to moderate (amplitude < 0,5 cm – 1cm); may be intermittent
____ Marked amplitude (1-2 cm)
____ Severe amplitude (> 2 cm)

Dysmetria - finger to nose test

Person is asked to stand still, legs together – arms outstretched, eyes closed. Finger tip should touch the nose. Examiner is watching and rates the dysmetria

____ Normal

____ Moderate pathologic

____ Severe pathologic

Dysdiadochokinesis

Person is asked to twist hands very quickly (alternating movements of the wrists (*Klockgether Score*)

____ Absent

____ Slight (minimal slowness of alternating movements)

____ Moderate (marked slowness of alternating movements)

____ Severe (severe irregularity of alternating movements)

____ Most severe (inability to perform alternating movements)

Tremor – eye lid

Eyes closed. Examiner is watching and rates the **tremor** (*Davao Pool score*)

____ None

____ Slight

____ Marked

LYING

Person is asked to lie on the examination bench.

Mentolabial reflex

____ Negative

____ Positive

Babinski reflex

____ Negative

____ Positive

Hoffmann reflex

____ Negative

____ Positive

Sucking reflex

____ Negative

____ Positive

Grasp

____ Negative

____ Positive

PSR (quadrizeps reflex)

____ No flex

____ Hyporeflexia

____ Normal

____ Hyperreflexia

____ Clonus

BSR (bizeps brachii reflex)

____ Normal
____ Hyporeflexia
____ Slight hyperreflexia
____ No reflex
____ Very brisk or reflex zone enlarged or
clonus

AR - Achillean tendon reflex, ankle jerk

____ Normal
____ Hyporeflexia
____ Slight hyperreflexia
____ No reflex
____ Very brisk or reflex zone enlarged or clonus

LYING – OTHER TESTS

Intentional Tremor- heel-to-shin test

Person is asked to touch with his heel the knee of the other leg. Then to move with the heel along the shin to the foot. Repeat and do it with both sides. Eyes first open, then closed. Rate tremor during heel-to-shin test (Klockgether Score)
____ Absent
____ Slight (slight terminal tremor)
____ Moderate (marked terminal tremor)
____ Marked (kinetic tremor throughout intended movements)
____ Severe (severe kinetic tremor heavily interfering with everyday life)
____ Most severe (maximal form of kinetic tremor making intended movements impossible)

Ataxia - heel-to-shin test

Rate ataxia (*Klockgether Score*)
____ Absent
____ Slight (slight hypermetria in heel-to-shin test)
____ Moderate (hypermetria and slight ataxic performance of heel-to-shin test)
____ Marked (marked swaying: unable to stand with feet together)
____ Severe (pronounced ataxia in performing heel-to-shin test)
____ Most severe (unable to perform heel-to-shin test)

Sensory disturbances

Sensory disturbances such as sensory impairment of the glove and-stocking type
____ Absent
____ Present Com-
ments_____

Bradykinesis

Rate your observation whether there was any sign of bradykinesis during the examination (slower active movements, absent or altered synkinesis of upper extremities during gait)
____ Absent
____ Present

Hypo-mimia

Rate your observation whether there you observed an hypo mimic expression of the face during the

examination)
____ Absent
____ Present

5. SPECIFIC TESTS

Date of the test: _____
Name of the tester: _____ Code _____

Memory Disturbances: (different memory tests can be used)
Forward digit span test (part of *Wechsler Memory Scale)*
Please repeat each column of numbers. Score longest series correctly repeated forward

	Score	Test
	4	6-4-3-9
	4	7-2-8-6
	3	4-2-7-3-1
	3	7-5-8-3-6
	2	6-1-9-4-7-3
	2	3-9-2-4-8-7
	1	5-9-1-7-4-2-3
	1	4-1-7-9-3-8-6
	0	5-8-1-9-2-6-4-7
	0	3-8-2-9-5-1-7-4

Match Box Test (from *MOT*)
Put **20 matches** on a table, half of each on one side of an open matchbox, approx. 15 cm
away. Take the time until all matches are put into the box. Use left and right hand
alternatively.
_____ seconds

Finger Tapping Test (from *MOT*)
Sitting at a table. Elbows should be placed on the table. Try to do as many points as
possible on a piece of paper with a pencil. Count the amount of points within **10 seconds**.
_____ points

Frostig Score

Draw a line from one symbol to the other. Do not interrupt while drawing. Do not touch the borders.
Please try to stay within the lines.

