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

in the Kyrgyz Republic

The first survey protocol

2017

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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 provide the data needed for the development of a global mercury monitoring plan, and baseline data on prenatal exposure to mercury in different population groups. The survey implementation will:

- extend the knowledge on baseline levels and sources of human exposure to mercury in Kyrgyz Republic (the city Aidarken);
- characterize the level and distribution of prenatal exposure in different population groups in participating countries, and particularly in hotspots (the mercury ore mining – close by town Aidarken);
- identify risk factors for exposure from different sources of mercury;
- develop effective measures to prevent the negative impacts of mercury on human health, and especially in vulnerable groups.

The objective of this protocol is to provide a uniform framework for all activities and tasks associated with the collection, analysis, assessment and reporting on prenatal exposure to mercury in mercury contaminated site in Kyrgyz Republic (further – Kyrgyzstan). It is supposed that this has to be applied consistently in all participating countries of the WHO regions to ensure comparability of data. Approach recommended by WHO has been accepted to perform the survey in Kyrgyzstan.

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 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 the Kyrgyzstan (Scintific and Productive Centre for Preventive Medicine)

The survey will be implemented by the Ministry of Health of the Kyrgyz Republic with the technical support of the WHO Regional Office for Europe and WHO Country Office in Kyrgyzstan. Both WHO and Kyrgyzstan 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 coordinators and the laboratory analyst on the survey design and implementation;

- to develop and provide Kyrgyzstan 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;
- to gather the data from Kyrgyzstan and to store them in a consolidated global database; to analyse the data gathered through the survey implementation on Aidarken town, 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 Kyrgyzstan, 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.

The role of Scientific and Productive Centre for Preventive Medicine, Kyrgyzstan in the protocol application is:

- to adapt the WHO protocol to national realities and to obtain approval from national ethics committees;
- to communicate any modifications in the WHO 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 collect data on exposure to mercury in target population groups; to fully comply with WHO SOPs on analysis of mercury in human scalp hair, cord blood and urine including non-invasive sampling procedures;
- 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 and to submit the national protocol to WHO;
- to report to WHO on results obtained in the survey, conducted according to the WHO protocol.

4. Developing a national protocol

The national protocol was developed by a national coordinator of the survey appointed by the Ministry of Health of Kyrgyzstan.

The national coordinator will be responsible for overall planning and implementation of the survey in Kyrgyzstan, assisted by the appropriately trained field staff. In particular, the national coordinator will assure that the survey meets all national ethical requirements for studies involving human subjects and correspond to the Who Master Protocol. The national coordinator is also responsible for coordination of mercury analysis in a reference laboratory identified by WHO.

The survey will be coordinated by Prof Ainash Sharshenova, Head of the Centre for Environmental Medicine and Human Ecology, Scientific and Production Centre for Preventive Medicine (SPCPM) of

the Ministry of Health of the Kyrgyz Republic.

5. Survey design

The survey involves mothers of newborn children recruited in the city of Aidarken 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 areas contaminated by industrial emissions or areas with high levels of consumption of contaminated foods.

The industrial plant is Khaidarkan Mercury Joint-Stock Company, which is located near the town Aidarken (500 m – 2 km) (fig.1). The Ministry of Health of the Kyrgyz Republic issued the directive (no. 478 from 11.08. 2016) and developed the plan of the survey implementation in Aidarken areas. The local representatives were involved in the survey from planning stage.

The Kyrgyz Republic, which have geographically defined populations with high levels of exposure to mercury are conduct the high-exposure arm and the general population arm (in order to have a national basis for comparison, or to develop “reference values”, defined as typical exposure levels in the general population of the country).

The survey in the general population arm was carried out in 1991-1996 in town Aidarken, Batken Region of Kyrgyz Republic.

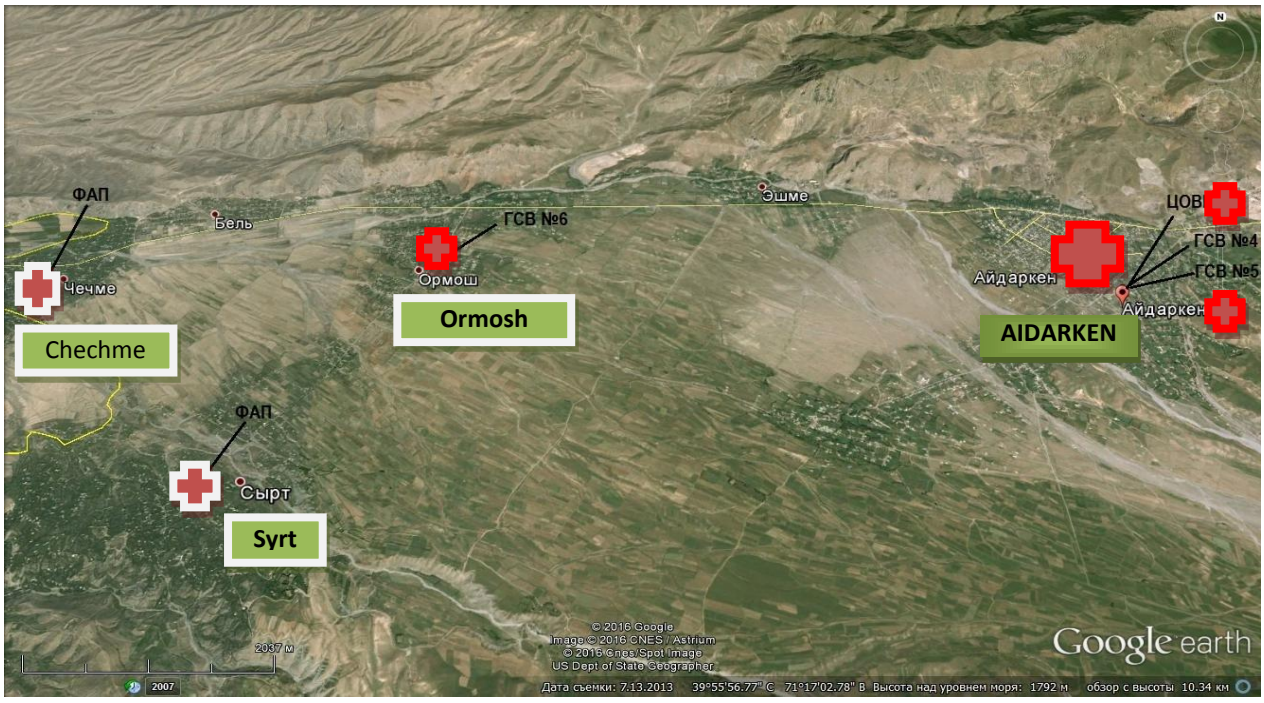

Fig 1. Aidarken area and medical facilities available and involved in the survey

It is very important to involve the community and local representatives in the survey from an early stage, so as 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 general population exposure to mercury involves representative samples of women at maternity wards existing in the area.

Aidarken area is supposed to be highly contaminated by mercury due to mercury primary mining which is the only industrial facility in the area.

This document provides a detailed description and sample size justification for the general population and high-exposure surveys.

The proposed survey design includes a limited set of biomarkers (scalp hair, cord blood and urine). They all will be collected in Kyrgyzstan.

5.1. Target population

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

All efforts should 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 should 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 during antenatal visits or in maternity wards (if it was not possible to recruit a woman during antenatal visit, for example in Syrt and Chechme) 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 (see a content of the information in Annex 2), 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, and collect a sample of scalp hair (following relevant SOPs). Samples of urine and cord blood will be collected by the medical personnel due to no entrance is permitted to maternity wards for non-staff people (following relevant SOPs).

Since the survey aims to characterize prenatal exposure to mercury, maternity hospitals are the preferred recruitment venue due to the availability of medical records and because they may be the easiest place for sampling hair, cord blood and urine, given especially that mothers spend several days in maternity wards after delivery. 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.

[1] No more than two weeks after delivery.

It is important to collect 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).

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 hours) 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.

5.2. Selection of hospitals and number of participating mothers

5.2.1. Number of participants

The total population in Aidarken is around 20000. And the target population is around 5000. According to WHO recommendations a minimum amount of recruitments should be 250. However, it is impossible to collect such a number of samples during the survey period in Aidarken, Kyrgyzstan.

Aidarken is of particular interest for the survey implementation because it is of primary mining of mercury. In agreement with WHO, the total number of samples collected in Kyrgyzstan will be 100 women.

For the further survey and surveys in other areas the approach described below will be applied.

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.

[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.

5.2.2. Identification of high-exposure areas

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

For the high-exposure survey, delimitation of the area of industrial hotspots or contaminated areas should take the following factors 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;
- meteorological and geographical characteristics of the area (e.g. wind direction, topography) in relation to the source of emissions.

The city Aidarken is situated in a high-mountain zone, 45 km from the district centre (city Kadamjai), 60 km away from the regional centre (city Batken). Climate is sharply continental; temperature range is +20 – 22 in the summer and -22 – +28°C in the winter. The city is situated at an altitude of 1980 m above the Sea level. North-west of the city Aidarken, on the right-side of the Osh-Batken highway there are situated villages Eshme, Sur, south-west of the city, on the left side of the same highway there are villages Shah-shah, Jal, Jany-Korgon, Ormosh, Syrt and Chechme.

Beginning in 1941 the Khaidarkan mercury integrated plant, now called Khaidarkan mercury joint-stock company (KMJSC), has developed mercury ore deposits of the largest size. Totally more than 40 th tons of metallic mercury was produced which constitutes approximately a half of the primary mercury produced by the former USSR. In the city Aidarken mercury production is active up to the present time.

The roughest estimates show that the production of this volume of mercury should result in an accumulation more than 15 mil tons of cinders containing not less than 400 tons (by data from preliminary sample collection in 2008 – about 3 000 tons) of residual mercury. Technological releases of gaseous mercury into atmosphere as a result of mercury vapour extraction from furnace gas, if taking only their condensation by water at 30°C, should give 275 tons in the least. Mercury loss with the dust is usually estimated as being 1% of its amount in the ore; this can give additionally 400 tons of mercury coming into the environment together with solid wastes and furnace gases.

The source of contamination of the air of the work-site of the metallurgical plant KMJSC are ore roasting furnaces, condensate of the central flue, mercury-absorbed working surfaces of constructive elements, facilities, a territory as a whole (mercury vapour is 2-8 times above the maximum allowable concentration).

Besides the above contamination sources, other contributors are the most contaminated areas of soil, dumps, cinders which is supported by the results of mercury vapour measurement in areas adjacent to the cinders: Kychy-Aidarken section, at the entrance to the city Aidarken. Notwithstanding the measurement being taken in the inter-seasonal period and in the cold period, mercury vapor concentrations in the air of these locations exceeded the maximum allowable concentration by 2 times.

The soil of areas within 500 m of the metallurgical plant KMJSC, the northern part of the Osh-Batken highway are strongly contaminated with mercury (more than 10 mg/kg). The soils of the area of the Administration of the KMJSC, the villages Sur, Jal, Shah-shah, Jany-Korgon are moderately contaminated with mercury (2.1 – 10 mg/kg). The main contamination occurred during the bloom of mercury production (until 1995) due to technological emissions and hot cinders being unloaded from the furnaces.

