Human biomonitoring survey
assessment of prenatal exposures to mercury
using biomarkers in cord blood, maternal urine and hair

in Chennai, India

The first survey protocol

2017

Contents

1. Background

Mercury is recognized by WHO as one of the top 10 chemicals or groups of chemicals of major public health concern. Its toxicity to human health has long been known, and the toxic effects of different forms of mercury extensively studied *(1)*.

Elemental and methylmercury are toxic to the central and peripheral nervous systems. The inhalation of mercury vapour can produce harmful effects on the nervous, digestive and immune systems, lungs and kidneys, and may be fatal. The inorganic salts of mercury are corrosive to the skin, eyes and gastrointestinal tract, and may induce kidney toxicity if ingested.

All humans are exposed to some level of mercury. Most people are exposed to low levels, often through chronic exposure (continuous or intermittent long-term contact). However, some people are exposed to high levels of mercury that can cause acute poisonings.

Fetuses are most susceptible to mercury. Methylmercury exposure in the womb can result from a mother's consumption of contaminated fish and shellfish. It can adversely affect a baby's growing and developing brain and nervous system, which leads to disorders of cognitive functions, memory, attention, language, and fine motor and visual-spatial skills later in life *(2, 3)*.

Human biomonitoring (HBM) is an effective and reliable tool to assess cumulative exposure to environmental pollutants and is an essential element in a strategy aiming to integrate health and environmental policies. Biomonitoring data directly reflect the total body burden (or biological effect) resulting from all routes of exposure, and inter-individual variability in exposure levels, metabolism and excretion rates. Determination of mercury levels in human tissues, such as hair, blood, nails, milk and urine, is recommended for assessing population exposure to mercury and its compounds *(4)*. The results of biomonitoring-based surveillance can be used for planning and assessing the effectiveness of risk prevention measures.

To protect human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds the Minamata Convention was adopted as the global legal instrument *(5)*. According to the Convention, the health sector is responsible for identification of population groups exposed to mercury and its compounds. HBM can be used by national governments to assess exposure to mercury for identification of populations at risks.

Since the period of in-utero development is the most vulnerable stage, in terms of long-term adverse neurodevelopmental effects of mercury, characterization of prenatal exposure is critical for evaluating the public health impact of mercury, and for assessing the public health benefits of reducing exposure. A harmonized approach is necessary to ensure provision of reliable and comparable results at national, regional and global level.

The basic intent of this document is to provide guidance for countries in constructing a national protocol for the monitoring of human exposure to mercury. This document was developed based on the outcomes of an international experts meeting held in Bonn, Germany on 24–25 June 2015 *(6)*. A number of other meetings and expert discussions provided important input to this methodology development.

The protocol comprises recommendations on survey design, recruitment and fieldwork, dealing with biological materials, data management and communication, and ethical considerations.

1.1. Scientific evidence and international consultations

This document is based on scientific information on mercury biomonitoring and health effects collected by WHO, including the following: *Guidance for identifying populations at risk from mercury exposure* (2008)*(4)*; *Mercury and Health* fact sheet (2016)*(1)*; *Mercury exposure and health impacts among individuals in the artisanal and small-scale gold mining community* (2014)*(7)*; documents on the work of WHO in coordinating the development of standardized protocols for HBM surveys on mercury, and planning pilot testing in volunteer countries, under the mandate of the Parma Declaration commitments to reduce early life exposure to environmental pollutants *(8)*; and the *Report on information on harmonized systems for measuring mercury body burden* (2011)*(9)*.

In April 2012, at a meeting in Catania, Italy, WHO experts discussed the overall approach, biological matrices and indicators for assessment of prenatal exposure to mercury for development of a harmonized approach to mercury HBM *(10)*. Women who had just delivered a child were agreed as the target population, and scalp hair, cord blood and urine as the matrices for assessment of prenatal exposure to mercury during last three months of pregnancy. *(10)*. The approach proposed by the experts was agreed by the representatives of WHO European Region Member States at the Second Extraordinary Meeting of the European Environment and Health Task Force (EHTF), The Hague, Netherlands, 31 May–1 June 2012 *(11)*.

The discussion continued during a number of forums including: the special session “Protecting human health from negative impact of mercury: from science to policy” at the International Conference on Mercury as a Global Pollutant (14–19 June 2015, Jeju, Korea)*(12)*; the session “Human biomonitoring as an instrument for assessment of exposure to mercury” at the meeting of representatives of the European Member States “Health sector involvement in the implementation of the Minamata Convention” (24–25 June 2015, Bonn, Germany)*(6)*; the international technical experts workshop “Harmonized approach to biomonitoring of human exposure to mercury” (26 June 2015, Bonn, Germany) (unpublished minutes); and during the session “Exposure assessment and health effects” organized by the National Institute for Minamata Disease, Japan, WHO Collaborating Centre for Studies on the Health Effects of Mercury Compounds at the Fifth Conference on Prenatal Programming and Toxicity (14–16 November 2016, Kitakuyshi, Japan)*(13)*.

International Ethical Guidelines for Health-related Research Involving Humans (2016) prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with WHO laid the basis for the ethical requirements included in the protocol *(14)*.

2. Aims and approach of the survey

The primary objectives of the survey are to get knowledge on baseline data on prenatal exposure to mercury in population in Chennai, India and to provide the data needed for the development of a global mercury monitoring plan. The survey implementation will:

- extend the knowledge on baseline levels and sources of human exposure to mercury in Chennai, India;
- characterize the level and distribution of prenatal exposure in population in Chennai as a potential hotspots due to a number of sources of mercury ;
- identify risk factors for exposure from different sources of mercury;

- contribute to the implementation of the Minamata Convention in India and development of effective measures to prevent the negative impacts of mercury on human health, and especially in vulnerable groups;
- provide analytical tools to monitor progress towards implementation of specific goals of the Minamata Convention (the WHO methodology involves assessment of exposure in a set of participants at a certain moment in time; such a cross-sectional survey is expected to be repeated at regular intervals, e.g. every five years).

The objective of this protocol is to provide a framework for all activities and tasks associated with the collection, analysis, assessment and reporting on prenatal exposure to mercury. This has to be applied consistently in all other surveys organized in India in a future to ensure comparability of data. WHO Master Protocol is a basis for the national protocol development. Information on identification of hotspots and hospitals selection is included in the protocol. The informed consent form is adapted to the national culture. No modifications against WHO Master Protocol are done.

Through expert recommendations and technical meetings, WHO has developed the following approach:

- Recruitment will be conducted during antenatal visits and exceptionally at maternity hospitals.
- Participants will be enrolled using a set of defined inclusion and exclusion criteria (legal adults, living in the catchment area of the hospital, live birth, etc.).
- A standardized questionnaire will be administered to participants to assess potential sources of exposure.
- The survey will use non-invasive sampling only (maternal hair, urine and cord blood); standard operating procedures (SOPs) for no risk sampling are provided by WHO.
- National surveys will involve a capacity-building component, to enable analysis of samples in domestic laboratories; methodological support will be provided by WHO, its temporary advisers and reference laboratories.
- Proficiency test and duplicate quality control samples will be analysed in reference laboratories, to ensure comparability of the results from different countries.

3. General principles

The following underlying principles should be considered when applying this protocol to developing a national protocol for monitoring of pre-natal exposure to mercury:

- Sampling of biological material (hair, cord blood and urine) should not harm or pose an undue burden on recruited women.
- Safeguarding the confidentiality of information should be assured.
- Ethical standards, including prior informed consent, should be respected.
- The protocol should be practical, feasible and sustainable.
- Emphasis should be placed on proficiency.
- Quality assurance of results should be independently confirmed.

3.1. Roles and responsibilities of WHO and India (Sri Ramachandra University, Chennai)

Both WHO and the responsible institution in India have roles and responsibilities in the application of the protocol.

The role of WHO in the protocol application is:

- to submit and get approval of the protocol from the WHO Research Ethics Review Committee (ERC) and to communicate modifications of national protocols to the ERC, requesting approval before their implementation;
- to organize a training for the national coordinator and the chief of the national laboratory ~~laboratory~~ on the survey design and implementation;
- to develop and provide India with training materials and SOPs for sampling of biological material, mercury analysis, and creation of national databases, as well as to develop and provide an eligibility screening form and a questionnaire to be completed by the survey participants;
- as an owner of data collected in the national pilot surveys, to gather the data from India and to store them in a consolidated global database; to analyse the data gathered through the survey implementation, and to report on the level and distribution of the exposure to mercury at national, regional and global scales to interested governmental and nongovernmental stakeholders (including experts and academia) at an international level;
- to provide technical assistance to India, if necessary, including in implementation of the survey, interpretation of results and risk communication;
- to update the protocol on a global level before each round of mercury HBM, if necessary;
- to coordinate the quality control process to ensure the quality of laboratory analysis of mercury in all participating in the pilot survey countries including India.

The role of India (Sri Ramachandra University, Chennai) in the protocol application is:

- to adapt the WHO protocol to national realities and to obtain approval from University and the national ethics committees;
- to communicate any modifications in the WHO protocol and to submit the national protocol to WHO before the survey implementation;
- to fully comply with the protocol principles when implementing the mercury HBM survey;
- to train the field staff involved in the survey implementation including, but not limited to, interviewers, maternity hospital staff, those responsible for collecting biological samples, those responsible for the storage and transportation of biological samples, laboratory analysts, those responsible for data handling and database creation, etc.;
- to coordinate the survey implementation with partner institutions such as Regional Occupational Health Centers (ROHCs), Indian Council of Medical Research (ICMR), the National Environmental Engineering Research Institute (NEERI), Council of Scientific and Industrial Research (CSIR)
- to collect data on exposure to mercury in target population in selected area; to fully comply with WHO SOPs on analysis of mercury in human scalp hair, cord blood and urine including non-invasive sampling procedures;
- as an owner of the national data, to collect and store the data in a national database;
- to analyse national data on the level and distribution of exposure to mercury and to report the data to interested governmental and nongovernmental stakeholders at the national level;
- to report on the application of the protocol to WHO;
- to report to WHO on results obtained in the survey, conducted according to the WHO protocol.

4. Developing a national protocol

This Protocol has been developed based on WHO Master Protocol on the survey. All ethical considerations from WHO Master Protocol are included in the national survey protocol. The WHO guidelines assisted the national coordinator in developing a national protocol to meet the aims of the survey. The national coordinator is responsible:

- for overall planning and implementation of the survey in the country, assisted by the appropriately trained field and laboratory staff;

- for assuring that the survey meets all national ethical requirements for studies involving human subjects;

- for communicating any changes in the protocol to the WHO team, who will communicate them in good time to the WHO ERC, requesting approval of the modifications before they can be implemented;

- for avoiding deviations to the WHO Master Protocol that can unintentionally result in the reduced reliability or comparability of data at regional and/or global level.

The national protocol was developed by the national coordinator of the survey: Dr Krishnendu MUKHOPADHYAY , Associate Professor & Academic Coordinator, Department of Environmental Health Engineering Sri Ramachandra University.

5. Survey design

The survey involves mothers of newborn children recruited during antenatal visits, or at maternity wards if it was not possible to recruit during antenatal visits. The randomized clustered design of the survey allows assessment of prenatal exposure to mercury in the general population and in exposure hotspots, such as Chennai areas contaminated by industrial emissions and due to high levels of consumption of fish at coastal areas. It is very important to involve the community and local representatives in the survey from an early stage to ensure support for the survey and proper communication of healthy behavioural habits to pregnant women to prevent avoidable exposure, if necessary. The proposed community involvement strategy is in Annex 4.

The survey of high-exposure populations in hotspots in India involves samples of women who are known or suspected to have increased levels of exposure to mercury and/or its compounds.

This document provides a detailed description and sample size justification for high-exposure surveys. In India, there are defined populations with expected high levels of exposure to mercury. The high-exposure survey is conducted. A “reference values”, defined as typical exposure levels in the general population of the country will be considered for mercury risk assessment. A detailed approach for selecting maternity hospitals in high-exposure areas, and criteria for recruiting highly exposed individuals will take into account local conditions.

The proposed survey design includes a limited set of biomarkers (scalp hair, cord blood, urine). Affordability and feasibility were important biomarker selection criteria as the survey is intended to be applicable in the majority of countries and in India, in the area with a number of mercury sources.