F1 ✏ .... ✈

Point: _____ 0 = good; 1 = bad; 2 = very bad

F2 ✏ .... ✈

Point: _____ 0 = good; 1 = bad; 2 = very bad

F3 ✏ .... ✈

Point: _____ 0 = good; 1 = bad; 2 = very bad

F4 ✏ .... ✈

Point: _____ 0 = good; 1 = bad

F5 ✏   ✈

Point: _____ 0 = good; 1 = bad; 2 = very bad

F6 ✏   ✈

Point: _____ 0 = good; 1 = bad; 2 = very bad

Please connect the symbols with a straight line.

F7 ☸   ☸

Point: _____ 0 = good; 1 = bad; 2 = very bad

Score: _____

MEMORY DISTURBANCES (new battery of tests):

Orientation to time - season:
_____ correct response
_____ incorrect response

Orientation to time - part of the day:
_____ correct response
_____ incorrect response

Orientation to place - name of the village
_____ correct response
_____ incorrect response

Orientation to place - name of the country:
_____ correct response

_____ incorrect response

Episodic memory (registration of 3 words): example: Fish, Ball, Tree
_____ Registered all 3
_____ Registered just 2
_____ Registered just 1
_____ Registered none

Copying figures
(Select some simple and more complex figures according to the degree of instruction of the patient; based on the quality, time and difficulty to perform the text, make your score for each figure)

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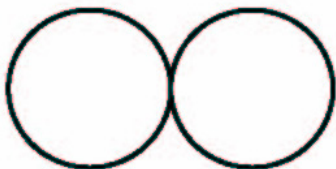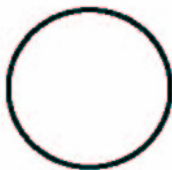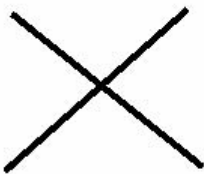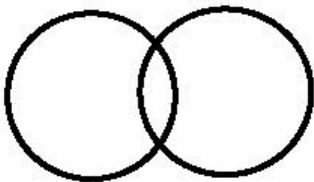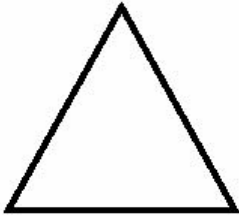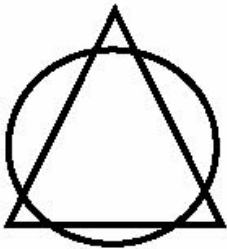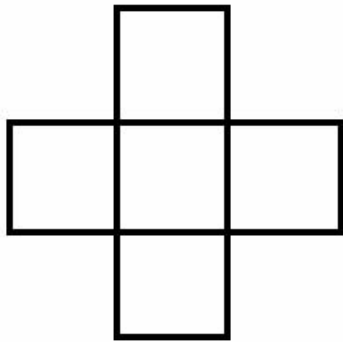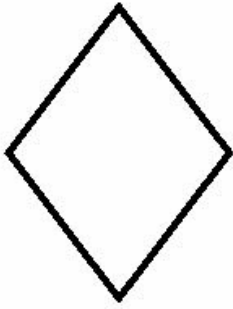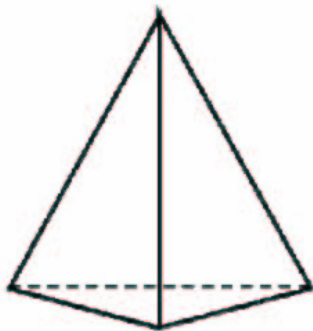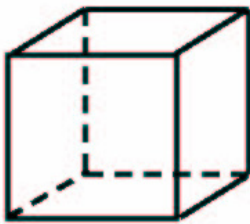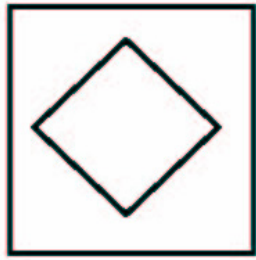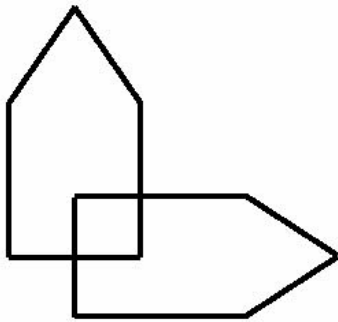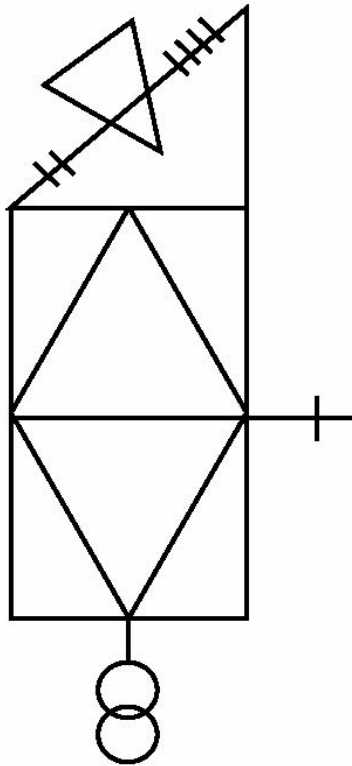
6. SPECIMENS