The tested samples of fruits and vegetables showed mercury levels from 0.028 to 1.06 mg/kg, which is 1.4 – 53 times higher than the maximum allowable concentration (less than 0.02 mg/kg).

In the city Aidarken the Kyrgyz make up 60%, the Tajik 35%, other nationalities (Russians, Tatars, Uzbeks). The Kyrgyz, the Tajik, Uzbeks, Tatars profess Islam, Russians profess Christian faith.

The target population is 107 mothers living in the city Aidarken and vicinity (villages: Kychy-Aidarken, Shahk-shahk, Djal, Eshme, Jany-Korgon, Sur, Ormosh, Syrt and Chechme).

Implementation of the WHO pilot survey in Kyrgyz Republic in Aidarken area has been agreed with WHO Regional Office for Europe.

5.2.3. Selection of hospitals

The hospitals involved in the survey were selected based on the following criteria:

- They serve areas were targeted population is living;
- The annual rate of deliveries is high enough to allow collection of 100 samples withing the survey duration (4 months);
- Professional staff for samples collection and recruitment (if necessary) is available;
- Emerging and follow up medical assistance can be provided if it is required.

The following hospitals were selected based on the criteria listed above:

- Aidarken Centre for General Medicine Practice (ACGMP) in the city Aidarken,
- Osh Inter-Regional Amalgamated Clinical Hospital (OIRACH) in the city Osh.

The ACGMP provide service to the urban and rural population and will participate in biomaterials sampling. The Aidarken Centre for General Medicine Practice is situated in 45 km from the district center town Kadamjai (from the Laboratory of Kadamjai District Centre for Disease Prevention and Sanitary-Epidemiologic Surveillance - KCDPSES). All Family Physician Groups (see fig. 1), Feldscher Accoucher Posts belong administratively to the Aidarken Centre for General Medicine Practice.

The identification code for the hospitals is as follows:

- Aidarken Centre for General Medical Practice, number 1 – KG1,
- Osh Inter-Regional Amalgamated Clinical Hospital, number 2 – KG2.

Expected numbers of recruited women is calculated based on available information on annual number of births. Average number of deliveries per year is in the Aidarken Centre for General Medicine Practice in 2014 – 662 children and in 2015 – 686 children.
Agreement with the hospitals for the survey implementation should include information about conditions for ensuring privacy for recruitment, questionning and sampling of hair (e.g. separate room in an entrance and 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 (general population) or in the selected survey area (high-exposure group) 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 State Agency Environmental Protection and Forestry under Government of the Kyrgyz Republic), 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)*, should be made available to exposed groups. Monitoring of fish contamination with mercury is established in Kyrgyzstan and will be coordinated based on the survey outcomes.

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.

It is agreed with local public health authorities that the local hospitals capacity will be used for medical follow-up if it is necessary.

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

An individual medical follow-up should be considered on a case-by-case basis, only for mothers with a confirmed high 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 should precede risk communication and planning of protective measures.

Neurological and cognitive development surveillance could be considered for children delivered by mothers with a very high concentration of mercury, within the first control at three months from delivery. It could be framed within the usual surveillance programme for newborns.

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

Recruitment and fieldwork will be organized by Scientific and Production Centre for Preventive Medicine (SPCPM) of Ministry of Health of the Kyrgyz Republic, in accordance with the directive no. 480 from 11.08.2016 as well as it will coordinate the project on implementation of the mercury biomonitoring survey.
The processes of recruitment and fieldwork are described briefly in this section.

6.1. Fieldwork management

Organization of fieldwork is the responsibility of the Scientific and Production Centre for Preventive Medicine (SPCPM) of MoH of the Kyrgyz Republic.
Fieldwork is the responsibility of the participating country. Each country decides on the organization of the fieldwork, including the following:

- notification and getting agreements with national and local authorities about the survey and to apply for ethical approval;
- using the standardized methodological documents provided by WHO as a starting point to prepare the SOPs,
- organization and preparing the documents and the plan of the survey and instruction (guidance) for fieldwork staff;

- training field personnel and supervising their work;
- selecting maternity hospitals;
- obtaining necessary permissions from national, district and local authorities;
- preparation and translation of all documents (informed consent, SOPs, etc.) in Russian and Kyrgyz languages;
- translation and validation of the questionnaire during a small-scale pre-pilot survey;
- prepare the agreements and recruitment of qualified survey personal;
- provision of a help-desk phone number for the survey staff and the participants;
- supervision of the fieldwork, help and advice if necessary;
- liaising with the local community, identifying and engaging local representatives to promote the survey;
- ordering and receiving goods and transportation of all lab things to the city Aidarken and Osh;
- developing an information leaflet for maternity hospitals and for survey participants;
- informing the recruited women, administering informed consent and conducting interviews;
- collecting, storing and shipping samples to the reference laboratory;
- entering the data into a data file and performing preliminary data cleaning;
- performance of internal quality control of fieldwork;
- evaluation and communication of the survey results;
- provision of the survey database and the national protocol to the WHO unit that performs data analysis and interpretation.
- 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.

The national coordinator will deploy experienced fieldwork personnel from the Scientific and Production Center for Preventive Medicine (SPCPM) and ask the maternity wards to support the field work by the hospitals' staff. The following basic tasks will be applied to select interviewers and local staff: experience with and knowledge of the topic, good experience in dealing with people, no reservations about people of different social classes or ethnic origin; training in sampling; in addition to that, the following will be considered: local knowledge of the sampling areas, a communication style that suits local cultural norms and experience in interview conduct.

Responsibilities of the research staff:
- to contact women and getting agreement from women to participate in the survey (provision of information sheet, eligibility screening);
- to recruit (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 samples;
- to collect medical records.

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

To ensure the adherence of hospital staff to the survey protocol, sufficient training, quality assurance and quality control measures must be in place. The following measures will be taken not to affect adversely the health care:

- 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;

- extra-hours for staff assisting with cord-blood sampling in maternity wards should be paid from the project budget or hospital budget if it is agreed so;
- enough staff units should be trained to perform the survey tasks and to avoid influencing negatively on delivery service and unacceptable burden to the hospitals staff.
- the maternity wards chief doctors will plan the staff workload accordingly.

To ensure the adherence of hospital staff to the survey protocol, sufficient training, quality assurance and quality control measures will 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 should either take place over the course of an entire year or during a specified season. All data collection activities should be conducted in a specific season.
In the case of a comparison study, sampling in the general population and in the high-exposure group should 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. Follow-up surveys in Kyrgyzstan should 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. All efforts should be made to provide information about the survey to women during antenatal visits, and to make the information leaflets available for women to take home. 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 should give 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.

The interviewers will need to be present at the maternity hospital. These could be either dedicated survey staff or trained employees of the hospital.

A female fieldworker might generally be a better choice to contact women shortly after delivery. The fieldworker should 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.

6.4. Questionnaire

All survey forms provided by WHO are translated into Russian and Kyrgyz (annex 1,2,3).. No changes are done in documents provided by WHO.

Preliminary questionnaire versions in national languages will be pilot tested prior to the main survey.

Screening interviews and obtaining consent (annexes 1 and 2) have to be done prior to administering the questionnaire.

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.

The questionnaire is aimed to characterize exposures during different periods of time.

Personal interviews conducted by trained interviewers are the most commonly used method to collect data on behavioural and nutritional exposure factors. However, this method has a tendency to under-report socially undesirable behaviours (for example smoking). This is known as the “social desirability” bias. On the other hand, interviews have the advantage over self-administered surveys that any misunderstanding can be resolved immediately, which leads to higher data completeness

and quality. Training of the interviewers is essential to ensure that the interviews are conducted in a standardized way. The training of interviewers has been shown to improve their performance, particularly in reducing under-reporting of pertinent information.

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 should 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, the training must be strategic and 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 hospital staff involved in the survey will be trained by the national coordinator and scientific field staff.

Establishing a technical help desk during the survey, starting from the moment the general protocol is adapted to the national situation, might increase consistency and promote adherence to survey protocols. The help desk could be available through a central website supporting the survey. It should provide answers that have been formulated by experts in the field in a timely manner.

If trained hospital personnel conduct interviews in addition to their regular duties, then additional motivation might be needed. The project budget included funds to cover honorarium for maternity wards staff (Annex 5).

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.

Samples collected in Kyrgyzstan will be analysed in a reference laboratory (Annex 6).

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, checklist including all important steps of the procedures will be prepared

for maternity wards staff. 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. The relevant SOP for analysis of mercury in hair, provided by WHO to the national

[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.

coordinators, 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 compounds. 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. 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.

The main source of exposure to mercury in Aidarken is supposed to be environment contamination by mercury due to primary mercury mining. That determined mothers' urine, scalp hair and cord blood as target matrices and their collection in this survey is an obligation.

7.2. Transportation of samples

In preparing samples for transportation, the national coordinator or 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, 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.

Detailed instructions for hair sampling and sample pre-analytical treatment can be found in the SOP for analysis of mercury in hair. The hair samples should be aliquoted and can be kept at room temperature.

The cord blood samples should be aliquoted (at least two aliquots) to enable mercury analysis in the national laboratory (as an inter-calibration to build national capacities) and the reference laboratory identified by WHO.

Urine samples should be aliquoted (at least three aliquots) to enable mercury and creatinine analysis in the national and the reference laboratories. The national survey coordinator is responsible for the samples transportation from hospitals to storage place before shipment to the reference analytical laboratory.

7.4. Analysis of samples

The 100 individual samples of each matrix (scalp hair, cord blood and urine) should be collected within the framework of the pilot surveys.

In Kyrgyz Republic, determination of total mercury in human urine will be carried out by cold vapor atomic absorption spectrometry (AAS) using mercury analyzer "RA - 915M" (Lumex limited company, Saint Petersburg, Russia).
The personnel of the Sanitary-Hygienic Laboratory has a capability for determining the presence of mercury in urine by cold vapor atomic absorption method. The analyzer RA 915M is available, which is obtained for temporary use from the State Agency of Environmental Protection and Forestry under the Government of the Kyrgyz Republic, there is a metrological verified technique for mercury determination in urine.

Methods of measurement of mass concentration of mercury in the urine M 07.06.2013 LLC " Lumex Marketing" (Russia, St. Petersburg), based on the reduction of mercury ions to atomic state high alkaline solution of tin dichloride (II) in the reaction vessel consoles, transfer analytical atomic mercury analyzer cuvette air current (method "cold vapor"), in which the resonant absorption (absorbance) of the radiation from the light source free of mercury atoms at a wavelength of 253.7 nm.
Formed quantitatively analytic signal is converted to a weight value of mercury using a preset calibration curve which is installed using the calibration solutions, obtained by diluting a standard sample of aqueous solution composition mercury.

Alternative standard operating procedures (SOPs) for the determination of total mercury in blood, hair and urine in the first part describes the procedure for processing samples of biological substrates. Hinge blood mineralized concentrated nitric acid in the presence of vanadium oxide (V), at a temperature of 90 °C. Next, determine the concentration of mercury is produced according to the above method, mercury analyzer.