The minimum recommended sample size for the hot-spot population survey is defined below, based on the experience of the European project COPHES/DEMOCOPHES for general population, and selected national HBM surveys.

5.1. Target population

The target population is mothers who have just delivered a child.

All efforts will be made to gain consent from women during antenatal care visits. In cases where women do not have an antenatal care visit during the two weeks before delivery, they can be contacted in maternity hospitals shortly before or after the birth.[1] The following criteria will be applied to determine whether a woman can be recruited and consent given at the time of delivery:

- low level of stress (no fear at childbirth)
- normal development of the childbirth process
- satisfactory physiological condition of the mother
- satisfactory physiological condition of the fetus
- no severe pain
- no emergency signs *(15)*.

Survey interviewers will briefly describe the objectives of the survey (information is available in Annex 2) and ask the women if they are interested in participating. If a positive answer is provided, the interviewer, using an eligibility screening form (Annex 1) will conduct a brief interview to check the eligibility of the candidate. If eligibility is confirmed, the interviewer will explain the purpose of the survey, specific activities and risks, and present the informed consent form (Annex 2). If consent is provided, the interviewer will then collect exposure information using the standardized questionnaire (Annex 3), obtain medical and anthropometrical data from the medical records (see specification below), and collect a sample of scalp hair (following relevant SOPs). Samples of urine and cord blood should be collected by the medical personnel in due course, depending on specific rules and procedures in the maternity ward (following relevant SOPs).

The total time of a woman involvement in the survey should not exceed the time necessary for recruitment, sampling and questioning (not more than 1.5 hour) including:
Recruitment – 10-30 min (depending on time that is necessary for a women to read information about the survey);
Hair sampling – 10-15 min;
Urine sampling incl. explanation – 15-20 min;
Questioning – 30-35 min.
Women should be informed about that in the prior consent form.

Since the survey aims to characterize prenatal exposure to mercury, maternity hospitals are the preferred venue for the survey implementation due to the availability of medical records and because they may be the easiest place for sampling hair, cord blood and urine. However, collection of hair and urine samples, and interviews can also be conducted in other settings, such as at home within two weeks after the delivery.

All relevant information on factors that may affect exposure to mercury (e.g. age, nutritional habits, occupation, socioeconomic status, education and use of chemicals and/or mercury-containing equipment at home) will be collected using an epidemiological questionnaire proposed by WHO.

[1] No more than two weeks after delivery.

5.2. Selection of the survey target area, hospitals and number of participating mothers

5.2.1. Number of participants

The International Federation of Clinical Chemistry (IFCC), endorsed by the International Union of Pure and Applied Chemistry (IUPAC), Clinical Chemistry Division, recommends the measurement of biomarker values in at least 120 individuals per group for the determination of baseline values (hereafter called "reference values"). The reference interval is defined as the 0.95 central interfractile intervals, or the interval between the 2.5 and the 97.5 percentiles of the distribution *(16)*.

Clustered design reduces the cost and improves logistical feasibility but requires a larger sample size due to the loss of statistical efficiency. A factor of 2 is used to increase the IFCC recommended sample size of 120 to 240 participants, based on the existing literature *(17)*. This sample size estimate takes into account the clustered design of the proposed survey (samples from the same maternity hospitals are not statistically independent). It is recommended that samples are taken from 10 additional participants in case some participants drop out of the survey. Thus, 250 women is a minimum recommended sample size for each cross-sectional HBM survey in the general population.[2] Based on the data on variability in mercury levels in hair samples in women from Flanders *(18)*, a sample size of 250 women can be assumed to be large enough to demonstrate a 27% change in the geometric mean mercury level between a baseline survey and follow-up cross-sectional surveys in a different set of women in the same country, at the conventional level of statistical significance and with 80% study power. This effect size is relevant in view of differences between countries and temporal changes in mercury levels already reported in the literature.

Despite the sample size looks less in comparison to high density population in the country to make a valid estimate; for the purpose of the project India accepted samples size recommended by WHO.

100 samples are planned to be collected to represent community at the coastal area and 150 samples from the population in Chennai city (comparison group).

5.2.2. Identification of the survey target area

For mercury exposure, proximity to the sea or other substantial water bodies can be used as a criterion for site selection. In India having access to the sea, it can generally be assumed that fish consumption and exposure to methylmercury are higher close to the sea.

Emissions of inorganic mercury from industrial sources are another relevant consideration for the identification of exposure hotspots in Chennai.

To identify the area of industrial hotspots or contaminated areas the following factors were taken into account:

- size, location and other pertinent characteristics of active pollution sources of concern;
- historical contamination of the area (presence of polluting activities in the past);
- concentrations of mercury in environmental samples (air, soil, surface water or sediment, groundwater, locally produced food) exceeding health-based guidance values and/or high consumption of contaminated local food products;
- health complaints by inhabitants or documented elevated rates of conditions related to mercury;

[2] The sample size calculation can be changed for other specified populations when the data on variability in mercury level in hair samples become available.

- meteorological and geographical characteristics of the area (e.g. wind direction, topography) in relation to the source of emissions.

Available information was analysed to select an area for the survey implementation: 3 coal fired thermal power station with the previous data 0.33 mg/kg Hg in coal; municipal dumping sites; common BMW treatment facility; coal fired brick manufacturing; fishing activities; refineries, e-waste recyclers. The analysis resulted in identification of coastal area and Chennai city as a hotspot and comparison population groups for the survey implementation.

5.2.3. Selection of hospitals

Two hospitals, namely RSRM hospital and SRMC hospital, are selected in Chennai, India for subject recruitment. One hundred paired samples (100 each for cord blood, urine and scalp hair) are planned to be collected from RSRM hospital and 150 paired samples (150 each for cord blood, urine and scalp hair) will be collected from SRMC hospital.

Selection of the first hospital has been anticipated to represent fish eater community (most of the participants are from coastal area), adjacent to the thermal power station and electronic dump-yards. The second one has been assumed to represent population of Chennai city.

Agreement with the hospitals should include information about conditions for ensuring privacy for recruitment, questionning and sampling of hair (e.g. separate room in an entrance and/or in the relevant clinical department) as well as for urine sampling.

5.3. Criteria for enrollment of mothers

With regard to the selection of potential participants, the recommended inclusion criteria are as follows:

- women at least 18 years of age (legally adult);
- live birth;
- normal term delivery (at least 37 weeks of pregnancy);
- singleton pregnancy;
- living in the catchment area of the maternity hospital in the selected survey area for the last three years and for most of the time during the last three months of pregnancy (spending not more than two weeks outside the area);
- hair at least 3 cm in length on the back of the head.

Immigrants should not be excluded as long as they have sufficient language ability in the interview language(s) and meet the other eligibility criteria.

A potential occupational exposure will not be considered an exclusion criterion.

The recommended exclusion criteria are as follows:

- women younger than 18 years old;
- delivery before 37 weeks of pregnancy;
- still-birth or delivery of a lifeless child;
- not a singleton pregnancy (twins, triplets, etc.);
- living in the catchment area of the maternity hospital or in the selected high-exposure area for less than three years before delivery;
- living outside the selected high-exposure area for more than two weeks during last three months of pregnancy;
- having hair shorter that 3 cm on the back of the head;

- not having sufficient language skills to understand information about the survey, the informed consent and other relevant information;
- women with mental disorders.
- women with hepatitis C, malaria, HIV and other contagious conditions, according to the relevant national regulations;
- women having lacerations during child delivery;
- women having complicated pregnancy.

5.4. Project follow-up: medical surveillance of people with high mercury concentrations

The main objective of the HBM survey is to generate data on the levels and distribution of prenatal exposure to mercury, in connection with different potential sources of mercury exposure, and to develop a global plan for mercury monitoring.

Elimination of mercury sources is the most important follow-up measure to reduce exposure and the associated health risks. In order to reduce exposure from industrial or environmental sources, the authorized governmental regulatory authorities such as environment protection authorities as well as local governments will be involved. For the reduction of exposure to methylmercury, public and individual advice, including dietary recommendations and guidance, based on the available scientific knowledge *(19)*, will be made available to exposed groups. Efforts will be taken to coordinate monitoring of fish contamination with mercury with HBM data.

The health impacts of mercury depend on its form and the level of exposure. Exposure to mercury vapours can cause acute and chronic kidney disorder. People chronically exposed to high concentrations of inorganic and organic mercury develop neurological symptoms.

If a high level of mercury is observed the survey coordinator should ensure that:

- for individuals with a high level of mercury in their urine, their doctors are contacted and a check-up of renal system functions is advised and arranged upon the woman's request;
- for individuals with a high level of mercury in their hair and blood, their doctors are contacted and a visit to a neurologist is advised and arranged upon the woman's request.

Implementation of the survey in big regional hospitals creates an opportunity to use existing hospital resources for organization of medical follow-up of the survey. This will be done if necessary in coordination with hospital administration.

However, it is unlikely that such clinical cases would be detected through the HBM survey.

An individual medical follow-up will be considered on a case-by-case basis, only for mothers with a confirmed high/increased level of mercury. Template letters to address a woman with high level of mercury in biological samples and template letter to her family doctor are in Annex 2.

Additional investigation of potential sources of exposure will precede risk communication and planning of protective measures.

To facilitate referral to appropriate specialists services, and the linkages with these services to allow for smooth the project follow up if necessary the national coordinator should take actions to build contacts with topical specialists (therapeutics, neurologists and gynaecologists/urologists) (see also chapter 9, Communication):

- at the project planning stage, to agree heads of hospitals a lecture to the hospital staff/topical specialists a lecture about mercury, its health effects, diagnosis of health effects that can be caused by exposure to organic and inorganic mercury;
- to agree involvement of scientists/experienced therapeutics who can advise on diagnosis and treatment of health effects potentially linked to exposure to mercury in the project if specific recommendations on medical follow up will be needed;
- when the mercury analyses results are available, to communicate them to the medical staff that can be potentially involved in the medical follow up (for example, through participation in hospital staff regular meeting); to ensure/provide contact details of specialists that can advise on additional investigation and treatment for the local therapeutics.

Two scenarios should be considered for the medical follow –up for women with confirmed high level of mercury in hair, or cord blood, or urine:

1) women with diagnosed neurological (mostly motor functions) and urinary system disorders as recorded in their medical data;

the main aim of the medical follow-up in this case is to reveal links between mercury contamination and previously diagnosed disorders: high level of mercury in hair and cord blood and neurological dysfunctions and high level of mercury in urine and renal dysfunctions; the following actions should be taken by the national survey coordinator :

a) contact women and or her family doctor (depending on answers to the relevant questions in the Informed Consent Form);

b) agree with her and with her family doctor a visit to the therapist (neurologist or gynaecologist/urologist);

c) contact the therapist and provide with an advise on additional tests to be performed to confirm/exclude mercury effects: investigate neurological disorders (mostly motor and coordination functions) or urinary system functions (to make urine analysis to reveal/exclude proteinuria);

d) advise on measures to prevent/reduce exposure to mercury;

2) women with confirmed high level of mercury with no recorded health disorders potentially link to exposure to mercury; the main aim is to diagnose if there are any health disorders potentially link to mercury contamination. The following actions should be taken to ensure medical follow-up:

a) contact women and or her family doctor (depending on answers to the relevant questions in the Prior Consent Form);

b) advise to women and family doctor on additional investigation to be performed to confirm/exclude mercury effects: investigate neurological disorders (mostly motor and coordination functions) or urinary system functions (to make urine analysis to reveal/exclude proteinuria); in case it can't be done by the family doctor to advise on what kind of specialists should be visited to check the health status; for example, using the local hospital capacities;

c) communicate measures to reduce exposure to mercury to the woman directly or/and to her family doctor.

Neurological and cognitive development surveillance will be considered for children delivered by mothers with a very high concentration of mercury, within the first control at three months from delivery. It will be discussed with each mother of concern in coordination with their family doctors is agreed.

The national survey coordinator is responsible for contacting mothers with high mercury concentration and/or their doctors and advising on neurological examination of a child.

6. Recruitment and fieldwork

The processes of recruitment and fieldwork are described briefly in this section.