Date of the specimen _____
Time of the specimen sampling _____
Name of the specimen taker: _____ Code _____

Blood (EDTA-blood 10 ml)
____ Yes
____ No

Malaria smear (only, if high prevalence of malaria in the area)
____ Negative
____ Positive

Urine (spontaneous urine sample 10 ml)

____ Yes
____ No

Urine total mercury (field test) (additional)

Result: ____ unit: ____

Proteinuria? (same test should be used)
____ negative
____ trace
____ +
____ ++
____ +++
____ ++++

Hair
____ Yes, sample collected
____ No

Hair total mercury (field test) (additional)
Result: ____ unit: ____

7. LABORATORY ANALYSISRESULTS

Material/test	Result	Unit
Blood		
Total mercury		
Methylmercury		
Selenium		
Urine		
Creatinine		
Total mercury		
Methyl mercury		
Hair		
Total mercury		
Methyl mercury		
Others (saliva, nails, breast milk, fae-ces...)		

Comments_____

8. MEDICAL SCORE SUM

Test	Score Points	Results
Anamnestic data		
Metallic taste	0/1	
Excessive salivation	0/1	
Tremor at work	0/1	
Sleeping problems at night	0/1	
Health problems worsened since Hg exposed	0/1	
Clinical data		
Bluish colouration of gingiva	0/1	
Ataxia of gait	0/1	
Finger to nose tremor	0/1	
Dysdiadochokinesis	0/1	
Heel to knee ataxia	0/1	
Heel to knee tremor	0/1	
Mento labial reflex	0/1	
Proteinuria	0/1	
Neuropsychological tests		
Memory test	0/1/2	
Matchbox test	0/1/2	
Frostig test	0/1/2	
Tapping test	0/1/2	
Maximum	21	

Medical score sum _____

NOTE:

Proteinuria 1 = more than trace, 0 = 0 or trace (correctness of this borderline needs to be checked, same test material should be used)
Memory test: 2 = score 0, 1 = score 1-2, 0 = score 3-4
Matchbox test: 2 = 21 seconds or more, 1 = 16-20 seconds, 0 = 0-15 seconds
Frostig test: 2 = 0-9 correct answers, 1 = 10-12 correct answers, 0 = 13-16 correct answers
Tapping test: 2 = 0-53 dots, 1= 54-64 dots, 0 = 65 or more dots

9. DECISION FOR THE DIAGNOSIS OF POSSIBLE EXCEEDENCE OF CHRONIC MERCURY THRESHOLD LIMITS FOR MERCURY

	Hg-blood (µg/L)	**Hg-urine** (µg/L)	**Hg-urine** (µg/g creatinine)	**Hg-hair** (µg/g)
HBM I	5	7	5	
HBM II	15	25	20	5 (in analogy)
WHO			50	7
BAT for metallic and inorganic Hg	25	100		
BAT for organic Hg	100			
BEI (Biological exposure index)	15 (after working)		35 (before working)	

Note: Toxicologically established threshold limits for mercury in blood, urine and hair (HBM = Human Bio-Monitoring; BAT = Biologischer Arbeitsstoff-Toleranzwert; BEI = Biological Exposure Indices). The BAT value is the maximum allowable concentration of a substance or its metabolites in body fluids. It should guarantee that the health of healthy people is not affected when being exposed 8 hours a day or 40 hours a week.

Decision for the diagnosis of a "chronic mercury intoxication"

		Medical Score Sum		
		0 – 4	5 – 9	10 - 19
Hg in all biomonitors	< HBM I	–	–	–
Hg at least in one biomonitor	> HBM I	–	–	+
	> HBM II	–	+	+
	> BAT	+	+	+

Decision for the diagnosis "chronic mercury intoxication" Intoxication
_____ No
_____ Yes

ANNEX C
SAMPLE COLLECTION PROCEDURES FOR URINE, BLOOD, AND HAIR

PROTOCOL FOR COLLECTING URINE SAMPLES

HOW MANY
> We would like you to collect a single urine sample. You will collect a sample from your first morning void.

SAMPLE ID: _____

TIME OF DAY
> We want you to collect a sample from your first morning void; that is, the time you first wake up in the morning to begin your day. (If you have a sleep schedule other than the usual overnight time period, please discuss the collection time with our staff).

HOW TO COLLECT THE SAMPLE
> It is very important to collect the sample using the following instructions so that the sample will not be contaminated with dust or dirt.

1. The night before, bring the urine sample cup and spare to the bathroom.
2. In the morning, before collecting the sample, wash your hands thoroughly with soap and water.
3. Remove the sample cup from the plastic bag. Remove the cap from the cup, put down the cap with the inside of the lid facing up.
4. Be careful not to touch the inside of the cup or the cap with your hands, clothing, or other material. If this happens, please use the second cup.
5. Urinate directly into the cup. Do not fill past the topmost line on the side of the cup.
6. Immediately place the cap on the collection cup. Again, do not touch the inside of the cap or collection cup.
7. Place the cup back into the plastic bag and seal the plastic bag. Put the collected sample into the plastic storage box in your freezer within 5 minutes.
8. Please complete the information for the urine sample:

_____
Date Collected:

_____
Time Collected:

_____
Time of last void before this sample:

PROTOCOL FOR COLLECTING BLOOD SPECIMENS

1. Have the following items on hand and available:

    *   Blue Absorbent Pad
    *   Powder free gloves
    *   Tourniquet
    *   Alcohol disinfectant swabs (individually wrapped)
    *   Gauze bandages (sterile, individually wrapped)
    *   21g or 23g vacutainer butterfly
    *   Vacutainer needle holder
    *   7 ml PURPLE top tube with Hemagard cap
    *   7 ml GREY top tube with Hemagard cap
    *   7 ml PURPLE top tube with Hemagard cap
    *   Bandage
    *   Sharps disposal container for used needles and butterflies