To check quality control for tests in use, the Sanitary-Hygienic Laboratory has special control procedures, for preparing reference samples, samples with additives, State Standard samples of mercury.
Control accuracy (stability) of the calibration method for determining the characteristics of mercury in urine is performed using 2.0 μg/dm^3 mercury solution.
From the control solution is analyzed two aliquots are mercury mass concentration for each input ($C_{k,1}$, $C_{k,2}$). The calibration characteristic is recognized stable if for each condition
$(C_{k,\,i} - C_0) \leq 0{,}1 \times C_0$
where C_0 - the actual value of the mass concentration of mercury in the test solution, μg/dm^3.

*$C_{k,\ i}$ - measured value for the control solution, µg/dm^3, where **i** = 1, 2.*
Control of measurement accuracy is carried out using the method of additives. Urine was divided in half and one of the portions of mercury injected. Analyze the initial portion and the portion with the addition of in full compliance procedure and obtained results of the analysis *(X_1* average, *X_2* average*, µg/dm^3)*. Control with positive results under the conditions:

$(X_{1\ \text{average}} - X_{2\ \text{average}} - C_д) \leq K_{пр}$,

where, *$C_д$ - value of the additive, µg/dm^3,*

$K_{пр}$ - control standard

The SHL for the first time organized mercury analyses in urine and human blood.

The analyzer will be operated under the control of a personal computer (PC). Data processing program for the mercury analyzer "RA - 915M" is included in program package.

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 spectroscopy (CVAFS).

Ideally, the laboratory that performs the analysis should be located in the country, but the main emphasis should be on analytical proficiency. Kyrgyzstan didn't perform well in proficiency test organized by WHO and all samples will be shipped to the reference laboratory (analysis (Research Centre for Toxic Compounds in the Environment, Masaryk University, Brno, Czech Republic).

7.5. Standardization

The laboratory (SHL) involved in the national survey will follow the standard SOPs for sampling and analytical methods, and the procedures for the quality assurance and quality control also in the pre-analytical phase. The availability of appropriate reference materials (samples with a certain level of mercury) supports internal quality assurance. External quality assurance should be done through international inter-laboratory comparison investigations (ICI).[4]

Internal quality control will include control of vials' purity, control of blank, control of inter-series repeatability and control of accuracy.
A proficiency test of the analysis of total mercury in cord blood and urine was organized by WHO, using freeze-dried samples as well as a mirror analysis of 20 samples of each biological matrix.
All collected samples will be sent to Czech Republic for the total mercury analysis (Research Centre for Toxic Compounds in the Environment, Masaryk University, Brno, Czech Republic).

7.6. Storage of samples and samples remaining after the mercury analysis

The two freezing refrigerators are available during this survey (1 - in the Kadamjai District Centre for Disease Prevention and Sanitary-Epidemiologic Surveillance; 2 – Aidarken Centre for General

[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.

Medicine Practice). Two -20° freezers are purchased to enable implantation of the UNEP project. For biosample storage, a freezer (-20°C and more) of the Bishkek city Center for State Sanitary-Epidemiologic Surveillance will be also use.

The samples will be destroyed after the analysis and confirmation of the results at national level and in the reference laboratory according to the Material Shipment Agreement (Annex 6).

8. Data management, analysis and evaluation

8.1. Data management

Data generated during the fieldwork will be further processed and merged in order to allow for final evaluation and results. 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 templates are provided by WHO. 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

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.

Kyrgyzstan 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 will be conducted in each participating country, while statistical data analysis can be conducted either at the national level or at WHO. Kyrgyzstan 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)

Kyrgyzstan will conduct statistical analyses at the national level and submit anonymized data 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 campaigns aim 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 leaders have to provide targeted information to the general public, policy-makers 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.

Population in Aidarken area and environment pollution due to primary mercury mining is of particular interest of many governments and international organizations promoting closure of primary mercury mining around the world. Improper and incorrect communication campaign can

harm the survey implementation and specific attention will be paid to materials prepared for the communication of the survey and its results.

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 should start before the recruitment itself begins. The recruitment process has 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.

In order to meet these goals, it is necessary to make sure information leaflets are tailored to the target population. The briefing of policy-makers and especially of local authorities in municipalities of cities and villages in Aidarken area should 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 will include contact details (name, address, telephone number and email address of the survey coordinators) and be available for participants.

The information leaflet and informed consent form will provide a brief summary of the survey and its aims, in plain language understandable for a non-professional audience in Russian and Kyrgyz languages. They both are used in the area. The leaflet and consent form will 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.

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. Scientific staff of SPCPM is responsible for that under a leadership of the national coordinator.

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. If the HBM survey reveals low exposure levels and low or negligible health risks, the main purpose will 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 will 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.

In general, 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 ant national and local level, 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, is an obligation.

It is crucial not only to prepare clear and understandable messages, tailored to the capacities and needs of the audience, but also to identify 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.). It is important to get support from central and local authorities 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, environment and economy 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. A preventive action plan will be developed if necessary

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), if any, 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 will be clearly communicated, focusing on population groups at risk; it will include recommendations on reducing exposure to mercury and/or preventing health risks.

The public perception of risks might affect the acceptability and the appropriateness of risk-reduction measures. Therefore, it is essential to ensure that the risk-communication process takes into consideration general public perceptions taking into account sensitivity of the issue in the population and the area due to mercury mining.

Most effective ways to communicate risks such as mass media will be explored. Involvement of topical experts will 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 and relevant safety levels, as well as any accidental mercury exposure, particularly of at-risk populations.

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

In cases where high concentrations of mercury are observed, 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. These could be paediatricians, gynaecologists and obstetricians, occupational physicians, and general practitioners serving specific communities (artisanal and small-scale miners, fishing communities, etc.). Organization of training for health-care professionals can be considered to help gain support for implementation of risk-reduction measures.

9.3.4. Communication of the survey results to participants

Individual results should be provided to survey participants, except those who do not wish to know their results. In sensitive situations such as situation in Aidarken area, topical experts 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 will be considered in cases where a high level of mercury has been detected. First, the analysis will be repeated to exclude any mistakes including 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 needs to be remembered that they will differ in cases of exposure to methylmercury and inorganic mercury.

It is important to explain to participants the meaning of their results 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. 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 needs to 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 is approved by the ethics committee of Scientific and Production Centre for Preventive Medicine of the Ministry of Health of the Kyrgyz Republic.

The ultimate objective is to guarantee the optimal protection of the rights and dignity of every survey participant (data subject). Special attention should therefore be 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 access personal results and the wish of participants to know or not to know their personal results;
    - the right for privacy for the enrolment discussion , screening process, answering questionnaire and taken samples of hair and urine;
    - 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 should 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:

_____

СКРИНИНГОВЫЙ ВОПРОСНИК / ТЕКШЕРҮҮ СУРООЛОРУ

1. Ваш возраст старше 18 лет? / Сиздин жашыңыз 18ден өткөнбү?
☐ Да / Ооба

☐ Нет / Жок

Если нет, не достигли 18 лет, то остановить интервьюирование (не включать в разработку!)
Эгерде 18 жашка чыга элек болсо маалымат алуу токтотулсун (изилдөө ишине киргизилбесин!).

2. Сколько дней прошло от родов (в случае если произошли роды) / Төрөгөнүңүзгө канча күн болду? (эгерде төрөгөн болсо)
____ дней / күн

Если более 14 дней, просим остановить проведение интервьюирование / Эгерде 14 күндөн ашык болсо маалымат алууну токтотууну суранабыз

3. Вы живете в _____.? [в районе изучения] / Сиз _____жашайсызбы? [излдөөгө алынган райондо]
☐ Да / Ооба

☐ Нет / Жок

Если нет, то просим остановить интервью / Эгерде жок болсо маалымат алууну токтотууну суранабыз

4. Как долго Вы живете в этой области/районе? / Бул областа/ райондо жашаганыңызга канча жыл болду?
_____ лет /жыл

Если менее 3 лет, то остановить интервьюирование / Эгерде 3 жылдан аз болсо маалымат алуу токтотулсун

5. Сколько дней в течение последних трех месяцев вы провели за пределами района [района изучения]? / Акыркы үч айдын ичинде сиз канча күн бул райондо эмес, башка жакта болдуңуз [излдөөгө алынган райондо]?
____ дней

Если более 14 дней, то просим остановить интервью / Эгерде 14 күндөн ашык болсо маалымат алууну токтотууну суранабыз

6. Достаточны ли знания языка, для заполнения интервью (оценивается интервьюером) / Маалыматты толтуруу үчүн тилди билүү деңгээли жетишерликпи (маалымат алып жаткан адам тарабынаан бааланат)
☐ Да / Ооба

☐ Нет / Жок

Если нет, то просим остановить интервью / Эгерде жок болсо маалымат алууну токтотуну суранабыз

7. Выборка волос возможна на основе визуальной оценки длины волос (по крайней мере, 3 см на задней части головы)? / Чачты талдоо чачтын узундугун кароонун негизинде бааланат (баштын арт жагынан жок дегенде 3 см)
☐ Да / Ооба

☐ Нет / Жок

8. Проба может ли зачислена в исследование? / Пробаны изилдөөгө киргизүүгө болобу?
   ☐ Да / Ооба

   ☐ Нет / Жок

9. Есть ли согласие на участие? Катышууга макулбу?
   ☐ Да / Ооба

   ☐ Нет / Жок

10. Участник дает письменное согласие на: (пожалуйста, отметьте все подходящие варианты) / Катышуучу жазуу түрүндө: (баардык туура келген варианттарын белгилеңиз)
    ☐ Образец волос / чачты

    ☐ Образец мочи / заараны

    ☐ Образец пуповинной крови / канды

    ☐ Доступ к медицинской документации / Медициналык документацияларды алуу мүмкүнчүлүгүнө карата макулдугун берет

11. Поступил в опрос? / Суроого катышууга кирдиби?

    ☐ Не имеют права/ Укугу жок

    ☐ Не желает участвовать / Катышууну каалабайт
    Причина / Себеби:_____

    ☐ Поступил на участие в исследовании? / Изилдөөгө катышууга кирдиби?

Если поступила в опрос / Эгерде катышууга кирсе

Имя участницы / Катышуучунун аты:_____

Домашний адрес / Үйүнүн дареги:_____

Дата поступления в больницу / Ооруканага келген күнү:_____

Дата рождения ребенка / Баланын төрөлгөн күнү:_____

Annex 2. Participant Information sheet and Informed consent form

Participant information sheet

Dear Participant,

The Scientific and Production Centre for Preventive medicine of the Ministry of Health with support from World Health Organization is organizing a pilot survey aiming at evaluation of health risks from mercury in the environment in Aidarken area of Kyrgyzstan. Based on this survey we will be able to assess exposure of population in Aidarken area 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.

Mercury and its compounds are used for production of different types of products and can be released to the environment as by-products during different type of combustion processed. Exposure to high concentrations of mercury and its compounds for a long time create a risk of neurological and urinary system disorders.

There is source of exposure to mercury for the population in Aidarken area such as primary mercury mining. The population in the area can be exposed to inorganic mercury. In waters, marine and fresh, mercury is transformed to methylmercury which can accumulate in fish and other sea products. Fish and other food contaminated by methylmercury is the main source of mercury for general population. The survey is aiming at investigating what mercury concentrations are in our organisms. That can be done through assessment of its concentrations in scalp hair, cord blood and urine.

