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**Intergovernmental negotiating committee
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**Preparation of a global legally binding instrument
on mercury**

Report on information on harmonized systems for measuring mercury body burden

Note by the secretariat

1. At its first session, held from 7 to 11 June 2010, the intergovernmental negotiating committee to prepare a global legally binding instrument on mercury requested the secretariat to prepare information on harmonized systems for measuring mercury body burden, starting on a pilot scale for the committee's second session, with the possibility of expansion during the remainder of the negotiation process. The committee noted that the secretariat would invite relevant partners, as needed, to provide the information requested.

2. In recognition of the statements made by the World Health Organization (WHO) during the committee's first session and its stated willingness to provide Governments with technical support relating to the management of health risks posed by mercury, the secretariat invited WHO to take the lead in carrying out the work to provide the report requested.

3. The annex to the present note contains the report developed by WHO, which has been reproduced as submitted, without formal editing.

* UNEP(DTIE)/Hg/INC.2/1.

Annex

Report on information on harmonized systems for measuring mercury body burden

Introduction

1. The present note, prepared by the World Health Organization, responds to the request of the intergovernmental negotiating committee at its first session to provide "(b) Information on harmonized systems for measuring body burden, starting on a pilot scale for the second session of the committee with the possibility for expansion during the remainder of the negotiation process".

2. Mercury exists in the environment in three forms: elemental (metallic or Hg^0), inorganic (Hg^{2+}; includes mercuric oxide, mercuric chloride, mercuric sulfide), and organic (e.g., methylmercury, thiomerosol). The form of the mercury affects its absorption, toxicokinetics, retention and ultimately the body burden. Measurement of body burden is done through the use of biomarkers. These issues are described in more detail below.

Environmental Forms of Mercury

Elemental

3. Elemental mercury exposure can result from accidental spills (e.g., broken thermometers, electrical switches, barometers, blood pressure monitors, etc.) and dental amalgams. Skin lightening creams and soaps, and some traditional medicines are known to contain both elemental and inorganic mercury. Elemental mercury is used to capture gold particles as an amalgam; the amalgam is then heated to vaporize the mercury. Mercury is used in some religious practices (e.g., Voodoo, Santeria, and Espiritismo).

4. Elemental mercury is poorly absorbed when ingested and is almost completely excreted in the feces, causing mild intestinal irritation. Little elemental mercury is absorbed from dermal contact. When inhaled, however, 80% of elemental mercury vapor is rapidly absorbed through the lungs and is readily distributed throughout the body crossing blood-brain and placental barriers.

5. Once it has entered tissues, elemental mercury is oxidized to ionic (Hg2+) mercury, retarding it from returning to general circulation. The ionic form does not cross biological barriers well and can be retained in tissues, brain and kidney in particular, for several weeks.

6. The pattern of excretion depends on how much elemental mercury is oxidized. Some elemental mercury may be exhaled, and a small proportion of elemental and/or ionic mercury may be excreted in saliva, sweat, and bile.

Inorganic Mercury

7. Inorganic mercury compounds such as mercuric chloride, mercuric oxide, mercuric iodide, mercurous acetate, and mercurous chloride are or have been used for their antiseptic, bactericidal, fungicidal, diuretic and/or cathartic properties.

8. Inorganic mercurial absorption via ingestion varies by the solubility and type of salt. Absorption decreases with decreasing water solubility. Increases in intestinal pH, a milk diet (relevant to neonates), and increased pinocytotic activity of the digestive tract have all been associated with an increased absorption of inorganic mercury. Due to these characteristics, infants are more at risk for increased absorption of inorganic mercury than adults. Absorption of inorganic mercury is reported to be as much as 20% by ingestion. Absorption of inorganic mercury following inhalation is not well studied but absorption via inhalation of mercuric chloride has been reported to be 40% in dogs. Inorganic mercury can be absorbed dermally as evidenced by studies of skin lightening creams and soaps. Inorganic mercury does not cross the blood-brain or placental barriers well and is accumulated in the kidneys. The reported half-life of inorganic (ionic) mercury in blood is 20 to 66 days. Ionic mercury from inorganic mercury salts are excreted in urine and feces but can also be found in breast milk.