2. Select the appropriate size butterfly and attach to the Vacutainer needle holder.

3. Wipe the three tube caps with an alcohol wipe **immediately** before collection.

4. Tie the tourniquet onto the upper arm so that it can be quickly released with one hand.

5. Swab the venipuncture area with an alcohol pad.

6. Wipe off excess alcohol with the gauze bandages. Allow to air dry for 5 - 10 seconds.

7. Puncture the vein with the butterfly needle.

8. Insert the **first 7ml purple top tube** into the barrel of the vacutainer needle holder and push until blood enters the tube. The tube will draw only 6.5 mL of blood. When full, remove tube and invert 4-6 times to mix.

9. Insert the **GREY top 7ml tube** into the barrel of the vacutainer needle holder and push until blood enters the tube. When full, remove tube and invert 4-6 times to mix.

10. Insert the **second 7ml purple top tube** into the barrel of the vacutainer needle holder and push until blood enters the tube.

11. Release the tourniquet when the last tube has filled half way. Allow tube to finish filling, remove from holder, invert 4-6 times to mix, and then apply pressure with sterile gauze to venipuncture site as you remove the needle.

12. Carefully remove vacutainer needle or butterfly from holder and dispose of it in the sharps container.

13. Mix all of the blood tubes well by inverting 4-6 times upon removal from the holder to ensure good distribution of the anticoagulant throughout the blood.

14. Immediately upon completion of venipuncture, while pressure is being applied to site, pick up collected tubes and invert 6-10 more times to mix.

15. Place pressure on the venipuncture site for a few minutes with a gauze pad. Cover the venipuncture site with a bandage.

16. Place a bar-coded ID label on the vacutainer tubes. Make sure that the label edge starts on the edge of the tube label and that there is a "window" so that one can see the tube contents. Place the label on the tube so that the barcode looks like a "ladder" when the tube is held upright.

17. Record the sample number on the collection log indicating results of the collection and appropriate collection comments if difficulties were encountered.

18. Place samples in the sample tube rack or box provided. Give the blood and urine specimens to the field survey personnel.

Notes:
If unable to collect blood after two tries, contact the survey laboratory personnel.

If the laboratory personnel are unable to collect a blood specimen after two additional tries then consult the MD.

PROTOCOL FOR COLLECTING HAIR SPECIMENS

1.1 Introduction
The purpose of hair collection is to obtain a suitable biological sample to determine total mercury levels in hair. Relationships exist between the concentrations of mercury in human scalp hair and dietary methylmercury exposures. Use the hair to characterize recent exposure to methylmercury over a relatively uniform time interval.

1.2 Specimen Requirement
Collect hair samples on primary male and female sample persons (SPs) ages 1-5, and women ages 16-49. Administer the questionnaire regarding hair treatment within the last month, and collect approximately 100 strands of hair from the occipital position of the head. Analysis requires a minimum of 50 mg. Collect as much as possible. Retain orientation of the hair strands, whenever possible.

1.3 Procedure Summary
Isolate a bundle of approximately 100 strands of hair in the occipital region and twist together. Cut hair as close as possible to the scalp. Fold a 3.5 cm x 5 cm Post-it Notes over the end of hair closest to the scalp, mark the Post-it with an arrow indicating the end of hair closest to the scalp, and attach a white plastic paper clip over the Post-it note. Place the hair sample in a zip closable bag. If the hair is too short to cut and clip together cut hair directly into the zip closable bag using chinning shears. Label the bag with the preprinted laboratory label, record collection results, and transport specimen to the laboratory.

1.4 Reagents and Materials
Equipment and Supplies
   1. Blunt tip scissors
   2. Thinning shears
   3. Plastic paper clip
   4. 3.5 cm x 5 cm Post-it Notes
   5. Plastic and aluminium hair clips
   6. Disposable combs
   7. Ziplock closable plastic bags (15 cm x 15 cm)
   8. Isopropyl alcohol (70% solution)
   9. Disinfecting container (instrument tray with cover)
   10. Disposable powder free gloves

11. Vacuum

1.5 Collection Procedure

1.5.1   *Preparation*

Obtain the sample person-specific, preprinted labels for the current session

Put on new gloves

Use a comb to partition the hair between the ears on the back of the head below the midline. This is the occipital area at the rear base of the head.