6.1. Fieldwork management

Fieldwork is the responsibility of the Sri Ramachandra University and the national coordinator. The following actions will be implemented to ensure success of the field work:

- using the standardized methodological documents provided by WHO as a starting point to prepare the SOPs, fieldwork manual and other documentation for the national survey and in local language if necessary (informed consent form and the questionnaire);
- training field personnel and supervising their work;
- obtaining necessary permissions from regional and local authorities;
- liaising with the local community, identifying and engaging local representatives to promote the survey;
- developing information leaflet for survey participants;
- informing the recruited women, administering informed consent and conducting interviews;
- collecting, storing and shipping samples to the respective laboratories;
- entering the data into a data file and performing preliminary data cleaning;
- analysing national data or submitting the data to a WHO-affiliated data analysis centre;
- communicating the results of the survey to the participants and national public health authorities.

Experienced fieldwork personnel from the University and the maternity hospitals will be deployed to perform the work.

Given that regular personnel of maternity wards will likely perform the survey tasks in addition to their normal duties, all possible efforts will be taken to avoid adversely affect their performance:

- most of the field work will be done by the scientific staff of the University;
- a number of partners will be involved in the field work to reduce workload related to the survey implementation on hospital staff, in particular, Regional Occupational Health Centers (ROHCs), Indian Council of Medical Research (ICMR), The National Environmental Engineering Research Institute (NEERI), Council of Scientific and Industrial Research (CSIR);
- personnel of the maternity staff (midwifes) should be responsible only for sampling of cord blood (in maternity wards) and urine before or after delivery; midwifes assisting with delivery should not be involved in recruitment and, especially, in recruitment of their own patients;
- physicians attending the birth should not be involved in recruitment and, especially, in recruitment of their own patients;
- the time schedule for the staff involved in the survey will be considered by the hospital's chief; together with the national coordinator he/she is responsible for exclusion of involvement of midwives assisting with delivery and physicians attending the birth in recruitment of their own patients;
- honorarium for the hospital staff is included in the budget and should be paid to compensate additional working time related to the survey.

To ensure the adherence of hospital staff to the survey protocol, sufficient training, quality assurance and quality control measures must be in place.

6.2. Timing of the survey

Exposure patterns, such as fish consumption, may vary by the season. To avoid a seasonal bias, sampling will be done during a specified time of the survey.

Sampling in the population of Chennai city and in the high-exposure group (coastal area) will take place in the same season to allow for the comparison of results.

It is envisioned that this survey will be repeated at regular intervals to monitor trends in exposure. Combining data from several data collection rounds would also increase the power of the statistical analysis of exposure determinants. It is supposed that follow-up surveys in India will use the same schedule (be conducted in the same season) to ensure data comparability. The baseline survey may produce important information on exposures and lead to policy interventions aiming at reducing exposures. Since new policy measures would require substantial time to take effect, conducting a follow-up survey is recommended.

6.3. Recruitment, interview, medical data collection and biological sampling

The recruitment of participants starts with distribution of an information leaflet (Annex 2) during antenatal visits This would give time to reflect on taking part in the study and would reduce the burden of consent process just before or after delivery. The leaflet can also be provided before or shortly after delivery.

The leaflet gives information on the survey's objectives, its scope, benefits for the women themselves, and the communication of the results. It should also provide information on the inclusion and exclusion criteria.

A female fieldworker might generally be a better choice to contact women shortly after delivery. The fieldworker will introduce themselves, and do the following:

- handover the information leaflet (unless it was made available to the woman during one of her antenatal visits), briefly describe the survey and ask whether the woman is interested in participating;
- conduct the screening interview and administer the informed consent form;
- collect the data on exposure, socioeconomic status, etc. using the questionnaire (it is preferable to do this in an interview rather than to leave the questionnaire with the woman for self-administration);
- collect a hair sample;
- arrange for the collection of urine and cord blood samples, strictly following the procedure recommended by WHO for sampling (note: if the recruitment is conducted after the delivery, it may be necessary to collect cord blood and urine samples prior to recruitment; if the woman is not eligible or does not agree to participate, the collected biological samples should be immediately discarded; samples must not be delivered to the analytical laboratory and analysed prior to obtaining informed consent; samples will be collected in the hospital and stored before shipment to an analytical laboratory; the national coordinator of the

survey should ensure that only samples from consenting women are shipped to the analytical laboratory for an analysis);

- obtain medical data on the woman and her child, including ICD-10 codes of diseases and conditions during pregnancy and delivery: nephropathies (N00-N16); polyneuropathy and encephalopathy (G50-G99); complications of labour and delivery (O60-O75) and delivery (O80-O84); and basic anthropometrical measurements of the infant (weight and height); such information could be used in the further analysis of the data on mercury concentration in biological matrices and the questionnaire data, and to facilitate formulation of exposure- and risk-reduction recommendations.

Experienced fieldwork personnel from the Sri Ramachandra University, Regional Occupational Health Centers (ROHCs), The National Environmental Engineering Research Institute (NEERI) as well the maternity hospital staff will be deployed to perform the work. To ensure the adherence of hospital staff to the survey protocol, sufficient training, quality assurance and quality control measures must be in place.

Responsibilities of the research staff include:
- to contact women and getting agreement to participate in the survey (information sheet, eligibility screening);
- to recruit women (prior informed consent); NB! Staff members contacting women at non-clinical stage shouldn't be involved in the recruitment process in the hospitals);
- to collect epidemiological information (main questionnaire);
- to collect hair samples;
- to organize storage of urine and blood samples;
- to collect medical records.

Responsibilities of medical staff in hospitals include:
- to collect cord blood samples in maternity wards and urine samples before or after delivery.

6.4. Questionnaire

All survey forms are available in English and translated into the local language of the area. Information from sources of exposure that are not ~~exist~~existing in Chennai has been excluded.

Preliminary questionnaire versions in national languages is been pilot tested prior to the main survey during the training. As pilot testing is an essential part of developing the questionnaires and national survey protocols, it should be conducted as early as possible.

The main questionnaire (Annex 3) will be used to interview the participants at the time of hair sampling. Completion of this questionnaire takes about 30 minutes, if administered by an interviewer. Section A comprises personal information, anthropometric data, ethnic origin, educational level of the family and socioeconomic status. Section B focuses on potential exposure pathways to mercury, and is divided into four parts: (1) occupational exposure, (2) exposure in the residential environment, (3) personal care and lifestyle (e.g. smoking behaviour), and (4) food and beverage consumption.

Personal interviews will be conducted by trained interviewers. It gives an opportunity be resolved immediately any misunderstanding and leads to higher data completeness and quality.

The national coordinator is in charge of generating a file with data from the questionnaire and assuring data quality using a template developed by WHO. The national survey coordinator is

responsible for developing SOPs for data handling and data quality control procedures, and for conducting pilot testing and evaluation of these procedures prior the beginning of a national survey.

The national coordinator will retain questionnaires from all the respondents until the end of the study, and they will be kept for future reference. Retention of all records will conform to national requirements and international norms concerning confidentiality. The national coordinator will complete a summary of information form about mothers donating samples and provide scanned copies of the questionnaires to WHO upon request.

6.5. Training of fieldwork staff

To ensure standardization of processes and successful implementation of the survey, the training will be organized as far in advance as possible. Training will involve a range of fieldworkers engaged in survey implementation, including interviewers, hospital staff, those responsible for collecting samples, those responsible for sample transportation and laboratory analysists.

All field staff planned to be involved in the project will be trained.

WHO Standard Operating Procedures (for quality control, sampling and mercury analysis) should be used for the training. Special attention should be paid to non-invasive sampling that allows avoiding any risks for women involved in the survey. Hospital staff involved in cord blood sampling should be instructed that according to WHO recommendations cord blood samples for this project may only be obtained by ex-utero collection of samples after delivery of placenta and clamping of the umbilical cord.

A technical help desk during the survey, starting from the moment the general protocol is adapted to the national situation will be established in the University to increase consistency and to promote adherence to survey protocols.

Given that trained personnel will conduct interviews in addition to their regular duties, then additional motivation is considered (see Annex 5 Budget).

6.6. Quality control measures

Quality control with respect to fieldwork and training of the project staff is considered by the national coordinator. It is in the interest of all partners involved that the fieldwork is controlled and checked. To avoid errors, checklists including all important steps of the procedures will be developed and used. In addition, field visits by supervisors and from experts not directly involved in fieldwork are planned.

7. Biological material

7.1. Overview of biomarkers for assessment of exposure to mercury

Justification for the selection of biomarkers of prenatal exposure to organic and inorganic mercury
In population-based HBM surveys, non-invasive matrices are preferred for assessing exposure to mercury in order to maximize the response rate. The selection of biological matrices for assessing human exposure depends on the mercury compounds (organic vs. inorganic), exposure pattern (chronic or acute) and time of sampling after the exposure *(4)*.

Maternal scalp hair
Exposure to methylmercury is reflected in the level of mercury in scalp hair *(4)*. Once incorporated into hair, mercury does not return to the blood, providing a good long-term marker of exposure. Mercury in maternal hair (close to the scalp) is a proxy of fetal mercury exposure *(20)*. Mercury concentration in 3 cm of scalp hair taken close to the scalp shortly after delivery reflects the exposure of the fetus during the last three months of pregnancy. However, the concentrations of mercury in hair can change to a certain extent due to the changing growth rate of hair *(21)*.

Hair-mercury concentrations can be affected by several factors, including hair colour and variable growth rates *(20)*. Previously conducted studies have shown that total mercury in maternal hair is a predictor of long-term neurotoxic effects in children *(22)*, despite some studies reporting inconsistent results, particularly when assessing the effects of exposure to low mercury levels *(23)*.

Mercury levels in populations consuming a very small amount of fish are normally below 0.5 µg/g in hair; in populations with moderate fish consumption total mercury in hair varies from below 1 to 2 µg/g; while people with frequent consumption of fish (once or more per day) may have mercury levels in hair exceeding 10 µg/g. The United States Environmental Protection Agency (US EPA) reference dose of 0.1 µg methylmercury per kilogram of body weight per day corresponds to approximately 1 µg/g mercury in hair in people with low fish consumption.

More recent calculations resulted in an adjusted biological limit corresponding to 0.58 µg/g in hair, the validity of which is supported by recent studies of developmental neurotoxicity at exposure levels close to the background *(24)*.

A tolerable limit proposed by WHO corresponds to a hair-mercury concentration of approximately 2.5 µg/g, which takes into account the possible compensation for methylmercury toxicity by beneficial nutrients in seafood. Due to the ease of collection and handling, maternal hair-mercury level is one of the most widely used biomarkers of prenatal exposure to methylmercury in population studies.

Cord blood
In contrast to hair, the presence of mercury in blood represents short-term exposure to organic and inorganic mercury, and does not provide information on long-term exposure and its variations *(4)*. Total mercury concentrations in cord blood are proportional to methylmercury concentrations in hair. As a biomarker of prenatal exposure, mercury in cord blood is preferable, as it provides information on both the exposure of mothers and prenatal exposures of their children *(25)*. Mercury in cord blood may have a stronger association with neurobehavioural deficits in the child compared to mercury in maternal hair *(26)*. Concentrations of total mercury in cord blood of individuals who do not eat fish are normally in the range of 0.5–5.0 µg/L. In cases of high fish consumption, values higher than 10 µg/L are frequently occurring. The reference value for mercury in cord blood based on the US EPA's reference dose is 5.8 µg/L. Mercury levels in cord blood and hair are recommended biomarkers of prenatal low-level methylmercury exposure due to its selective transfer through

biological barriers such as blood, hair and placenta *(27–29)*. Cord blood is a non-invasive matrix, but should be collected by the nurse after birth.

Maternal urine

Urine is the matrix of choice for assessing exposure to inorganic and elemental mercury *(30, 31)*. In an occupationally non-exposed population, the number of amalgam surfaces was found to be associated with urinary mercury *(32)*. In the general population, urinary mercury can be elevated also due to high fish consumption, as a consequence of demethylation and excretion of inorganic mercury and partially also due to limited excretion of methylmercury through urine. Urine is a non-invasive matrix, is easy to collect and is commonly used to assess exposure to elemental and inorganic mercury, particularly in occupational health settings where biomonitoring of random spot urine samples is routinely practiced.