When a woman is exposed during pregnancy to high concentrations of mercury, mercury can be transferred to the fetus, and affect the developing organs and systems. Prenatal exposure to mercury in high concentrations is linked to an increased risk of certain diseases and conditions in a child. That's why we are addressing you and willing to assess your and your child exposure to this chemical during last three months of pregnancy.

After the survey we will have information about your body contamination by mercury and risks of your child exposure to mercury. 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.

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 after delivery of the child and the placenta. A nurse will instruct you how to collect urine sample when you are in hospital or after that.

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. For that, just to inform the national coordinator about your decision. The national coordinator contact details are provided below.

We plan to complete the survey in 3-5 months depending of a number of deliveries during this period. One hundred 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 of your time during your staying in a hospital.

This survey strictly follows all ethical standards. 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.

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 national survey coordinator

Prof Ainash Sharshenova

E-mail: spcpm@rambler.ru

Phone: +996-312-544573

Информационный лист участника

Дорогая участница,

Научно-производственный центр по профилактической медицине Министерства здравоохранения при поддержке Всемирной организации здравоохранения организует экспериментальное исследование, направленное на оценку рисков для здоровья, связанных с ртутью в окружающей среде в районе Айдаркен Кыргызстана. На основе этого опроса мы сможем оценить воздействие ртути на население Айдаркенской области и предложить, при необходимости, профилактические меры, а также поддержать усилия ВОЗ по разработке глобального плана мониторинга воздействия ртути.

Ртуть и ее соединения используются для производства различных видов продуктов и могут выделяться в окружающую среду в качестве побочных продуктов при сжигании. Воздействие высоких концентраций ртути и ее соединений в течение длительного времени создает риск нарушений неврологической и мочевой систем.

Существует источник воздействия ртути для населения в районе Айдаркен, такой как первичная добыча ртути. Население в этом районе может подвергаться воздействию неорганической ртути. В водах, морских и речных/озерных, ртуть превращается в метилртуть, которая может накапливаться в рыбе и других морских продуктах. Рыба и другие продукты, загрязненные метилртутью, являются основным источником ртути для населения в целом.

Исследование нацелено на выявление того, какие концентрации ртути находятся в наших организмах. Это можно сделать путем оценки ее концентраций в волосах кожи головы, пуповинной крови и моче.

Когда женщина подвергается воздействию высоких концентраций ртути во время беременности, ртуть может передаваться плоду и воздействовать на развивающиеся органы и системы. Пренатальное воздействие ртути в высоких концентрациях связано с повышенным риском некоторых заболеваний и состояний у ребенка. Вот почему мы обращаемся к вам и готовы оценить воздействие на Вас и вашего ребенка этого химиката в течение последних трех месяцев беременности.

После обследования у нас будет информация о загрязнении вашего тела ртутью и о рисках воздействия ртути на вашего ребенка. Имея эту информацию, мы предоставим вам рекомендации о том, как свести к минимуму или избежать воздействия ртути и предотвратить ее вредные последствия для вашего ребенка.

Для анализа концентрации ртути мы возьмем от вас образцы волос головы, пуповинной крови и мочи. Все эти процедуры не причинят вам вреда. Мы возьмем несколько прядей волос с затылка. Это не будет заметно. Пуповинная кровь будет собрана специалистами в родильном отделении после родов ребенка и отделения плаценты. Медсестра проинструктирует вас, как собирать образец мочи, когда вы находитесь в больнице или после этого.

Участие в опросе является добровольным. Вы можете отказаться от участия по разным причинам. Это никак не повлияет на уровень и качество медицинской помощи. Кроме того, вы можете снять свое участие в любое время, прежде чем покинуть больницу. Для этого просто проинформируйте национального координатора о вашем решении. Контактная информация национального координатора приведена ниже.
Мы планируем завершить исследование в течение 3-5 месяцев в зависимости от количества родов за этот период. В опросе вместе с вами будут участвовать еще сто женщин.

В общей сложности, участие в опросе займет около 1,5 часов вашего времени во время вашего пребывания в больнице.

Этот опрос строго следует всем этическим стандартам. Информация, которую мы собираем во время опроса, будет считаться конфиденциальной. Ни ваше имя, ни имя вашего ребенка не будут опубликованы. Все данные будут анонимизированы, и идентификационный код, присвоенный вам, будет использоваться для целей анализа.

Образцы, собранные в ходе обследования, будут уничтожены в лаборатории после завершения анализа. Они не будут использоваться для каких-либо других целей, кроме цели этого опроса.

Национальный координатор

Проф. Айнаш Шаршенова
E-mail: spcpm@rambler.ru
Телефон: + 996-312-544573

Informed consent form

CONSENT FORM for participation in a human biomonitoring survey to assess exposure to mercury, research project conducted in accordance with the Ministry of Health order N 480 from 11.08.2017 by the scientific staff of the Joint institution “Prophylactic Medicine” of the MoH of Kyrgyzstan, with support from the World Health Organization (WHO).

Dear participant,

We would like to invite you to take part in a study aiming to assess exposure to mercury to be able to assess risks and to recommend on protective measures.

Purpose

This study paid specific attention to children health and is conducted for assessment of contamination of the area where you live. The main purpose of the survey is to collect information on exposure to mercury before delivery.
Based on the results of the survey, we will provide data on intrauterine exposure to mercury, assess the level and distribution of exposure, identify the main risk factors of exposure in a population and advise the government on protective measures to reduce exposure if needed.

The survey is supported by the WHO as a part of a global initiative aiming at the development of a global plan of assessment of exposure to mercury and characterization of the global and regional distribution of exposure. It is necessary to plan protective measures and evaluate the effectiveness of their implementation at a global, regional and country level.

Background

Mercury is present in air, soil and food and finds its way into the human body, disturbing biological processes and in some cases affecting our health. When a woman is exposed during pregnancy, mercury can be transferred to the fetus, and affect the developing organs and systems. Prenatal exposure to mercury in high concentrations is linked to an increased risk of certain diseases and conditions in a child. Analysis of biological material from mothers (such as hair and urine) and of cord blood helps to characterize prenatal exposures to mercury and to provide valuable information. This helps to assess health risks at the population level and to support policy interventions aiming at reducing pollution and protecting health. It can also be used to provide recommendations on how to protect you and your child from exposure to mercury and reduce risk in cases of detected higher mercury concentrations.

Selection procedure on assessing prenatal exposure to mercury

Scientifically sound methods to assess prenatal exposure to mercury are well established. The methodology applied in the survey has been developed and is recommended by WHO. It enables an assessment of exposure to mercury during the last trimester of pregnancy, through measuring concentrations of mercury and its compounds in the cord blood, scalp hair and urine. The most valuable data to assess prenatal exposure to mercury can be obtained if samples of biological material are taken immediately after delivery. For that reason, we approach women during their stay at maternity hospitals. If you are interested in getting more information about your and your

child's exposure to mercury, and you meet the eligibility criteria, you are invited to participate in the survey.

Procedures

If you agree to participate in this survey we will ask the following biomaterials from you:
• Cord blood, taken by a midwife during childbirth.
• Your urine sample (maternal urine)
• Your hair (a small cut strand of hair, close to the scalp at the back of the head)
• Reply to the questionnaire containing information about your diet, at work and at home, lifestyle and health; it will take around 30 min;
• Your consent to receive some information from you and your child's medical records, such as weight, height, the official diagnosis of (congenital) diseases and conditions.

We would like to measure the total amount of mercury in the hair, strands take at least 3 cm from the head, because this reflects the impact of this contaminant in the last three months. We would like to measure the level of mercury in cord blood and in urine.

Samples collected in this survey will be sent to Mazaryk University, Czech Republic for mercury analysis. All samples will be destroyed in a laboratory after analyses are completed. The same confidentiality rules are applied: only samples ID will be communicated to the researches in the Masaryk University. No private information will be available for anyone except of the national survey coordinator.

Voluntary participation/discontinuing participation

You do not have to take part in this research if you do not wish to do so. Refusing to participate will not affect your treatment at this hospital in any way.

Also, if you decide to participate in the survey, you will be able to discontinue your participation at any time. All you have to do is to inform the researchers that you no longer want to participate. Furthermore, you can ask for all the samples that you have provided to be destroyed. If you decide to withdraw your participation and ask for the destruction of your samples, please do it before leaving the hospital. Withdrawing your participation will not affect your medical treatment or access to medical services in any way.

The results of the analyses that have already been completed will remain in the survey database and will be used in survey reports.

In total, participation in the survey will take around 1,5 hours of your time.

Benefits of the survey

The results from all survey participants will be analysed collectively to characterize exposures to mercury and to guide policy-makers to make informed decisions for the benefit of public health.

Your results will be compared to health-based guidance values, when they are available. If necessary, you will receive recommendations on how to reduce the level of a pollutant in your body or to avoid future exposures.

You can ask that your individual test results be sent to you or to your doctor. If you choose to have the results sent to your doctor, we will ask you to provide their name and address in writing.

You can also specify to not receive your results if you do not wish to know.

Costs

No costs associated with this study will be charged to the participants.

Possible risks

No risks are anticipated associated with participation in this survey. There is no health risk related to the collection of cord blood. The procedure will not have any influence on the normal delivery procedures. Possible inconveniences are limited to the time you will have to spend on providing the hair and urine samples and responding to the questionnaires. The questionnaires and medical records contain information that can be viewed as sensitive. However these data will be kept strictly confidential. We will use coding and anonymized data at the data analysis stage. Your personal information will only be available to authorized investigators.

Confidentiality

Researchers will process the information from the questionnaires and the samples. Your name and address will be replaced by a code. If the results of this study are published in a report or scientific journal your name will not be mentioned and no information that can identify you will be included in such a report or publication. All information will be treated confidentially in accordance with relevant privacy laws. . We will ensure your privacy for collection of hair and urine samples as well as for answering questionnaires.

Information about the survey

You have the right to ask for additional information about the research project and the procedures described in this document. The main investigator (contact details are provided below) will respond to requests for information, as much as she is aware of it. Researchers will inform you of significant changes in the procedure, the occurring risks or benefits of this study. All samples collected in this survey will be destroyed as soon as all analyses are performed.

The form of consent for participation in conducting a pilot study on mercury biomonitoring for assessing prenatal exposure, the research project is carried out in accordance with the Directive of the Ministry of Health of the Kyrgyz Republic No. 480 dated ----, with the participation of the employees of the Scientific Production Association "Preventive Medicine" of the Ministry of Health of the Kyrgyz Republic and support from the World Health Organization (WHO).

I read the information booklet to participate in the human biomonitoring program and I want to participate in the study. I understand the potential risks and benefits of this study and take a voluntary part in this study. I understand that this information will be kept strictly confidential and that the study was approved by the ethics committee.

Mother's name (please print):

_____

Signature of the mother: _____

Name and surname of the child:

_____

Date of birth of the child (dd / mm / yyyy) _____

Results:

I do not want to get personal results.

I would like to receive personal results at my home address:

_____

I wish my personal results were sent to my doctor.