Fasten the hair above the ears out of the way with plastic or aluminium hair clip(s).

1.5.2   *Collection*

Isolate a small bundle of hair that is approximately the size of a pencil eraser (0.75-1.0 cm diameter).

Twist the hairs together into a bundle.

Cut the hair as close to the scalp as possible with the blunt tip curved scissors.

Fold a 3.5 cm x 5 cm Post-it Note around the hair closest to the scalp.

Attach a white plastic paper clip to the Post-it Note.

Draw an arrow on the Post-it Note to designate the end closest to the scalp.

Place the cutting with the Post-it Note and plastic paper clip into the zip closable bag that contained the scissors and comb or use a clean unused zip closable bag. Immediately close and seal the zip closable bag, making sure hairs are not protruding through the opening. If necessary, use the comb to push hair completely into the bag or leave the comb in the bag with the hair.

Cut from a second and third location in the occipital area if it is necessary to collect a sufficient sample.

If hair is too short to be cut and clipped together, cut hair directly into the storage bag using thinning shears. Use a comb to lift up the hair. Place the shears close to the scalp and clip 2 or 3 times in the same location. Place the comb behind the shears and pull the comb and shears together

1.5.3   *Concluding the Procedure*

Remove the clip(s) from the hair.

Remove and discard gloves.

Disinfect the scissors and clips by placing them in 70% isopropyl alcohol in a sealed disinfecting container. Allow these supplies to remain in the disinfecting container until the end of the session or for at least 20 minutes. Remove and place the clips and scissors on clean paper towels and allow them to air dry.

Make up new individual collection kits. Place one pair of scissors and one new comb in a clean zip closable bag.

1.6 Specimen Transport

Transport the labelled specimen to the laboratory in a sealed zip closable bag.

Store the specimen in a zip closable bag at room temperature.

1.7 Specimen Shipment

Ship specimens periodically at ambient temperature.

1.8 Quality Control Sample

1.8.1   *Container Blanks*

Unused zip closable bags serve as container blanks. Container blanks assess the potential for sample contamination, or are used for direct post-study measurement with suitable QC material. When a new lot of zip closable bags are received at the warehouse, at least six bags are labelled as "container blanks" and are sent directly to the testing laboratory. All untested bags are quarantined until the testing laboratory returns the results and approves their use.

Instructions for hair sampling for mercury analysis

A small lock of hair (thickness about a match) from the back of the neck is tied together with a cotton string. The knot is tied about 1 cm from the scalp.

The lock is cut as close to the scalp as possible and placed is a marked paper envelope (not plastic due to problems with static electricity). The hair sample below to the right is ideal, because the hair strands are aligned, and proximal end of the hair is easily identified (the yellow arrow).

The envelopes with hair samples can be stored at room temperature.

Please label the envelope with the following information:

> Project name or number
> Subject name and/or code
> Date of sampling
> Sampling number (if appropriate)

Trace Elements Laboratory
University of Southern Denmark/ Odense University Hospital
April, 2005

ANNEX D
EXAMPLE OF A FOOD FREQUENCY QUESTIONNAIRE

Characterization of Diet and Mercury in the Community

FREQUENCY OF TRADITIONAL FOOD

ID: _____

Date:_____

Respondent's gender _____

This questionnaire concerns traditional food: traditional food comes from the local land and environment (animals, birds, fish, wild plants…)

For each season, that for the **winter** (*December, January, February*), for the **spring** (*March, April, May*), for the **summer** (*June, July, August*) and for the **fall** (*September, October, November*), please recall as exactly as you can, how many **days a week in a season**, or for foods eaten less often, how many **days per season**, you personally ate the following food:

FISH

Species: **Arctic char** **Yes** **No**	Frequency – meals per week in a season (MPW) or meals per season (MPS)[1]				Cooking methods (dried, fried, smoked, etc; if fried, specify type of oil used)
	Winter	**Spring**	**Summer**	**Fall**	
Whole	_____	_____	_____	_____	_____
Flesh	_____	_____	_____	_____	_____
Skin Yes No	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Eggs	_____	_____	_____	_____	_____

[1] Interviewer: make sure to write down if the amount eaten is MPW or MPS.