Due to wide variability in urinary excretion rates among individuals, as well as the great temporal variability in urine composition within individuals *(33)*, the results should be expressed per gram of creatinine or adjusted for the specific gravity. Concentrations of total mercury in urine of non-exposed individuals are normally in the range of <0.1–5.0 µg/L. In cases of non-occupational exposure to inorganic and elemental mercury, values of up to 10 µg/L have been reported, while workplace exposures can result in levels higher than 50 µg/L. The health-based German HBM I,[3] which corresponds to the concentration of total mercury in urine below which adverse health effects are not expected, is 7 µg/L, or 5 µg/g creatinine; the German HBM II value that corresponds to the concentration above which there is an increased risk of adverse health effects in susceptible individuals of the general population is 20 µg/L, or 25 µg/g creatinine *(34)*.

7.1.1. Choice of the matrices for the survey and sample collection

The literature provides adequate evidence that mercury in maternal hair (close to the scalp) is an appropriate biomarker of fetal mercury exposure *(26)*. Moreover, this biomarker has been used to show an association between prenatal mercury exposure and long-term neurotoxic effects in children *(22)*.

Human hair has the advantage of being a non-invasive matrix that is easy to collect through a simple procedure that requires minimal training of survey personnel. Hair samples can be transported and stored in a zipper bag or a paper envelope at room temperature *(35)*. Hair samples have been used extensively in studies of methylmercury exposure from fish consumption *(36, 37)*.

Once incorporated in the hair, mercury remains there, providing information on exposure during the hair growth period. Most mercury in hair is in the form of methylmercury, especially among populations that consume fish. It is an accurate and reliable method to measure methylmercury intake levels. It is valuable indicator of assessment of exposure to mercury in population in coastal area of Chennai which supposed to have high-level fish consumption. The relevant SOP for analysis of mercury in hair, provided by WHO to the national coordinator, describes in detail the place on the head for collecting hair samples, the amount of hair to be collected and the principles of sample storage.

Cord blood can be collected by the nurse after birth and does not cause any pain to the mother or baby. Mercury levels measured in cord blood reflect exposure of the fetus to mercury and its

[3] These values are based on the German Environmental Surveys (GerESs), nationwide population surveys that have been carried out in Germany periodically since the mid-1980s.

compounds. Given that it provide information both to methylmercury and non-organic mercury it is valuable indicator to assess exposure of population living in areas with high-level fish consumption and mercury releases due to industrial activities. A detailed description of the collection of cord blood is given in the relevant SOP for analysis of mercury in cord blood, provided by WHO to the national coordinators. The procedures described in this SOP are only suitable for mercury.

Urine is another non-invasive matrix, which is easy to collect. Urinary concentrations of pollutants, including mercury, can be influenced by the composition of urine. Therefore, creatinine levels or special gravity should be measured as well. The results for primary biomarkers are expressed as adjusted for the creatinine content or special gravity measurement results. Mercury in urine should be analysed in populations exposed to mercury releases that is the case in Chennai. Urine collection is described in detail in the SOP for analysis of mercury in urine, provided by WHO to the national coordinators.

For the collection of cord blood and urine samples, appropriate containers should be used to prevent background contamination. Prior to sample collection, the batch of containers for urine and blood should be tested for the presence of interfering chemicals. The containers for the collection of cord blood should contain ethylenediaminetetraacetic acid (EDTA) to inhibit blood coagulation.

Given complex exposure to mercury in Chennai province, three matrices recommended by WHO are collected:

Hair – to analyse mother exposure to organic mercury
Cord blood – to analyse foetus and mother exposure to inorganic and organic mercury
Urine – to analyse mother exposure to inorganic mercury

7.2. Transportation of samples

In preparing samples for transportation, the responsible fieldworker must ensure that samples will not be destroyed or lost during transportation and that any person coming into contact with them will not be infected.

Hair samples do not require any special transport conditions; they can be transported at room temperature. However, it should be checked that the corresponding documents, including a sheet listing all samples, is sent in the package and information on any event that occurred during sampling that could affect the sample, has also been included.

Cord blood and urine samples must be kept at 4°C until their arrival at the laboratory, where they will be aliquoted and analysed or stored until analysis. Alternatively, the samples can be aliquoted and frozen in the maternity ward if agreed with hospitals staff, and then transported to the laboratory under proper conditions. Furthermore, urine and cord blood samples must be transported in compliance with the relevant shipping regulations for biological material.

7.3. Preparation of samples

A specific form will be used to document the sampling, labelling, processing and shipping of the samples.

Hair sampling and sample pre-analytical treatment will be conducted according to the WHO SOP for analysis of mercury in hair.

The cord blood samples will be aliquoted (at least two aliquots) to enable mercury analysis in the national laboratory and/or the reference laboratory according to the WHO SOP.

Urine samples should be aliquoted (at least three aliquots) to enable mercury and creatinine analysis in the national and/or the reference laboratories according to the WHO SOP.

7.4. Analysis of samples

The 250 individual samples of each matrix (scalp hair, cord blood and urine) are planned to be collected within the framework of the pilot surveys. All three matrices will be analysed for mercury concentrations.

Analysis of samples should be performed following the relevant SOPs, developed by WHO: in cord blood and urine using cold vapour atomic absorption spectrometry (CVAAS), and in scalp hair using thermal decomposition-gold amalgamation-atomic absorption spectroscopy. An alternative SOP was developed by WHO for laboratories that have access to instruments with flow injection analysis and gold amalgamation, processes that would be followed by either CVAAS or cold vapour atomic fluorescence detection.

Analytical protocol for Hg analysis in human bio-specimen using microwave digestion followed by ICP-MS analysis

All bio-specimen samples were digested using microwave digester (OneTouch, MARS) equipped with the Teflon digestion tubes. Appropriate sample weight (0.2mg for hair and cord-blood and 2ml urine) should be weighed directly into the digestion tubes. To each tube, add 2.5ml of trace select concentrated nitric acid (≥69%) followed by 2.5mL of distill water to a final volume of 5mL. Microwave digestion was programmed for a total run time of 45min with temperature set to reach to 210°C with holding time of 15min. Pour the digested sample into 10ml standard flask and make-up the volume to 10ml using DI water. Mix the contents thoroughly and 1ml sample was used for analysis using ICP-MS.

ICP-MS system (7700 series X, Agilent Technologies) must be conditioned prior to analysis set-up by checking nebulizer uptake and peri-pump parameters, and by checking several blank (DI water) rinse readings. Calibration solutions must be prepared by weighing rather than by volume in 3% nitric acid solution. Linearity was tested for the range of concentration between 0.5ng/ml to 10ng/ml. Calibration blanks must be tested for instrument background noise. Samples must be analyzed with QC samples for every 6-10 samples and concentration expressed in mg/kg was calculated as a follows

$C\ (mg/kg) = (Cs-Cb)*10*f/m$

C = concentration of analyte in mg/kg
Cs = test solution concentration (mg/L)
Cb = blank test solution concentration (mg/L)

m = test portion mass (g)
f = possible dilution factor

7.5. Standardization

Results of the measurements must be analytically comparable between laboratories. To ensure this, the national survey must follow the WHO SOPs for sampling and analytical methods, and develop procedures for quality assurance and quality control that cover the pre-analytical phase. The availability of appropriate reference materials (samples with a certain level of mercury) supports internal quality assurance. External quality assurance will be organized by WHO through international inter-laboratory comparison investigations (ICI).[4]

A proficiency test of the analysis of total mercury in cord blood and urine needs to be organized the reference laboratory selected by WHO, using freeze-dried samples. Mirror analysis of 20 samples of each biological matrix is performed in the reference laboratories identified by the WHO.

7.6. Storage of samples remaining after the mercury analysis

Biological samples will be storage in the analytical laboratory according to the SOPs prepared by WHO before mercury analysis is complited and distroyd right after that. No biobanking procedures are developed and enforced in the University for environmental studies.

8. Data management, analysis and evaluation

8.1. Data management

Data generated during the fieldwork will need to be further processed and merged in order to allow for final evaluation and results using templates provided by WHO. A database will combine the laboratory data files and the questionnaire database. The database is constructed as a matrix with one row per subject and all separate variables in columns. The data from each participant are identified by a unique identity number (ID number). Please see the following example:

ID number	Variable name	Matrix	Biomarker	Unit	Data source
XXXXX	HM_HG	Hair Blood Urine	Total mercury	ng/mg	Lab result

The data will be stored in a uniform format recommended by WHO. Information on the structure of the database, including variable names, formats, units and rules for handling missing values or values below the limit of quantification, will be included in a codebook.

[4] ICI is a measure to harmonize analytical methods and their application so as to improve the comparability of analytical results. ICI is carried out before the laboratories begin to analyse the samples.

The national coordinator in consultation and agreement with the project coordinator in WHO, will choose its software for database management and statistical analysis based on the following criteria:

- suitable for importing data from external data files provided by chemistry laboratories (most commonly Excel or Access files);
- allows input of the questionnaire data;
- sufficient database management functionality;
- capacity to perform statistical analyses;
- possibility to deliver external databases to a WHO database.

Based on experience in other multicentre studies, statistical analysis programs like R, SPSS or SAS meet these criteria and are thus recommended.

Data processing shall be conducted in in Sri Ramachandra University and in WHO. The national coordinator will transfer the data to WHO for creation of a database at the global level, and analysis of levels and distribution of exposure to mercury at national, regional and global levels.

8.2. Statistical analysis

8.2.1. Data analysis at the national and the international level (recommended approach)

The data collected in India will be statistically analysed at the national level and submitted in anonymized format for statistical analysis to a central database. The aim of a statistical analysis at the international level is to assess associations between biomarker values and predictors such as age, gender, fish consumption habits, etc. in a pooled dataset. However, in some cases WHO can make its own statistical analysis based on data provided by the national coordinator.

Data analysis will involve descriptive statistics and regression analysis. At the descriptive statistics stage, response rates and distributions of parameters will be evaluated, outliers identified and checked.

The regression analysis stage will involve analysis of biomarker data in relation to predictors. The associations will be studied using univariate and multiple regression models.

8.2.2. Data evaluation

The interpretation and evaluation of the HBM results will be dealt with in separate steps. Some of the questions that the HBM survey aims to answer are outlined below:

- Are the observed levels of exposure important/significant in terms of health risk?
- Are elevated exposure levels associated with specific types of exposure source?
- How specific biomarkers are distributed among defined/selected survey population strata/subgroups of the general and exposed populations?
- What is the spatial variability in exposure levels in participating countries globally?

Additionally, it will be valuable to compare the results of the HBM survey with existing data available in the literature.

9. Communication

Communication campaign in the survey framework aims to promote awareness, encourage stakeholder involvement, maximize recruitment and retention, ensure transparency and openness towards stakeholders, and to safeguard translation into precautionary and preventive policy. Apart from providing information to the survey participants, the survey leader has to provide targeted information to the general public, policy-makers in health and environment sectors and public health professionals.

Effective communication can help to raise awareness in the population and to stimulate preventive action at the population and individual levels. At the same time, it is important to avoid inducing anxiety in survey participants when corrective actions are not warranted at the individual level.

Three periods of extensive communication campaigns are identified: prior to and at the onset of the sampling period, during the survey, and at the results dissemination stage.

9.1. Communication prior to the survey

Measures to enhance recruitment will start before the recruitment itself begins to reach two main goals: (1) to recruit individuals that adequately represent the target population; and (2) to recruit a sufficient number of participants to meet the sample size and power requirements. Therefore the initial campaign should start as soon as the protocol is ready.

Information leaflet tailored to the target population is prepared. The briefing of policy-makers in the health and environment sectors will start at the same time.

It is important that the participants have sufficient opportunities to ask questions, to encourage uptake and to reduce withdrawal from the survey. The survey information leaflet and other materials include contact details (including name, address, telephone number and email address of the national survey coordinators) and are available for participants.

The information leaflet and informed consent form provide a brief summary of the survey and its aims, in plain language understandable for a non-professional audience. The leaflet and consent form also explain what participation means in practice: how long it takes, where it takes place and what it involves. The following list is not exhaustive but gives an idea of the main topics to be covered:

- nature and aims of the survey;
- promise of confidentiality, that the participant's responses will not be linked to their name or any other identifiable information;
- description of what participation means in practice (when, where, who, what);
- inclusion and exclusion criteria for participating in the survey;
- possible risks, inconveniences or discomforts that could reasonably be expected to result from the survey;
- possible benefits for participants (if relevant, as there might not be any direct benefits);
- participating country's institutional contact details;
- information about how the survey leader obtained the potential participant's contact information;
- information about what will happen to the results;

- explanation that participation is always voluntary and that participants can withdraw at any time;
- explanation about how privacy and confidentiality will be maintained over the time data is stored;
- description of data storage in a biobank (if applicable) and possible uses of data in the future.