Name and surname of the doctor:

_____

Doctor's address:

_____

The national coordinator:

Dr Ainash SHARSHENOVA (national coordinator)
Head, Centre for Environmental Medicine and Human Ecology, Scientific and Production Centre for Preventive Medicine (SPCPM) of the Ministry of Health of the Kyrgyz Republic

Email: spcpm@rambler.ru

Tel: +996-312-544573

We thank you for participation in the survey!

Информационный буклет для участия в программе биомониторинга человека

Форма согласия на участие в проведении пилотного исследования по биомониторингу ртути для оценки пренатального воздействия, исследовательский проект осуществляется в соответствии с Указанием МЗ КР №480 от 11.08.2016 при участии сотрудников Научно-производственного объединения «Профилактическая медицина» Министерства здравоохранения Кыргызской Республики и при техническом содействии Всемирной организации здравоохранения (ВОЗ).

Уважаемая участница!
Мы хотели бы пригласить Вас принять участие в исследовании, направленного на защиту здоровья детей

Цель

Это исследование уделяет особое внимание новорожденным детям и проводится для изучения воздействия загрязнения в вашем районе проживания. Основная цель данного исследования заключается в предоставлении данных о дородовом воздействии химических веществ и вредных веществ, таких как ртуть. Цель направлена на оценку влияния факторов риска, влияющие на здоровье человека, воздействия загрязнения, и после повторного обследования в течение нескольких лет в новой группе участников.

Процедуры

Если вы соответствуете вышеуказанным критериям, согласны ли Вы на участие в данном опросе и сдать следующие биоматериалы:
• Пуповинная кровь, берется акушеркой при родах.
• Ваш образец мочи (материнская моча)
• Ваши волосы (небольшая срезанная прядь волос, близкая к коже головы на затылке)
• Ответ на вопросник, содержащий информацию о Вашей диете, на работе и дома, образ жизни и здоровья.
• Ваше согласие получить некоторую информацию от вас и медицинские записи вашего ребенка, такие как вес, рост, официального диагноза (врожденных) заболеваний и состояний.

Мы хотели бы измерить общее количество ртути в волосах, прядь берут не менее 3 см с головы, потому что это отражает воздействие данного загрязнителя в течение последних трех месяцев. Мы хотели бы измерить уровень ртути в пуповинной крови и в моче.

Образцы, собранные во время исследования будут отправлены для анализа ртути в Мазарикский Унивеситет, Чехия. После анализа оставшие образцы будут уничтоженыю Требования конфиденциальности будут соблюдены: только индентификационные коды будут представлены исследователям в Чехии. Личная информация будет недоступна никому, кроме национального координатора.

Добровольное участие/Отклонение

Вы можете отказаться от участия в данном исследовании, если вы не хотите участвовать. В любом случае отказ от участия не повлияет на лечение в этом центре. Даже если Вы подписали данное соглашение, Вы можете прекратить процесс в любой момент. Все, что вам придется сделать, это проинформировать исследователей, что Вы больше не хотите участвовать. Кроме того по Вашей просьбе, все образцы, которые Вы дали для исследования могут быть уничтожены. В любом случае Ваше лечение или доступ к медицинским услугам, не будут затронуты. Результаты проведенного анализа останутся для изучения.

Преимущества исследования

Результаты исследования будут проанализированы, характеризуя экспозицию в образце матери / ребенка. Ваши результаты будут сравниваться с ориентировочными значениями здоровья, основываясь на доступных значениях.
Консультации о том, как снизить риски в вашем доме или производственных условиях. Вы можете попросить, чтобы ваши индивидуальные результаты тестирования выслали вам или вашему врачу. Если вы хотите чтобы результаты были направлены вашему врачу, мы просим Вас предоставить его / ее имя и адрес в письменной форме. Можно также указать, что не хотите получить результаты.

Расходы

Все расходы, связанные с этим исследованием будут для участника бесплатным.

Возможные риски

Нет ожидаемых рисков, связанных с участием в данном исследовании. Нет риска для здоровья, связанная со сбором пуповинной крови. Процедура не будет иметь никакого влияния на обычное состояние. Возможные неудобства – это затрата времени на предоставление волос, мочи и заполнение вопросника. Эти данные (анкеты и медицинской карты) будут храниться строго конфиденциально. Мы будем использовать кодирование и процесс анонимного наблюдения на этапе анализа данных. Ваша персональная информация будет предоставляться только уполномоченным исследователям.

Конфиденциальность

Исследователи будут обрабатывать информацию из анкет и образцов. Имя и адрес будет заменен кодом. Если результаты этого исследования будут опубликованы в отчетах, научный журналах, докладах или публикациях не будет упомянуто ваше имя и никакая информация, которая может идентифицировать вас. Вся информация будет рассматриваться конфиденциально в соответствии с законом о конфиденциальности. Мы предоставим Вам возможность уединения для сбора образцов волос, мочии проведения анкетирования.

Информация об исследовании

Вы имеете право обратиться за информацией о научно-исследовательском проекте и процедурах, описанных в данном документе. На запросы о предоставлении информации будет отвечать главный исследователь в меру ее осведомленности. Исследователи будут информировать вас о существенных изменениях в процедуре, происходящих рисках или преимуществах данного исследования. В конце исследования, Вы будете проинформированы о результатах исследования образцов, которые до сих пор сохранились и любого потенциального использования этих образцов в будущем.

Форма согласия на участие в проведении пилотного исследования по биомониторингу ртути для оценки пренатального воздействия, исследовательский проект осуществляется в соответствии с Указанием МЗ КР №480 от ------ при участии сотрудников Научно-производственного объединения «Профилактическая медицина» Министерства здравоохранения Кыргызской Республики и при техническом содействии Всемирной организации здравоохранения (ВОЗ).

Я прочитала информационный буклет для участия в программе биомониторинга человека и хочу принять участие в исследовании. Я понимаю, потенциальные риски и преимущества данного исследования и принять добровольное участие в этом исследовании. Я понимаю, что эта информация будет храниться строго конфиденциально и что, исследование было одобрено этическим комитетом.

Имя матери (печатными буквами):
_____

Подпись матери: _____
Имя и фамилия ребенка:

_____
Дата рождения ребенка (дд/мм/гггг) _____
Результаты:
Я не хочу получить персональные результаты.
Я желаю получить персональные результаты на мой домашний адрес:
_____
Я желаю, чтобы мои персональные результаты были отправлены к моему врачу.
Имя и фамилия врача:
_____
Адрес врача:
_____
Национальный Координатор

Проф Айнаш Шаршенова
Руководитель Центра медицины окружающей среды и экологии человека
Научный и производственный центр Превентивной медицины Министерства здравоохранения Республики Киргизстан
Email: spcpm@rambler.ru
Tel: +996-312-544573

Благодарим за Ваше участие!

Адамдын биомониторинги программасына катышуу үчүн маалымат буклети

Пренаталдык таасирди баалоо үчүн сымаптын биомониторинги боюнча пилоттук изилдөөлөрдү жүргүзүүгө катышуудагы макулдашуу формасы КР ССМ 11.08.2016 ж. №480 Көрсөтмөсүнө ылайык, Кыргыз Республикасынын Саламаттык сактоо Министрлигине караштуу «Алдын алуучу медицина» Илимий Өндүрүштүк Бирикмесинин кызматкерлеринин катышуусунда жана Дүйнөлүк саламаттык сактоо уюмунун (ДССУ) техникалык жардамындагы изилдөө долбоорунда иш жүзүнө ашырылат.

Урматтуу катышуучу!

Биз балдардын ден соолугун коргоого багытталган изилдөөгө катышууга Сизди чакырабыз

Максаты

Бул изилдөөлөр жаңы төрөлгөн балдарга өзгөчө көңүл бурат жана сиз жашаган райондун булганууусунун таасирин изилдөө үчүн жүргүзүлүүдө. Бул изилдөөлөрдүн негизги максаты химиялык заттардын жана сымап сыяктуу зыяндуу заттардын төрөткө чейинки таасири жөнүндөгү маалыматтарды көрсөтүү болуп саналат. Максат бир нече жылдан кийин катышуучулардын жаңы тобундагы кайрадан изилдөөдө адамдын ден соолугуна таасир берүүчү тобокелдик факторлордун таасирин, булгагычтардын таасирин баалоого багытталган.

Изилдөөгө катышуу үчүн болгон критерийлер

•Сиз 18 жаштасыз жана андан улуусуз;

•Сиз акыркы 3 жылдан бери жана кош бойлуулуктун акыркы 3 айындагы көпчүлүк убагында (башка жерде эки жумадан көп эмес) Айдаркен ш. жана анын тегерегиндеги – Айдаркендеги жалпы врачтардын практикалык борбору (төрөт үйү) тейлеген райондордо жашайсыз;

•Бала тирүү төрөлдү.

Процедуралар

Эгерде сиз жогоруда көрсөтүлгөн критерияларга ылайык келсеңиз, Сиз суроолорго жооп берүүгө катышууга жана кезектеги биоматериалдарды тапшырууга макулсузбу:

• Киндик канын, төрөт учурунда акушерка алат.

• Сиздин заарацыздын үлгүсү (энесинин заарасы)

• Сиздин чачыңыз (баштын аркасынан, териге жакын жеринен анча чоң эмес кесилген бир тутам чачыңыз)

• Сиздин тамактануунуз, иштеги жана үйдөгү жашоо абалыңыз, ден соолугуңуз жөнүндө камтыган маалымат суроолоруна жооптор.

• Сизден кээ бир маалыматтарды жана балаңыздын салмагы, боюнун өсүшү, оорунун официалдуу (тубаса) диагнозу жана абалы сыяктуу медициналык баяндамасын алууга сиздин макулдугуңуз.

Биз сымаптын чачтагы жалпы сандык көлөмүн ченеп көрүүнү каалайбыз, баштан 3см анча чоң эмес кесилген бир тутам чач алынат, себеби бул акыркы үч айдын ичинде ушул булгагычтардын таасирин көрсөтөт. Биз киндик кандагы жана заарадагы сымаптын деңгээлин ченеп көрүүнү каалайбыз. Кандын жана зааранын калып калган бөлүгү изилдөөчүлөр тарабынан эч болбогондо дагы 5 жылга сакталат жана келечекте кошумча изилдөөлөр үчүн колдонулушу мүмкүн. Баардык анализдер булгагычтарды өлчөө менен байланыштырылат. Каалагандай кошумча изилдөөлөр этникалык комитеттин макулдугун алгандан кийин гана жүргүзүлөт. Биз кийинчерээк кошумча текшерүүлөр үчүн сиз менен байланыша алабыз. Бул учурда сиз катышуу жана баш тартуу мүмкүнчүлүгүнө дайыма ээсиз.

Өз эрки менен катышуу/катышуудан баш тартуу

Эгерде сиз катышууну каалабасаңыз, бул изилдөөлөргө катышуудан баш тартсаңыз болот. Кандай гана учур болбосун катышуудан баш тартууңуз бул борбордон дарылануунузга таасир бербейт. Эгерде сиз бул макулдашууга кол койгон учурда да Сиз бул процессти каалаган

учурда токтото аласыз. Сиз болгону мындан ары катыша албай турганыз жөнүндө изилдөөчүлөргө маалымат берүүңүз керек. Мындан тышкары Сиздин суранычыңыз боюнча изилдөөгө тапшырган бардык үлгүлөр жок кылынышы мүмкүн. Кандай болсо дагы Сиздин дарылануунузга жана медициналык кызматынан жардам алууңузга таасирин тийгизбейт. Жүргүзүлгөн анализдин жыйынтыктары изилдөө үчүн калат.