Organic Mercury

9. Exposure to organic mercury is primarly in the form of methyl mercury. Minor organic mercury exposures include thiomerosol (a vaccine preservative) and other pharmaceuticals. Exposure to methylmercury primarily results from eating fish and seafood.

10. When ingested, 95% of methylmercury is absorbed. Methylmercury crosses the blood-brain and placental barriers and is able to enter cells. It is oxidized in the brain, so that it cannot re-cross the blood-brain barrier, allowing for accumulation of mercury. Some methylmercury is converted to inorganic mercury and excreted. The half-life of methylmercury in humans is relatively long; estimates range from 44 to 80 days. Excretion occurs primarily in feces and hair and about a third in urine. Some methylmercury may be excreted in milk but to a much lesser extent.

Biomarkers of Mercury Exposure

11. The body burden of mercury is estimated by the measurement of mercury in various human biological media (e.g., blood, cord blood, cord tissue, urine, milk, hair and nails). Measurements in such media are referred to as biomarkers of exposure. These media have the advantages that they can be stored easily, and with the exception of blood, all can be collected non-invasively. For some of these biomarkers, relationships have been established with health effects (e.g., hair mercury and IQ deficits). Mercury in various biological media is usually reduced to its elemental state prior to analysis. Thus knowledge about the chemical form of mercury exposure (elemental, ionic, organic) is generally not available from biomarker analysis. As described below, however, the presence of mercury in certain biologic media will provide some clues as to the environmental form of mercury exposure.

Blood

12. The presence of mercury in blood indicates current or recent exposure. There is a direct relationship between consumption of fish contaminated by methylmercury and mercury concentration in blood. Methylmercury is readily absorbed by the gastrointestinal tract, peaks in blood within 4 to 14 hours and undergoes clearance to other body tissues within 20 to 30 hours. Inorganic and elemental mercury concentrations in blood also peak in a relatively short period of time. WHO considers the normal mean concentration of mercury in whole blood to be 5 to 10 µg/L.

Urine

13. Urine is the best measure of recent exposure to elemental mercury vapor or inorganic mercury. Since inorganic mercury can accumulate in the kidneys and be slowly released, urinary mercury may represent current or past exposure. Urinary mercury is thought to best indicate the level of mercury in the kidneys. Waste product concentration, including mercury, can vary with urine dilution and is expressed in units of creatinine. Mercury in urine correlates well with moderate and high elemental mercury vapor exposure. Normal urinary mercury is less than 5 µg/g creatinine.

Hair

14. Mercury in hair is an excellent biomarker for methylmercury. 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 is the preferred choice for many studies as it provides a simple, integrative, and non-invasive sample for estimating long-term average exposure. Methylmercury is incorporated into hair as the hair is formed and has a direct relationship with blood mercury levels. Hair allows for peaks in mercury concentration to be detected and can put exposure in temporal context as hair grows about 1 cm each month. Inorganic and elemental forms of mercury are not excreted to any significant amount in scalp hair, making hair an inappropriate biomarker of inorganic or elemental mercury exposure. Among fish consumers, 80% of the mercury in hair is from methylmercury. Age, hair coloring and treatments, and ethnicity (hair type varies by ethnicity) may affect uptake of mercury by hair. In people who do not consume contaminated fish, 1 to 2 ppm of mercury in hair is normal while those consuming contaminated fish may have 10 ppm or higher mercury in hair.

Cord Blood and Tissue

15. Cord blood concentrations have been found to be better in characterizing children's prenatal methylmercury exposures than maternal hair levels. Samples are easy to collect for births in medical settings. When expressed in relation to the dry weight of cord tissue, cord mercury concentration correlates well with that of cord blood. In fact, dry-weight cord mercury concentration was found to be almost as good a predictor of methylmercury-associated neuropsychological deficits at 7 years of age as was the cord-blood mercury concentration.

Milk

16. Human milk reflects mercury intake during pregnancy not the breast-feeding period and does not correlate with infant or mother's hair mercury. Milk represents a major route of excretion of lipophilic substances. Most forms of mercury, however, are not lipophilic and what mercury is excreted in milk depends on many maternal factors (age, nutritional status, body mass index, time of sampling, lactation period, and milk fat content).

Nails

17. Fingernail and toenail mercury levels have also been used to measure the body burden of mercury. The extent to which finger and toenail levels correlate with external mercury exposure has not been established, however.