A withdrawal form will be available for any survey subject who decides that they would like to withdraw from the survey. Survey participants may withdraw at any time; they will be asked to confirm their withdrawal with a signature.

9.2. Communication during the survey

Communication will continue during the survey implementation to react quickly and effectively to any upcoming questions.

To facilitate communication, a contact point is identified (with his name, phone number and email address) to receive and answer questions and queries.

9.3. Communication of the survey results

Before communicating the result of the HBM survey, careful consideration will be given to the assessment of individual and population risks, based on the measured concentrations of mercury and the questionnaire data, as well as on the main goals of risk communication, taking into account different target groups and their needs. The level and distribution of mercury levels and the associated risk determine the main communication aims. For example, if the HBM survey reveals low exposure levels and low or negligible health risks, the main purpose would be to inform participants of the results and to use this as an opportunity to raise awareness and educate. Whereas, if the survey showed a high level of exposure to mercury, communication of results would include more information about health risks and risk-reduction measures, including on preventing exposure and promoting safer behaviours. It is critically important to distinguish between communication addressed to individuals and to the wider population (e.g. different approaches to risk assessment, recommended risk-reduction measures, and defining of responsibilities of individuals and relevant authorities, etc.) as well as to involve different stakeholders according to their roles and capacities.

The fundamental goal of risk communication is to provide meaningful, relevant and accurate information in clear and understandable terms, targeted to a specific audience. It should facilitate understanding of complex technical issues – such as exposure to mercury, the associated health risks and risk-reduction measures – to bridge the gap between lay people and experts and to help people make more informed and healthier choices.

All stakeholder categories – including policy-makers in health and environment sector, health-care professionals, the general public, local communities and individuals involved in the survey – will be included in the mercury risk communication. When communicating the results, consideration will be given to the meaning of HBM results, their interpretation at individual and population level, and their potential health relevance (health risk, predictive value of biomarkers, etc.), including communication about uncertainty. Furthermore, communication on available protective and preventive measures at individual and population level, especially in the case of observed high mercury concentrations, will be considered.

The most effective channels to communicate the message (e.g. through publications, mass media, scientific reports, leaflets, lectures, involvement of an expert or a recognized community leader, etc.) are considered to communicate the survey results. It is important to get support from central and local authorities, especially in the health and the environment sectors and the medical community.

9.3.1. Communication of the survey results to policy-makers, including government health-care and environmental protection bodies

Policy-makers, particularly in the health and environment sectors, will receive a summary of the HBM survey findings with recommendations on further steps and available risk-reduction measures. The summary will include information about the levels and distribution of exposure to mercury in a population, existing and projected health risk at population level, the main sources of exposure to mercury, as well as available and feasible actions and measures to reduce exposure and health risk. Development of a preventive action plan will be proposed if necessary. Inclusion of information on good practices will be considered to demonstrate the potential benefits of implementation of risk-reduction measures. The relevant policy framework at national and international level provides a context for presenting the survey results and the proposed actions.

9.3.2. Communication of the survey results to the general population and communities involved in the survey

Risk-communication messages for the general public and communities will be formulated in a way that avoids misunderstandings and undue concerns. Prior to formulating risk-communication messages the population-level risks will be carefully evaluated, using all information available, and population groups at higher risk (of exposure and health effects) will be identified. A clear distinction will be made between interpretation of HBM results at individual and population levels.

The meaning of the HBM survey results should be clearly communicated, focusing on population groups at risk; it should include recommendations on reducing exposure to mercury and/or preventing health risks. An example of this is fish consumption advice; if this advice is necessary, it will be adopted to local conditions (fish and seafood types, fishing patters, cultural aspects, etc.) and will be presented in the context of the health benefits of fish consumption.

The most effective way to communicate risks is through mass media: an article in the newspaper or a programme on regional or local radio and/or television will be used for this purpose. Involvement of topical experts can be considered to strengthen the message and support the recommended risk-reduction measures in certain cases. Information about the results of the HBM survey, including on the observed levels and distribution of mercury, will be put in the context of levels of mercury in the ambient environment, if data available, and relevant safety levels.

9.3.3. Communication of the survey results to health-care professionals

In cases of the observed high concentrations of mercury , communication prepared for health-care professionals will include general information on mercury and its health effects, the main sources of exposure, principles of diagnosis and treatment, risk-reduction measures and vulnerable population groups, for example pregnant women. Identification of target groups for communication efforts among health-care professionals depends on the population groups at higher risk. Involvement of

paediatricians, gynaecologists and obstetricians, occupational physicians, and general practitioners serving specific communities (artisanal and small-scale miners, fishing communities, etc.) is an obligation.

9.3.4. Communication of the survey results to participants

Individual results will be provided to survey participants, except those who do not wish to know their results (see Annex 2). In sensitive situations, experts in social sciences and communication might be consulted in order to understand public perceptions and to develop optimal communication strategies.

Prior to communicating the survey results to participants, the following measures are recommended in cases where a high level of mercury has been detected. First, the analysis should be repeated to exclude any mistakes, and to test the samples in a reference laboratory. The next step, after checking the quality of the measurements and confirming the result, is to evaluate risks using all available information on potential sources of exposure and the associated health risks.

When communicating risk-reduction measures, it will differ in cases of exposure to methylmercury and inorganic mercury.

The meaning of their results will be explained to participants as clearly as possible. The results can be communicated to the survey participants through direct contact or through their family doctors.

Personal communication with individuals at high risk is the most effective way to discuss the problem and the recommended preventive measures and risk minimizing actions. All efforts will be taken to explore this approach. Involvement of a family doctor and/or family members might be considered, subject to agreement of the participant. It is critical to be prepared to provide clear evidence-based answers to questions about the health effects and medical follow-up, to avoid any misunderstanding or exaggeration of the problem.

Communications at the country level and at WHO level should be coordinated and consistent. At the same time, it should allow customized, country-specific messages according to the local context (e.g. country characteristics, concerns). Confidentiality of personal data and testing results must be guaranteed. At the same time, all aggregated results can be made publically available, providing that no link can be made to specific individuals.

10. Ethics

The survey must adhere to the legal and ethical framework established by international directives, conventions and guidelines, and by domestic laws in India.

Approval of a national ethical committee has been obtained.

The ultimate objective is to guarantee the optimal protection of the rights and dignity of every survey participant (data subject). Special attention is therefore paid to:

- defining and explaining the specific, explicit and legitimate purposes of the survey to all actors involved;
- asking for written consent (informed, free, explicit, specific and documented) prior to the commencement of research. Informed consent includes:

- the survey objective;
- the targeted population and recruitment method;
- possible risks and benefits to the participants;
- approval of the survey protocol by an ethics committee;
- the right to refuse consent or to withdraw consent at any time without giving reasons and without being subject to any form of discrimination;
- the right to privacy for the enrolment discussion , screening process, answering questionnaire and taken samples of hair and urine;
- the right to access personal results and the wish of participants to know or not to know their personal results;
- the procedure for dealing with critically high biomarker values;
- recipients of the survey data;
- measures to assure the confidentiality of personal data.

When communicating results at the individual level, explaining their health significance (if known) is extremely important. When further evaluation or intervention is warranted due to a critically high biomarker value, communication at the individual level will involve professional counselling.

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Annex 1. Eligibility screening form

1. Are you at least 18 years of age?
   - ☐ Yes
   - ☐ No

   If no → not eligible, stop the interview politely

2. How many days ago was your delivery (if done after delivery)?

   ____ days

   If more than 14 days → not eligible, stop the interview politely

3. Do you live in [*the catchment area of the hospital*]?
   - ☐ Yes
   - ☐ No

   If no → not eligible, stop the interview politely

4. How long have been living in this area?

   ____ years

   If less than three years → not eligible, stop the interview politely

5. How many days during the last three months have you spent outside the [*catchment area of the hospital*]?

   ____ days

   If more than 14 days → not eligible, stop the interview politely

6. Sufficient language ability in the interview language? (assessed by the interviewer)
   - ☐ Yes
   - ☐ No

   If no → not eligible, stop the interview politely

7. Hair sampling possible (based on visual assessment – hair length of at least 3 cm on the back of the head)?
   - ☐ Yes
   - ☐ No

   If no → not eligible, stop the interview politely

8. Eligible for enrolment?
   - ☐ Yes
   - ☐ No

9. If eligible, consented to participate?
   - ☐ Yes
   - ☐ No

10. Participant gave written consent to (please mark all that apply):

- ☐ Hair sample
- ☐ Urine sample
- ☐ Cord blood sample
- ☐ Access to medical records

11. Enrolled in the survey?

- ☐ Not eligible
- ☐ Eligible but not willing to participate
- ☐ Enrolled to participate

IF ENROLLED IN THE SURVEY

Name of participant:

_____

Home address:

_____

Date of admission to the hospital:

_____

Date of delivery of child:

_____

Annex 2. Information sheet and Informed consent form

The informed consent form should be signed by all recruited women.

Information sheet for participants

(the researcher must provide this information to all women contacted for the survey)

Sri Ramachandra University is conducting a survey to assess exposure of population in Chennai province to mercury in cooperation with WHO. We are contacting you to invite to take part in the survey.

There are several sources of mercury for the population in Chennai including releases into air from coal power plants, wastes management, and a cement production plant. In the coastal area people consume a lot of fish and seafood that can be contaminated due to global mercury pollution. Given that we all can be exposed to mercury. The survey is aiming at investigating what concentrations of mercury are accumulated in our organisms.

Participation in the survey is voluntary. You can refuse to participate for different reasons. It won't influence anyhow to the level and quality of medical care. Moreover, you can withdraw your participation any time before living hospital. All need is to inform the national coordinator. His contact details are provided below.

This survey has two main purposes, in particular, to assess exposure of population in Chennai to mercury and propose prevention actions if necessary as well as to support WHO efforts in developing of global plan for monitoring of exposure to mercury.

We plan to complete the survey in 4-5 months depending of a number of deliveries during this period. Two hundred fifty women will participate in the survey together with you.

Participation in the survey is no cost for you.

In total, participation in the survey will take around 1.5 hour.

You will inform you about the study results if you wish to get them. You can indicate it in the form confirming that you are informed about the survey and agreed to participate.

To analyse mercury concentration we will take samples of scalp hair, cord blood and urine from you. All these procedures won't harm you. We will take several strands of hair from back of your head. It won't be notable. Cord blood will be taken by professionals in maternity room. Nurse will instruct you how to collect urine sample after the delivery.

After the survey we will have information about your body contamination by mercury and risks of intrauterine exposure of your child to mercury during last trimester of pregnancy. Mercury in high concentration can cause neurological/cognitive disorders in children. Having this information we will provide you with advice on how to minimise or avoid exposure to mercury and prevent its harmful effects to your child.

Your participation will also contribute to development of preventive and risks minimization measures for the population in Chennai.

We will provide you with information on exposure to mercury as soon as we complete the analysis. We will take all efforts to make it as soon as possible and no later than in 4-5 months after samples are collected. In case of high level concentration is observed, additional medical examination will be recommended for you and/or your child with no costs for you.

Information we collect during the survey will be treated as confidential. Neither your name nor name of your child will be published or reported. All data will be anonymized and ID code given to you will be used for analysis purpose.

Indian legal requirement for confidentiality of personal information are fully applied to this survey.

Samples collected in the survey will be destroyed in a laboratory after all analysis is completed. They won't be used for any other purposes except of the purpose of this survey.

The survey protocol has been approved by the national and international ethics research committees. This survey strictly follows all ethical standards.

DEPARTMENT OF ENVIRONMENTAL HEALTH ENGINEERING

SRI RAMACHANDRA UNIVERSITY

CHENNAI - 600116

INFORMED CONSENT

Project Title: Development of a Plan for Global Monitoring of Human Exposure to and Environmental Concentrations of Mercury: A pilot survey in India

Principal Investigator:

Dr. Krishnendu Mukhopadhyay, MSc, PhD
Associate Professor
Department of Environmental Health Engineering
Sri Ramachandra University
Porur, Chennai 600116

Description of the Study: Mercury is harmful for human beings. It is especially harmful for foetus because exposure to mercury can impact development of nervous system. Thus, to characterize pre-natal exposure is critical for evaluating public health impacts of mercury and assessing public health benefits of exposure reduction measures.