Изилдөөнүн артыкчылыгы

Изилдөөнүн жыйынтыктары эне/бала үлгүсүн баяндоо мүнөзүндө анализденет. Сиздин анализдин жыйынтыктары мүмкүн болгон өлчөмдөргө негизделүү менен, ден соолуктун болжолдуу ченемдери менен салыштырылат. Сиздин үйдө жана өндүрүш ишкана шартында тобокелдикти кантип төмөндөтүү керек жөнүндөгү консультация алуу. Сиз жеке изилдөө жыйынтыктарын сизге же сиздин врачка жиберүүнү сурансаңыз да болот. Эгерде сиз изилдөө жыйынтыктарын сиздин врачка жиберүүнү кааласаңыз биз сизден анын аты-жөнүн жана дарегин жазуу формасында берүүңүздү суранабыз. Анализдин жыйынтыктарын алууну каалабай тургандыгыңызды да көрсөтсөңүз болот.

Чыгымдар

Бул изилдөөлөргө байланыштуу болгон чыгымдар катышуучулар үчүн бекер.

Мүмкүн болгон тобокелдиктер

Бул изилдөөлөргө катышууга байланыштуу болгон күтүлүүчү тобокелдиктер жок. Киндик канын алууга байланыштуу болгон ден соолук үчүн тобокелдиктер жок. Процедуралар кадимки абалга эч кандай таасир бербейт. Мүмкүн болгон ыңгайсыздыктар – чачты, заараны алууда жана суроо-жооп баракчасын толтурууга убакыттын кетиши. Бул маалыматтар (анкеталар жана медициналык карталар) жарыялоого болбой турган талаптуулукта сакталат. Биз маалыматтарды анализдөө этабында код коюу жана анонимдик байкоо процесстерин колдонобуз. Сиздин жеке маалыматыңыз бир гана тийиштүү изилдөөчүлөргө гана берилет.

Жарыялоого болбой турган талаптуулук

Изилдөөчүлөр анкетадагы жана үлгүлөрдөгү маалыматтарды иштеп чыгат. Аты жана дареги код менен алмашылат. Эгерде бул изилдөөлөрдүн жыйынтыгы отчеттордо, илимий журналдарда, докладдарда жарыяланса сиздин атыңыз жана сизди идентификациялоочу кандайдыр бир маалыматтар айтылбайт. Баардык маалыматтар жарыялоого болбой турган талаптуулук жөнүндөгү законуна ылайык каралат.

Изилдөөлөр жөнүндө маалымат

Сиз бул документтерде жазылган илимий-изилдөө долбоору жана процедуралар жөнүндөгү маалыматтар үчүн кайрылууга укуктуусуз. Маалымат берүү жөнүндөгү суроого башкы изилдөөчү өзүнүн кабардар болгондук чегине жараша жооп берет. Изилдөөчү процедурадагы көрүнүктүү өзгөрүүлөр, болуп өткөн тобокелдиктер же бул изилдөөнүн артыкчылыктары жөнүндө сизге маалымат берет. Изилдөөнүн аягында сиз азыркыга чейин сакталып турган, изилдөөгө алынган үлгүлөрдүн жыйынтыктары жөнүндө жана келечекте бул үлгүлөрдү каалагандай потенциалдуу колдонуу жөнүндө маалымат аласыз.

Сиздин катышууңузга ыраазычылык билдиребиз!
Форма информированного согласия

Ф.И.О. главного исследователя: Шаршенова Айнаш Акыновна

Другие контактные лица: Айдаркенский центр общеврачебной практики

Макулдашуу маалымат формасы

Башкы изилдөөчүнүн Ф.А.О.: Шаршенова Айнаш Акыновна

Башка байланышуучу адамдар: Айдаркендеги жалпы врачтардын практикалык борбору

Пренаталдык таасирди баалоо үчүн сымаптын биомониторинги боюнча пилоттук изилдөөлөрдү жүргүзүүгө катышуудагы макулдашуу формасы КР ССМ 11.08.2016 ж. №480 Көрсөтмөсүнө ылайык, Кыргыз Республикасынын Саламаттык сактоо Министрлигине караштуу «Алдын алуучу медицина» Илимий Өндүрүштүк Бирикмесинин кызматкерлеринин катышуусунда жана Дүйнөлүк саламаттык сактоо уюмунун (ДССУ) техникалык жардамындагы изилдөө долбоорунда иш жүзүнө ашырылат.

Мен адамдын биомониторинги программасына катышуу үчүн маалымат буклетин окуп чыктым жана изилдөөгө катышууну каалайм. Мен бул изилдөөлөрдүн потенциалдуу тобокелдигин, артыкчылыктарын жана өз эркимен бул изилдөөлөргө катышууну чечүүнү түшүнөмүн. Бул маалыматтар талаптуулук менен жашырундуулукта сакталарын түшүнөм жана этникалык комитет тарабынан жактырылган.

Эненин аты (басма тамгалары менен):

Эненин колу: _____

Баланын аты жана фамилиясы:

Баланын туулган күнү (тк/аа/жжжж) _____

Жыйынтыгы:

Жеке жыйынтыкты алгым келбейт.

Менин жеке жыйынтыктарымды үйүмдүн дарегинде алгым келет:

Менин жеке жыйынтыктарым менин врачыма жиберилүүсүн каалайм.

Врачтын аты жана фамилиясы:

Врачтын дареги:

Letter to a family doctors of women with high level of mercury in biological sample(s) (template)

Dear Mr/Ms -----

Scientific and Production Centre for Preventive Medicine (SPCPM) of the Ministry of Health of the Kyrgyz Republic 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

Prof Ainash Sharshenova, Head of the Centre for Environmental Medicine and Human Ecology
Phone: +996-312-544573
E-mail: spcpm@rambler.ru

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 the Scientific and Production Centre for Preventive Medicine of the Ministry of Health of the Kyrgyz Republic 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

Prof Ainash Sharshenova, Head of the Centre for Environmental Medicine and Human Ecology
Phone: +996-312-544573
E-mail: spcpm@rambler.ru

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
Artisanal and small-scale gold mining	O	O	O	O	O	O
Production of goods that contain mercury, such as traditional remedies, cosmetics, etc.	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
Artisanal and small-scale gold mining	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
Mining operation	O	O	O
Artisanal small-scale mining	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	O	O	O	O

(including in herb teas)				

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

Types of fish	At least once per day	At least once per week	At least once per month	Less than 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

Основная анкета для участников / **Катышуучу үчүн негизги анкета**

Ф.И.О. участника / Катышуучунун Ф.А.О.	
Номер медицинской записи Медициналык жазууларынын номери	
Идентификационный номер участника Катышуучунун идентификациялык номери	
Дата интервьюирования Суроо-жооптун алынган күнү	*Дата (день/месяц):* Күнү(күнү/айы): «_____» _____ 2016
Дата рождения ребенка Баланын төрөлгөн күнү	*Дата (день/месяц):* Күнү(күнү/айы): «_____» _____ 2016

А. *Информация о персоне* / Катышуучу жөнүндө маалымат

А.1. *Мать ребенка (участник опроса) ФИО /*Баланын энеси (суроо-жооптун катышуучусу) ФАО
_____

А.1.1. *Какая Ваша национальность?* / Сиздин улутуңуз? / _____
А.1.2. *Были ли у Вас дети ранее?* / Мындан мурун да балдарыңыз болду беле?

- *Нет* / Жок
- *Да* / Ооба *Сколько детей?/* Канча балаңыз бар?_____

А.1.3. *Какой у Вас уровень образования? Пожалуйста, выберите **один** ответ* (ˇ)
Сиздин билим деңгээлиңиз кандай? **Бир** жоопту тандаңыз.

- *Среднее (окончил школу)/* Орто билимдүү (мектепти бүткөн)
- *Среднее специальное образование (Колледж, технич. колледж или незаконченное высшее образование) /*Орто атайын билимдүү (колледж, техник. колледж же толук эмес жогорку билимдүү) /
- *Высшее образование* / Жогорку билимдүү

А.2. *Отец ребенка* / Баланын атасы
А.2.1. *Какой уровень образования у отца? Выберите **один** ответ /*
Атасынын билим деңгээли кандай? Бир жоопту тандаңыз

- *Среднее (окончил школу)* / Орто билимдүү (мектепти бүткөн)
- *Среднее специальное образование (Колледж, технич. колледж или незаконченное высшее образование) /* Орто атайын билимдүү (колледж, техник. колледж же толук эмес жогорку билимдүү) /
- *Высшее образование /* Жогорку билимдүү

А.3. *Экономический статус Вашей семьи (домохозяйства)/* Сиздин үйбүлөөңүздүн экономикалык статусу (үй чарбасы)
А.3.1. *Как легко Вам справиться с финансовыми средствами? Выберите **один** ответ /*Финансы каражаттарын кандай чечесиз? **Бир** жоопту тандаңыз.

- *Трудно, не всегда можем позволить себе необходимое* / Кыйын, өзүбүзкө керектүүнү дайыма эле ала албайбыз
- *Доход ограничен, но можем позволить себе необходимое* / Киреше (доход) чектелүү, бирок өзүбүзгө керектүүнү ала алабыз
- *Жить комфортно, но нет избытка располагаемого дохода* /Жайлуу жашоо, бирок ашык киреше жок

- *Устойчивое финансовое положение, в состоянии позволить себе продукты высокого качества и услуги* / Туруктуу финансылык абал, жогорку сапаттагы азык-түлүк жана кызматын алуу мүмкүнчүлүк бар

B. *Потенциальное воздействие ртути* / Сымаптын потенциалдуу таасири
B.1. *Профессиональное воздействие* /Профессионалдык (кесиптик) таасир

B.1.1. *Прежде чем выйти в декретный отпуск, Вам был оплачен неполный или полный рабочий день (наемный работник, работодатель, частный предприниматель)?*
Декреттик отпускага кетерден мурун Сизге толук же толук эмес жумушчу күнү төлөнүп берилдиби (жалданган жумушчу, жумуш берген адам, жеке ишкер адам)?

- *Нет* / Жок
- *Да* / Ооба

Если нет, пожалуйста, переходите на вопрос секции Б.1.5
Эгерде жок десеңиз, кийинки Б.1.5. суроолоруна өтүңүз

B.1.2. *Вы когда-нибудь работали в промышленности или/секторах. Пожалуйста, отметьте все что подходит. /* Сиз бир кездерде өндүрүш ишканаларда/секторлордо иштедиңиз беле. Тийиштүүсүн белгилеңиз (кайсынысы туура келсе ошонун баарын белгилеңиз).