Harmonized System for Measuring Body Burden

18. Hair sampling is the preferred method for measuring methylmercury concentrations, as obtaining hair samples is minimally invasive, presents little risk of disease transmission, and does not require medical supervision. There are also fewer cultural barriers to obtaining hair samples, although in some regions of Africa and Latin America hair may be of superstitious or magical significance. Other factors to consider include sampling of persons who are bald or have short hair, and the use of certain hair treatments (artificial waving may reduce mercury content while mercury-containing soaps may increase it). Population-based studies of this sort have not been conducted in many countries; often, only sparse data on mercury levels or fish consumption are available for highly exposed subgroups. Focused sampling of populations believed to have high methylmercury exposure can be useful for estimating the burden of disease among groups with the greatest risk. This requires careful consideration of sites to be studied and how the results can be extrapolated to non-sampled areas. Subsistence fishing, location near environmental hotspots, and differences in other relevant behaviors and exposures throughout the region must be considered. Although mercury concentration data in children and males may be useful for other public health purposes, they are not required to estimate the potential IQ decrements resulting from in utero methylmercury exposure. Therefore, if resources are limited, mercury samples need only be collected from women of childbearing age to estimate potential IQ deficits in the population's children. It is essential that protocols for collection and analysis of the hair be carefully followed to avoid error in the interpretation of results.

19. Urine samples are considered to be the best determinant of body burden of mercury from long-term exposure to elemental and inorganic mercury. Urinary mercury measurement is reliable and simple and provides rapid identification of individuals with elevated mercury levels. It is a more appropriate marker of exposure to inorganic or elemental mercury, since organic mercury represents only a small fraction of urinary mercury. Blood samples are useful primarily in cases of short-term, higher-level exposures to these mercury forms, but are not as reliable as an indicator of total body burden in longer term exposures.

Potential Pilot Studies

20. As described in document UNEP(DTIE)/Hg/INC.2/5 concerning the health impacts of mercury, methylmercury is the most toxic and the most common form of mercury found in the environment. Hair sampling is the preferred method for measuring methylmercury concentrations for the reasons outlined above.

21. Despite the relative ease of sample collection (hair), little information in the open scientific literature is available on hair mercury in the general population of countries with high fish consumption. Most studies that have examined hair mercury were of populations where there was a known source of mercury in the vicinity (e.g., artisanal gold mining) or the population was a select group (e.g., subsistence fishers).

22. Pilot studies should focus on the collection of hair samples from pregnant women and women of child-bearing age in countries with high fish consumption. The focus on pregnant women and women of child-bearing age is because there is a direct correlation between neurodevelopmental deficits and mothers' hair mercury. Furthermore a methodology to estimate the neurodevelopmental burden of disease based on hair mercury in women of child-bearing age has been developed (See: WHO. 2008. Mercury: Assessing the Environmental Burden of Disease at National and Local Levels. Environmental Burden of Disease Series, No. 16). It is critical that the results of the pilot studies be presented as distributions to allow health risk assessors to make optimum use of the information.

23. It is essential in the undertaking of any pilot studies that biological specimens be collected 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. Personal information must be handled and maintained confidentially. 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.

Further Information

24. The present note is based on World Health Organization and other United Nations documents on mercury. It is beyond the scope of the note to capture all of the information described in those documents. The reader is therefore referred to several WHO documents for a more complete description on the collection of biological samples (e.g., hair, nails, urine), and analysis of mercury in these samples. These documents include, but are not limited to:

- JECFA. 2010. Seventy-second meeting. Rome, 16–25 February 2010. Summary and conclusions. Issued 16th March 2010
- WHO and UNEP. 2008. Guidance for Identifying Populations at Risk from Mercury Exposure. Geneva, Switzerland. [1]
- WHO. 2008. Mercury: Assessing the Environmental Burden of Disease at National and Local Levels. Environmental Burden of Disease Series, No. 16. WHO. Geneva, Switzerland.
- WHO and UNEP. 2002. Global Mercury Assessment.
- WHO. 2003. Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects. Concise International Chemical Assessment Document 50. Geneva, Switzerland.

1 Note from the secretariat – An executive synopsis of this guidance document is available to the committee as document UNEP(DTIE)/Hg/INC.2/19.