The standardized methodological documents for the mercury exposure surveillance, including survey design, recruitment procedures for national field staff, standard operating procedures for human hair, cord blood and urine sampling and analysis, and data analysis plan, have been developed to facilitate the implementation of mercury human biomonitoring in the pilot countries participating in WHO initiative related to mercury HBM.

The target population group(s) and hospitals/medical facilities for the pilot survey implementation were identified by national experts in countries involved in the pilot survey, including in India. Three biological matrices were selected for the purpose of the project: scalp hair, cord blood and urine. Concentrations of mercury should be estimated in at least 250 individuals using at least 2 sample matrices in India as well as in other participating country.

Procedures: To assess exposure to mercury and its compounds, we will analyse its concentrations in cord blood, scalp hair and urine, following your agreement to provide this biological material. All samples will be collected in a non-invasive manner. A sample of umbilical cord blood will be collected by midwifes after delivery your child and placenta; a sample of your hair will be collected by cutting a small strand of hair close to the scalp from the back of your head; and, a spot sample of your urine will be collected in the container provided by the survey staff. We will provide instructions and explanation how to do it. We will also ask you to answer a questionnaire with a number of questions about your diet, home and work environment, lifestyle and health. This information will help us to learn more about potential sources of mercury. Completion of the questionnaire should not take more than 30 minutes. All procedures will be conducted by trained personnel, who will also be ready to answer your questions. Participation in the survey will take not more than 1.5 hour in total.

We would highly appreciate it if you allowed us to access the following information from your and your child's medical records: your child's weight and height at birth, as well as your diseases and conditions during pregnancy and delivery. This information, together with the analysis of mercury concentrations, will allow the national survey coordinator to provide you with advice on how to minimize your exposure, if necessary.

Possible Risks to the participant: There are NO risks involved in the study.

Possible Benefits to the participant: You will be benefited by knowing the exposure levels of mercury which will help adopting possible control measures.

Cost and Payments to the participant: There is no cost for participation in this study. Participation is completely voluntary and no payment will be provided.

Confidentiality: Information obtained in this study will be kept confidential. Your privacy is very important to us and we will make every effort to protect it:

- We will remove your name and other identifiers from your sample and information, and replace them with a code number.
- We will keep the list that links the code number to your name separate from your sample and other information.
- Only the national coordinator will have access to the list and he is responsible to keep identical information about you confidential.
- Researchers who study your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
- We will not give information that identifies you to anyone, except if required by the national legislation.

We will also take actions to ensure privacy for all actions you are involved in the survey framework

Participants' right to withdraw from the study: You have the right to refuse to participate in this study, the right to withdraw from the study and the right to have your data destroyed at any point during or after the study, without penalty.

Voluntary consent by the participant: PARTICIPATION IN THIS STUDY IS COMPLETELY VOLUNTARY, AND YOUR CONSENT IS REQUIRED BEFORE YOU CAN PARTICIPATE IN THIS STUDY.

Information about the survey: You have the right to ask for additional information about the research project and the procedures described in this document. All reasonable requests for information will be answered by the principal investigator to the best of their knowledge. The researchers will inform you if and when any major changes in the procedures, risks or benefits of this study occur.

Information on the progress of the survey can be requested from the national coordinator. The national coordinator contact details are as follows:

Dr. Krishnendu Mukhopadhyay, MSc, PhD
Associate Professor
Department of Environmental Health Engineering
Sri Ramachandra University
Porur, Chennai 600116

Phone: +91 44 4592 8547

E-mail: krishnendu@ehe.org.in

I have read this consent form and I fully understand the contents of this document and voluntarily consent to participate in the study.

All of my questions concerning this study have been answered. If I have any questions in the future about this study they will be answered by the investigator listed above. I understand that this consent ends at the conclusion of this study.

By signing this form, I agree to participate in this study. A copy of this form has been given to me.

Child's first and last names (if given):

_____

Child's date of birth (DD/MM/YYYY):

_____

Witness signature Participant's signature

Name: Name:

Date: Date:

Communication of results

The quality checked human biomonitoring survey results, including concentrations of mercury in hair, urine and cord blood, are expected to be available no later than three months after the sampling. Please indicate below, whether and how you want to obtain your individual results.

[ ] I do not wish to receive my results.

[ ] I wish to receive my results at my home address:

_____

_____

[ ] I wish that my results be sent to my doctor.
Doctor's first and last name:

_____

Doctor's address:

_____

_____

Informed Consent Form (local language)

परियोजना का शीर्षक: बुध की बुधवार को मानव एक्सपोजर और पर्यावरण सांद्रता की वैश्विक निगरानी के लिए एक योजना का विकास: भारत में एक पायलट सर्वेक्षण

मुख्य जाँचकर्ता:
डॉ कृष्णेंदु मुखोपाध्याय, एमएससी, पीएचडी
सह - प्राध्यापक
पर्यावरण स्वास्थ्य इंजीनियरिंग विभाग
श्री रामचंद्र विश्वविद्यालय
पोहर, चेन्नई 600116

अध्ययन का विवरण: बुध मनुष्यों के लिए हानिकारक है। यह भ्रूण के लिए विशेष रूप से हानिकारक है क्योंकि पारा के संपर्क में तंत्रिका तंत्र के विकास पर प्रभाव पड़ सकता है। इस प्रकार, पारा के सार्वजनिक स्वास्थ्य प्रभावों के मूल्यांकन और एक्सपोजर कम करने के उपायों के सार्वजनिक स्वास्थ्य लाभों का आकलन करने के लिए जन्मपूर्व प्रसव को चिह्नित करने के लिए महत्वपूर्ण है। पारा के कार्यान्वयन की सुविधा के लिए सर्वेक्षण डिजाइन, राष्ट्रीय फील्ड स्टाफ के लिए भर्ती प्रक्रिया, मानव बाल, मानक गर्भनाल रक्त और मूत्र नमूनाकरण और विश्लेषण, और डेटा विश्लेषण योजना के लिए पारा के प्रदर्शन के लिए मानकीकृत पद्धतिगत दस्तावेजों को विकसित किया गया है। पायलट एचबीएम से संबंधित डब्ल्यूएचओ की पहल में भाग लेने वाले पायलट देशों में मानव बायोमनीटरिंग भारत में पायलट सर्वेक्षण में शामिल देशों के राष्ट्रीय विशेषज्ञों द्वारा पायलट सर्वेक्षण कार्यान्वयन के लिए लक्षित जनसंख्या समूह और अस्पतालों / चिकित्सा सुविधाओं की पहचान की गई थी। परियोजना के उद्देश्य के लिए तीन जैविक मैट्रिक्स का चयन किया गया था: सिरप बाल, गर्भनाल रक्त और मूत्र। भारत के कम से कम 2 नमूने मैट्रिक्स और साथ ही अन्य भाग लेने वाले देश में कम से कम 250 व्यक्तियों का उपयोग करके पारा के सांद्रता का अनुमान होना चाहिए।

प्रक्रियाएं: पारा और उसके यौगिकों के जोखिम का आकलन करने के लिए, हम इस जैविक सामग्री प्रदान करने के लिए अपने समझौते के बाद, गर्भनाल रक्त, खोपड़ी बाल और मूत्र में अपनी सांद्रता का विश्लेषण करेंगे। सभी नमूने एक गैर-इनवेसिव तरीके से एकत्र किए जाएंगे। आपके बच्चे और नाल के प्रसव के बाद मिडवाइफ द्वारा गर्भनाल गर्भनाल रक्त का एक नमूना एकत्र किया जाएगा; अपने सिर के पीछे से खोपड़ी के करीब बाल के एक छोटे किनारों को काटने के द्वारा आपके बाल का एक नमूना एकत्र किया जाएगा; और, आपके मूत्र का स्थान नमूना सर्वेक्षण कर्मचारियों द्वारा प्रदान कंटेनर में एकत्रित किया जाएगा। हम निर्देश और स्पष्टीकरण देंगे कि यह कैसे करना है। हम आपको अपने

आहार, घर और काम के माहौल, जीवनशैली और स्वास्थ्य के बारे में कई प्रश्नों के साथ प्रश्नावली का उत्तर देने के लिए भी कहेंगे। यह जानकारी हमें पारा के संभावित स्रोतों के बारे में अधिक जानने में मदद करेगी प्रश्नावली को पूरा करना 30 मिनट से ज्यादा नहीं लेनी चाहिए। सभी प्रक्रियाएं प्रशिक्षित कर्मियों द्वारा आयोजित की जाएगी, जो आपके सवालों के जवाब देने के लिए भी तैयार होंगी। सर्वेक्षण में भागीदारी कुल में 1.5 घंटे से अधिक नहीं ले जाएगा।
हम अत्यधिक सराहना करते हैं यदि आप हमें अपने और आपके बच्चे के मेडिकल रिकॉर्ड से निम्नलिखित जानकारी का उपयोग करने की अनुमति देते हैं: जन्म के समय आपके बच्चे का वजन और ऊंचाई, साथ ही आपके रोग और शर्तों के दौरान गर्भावस्था और वितरण के दौरान। पारा सांद्रता के विश्लेषण के साथ, यह जानकारी, राष्ट्रीय सर्वेक्षण समन्वयक को आपको सलाह प्रदान करने की अनुमति देगा कि यदि आवश्यक हो, तो अपने जोखिम को कम करने के तरीके के बारे में बताएं।

प्रतिभागी को संभावित जोखिम: अध्ययन में शामिल कोई जोखिम नहीं है।

प्रतिभागी को संभावित लाभ: आप पारा के जोखिम के स्तर को जानकर लाभान्वित होंगे जो संभव नियंत्रण उपायों को अपनाने में सहायता करेंगे।

प्रतिभागी को लागत और भुगतान: इस अध्ययन में भाग लेने के लिए कोई शुल्क नहीं है। भागीदारी पूरी तरह से स्वैच्छिक है और कोई भुगतान नहीं किया जाएगा।

गोपनीयता: इस अध्ययन में प्राप्त जानकारी को गोपनीय रखा जाएगा। आपकी गोपनीयता हमारे लिए बहुत महत्वपूर्ण है और हम इसे बचाने के लिए हर संभव प्रयास करेंगे:
• हम आपके नमूने और जानकारी से अपना नाम और अन्य पहचानकर्ता निकाल देंगे, और उन्हें एक कोड नंबर के साथ बदल देंगे।
• हम उस सूची को रखेंगे जो आपके नमूने और अन्य सूचनाओं से अलग कोड नाम आपके नंबर से जोड़ता है।
• केवल राष्ट्रीय समन्वयक के पास सूची तक पहुंच होगी और वह आपके बारे में गोपनीय जानकारी रखने के लिए जिम्मेदार है।
• आपके नमूने और जानकारी का अध्ययन करने वाले शोधकर्ता नहीं जानते कि आप कौन हैं उन्हें एक समझौते पर भी दस्तखत करना चाहिए कि वे यह पता लगाने की कोशिश नहीं करेंगे कि आप कौन हैं
• हम राष्ट्रीय कानून द्वारा आवश्यक जानकारी को छोड़कर किसी को भी आपकी पहचान नहीं करेंगे।

हम सर्वेक्षण ढांचा में शामिल सभी कार्यों के लिए गोपनीयता सुनिश्चित करने के लिए हम कार्रवाई भी करेंगे

अध्ययन से वापस लेने का प्रतिभागियों का अधिकार: इस अध्ययन में भाग लेने से इंकार करने का अधिकार है, अध्ययन से या उसके बाद किसी भी बिंदु पर बिना दंड के अध्ययन के लिए अपना अधिकार निकालने का अधिकार और आपके डेटा को नष्ट करने का अधिकार है

प्रतिभागियों द्वारा स्वैच्छिक सहमति: इस अध्ययन में भागीदारी पूरी तरह से स्वैच्छिक है, और इससे पहले कि आप इस अध्ययन में भाग लेंगे आपकी सहमति आवश्यक है।