Тип промышленности Индустриянын түрү	*Никогда* Эчкачан	*Меньше 6 месяцев* 6 айдан азыраак	*Между 6 месяцами - 1 год* 6 айдын ортосунда - 1 жыл	*1–5 лет* 1–5 жыл	*Больше 5 лет* 5 жылдан көп	*Совсем не работала в период этой беременности* Ушул кошбойлуулук кезде такыр иштеген жокмун
Химическая/нефтяная Химиялык/нефти иш						
М*еталлоплавильные* Металл эритүүчү						
Металлообработка Металл иштетүүчү						
Хлорно - щелочной завод Хлордук-щелочтук заводу						
Химическая лаборатория Химиялык лаборатория						
Стоматология						
*Обращение с отходами (общее) /*Таштандылар менен иштөө (жалпы)						
Управление электронными отходами /Электрондук таштандыларды башкаруу						
Кустарная и мелкомасштабная добыча золота /Алтынды кустардык (жөнөкөй кол менен жасалган) жол менен жана кичине өлчөмдө өндүрүп алуу						

Производство товаров, содержащих ртуть, такие как традиционные средства косметика и т.д./ Сымап кошулган традициялык (адат болгон) каражаттарды, косметикалык жб.у.с. товарларды өндүрүү						

B.1.2.1. *Пожалуйста, укажите название и адрес промышленного предприятия где вы работали до или во время этой беременности* / Ушул кош бойлуулук учурунда жана ага чейин сиз кайда иштегенсиз, мүмкүн болсо ошол өндүрүш ишканасынын аталышын жана дарегин айтсаңыз.
_____
_____

B.1.3. *В своей работе, Вы имели контакт со следующими веществами? Пожалуйста, отметьте все, что относится* / Сиздин иштеген ишиңиз төмөнкү заттар менен байланыштуу болду беле? Кайсы заттар кирсе ошону белгилесеңиз.

Вещество / Заттар	*Не знаю* Билбейм	*Никогда* Эчкачан	*Меньше 6 месяцев* 6 айдан азыраак	*Между 6 месяцами и 1 год* 6 айдын ортосунда - 1 жыл	*1–5 лет* 1–5 жыл	*Больше 5 лет* 5 жылдан көп	*Каждый раз во время этой беременности* Ар бир жолу ушул кошбойлуулук кезде
Металлическая пыль / Металл чаңы							
Ртуть /Сымап							
Амальгама /Амальгама							
Пестициды /Пестициддер							
Испарения от сжигания угля /Көмүр жакканда бөлүнгөн буулануулар							
Испарения от сжигания электронных отходов/ Электрондук таштандыларды жакканда бөлүнгөн буулануулар							

B.1.4. *Если Вы работали в любом из ранее упомянутых отраслей или имели воздействие, как указано в предыдущих вопросах (Вы ответили «**Да**» на любой вопрос в пункте B.1.2 – B.1.3), пожалуйста, представьте дополнительную информацию ниже. Отметить все, что подходит.* Мурунку суроолордо көрсөтүлгөндөй эгерде сиз жогоруда айтылган ишканалардын биринде иштеген болсоңуз же таасир кылган болсо (сиз B.1.2 – B.1.3 баардык суроого «ооба» деп жооп берсеңиз) сураныч, кошумча төмөнкү маалыматтарды белгилей кетсеңиз. Кайсынысы туура келсе ошонун баарын белгилеңиз.

	Всегда Дайыма	*Иногда* Кээде	*Нет* Жок
Вы меняли рабочую одежду перед тем как пойти домой? Сиз үйгө кетээрдин алдында жумушка кийген киймиңизди алмаштырасызбы?			
Вы меняли рабочую обувь перед тем как пойти домой? Сиз үйгө кетээрдин алдында жумушка кийген бут киймиңизди алмаштырасызбы?			
Вы принимали душ после рабочей смены, прежде чем идти домой? Сиз жумуштан кийин, үйгө кетээрдин алдында душка түшөсүзбү?			
Когда-нибудь приносили свою рабочую одежду или другие загрязненные предметы домой? Бир учурларда өзүңүздүн жумушка кийген кийимдериңизди же башка булганган буюмдарыңызды үйгө алып келдиңиз беле?			
Если вы ответили «ДА» на предыдущий вопрос то, стирали ли вы рабочую одежду отдельно от любой другой одежды? Эгерде сиз мурунку суроого «Ооба» деп жооп берсеңиз анда жумушчу киймиңизди башка кийимдериңизге кошпой, өзүнчө бөлүп жуудуңузбу?			

B.1.5. *Во время беременности ваш муж / партнер или кто-либо живущий в вашем домохозяйстве еще работал в следующих отраслях / секторах? Пожалуйста, отметьте все подходящие варианты.* Сиз кошбойлуу кезде сиздин күйөөңүз/партнеруңуз же сиздин үйүңүздө жашаган кимдир бирөө төмөнкү тармактарда /секторлордо иштеди беле? Туура келген баардык варианттарды белгилеңиз.

Тип отрасли Тармактардын түрү	*Да* /Ооба	*Нет* /Жок	*Не знаю* /Билбейм
Химическая /нефтяная Химиялык /нефти иш			
Металлоплавильные / Металл эритүүчү			
Металлообработка/ Металл иштетүүчү			
Хлорно-щелочной завод/ Хлордук–щелочтук заводу			
Управление с отходами и электронными отходами/ Таштандыларды жана электрондук таштандыларды башкаруу			
Химическая лаборатория /Химиялык лаборатория			
Стоматология			
Кустарная и мелкомасштабная добыча золота /Алтынды кустардык (жөнөкөй кол менен жасалган) жол менен жана кичине өлчөмдө өндүрүп алуу			

B.1.5.1. *Пожалуйста, укажите имя и адрес промышленного предприятия, на котором ваш муж / партнер работал до / во время этой беременности. /*
Ушул кош бойлуулук учурунда же буга чейин сиздин күйөөңүз/партнеруңуз иштеген өндүрүш ишканасынын аталышын жана дарегин айтсаңыз /

_____
_____

B.1.6. *Во время вашей беременности, Ваш муж/партнер имел регулярные профессиональные контакты или хобби, связанное со следующими веществами?/*
Сиз кошбойлуу кезде сиздин күйөөңүз/партнеруңуз профессионалдык же өзү кызыккан иштери (хобби) боюнча төмөнкү заттар менен байланышы болгонбу?

Вещество /Заттар	*Да/* Ооба	*Нет/* Жок	*Не знаю* /Билбейм
Металлическая пыль /Металл чаңы			
Ртуть /Сымап			
Амальгама /Амальгама			
Пестициды /Пестициддер			
Испарения от сжигания угля Көмүр жакканда бөлүнгөн буулануулар			
Испарения от сжигания электронных отходов/ Электрондук таштандыларды жакканда бөлүнгөн буулануулар			

B.1.7. *Если ваш муж /партнер или любой другой член вашей семьи работал на промышленном предприятии (вы ответили утвердительно на любой вопрос в пунктах B1.5- B 1.6) просьба представить дополнительную информацию в приведенной ниже таблице. Отметить все подходящие варианты /*
Эгерде сиздин күйөөңүз/партнеруңуз же үй-бүлөөңүздөн кимдир бирөөсү өндүрүш ишканасында иштеген болсо (сиз B1.5 - B1.6 баардык суроого «ооба» деп жооп берсеңиз) сураныч, кошумча төмөнкү маалыматтарды белгилей кетсеңиз. Кайсынысы туура келсе ошонун баарын белгилеңиз.

	Всегда Дайыма	*Иногда* Кээде	*Нет* Жок
Он менял рабочую одежду перед тем как пойти домой? Ал үйгө кетээрдин алдында жумушка кийген киймин алмаштырабы?			
Он менял рабочую обувь перед тем как пойти домой? Ал үйгө кетээрдин алдында жумушка кийген бут киймин алмаштырабы?			
Он принимал душ после рабочей смены, прежде чем идти домой? Ал жумуштан кийин, үйгө кетээрдин алдында душка түштөбү?			
Он когда-нибудь приносил свою рабочую одежду или другие загрязненные предметы домой? Ал бир учурларда өзүнүн жумушка кийген кийимдерин же башка булганган буюмдарын үйгө алып келди беле?			
Если вы ответили «ДА» на предыдущий вопрос то, стирали ли вы его рабочую одежду отдельно от любой другой одежды? Эгерде сиз мурунку суроого «Ооба» деп жооп берсеңиз анда анын жумушчу киймидерин башка кийимдерге кошпой, өзүнчө бөлүп жуудуңузбу?			

B.2. *Место жительство* / Жашаган жериңиз
B.2.1. *Где находится ваше место жительство? /*Жашаган жериңиз каякта?

- *В городе* / Шаарда
- *В сельской местности* / Айылда

B.2.1.1. *В каком районе или жилом районе вы живете? /*Кайсы райондо же кайсы турак жай районунда жашайсыз? /

- *Пожалуйста, укажите название города / села* Шаардын/айылдын атын жазыңыз:_____
  _____
- *Пожалуйста, предоставьте название местности*:/ Жергиликтүү жашаган жериңиздин аталышы:
  _____

B.2.2. *Есть ли какие-либо из следующих действий в непосредственной близости от вашего дома (до 2 км)? Пожалуйста, отметьте все подходящие варианты*.

Сиздин үйүңүзгө жакын (2км чейинки) аралыкта кандайдыр бир төмөнкүдөй иш аракеттер барбы? Баардык ылайыктуу варианттарын белгилеңиз.

	Да Ооба	*Нет* Жок	*Не знаю* Билбейм
Бизнес по металлообработке /Металл иштетүү бизнеси			
Завод по сжиганию отходов /Таштандыларды өрттөө боюнча заводу			
Предприятие по производству цемента / Цементти өндүрүү ишканасы/			
Хлор-щелочной завод / Хлордук – щелочтук заводу			
Муниципальная свалка /Муниципалдык таштандылар			
Полигон для промышленных побочных продуктов / отходов Өдүрүштүн кошумча продуктылары/таштандылары үчүн аянты			
Крематорий			
Добыча полезных ископаемых /Пайдалуу кендерди өндүрүү			
Кустарная мелкомасштабная / Кустардык (жөнөкөй колдо жасалган) жол менен жана кичине өлчөмдө өндүрүп алуу			
Теплоэлектростанция /Жылуулукэлектростанция			
Демонтаж электронных отходов Электрондук таштандыларды демонтаждоо			

B.2.3. *Когда ваш дом был построен?/* Сиздин үйүңүз качан курулган?

- *В 2000 или недавно* / 2000 ж. же жакында курулган
- *Между 1980 и 1999 годами* /1980 жана 1999 жылдардын ортосунда
- *В период с 1950 по 1979 год* / 1950 жылдан 1979 жыл мезгилдеринде
- *До 1950 года* / 1950 жылга чейин
- *Не знаю* / Билбейм

B.2.4. *Какое топливо или источник энергии, вы в основном используете для приготовления пищи и для отопления в вашего дома? Пожалуйста, отметьте только один для каждого варианта ответов.*

Тамак даярдоодо жана үйдү жылытууда негизинен сиз отундун кайсы түрүн же кайсы энергия булагын колдоносуз? Ар бир вариантка бирөөнү белгилеңиз.