Species: **Eel** **Yes** **No**	Frequency – meals per week in a season (MPW) or meals per season (MPS)[1]				Cooking methods (dried, fried, smoked, etc; if fried, specify type of oil used)
	Winter	**Spring**	**Summer**	**Fall**	
Whole	_____	_____	_____	_____	_____
Flesh	_____	_____	_____	_____	_____
Skin Yes No	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Eggs	_____	_____	_____	_____	_____

[1] Interviewer: make sure to write down if the amount eaten is MPW or MPS.

Species: Lake Trout Yes No	Frequency – meals per week in a season (MPW) or meals per season (MPS)[1]				Cooking methods (dried, fried, smoked, etc; if fried, specify type of oil used)
	Winter	**Spring**	**Summer**	**Fall**	
Whole	_____	_____	_____	_____	_____
Flesh	_____	_____	_____	_____	_____
Skin Yes No	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Organ (_____)	_____	_____	_____	_____	_____
Eggs	_____	_____	_____	_____	_____

[1] Interviewer: make sure to write down if the amount eaten is MPW or MPS.

ANNEX E
EXAMPLE OF A 24-HOUR RECALL QUESTIONNAIRE

Characterization of Diet and Mercury in the Community

INDIVIDUAL 24-HOUR RECALL

ID: _____   Date: _____

Administered by: _____   Time: _____

For women only:

Are you pregnant? Yes ☐   No ☐   Are you breast-feeding an infant? Yes ☐   No ☐
Were you pregnant the last six months? Yes ☐   No ☐
Did you make a miscarriage the last six months? Yes ☐   No ☐

Write all what you have eaten since 24 hours. **Remember:** lard, butter, margarine, garlic, barley, salad dressing and other condiments, type of oil in the cooking, the milk/creamer/sugar in beverages, any juice, alcohol, jam/honey/peanut butter...? Any snacks, beverages, or foods consumed outside the home?

Time	Food/drink name	Description of preparation (raw, cooked, smoked, …)	Amount (serving)

Time	Food/drink name	Description of preparation (raw, cooked, smoked, …)	Amount (serving)

Would you consider yesterday to be a usual day?

<div align="right">Yes</div>

Thank you.

ANNEX F
EXAMPLE OF A SYSTEMATIC OCCUPATIONAL DATA COLLECTION SHEET

Date of visit   _____

Name of company   _____

Person in charge   _____

General Working Environment

Number of employees   _____

Number of women   _____

Number of men   _____

Temperature   _____

Humidity   _____

Surface of the plant   _____

Ventilation: general and
local exhaust for chemicals   _____

Description of Work Process

What type of production   _____

Level of production   _____

Different phases of work process (describe)
and time allocated for each phase of work
process   _____

Chemicals that are used:	**Chemical 1**	**Chemical 2**	**Chemical 3**
Data sheet information available?			
Supplier?			
Frequency of utilization?			
Quantity used?			
Number of workers involved in process using chemicals?			
Personal protective equipment?			
Chemicals stored in warehouse?			
Presence of waste disposal system?			

ANNEX G
STEP BY STEP RISK COMMUNICATION GUIDE
FOR MERCURY IN FISH

1. **Risk Assessment & Risk Management**

    o Do you have a problem with mercury in fish in your population?

    o Who are your target populations at risk?

    o How will communication assist in managing this problem?