सर्वेक्षण के बारे में जानकारी: आपको अनुसंधान परियोजना के बारे में अतिरिक्त जानकारी और इस दस्तावेज़ में वर्णित प्रक्रियाओं के बारे में पूछने का अधिकार है। जानकारी के लिए सभी उचित अनुरोधों का प्राचार्य अन्वेषक द्वारा उनके ज्ञान का सबसे अच्छा जवाब दिया जाएगा। शोधकर्ता आपको सूचित करेंगे कि इस अध्ययन की प्रक्रियाओं, जोखिमों या लाभों में कोई भी बड़ा परिवर्तन होने पर और क्या होगा।
राष्ट्रीय समन्वयक से सर्वेक्षण की प्रगति की जानकारी का अनुरोध किया जा सकता है। राष्ट्रीय समन्वयक संपर्क विवरण निम्नानुसार हैं:

डॉ कृष्णेंदु मुखोपाध्याय, एमएससी, पीएचडी
सह - प्राध्यापक
पर्यावरण स्वास्थ्य इंजीनियरिंग विभाग
श्री रामचंद्र विश्वविद्यालय
पोहर, चेन्नई 600116
फोन: +91 44 4592 8547
ई-मेल: krishnendu@ehe.org.in

मैंने इस सहमति फॉर्म को पढ़ लिया है और मैं इस दस्तावेज़ की सामग्री को पूरी तरह से समझता हूं और अध्ययन में भाग लेने के लिए स्वेच्छा से सहमति देता हूं।

इस अध्ययन से संबंधित सभी प्रश्नों का उत्तर दिया गया है। यदि मुझे इस अध्ययन के बारे में भविष्य में कोई प्रश्न पूछना है तो उन्हें ऊपर दिए गए जांचकर्ता द्वारा उत्तर दिया जाएगा। मैं समझता हूं कि यह सहमति इस अध्ययन के समापन पर समाप्त होती है।

इस फॉर्म पर हस्ताक्षर करके, मैं इस अध्ययन में भाग लेने के लिए सहमत हूं। इस फॉर्म की एक प्रति मुझे दी गई है।

बच्चे का पहला और अंतिम नाम (यदि दिया गया है):

बच्चे की जन्म तिथि (डीडी / एमएम / वाई वाई वाई वाई वाई):

साक्षी हस्ताक्षर	प्रतिभागी के हस्ताक्षर
नाम	नाम:
दिनांक:	दिनांक:

परिणामों का संचार

गुणवत्ता वाले मानव biomonitoring सर्वेक्षण के परिणाम, बाल, मूत्र और गर्भनाल रक्त में पारा की सांद्रता सहित, जांच की उम्मीद है नमूना लेने के बाद तीन महीने के बाद उपलब्ध नहीं होगा। कृपया नीचे बताएं, क्या आप अपने व्यक्तिगत परिणामों को प्राप्त करना चाहते हैं।

[] मैं अपने परिणाम प्राप्त नहीं करना चाहता
[] मैं अपने परिणामों को अपने घर के पते पर प्राप्त करना चाहता हूं:

[] मैं चाहता हूं कि मेरे परिणाम मेरे डॉक्टर को भेजे जाएं ।
डॉक्टर का पहला और अंतिम नाम:

डॉक्टर का पता:

Interviewer Statement

I have read this consent form to the participant …….residing at ……. and he/she fully understands the contents of this document and voluntarily consents to participate in the study. All of his/her questions concerning this study have been answered. If he/she has any questions in the future about this study they will be answered by the investigators listed below. The participant understands that this consent ends at the conclusion of this study.

Contact Address:

Principal Investigator

Dr. Krishnendu Mukhopadhyay, MSc, PhD
Associate Professor
Department of Environmental Health Engineering
Sri Ramachandra University
Porur, Chennai 60011

By signing this form, the interviewer confirms that the participant has agreed to participate in this study. A copy of this form has been given to him/her.

Interviewer's signature: Name:

A letter to the family doctors of a woman with high level of mercury in biological sample(s) (template)

Dear Mr/Ms -----

Sri Ramachandra University with support from World Health Organization conducted a survey to evaluate the population exposure to mercury.

We recruited women in maternity hospitals and assessed concentration of mercury in scalp hair, cord blood and urine.

Your patient Ms ------- participated in the survey. We found exceeded level of mercury in her *hair/blood/urine*. She instructed us to inform you about the results of laboratory analysis of her biological samples. The observed level of mercury in your *hair/urine/cord blood* is ----- *µg/g (µg/L).* The normal range of total mercury in blood varies from 1.0 to 5.0 µg/L, in hair – from 1.0 to 5.0 µg/g, and in urine from 0.4 to 7.0 µg/L. In some cases, clinical manifestations of mercury poisonings were not observed with mercury level in biological samples 10-50 times and even higher than average level in population.

However, medical examination is necessary to exclude mercury poisoning.

Please, find below some information about mercury and its health effects for your consideration.

There are three main forms of mercury: metallic mercury, inorganic mercury (mercury salts) and organic mercury (methylmercury). These forms of mercury differ in their degree of toxicity and in their health effects. High level of mercury in hair reflects exposure mostly to methylmercury, in urine – mostly to inorganic mercury, and in cord blood – to both organic and inorganic mercury.

Repeated or continuous exposure ***to elemental mercury*** due to briefing of contaminated air in occupational environment or evaporation from mercury spills (broken thermometers or fluorescent lamps) can result in damage to the nervous system and kidneys. Classic symptoms of poisoning include neuropsychiatric effects and renal impairment. The neuropsychiatric effects include tremor, anxiety, emotional lability, forgetfulness, insomnia, anorexia, erythrism (abnormal irritation, sensitivity, or excitement), fatigue, and cognitive and motor dysfunction.

Methylmercury may affect many different areas of the brain and their associated functions, resulting in a variety of symptoms. These include personality changes (irritability, shyness, nervousness), tremors, changes in vision (constriction (or narrowing) of the visual field), deafness, muscle incoordination, loss of sensation, and difficulties with memory. The main source of exposure to methylmercury is contaminated fish or shellfish.

Exposure to ***inorganic mercury*** is unlikely in investigated population groups. The inorganic salts of mercury are corrosive to the skin, eyes and gastrointestinal tract, and may be toxic for kidney if ingested.

All forms of mercury can cause kidney damage if large amounts enter the body. Kidney effects can range from increased protein in the urine to kidney failure in case of a massive poisoning. The kidneys are likely to recover once the body clears itself of the contamination.

All mercury effects to adults are reversible. But measures should be taken to reduce the mercury body burden.

We kindly ask you organize medical follow-up for your patient to check if there is a clinical manifestation of mercury poisoning.

We are ready to provide you with advice what measures can be recommended to reduce exposure and prevent any negative health impact.

Feel free to contact me if additional information or clarifications are necessary.

The national survey coordinator

Dr. Krishnendu Mukhopadhyay, MSc, PhD
Phone: +91 44 4592 8547
E-mail: krishnendu@ehe.org.in

A letter to a woman with high mercury level in biological sample(s) *(template)*

Dear Madam/Ms ------,

We would like one more time to thank you for the participation in the survey on evaluation of exposure to mercury organized by Sri Ramachandra University with support from World Health Organization.

Following your instruction to contact you directly provide the survey results, we would like to inform you about mercury level in your hair and urine, and in the cord blood.

We found elevated level of mercury in your *hair/urine/cord blood* sample(s). We would like to stress that it doesn't mean that you have health disorders caused by exposure to mercury. Clinical symptoms are developed only as a result of exposure to very high concentrations of mercury for a long time and significantly depend on many other factors e.g. form of mercury, pathways of exposure, nutrition status, etc.

The observed level of mercury in *your hair/urine/cord blood is ----- µg/g (µg/L)*. The normal range of total mercury in blood varies from 1.0 to 5.0 µg/L, in hair – from 1.0 to 5.0 µg/g, and in urine from 0.4 to 7.0 µg/L. In some cases, clinical manifestations of mercury poisonings were not observed with mercury level in biological samples 10-50 times higher than average level in population.

However, it does mean that actions should be taken to reduce your and your child exposure to mercury.

We kindly recommend you to have medical examination to exclude any symptoms of mercury effects to your health. Please, address your family doctor. Very simple tests such as investigation of your neurological and kidney functions can be done. Your family doctor can do it and recommend more specific medical examination if needed.

You also should know that mercury health effects are reversible and fully disappear when mercury is released from your organism. We will provide you with an advice on how to reduce exposure to mercury and decrease its level in your body. It can be done by correcting your life habits.

We also can provide your doctor with the advice to support you if you decide so.

Please, call or write me if additional information, clarification or support is necessary.

Kind regards,

The national survey coordinator

Dr. Krishnendu Mukhopadhyay, MSc, PhD
Phone: +91 44 4592 8547
E-mail: krishnendu@ehe.org.in

Annex 3. Main questionnaire for participants

Name of participant	
Medical record number	
Identity number of participant	
Date of interview	Date (day/month/year): _ _/ _ _/ _ _ _ _
Date of child delivery	Date (day/month/year): _ _/ _ _/ _ _ _ _

A. Personal information

A.1. Mother of the child (survey participant)

A.1.1. What is your ethnicity (or nationality)?

.....

A.1.2. Have you had children previously?

O No

O Yes How many? _____

A.1.3. What is your education level? *Please select **ONE** answer.*

O Primary (completed primary school)
O Secondary (completed secondary/high school)
O Post-secondary (college, university)

A.2. Farther of the child

A.2.1. What is the education level of the farther? *Please select **ONE** answer.*

O Primary (completed primary school)
O Secondary (completed secondary/high school)
O Post-secondary (college, university)

A.3. Economic status of your household

A.3.1. How easy is it for you to cope financially? *Please select **ONE** answer.*

O Difficult, not always able to afford the necessities
O Income is limited but can afford the necessities
O Live comfortably, but no excess in disposable income
O Stable financial situation, able to afford high-quality products and services

B. Potential exposure to mercury

B.1. Occupational exposure

B.1.1. Before your maternity leave/pregnancy, did you have a paid full-time or part-time job?
(as an employee, employer or self- employed)

O No
O Yes

If NO, please go directly to section B.1.5.

B.1.2. Have you ever worked in the following industries or sectors? *Please mark all that apply.*

Industry type	Never	Less than 6 months	Between 6 months and 1 year	1–5 years	More than 5 years	Any time during this pregnancy
Chemical/petroleum	O	O	O	O	O	O
Metal smelting	O	O	O	O	O	O
Metalworking	O	O	O	O	O	O
Chloralkali plant	O	O	O	O	O	O
Chemistry laboratory	O	O	O	O	O	O
Dentistry	O	O	O	O	O	O
Waste management (general)	O	O	O	O	O	O
Electronic waste management	O	O	O	O	O	O

B.1.2.1. Please provide the name and address of the industrial enterprise where you were working before/during this pregnancy.

……..

……

B.1.3. In your job, did you have contact with the following substances? *Please mark all that apply.*

Substance	Don't know	Never	Less than 6 months	Between 6 months and 1 year	1–5 years	More than 5 years	Any time during this pregnancy
Metallic dust	O	O	O	O	O	O	O
Mercury	O	O	O	O	O	O	O
Amalgam	O	O	O	O	O	O	O
Pesticides	O	O	O	O	O	O	O
Fumes from burning coal	O	O	O	O	O	O	O
Fumes from burning electronic waste	O	O	O	O	O	O	O

B.1.4. If you have worked in any of the previously mentioned industries or have had exposures as listed in the previous questions (you answered YES to any questions in B.1.2–B.1.3), please provide additional information below. *Please mark all that apply.*

	Always	Occasionally	No
Did you change work clothes before entering your home?	O	O	O
Did you change work shoes before coming home?	O	O	O
Did you take a shower after your work shift before coming home?	O	O	O
Did you ever bring your dirty work clothes or other contaminated items home?	O	O	O
If you answered YES to the previous question – Did you wash your work clothes separately from any other clothes?	O	O	O

B.1.5. During your pregnancy, did your husband/partner or anyone else living in your household work in the following industries/sectors? *Please mark all that apply*.

Industry type	Yes	No	Don't know
Chemical/petroleum	O	O	O
Metal smelting	O	O	O
Metalworking	O	O	O
Chloralkali plant	O	O	O
Waste management (general)	O	O	O
Electronic waste management	O	O	O
Chemistry laboratory	O	O	O
Dentistry	O	O	O

B.1.5.1. Please provide the name and address of the industrial enterprise where your husband/partner worked before/during this pregnancy.