2. **Goals & Objectives**

    o Define what it is you are aiming to achieve and who your target audience is, **for example:**

        i.   Educating target audience, such as women of child-bearing age, people who consume large amounts of fish.

        ii. Educating public health professionals, seafood industry, educators and other stakeholders.

        iii. Improving the quality of information in the public domain on the issue.

3. **Communication Landscape and Consultation**

    o What kinds of expertise do you need in your programme planning group?

    o Who are the people that your target audience turn to for advice?

    o Are there opinion leaders/influencers (public health professionals, community groups) that can help you communicate your message?

    o Start consultation early - these people can help you develop your key messages and decide on the best communication channels.

    o Continue consultation on an ongoing basis.

4. **Understand your target audience**

    Campaigns with clearly identified target audiences usually work more effectively than general campaigns

    o From Step 2 and 3 above, who are the groups that you should target?

    o Incorporate information about their typical diet, especially level of fish consumption, and level of methylmercury in those fish (would partly be covered by Step 1).

    o How do they source their fish - through direct catch, market, fish shop?

    o What is their literacy level?

    o Do they have access to technology – such as internet?

    o Where do they currently get information regarding diet and health – such as doctors, nurses, media, literature, internet ?

    o What other ways may be possible to access them – such as community organizations, point of sale, etc.

5. **Key Messages**

    o   Be sure to include information on the benefits of fish as well as the risks.

    o   Usually helps to start with the benefits and then move onto the risks.

    o   Offer simple, positive and feasible choices.

    o   Underlying messages might include, for example:

        iv.   Fish is an important part of a balanced diet and has many important nutrients.

        v.   However **some** fish (large predatory fish - such as shark, swordfish and marlin) have elevated mercury levels and their consumption should be limited.

        vi.   Many other fish and shellfish are low in mercury and their consumption should be encouraged.

        vii. It is important that you know how to pick the right kind of fish so you can get all of the benefits without the risks.

6. **Communication methods**

    o   Identify the most appropriate method(s) for delivering the message. List some? Written materials, public meetings, media, partnerships with stakeholders.

    o   Consider the various channels which can be used to communicate your message, **for example**:

        viii. Places where pregnant women go to for advice - Public health professionals (doctors, nurses, midwives);

        ix.   Community groups;

        x.   Fish shops/markets;

        xi.   Media (care should be taken to ensure the message is properly delivered).

    o   Using multiple channels is more effective than using a single channel.

    o   Consider whether your channels need to be educated prior to embarking on the campaign - make sure they are well equipped with appropriate advice to communicate of your behalf – for example, you may wish to hold workshops for midwives/doctors, or maybe prepare an article for a medical journal, do fish retailers need more information?

    o   Test the key messages for the method of dissemination selected.

7. **Support Materials**

    o   What type of support materials will work for your target audience, consider the following:

        i.   Literacy levels - will pictures work better than words?

        ii.   Translate materials into appropriate languages; or

        iii. Access to technology

    o   Example of possible support materials:

        xii. Brochure;

        xiii. Poster;

        xiv. Information card;

        xv.   Website; or

        xvi. Combination of above.

o   You may need to think of new ways to reach your target audience - you are often competing for their attention.

o   Make sure you have further information accessible to those who want it – for example, you may want to prepare a summary paper for doctors.

8.   Distribution and Implementation

o   Plan on how to distribute your materials - in many cases the organizations that you consult with can assist with this.

o   If you intend to do media launch, prepare your spokespeople adequately, prepare possible questions and answers.

o   Ensure you have more information available for those who want it.

o   Plan for the longevity of the campaign. For example, each generation of pregnant women is constantly renewing, make sure you have ways to keep the information replenished - this is not a one time campaign.

9.   Evaluation

o   Consider how to measure the effectiveness of your campaign using appropriate indicators.

o   Consult with your partner organizations and target audience.

o   There are ways to continually improve on your work.

o   Remember this is an ongoing campaign; you can improve on it as you learn more.