……

……

B.1.6. During your pregnancy, did your husband/partner have regular occupational or hobby-related contact with the following substances?

Substance	Yes	No	Don't know
Metallic dust	O	O	O
Mercury	O	O	O
Amalgam	O	O	O
Pesticides	O	O	O
Fumes from burning coal	O	O	O
Fumes from burning electronic waste	O	O	O

B.1.7. If your husband/partner or any other member of your household worked at an industrial enterprise (you answered YES to any question in B.1.5–B.1.6), please provide additional information below. *Please mark all that apply.*

	Always	Occasionally	No
Did your husband/partner change work clothes before entering your home?	O	O	O
Did your husband/partner change work shoes before coming home?	O	O	O
Did your husband/partner take a shower after work, before coming home?	O	O	O
Did your husband/partner bring dirty work clothes or other contaminated items home?	O	O	O
If you answered YES to the previous question – Did your husband/partner always wash work clothes separately from any other clothes?	O	O	O

B.2. Residential environment

B.2.1. Where is your place of residence located?

O In the city
O In a rural area

B.2.1.1. In what neighbourhood or residential area do you live?

O *Please provide name of the city/village*: ……..
O *Please provide the name of the area*: ……

B.2.2. Are there any of the following in the vicinity of your home (up to 2 km)? *Please mark all that apply*

	Yes	No	Don't know
Metalworking business	O	O	O
Waste incineration plant	O	O	O
Cement production plant	O	O	O
Chloralkali plant	O	O	O
Municipal landfill	O	O	O
Landfill for industrial by-products/waste	O	O	O
Crematorium	O	O	O
Thermo-power plant	O	O	O
Electronic waste dismantling	O	O	O

B.2.3. What fuel or energy source do you mainly use for cooking and for heating inside your home? *Please mark only one fuel source for each*.

Fuel source	Cooking	Heating
Natural gas	O	O
Coal or charcoal	O	O

Electric power	O	O
Wood or biomass	O	O
Hot water or hot air from central heating system (district heating or central boiler for a multi-apartment building)	O	O
Kerosene	O	O

B.2.4. What is your main source of water for drinking and cooking? *Please select only one water source for each*.

Water source	Drinking	Cooking
Public water supply	O	O
Private well or spring	O	O
Bottled water	O	O
Surface water (river, lake, etc.)	O	O

B.2.5. Has a thermometer or any other device containing liquid mercury (like a sphygmomanometer) been broken in your home during the last two years?

O No
O Yes. If yes, how long ago? Please specify below:
  O Less than 30 days ago
  O from 30 to 90 days (three months) ago
  O From 91 days to 6 months ago
  O More than 6 months ago but within the last 2 years
O Don't remember/don't know

B.2.6. Has an energy saving fluorescent lamp been broken in your home during the last three months (90 days)?

O No
O Yes. If yes, how many days ago? _____days
O Don't remember/don't know

B.2.7. Has anyone worked regularly with metals in your home in the last three months (e.g. soldering metals as part of do-it-yourself and hobby activities)?

O No
O Yes
O Don't know

B.3. Personal care and lifestyle

B.3.1. Do you have any dental amalgam fillings (dark-coloured fillings)?

O No
O Yes. If yes, how many amalgam dental fillings do you currently have? .....
O Don't know

B.3.2. Do you often use chewing gum or habitually chew (leaves/tobacco, etc.)?

O No
O Yes

B.3.3. Have you ever smoked cigarettes or other tobacco products in your life time?

O I have never smoked. *Go to question B.3.5.*
O I used to smoke, but quit prior to this pregnancy
O I was smoking during this pregnancy

B.3.4. How often did you smoke, on average, before and during pregnancy?

Frequency	Before	During
Did not smoke	O	O
Smoked less than once per week	O	O
Smoked at least once per week, but not every day	O	O
Smoked daily	O	O

B.3.5. How often did you drink alcoholic beverages during this pregnancy?

O Never
O At least once per month
O At least once per week

B.3.6. Do you regularly use skin-lightening products?

O No
O Yes

B.3.7. Did you use skin-lightening products during this pregnancy?

O No
O Yes. If yes, how often? *Please specify below*:
    O At least once per day
    O At least once per week
    O At least once per month
    O Less that once per month

B.3.8. Do you regularly use traditional remedies/medicines that may contain mercury (containing cinnabar)?

O No
O Yes

B.3.9. Did you use traditional remedies/medicines that my contain mercury (cinnabar) during this pregnancy?

O No
O Yes. If yes, how often? *Please specify below*:

O At least once per day
O At least once per week
O At least once per month
O Less that once per month

B.4. Food and beverage consumption

B.4.1. How often do you eat the following foods? *Please mark each category.*

Type of product	At least once per day	At least once per week	At least once per month	Less than once per month
a. Any type of fish/shellfish/sea weed (such as tuna in salad or sandwich, pizza, prawn cocktail, etc.)	O	O	O	O
a.1. Fish from shop	O	O	O	O
a.2. Shellfish from shop	O	O	O	O
a.3. Seaweed	O	O	O	O
a.3. Locally produced seafood (any type)	O	O	O	O
b. Cereal and grain products (any type)	O	O	O	O
b.1. Rice and rice products from shop	O	O	O	O
b.2. Bran and germ	O	O	O	O
b.3. Locally grown rice				
c. Meat and meat products (any type)	O	O	O	O
c.1. Game meat	O	O	O	O
c.2. Edible offal (liver, kidney, etc.)	O	O	O	O
c.3. Chicken	O	O	O	O
d. Vegetables and mushrooms	O	O	O	O
d.1. Wild mushrooms	O	O	O	O
d.2. Leafy vegetables from shop	O	O	O	O
d.3. Legumes from shop	O	O	O	O
d.4. Root vegetables from shop	O	O	O	O
d.5. Locally grown vegetables (your own or purchased at a local market)	O	O	O	O
g. Herbs collected locally (including in herb teas)	O	O	O	O

B.4.2. How often did you eat the following types of fish during the last three months?

Types of fish	At least once	At least once	At least once	Less than

	per day	per week	per month	once per month
a. Swordfish, tuna	O	O	O	O
b. Oily fish (sardines, herring, mackerel, salmon, etc.)	O	O	O	O
c. Whitefish, cod, haddock, plaice	O	O	O	O
d. Freshwater fish (trout, perch, others) from shop	O	O	O	O
e. Freshwater fish locally caught	O	O	O	O
f. Shellfish	O	O	O	O
g. Seaweed	O	O	O	O
h. Canned fish	O	O	O	O

Annex 4. Community involvement strategy

Community involvement in the survey has the potential to positively influence the response rate and retention of participants, as well as implementation of possible risk-reduction measures, as the project follow-up. In terms of survey in Chennai, the community is large and communication strategy will be planed accordingly. Most probably, it will be unfeasible to identify and involve all at the very beginning of the survey. It will be done on the stage of communication of results.

The community needs to be involved in all stages: prior to the survey, during its implementation and in survey follow-up, especially if risk-reduction measures are to be implemented.

Community involvement will be beneficial and is necessary:

- to enable planning of the survey to take into account community needs;
- to ensure support for project implementation from the local authorities and population, and get a higher response rate for the survey; this will positively influence the reliability of survey results;
- to create a sense of participation and co-ownership, and to build trust towards the survey and the survey field staff;
- to increase acceptance of the survey results;
- to strengthen community knowledge and skills to understand the problem and implement risk-reduction measures;
- to ensure implementation of risk-reduction measures if they are needed.

Development of a comprehensive community involvement strategy will add value to both the professionals involved in the survey matter and to society. The main guiding principles to be followed in this process include:

- align the strategy with stakeholders needs
- establish the goals and expected outcomes of the strategy
- explore best practices for community involvement.

The next steps involve creation and execution of a community involvement plan, following the main principles:

- establish an evaluation plan, including measuring, assessing and reporting
- build effective communication skills and strategies to advance community involvement
- advance community relationships into shared value partnerships
- institutionalize community involvement within your organization.

Several steps are recommended for the development and implementation of the strategy and action plan for community involvement.

1. Learn more about the community

Basic information on communities which are potentially involved is partly available: it is fishery communities and Chennai city population. It includes information on community profile; environment pollution information; potential risks and threats of the survey; additional information should be collected on communities needs and problems should be collected.

2. Develop a communication package about the survey

Information about the project will adapted to the target audience – the health and environment sectors and survey participants; development of a different set of information for the local authorities should be considered. The following information will be included in the information package: the rational for the survey and its objectives; who will be involved; how the survey will be implemented; what risks it could pose to the community and its members, if any; what the benefits for the community are; how the survey results will be communicated; what the follow-up is, in particular, if high levels of exposure to mercury are detected.

3. Ensure support from influential people

Information about the planned survey will be first communicated to people with authority; heads of local health and environment administration, mayors, heads of small fishery communities, heads of hospitals involved in the survey, family doctors and relevant research associations. . Engagement and support from those people will allow better understanding of the community's needs, and help to gain trust of the community in the planned survey.

4. Communicate information about the survey to community members

Information about the survey will be communicated to community members through:

- developing and disseminating an information leaflet about the planned survey;
- agreeing joint antenatal visits with gynaecologists and obstetricians serving the community;

5. Keep contact open during the survey implementation

Communication channels need to be maintained during the implementation of the survey in order to respond quickly and effectively to any problems which the survey field staff might face, but also to answer any questions and to provide further clarification to the community and its members, if requested.

6. Communicate the survey results

The survey results will be communicated irrespective of the measured concentrations of mercury. In cases where high levels of exposure to mercury are detected, the communication of the project results should include a proposal for risk-reduction measures (see Section 9 Communication). Furthermore, information about possible future (longer-term) actions will be provided.

7. Follow up with community members who need specific attention and support in implementation of risk-reduction measures, if necessary

In cases of high level concentrations of mercury in biological samples, the participants will receive additional information on how to interpret the results and recommendations on individual preventive measures to reduce exposure. In the unlikely case of very high mercury concentrations, recommendations for individual medical consultations with health-care workers will be communicated directly to the affected participants. Further to providing information at individual level, risk-reduction measures will be recommended for implementation at the community level. This requires active interaction and full engagement of the local authorities in the development and implementation those measures that will be considered.

Annex 5 Budget

Budget line/expenses	Cost per unit (INR&USD)	Total cost (INR)	WHO project budget (Europe) (INR)	WHO project budget SEARO) (INR)	Country contribution (INR)
1. Staff costs					
1.1.National coordinator	INR 380.5/day x 45 days	171234		171234	
1.2.Field staff	INR 25821/monthX4 months	103284		103284	
Subtotal		***274518***		***274518***	
2. Training					
2.1.National coordinator	$56 per day X 5 days	18771.2	18771.2		
2.2. Printing materials	$0.20 per page x 2500 pages	33520	33520		
2.3. Rent of a meeting room	$100/day X 5 days	33520			33520
2.4. Meal, coffee break	$10 per person x 50 persons	33520	33520		
2.5. Travel of meeting participants	$30 per person x 50 persons	100560	100560		
2.6. Travel of trainers	$50 per person x 2	6704	6704		
Subtotal		***226595.2***	***193075.2***		***33520***
3. **Field work (travel)**					
3.1.Field travel	INR 22075 per month x 4 months	132300		132300	
3.2.Travel from Chennai to Slovenia for laboratory training	$1475	94621.25		94621.25	
3.3.Subsistence allowance		200543.15		200543.15	
Subtotal		***427464.40***		***427464.40***	
4. **Lab analysis**					
4.1.Optimization of analytical protocols	INR 1359.2x28days	106545.6		106545.6	
4.2.Mirror analysis cord blood	INR 1359 per sample x 20 samples	27180		27180	
4.3.Mirror analysis Urine	INR 1359 per sample x 20 samples	27180		27180	
4.4.Mirror analysis hair	INR 1359 per sample x 20 samples	27180		27180	
4.5. Shipment of	$2000	128300		128300	

samples					
Subtotal		***316385.6***		***316385.6***	
Total direct costs		1217963.6	193075.2	1018368	33520
Institutional overheads		242289	242289		
Total		**1702541.6 $26066**	**1669021.6 $25553**		**33520 $513**