Источник топлива Отун булактары	*Приготовление еды* Тамак даярдоо	*Отопление* Үйдү жылытуу
Природный газ /Табигый газ		
Уголь или древесный уголь / Көмүр же жыгач отун		
Электроэнергия /Электроэнергиясы		

Дерево или биомасса /Жыгач же биомассасы		
Горячая вода и система центрального отопления (централизованное теплоснабжение или центральное отопление для жилого дома)/ Ысык суу же жылытуу борборлоштурулган жылытуудан (борборлоштурулган жылуулук менен камсыз кылуу же борборлоштурулган жылытуу негизги турак жайы үчүн)		
Керосин / Керосин		

B.2.5. *Какой Ваш главный источник воды для питья и приготовления пищи? Пожалуйста, выберите только один для каждого*
Сиздин ичүү жана тамак даярдоо үчүн болгон негизги суу булактарыңыз? Ар бирине бирөөнү белгилеңиз.

Источник воды Суу булактары	*Питьевая вода* Ичүүгө жарактуу суу	*Приготовление пищи* Тамак даярдоо
Общественное водоснабжение Коомдук суу менен камсыз кылуу системасы		
Частный колодец или родник Жеке кудук же булак		
Бутилированная вода Бутулкадагы суу		
Поверхностные воды (река, озеро и т.д.)/ Үстүнкү ачык суулар (дарыя, көл жб.)		

B.2.6. *Термометр или любое другое устройство, содержащее жидкую ртуть (как сфигмоманометр, аппарат для измерения давления) был ли сломан в вашем доме в течение последних двух лет?/* Акыркы эки жылдын ичинде сиздин үйдө сымап термометри же башка сымап кошундусу менен болгон (сфигмоманометр сыяктуу) башка бузулган жабдуулар же приборлор барбы?

- Нет / Жок
- Да / Ооба

Если «Да» то, как давно это было? Просьба уточнить ниже / Эгерде «Ооба» болсо канча убактан бери? Сураныч, төмөнкүлөрдү тактаңыз:

- *Менее чем 30 дней назад* / Мындан 30 күндөй мурунураак
- *От 30 до 90 дней (три месяца) назад* / Мындан 30дан 90 күнгө чейин мурунураак (үч ай)
- *От 91дней до 6 месяцев назад* / Мындан 91ден 6 айга чейин мурунураак
- *Более 6 месяцев назад, но в течение последних 2-х лет /* Мындан 6 айдан ашыгыраак мурун, акыркы эки жылдын ичинде
- *Не помню, не знаю* / Эсимде жок, мен билбейм.

B.2.7. *Была ли нарушена (сломана) энергосберегающая люминесцентная лампы в вашем доме в последние 3 месяца (90 дней)? /* Сиздин үйдө акыркы 3 айда (90 күндө) энергияны үнөмдөөчү люминесценттик лампанын иштөөсүнүн бузулуусу болду беле?

- *Нет* /Жок
- *Да* / Ооба
  Если «Да» то, сколько дней назад? Эгерде «Ооба» болсо канча күн мурун? _____ дней/күн

- *Не помню, не знаю* / Эсимде жок /мен билбейм.

B.2.8. К*то-нибудь в вашем доме работал регулярно с металлами в течение последних трех месяцев? (например: пайка металлов, как часть хобби своей деятельности)*
Акыркы үч айдын ичинде сиздин үйбүлөөңүздөн кимдир бирөө дайыма металл менен иштеди беле? (мисалы: металлдарды эритүү, өзүнүн жеке кызыккан иши катары)

- *Да* / Ооба
- *Нет* / Жок
- *Не знаю* / Билбейм

B.3. ***Личный уход и образ жизни /*** **Жеке өзүн кароо жана жашоо образы**

B.3.1. *Есть ли у вас зубные пломбы из амальгамы (темного цвета) пломбы?*
Сизде амальгам пломбасынан (кара түстөгү) коюулган тиш пломбасы барбы?

- *Нет* / Жок
- Да / Ооба
  Если «Да», укажите сколько амальгамы зубных пломб у вас сейчас есть?/
  Эгерде «Ооба» болсо азыр сизде канча амальгам тиш пломбасы бар? _____.
- *Не знаю /* Билбейм.

B.3.2. *Часто ли вы используете жевательную резинку или обычно жуете (листья / табак и т.д.)?*
Сиз сагызды тез-тез колдоносузбу же адатта чайнайсызбы (тамеки жалбырагын жб)?

- *Да* / Ооба
- *Нет* / Жок

B.3.3. *Вы когда-нибудь курили сигареты и другие табачные изделия в вашей жизни? Отметьте все подходящие варианты?*
Сиз кайсы бир учурларда тамеки же башка тамеки каражаттарын тарттыңыз беле? Ылайыктуу баардык варианттарын белгилеңиз?

- *Я никогда не курила. Переходите к вопросу B.3.5.*
  Мен эч качан тамеки тарткан эмесмин. B.3.5. суроосуна өтүңүз.
- *Я употребляла табачные изделия, но бросила курить до этой беременности*
  Тамеки каражаттарын колдончумун, бирок ушул кош бойлуулукка чейин таштагам
- *Я употребляла табачные изделия в течении этой беременности*
  Кош бойлуу учурунда да тамеки тартам

B.3.4. *Как часто вы курили, в среднем **до** и **во время беременности**?*
Сиз кош бойлуу кезиңизде жана ага чейин орточо алганда канчалык тез-тез тамеки чеккенсиз?

Периодичность / Мезгилдүүлүгү	*До* Кош бойлуу боло элек кезге чейин	*Во время* Кош бойлуулук кезиңизде
Не курила /Тамеки тарткан эмесмин		
Реже одного раза в неделю / Жумасына бир жолудан аз эмес		
По крайней мере, один раз в неделю, но не каждый день / Жок дегенде жумасына бир жолу, бирок күн сайын эмес		
Ежедневно / Күн сайын		

B.3.5. *Как часто вы употребляли алкоголь содержащие напитки во время этой беременности?*
Сиз алкоголь кошулган ичимдиктерди канчалык тез-тез колдонгонсуз?

- *Никогда* / Эч качан
- *По крайней мере 1 раз в месяц* / Жок дегенде айына бир жолу
- *По крайней мере 1 раз в неделю* / Жок дегенде жумасына бир жолу

B.3.6. *Вы используете осветляющие кожу продукты (крема, мази) регулярно?*
Сиз терини агартуучу каражаттарын (крем, мазь жб.) дайыма колдоносузбу?

- *Нет* / Жок
- *Да* / Ооба

B.3.7. *Регулярно ли вы использовали осветляющие кожу продукты (крема, мази)* ***во время*** *этой беременности?*
Сиз терини агартуучу каражаттарын (крем, мазь жб.) ушул кошбойлуулук учурунда дайыма колдондуңузбу?

- *Нет* / Жок
- *Да* / Ооба

*Если «**Да**», то как часто? Пожалуйста, укажите ниже*
Эгерде «**Ооба**» десеңиз канчалык тез-тез колдондуңуз? Төмөндө көрсөтсөңүз:

- *По крайней мере, один раз в день* / Жок дегенде күнүнө бир жолу
- *По крайней мере, один раз в неделю* / Жок дегенде жумасына бир жолу
- *По крайней мере, один раз в месяц* / Жок дегенде айына бир жолу
- *Один раз в 2-3 месяца* / 2-3 айда бир жолу

B.3.8. *Используете ли вы регулярно традиционные средства / лекарства, которые содержат ртуть (содержащие киноварь)?*
Традициялык каражаттарды дайыма колдоносузбу / курамына сымап кошулган дарыларды (киноварь кошулган)?

- *Нет* / Жок
- *Да* / Ооба

B.3.9. *Используете ли вы регулярно традиционные средства / лекарства, которые содержат ртуть (содержащиекиноварь) во время этой беременности?*
Традициялык каражаттарды ушул кош бойлуулук кезиңизде дайыма колдондуңузбу/ курамына сымап кошулган дарыларды (киноварь кошулган)?

- *Нет* / Жок
- *Да* / Ооба

*Если «**Да**», то как часто? Пожалуйста, укажите ниже*
Эгерде «**Ооба**» десеңиз канчалык тез-тез колдонгонсуз? Төмөндө көрсөтсөңүз:

- *По крайней мере, один раз в день* / Жок дегенде күнүнө бир жолу
- *По крайней мере, один раз в неделю* / Жок дегенде жумасына бир жолу
- *По крайней мере, один раз в месяц* / Жок дегенде айына бир жолу
- *Один раз в 2-3 месяца* / 2-3 айда бир жолу

B.4. *Продукты питания и напитки потребления/* Керектелүүчү тамак азыктары жана суусундуктар
B.4.1. *Как часто вы едите следующие продукты? Пожалуйста, проверьте по каждой категории./* Төмөнкү тамак азыктарын канчалык тез-тез жедиңиз? Ар бирин текшерип көрүңүз.

Тип продукта / Тамак азыктарынын түрү	*1раз в день* Күнүнө 1 жолу	*1 раз в неделю* Жумасына 1 жолу	*1 раз в месяц* Айына 1 жолу	*Один раз в 2-3 месяца* 2-3 айда бир жолу
A. *Любой вид рыбы / моллюсков / морских водорослей (например, тунец в салате или бутерброде, пицца, креветки коктейль и т.д.)/* Балыктын баардык түрү / деңиз балырлары (салаттагы тунецти же бутербродду кошуу менен, пицца, креветка коктейли жб.)				
a.1. *Рыба купленная в магазине /* Дүкөндөн сатып алынган балыктар				
a.2. *Моллюски из магазина /* Дүкөндөн сатып алынган моллюскалар				
a.3. *Морские водоросли* /Деңиз балырлары				
a.4. *Местная пойманная рыба (все виды) /*Жергиликтүү кармалган балыктар (баардык түрү)				
B. *Зерновые и крупяные* /Дан жана акталган дан азыктары				
в.1 *Рис и рис содержащие продукты из магазина* /Дүкөндөн алынган күрүч жана күрүч кошулган азыктары				
в.2. *Отруби* /Улпак, кебек				
в.3. *Местный выращенный рис /* Жергиликтүү өстүрүлгөн күрүч				
C. *Мясо и мясные продукты (все виды)* Эт жана эт азыктары (баардык түрү) /				
c.1. *Мясо* / Эт				
c.2. *Субпродукты (печень, почки и т.д.) /*Малдын ич эттери (боор, бөйрөк жб.)				
c.3. *Курица* /Тоок				
D. *Овощи и грибы /* Жашылчалар жана козу карындар				
d.1. *Лесные грибы* /Токой козу карындары				
d.2. *Овощи из магазина* /Магазинден алынган жашылчалар				
d.3. *Бобовые из магазина* /Магазинден алынган буурчак түркүмүндөгү азыктар				
d.4. *Корнеплоды из магазина/* Магазинден алынган тамыр жемиштери /				
d.5. *Выращенные овощи (самостоятельно или купленные на местном рынке)/* Өстүрүлгөн жашылчалар (өзүңүз же жергиликтүү базардан сатып алынган) /				
g. *Травы, местные (чай) /*Чөптөр (чай)				

B.4.2. *Как часто вы ели следующие виды рыбы в течение последних 3-х месяцев?*
Сиз акыркы үч айдын ичинде төмөнкү балыктардын түрүн канчалык тез-тез жедиңиз?

Тип рыбы Балыктардын түрү	*1раз в день* Күнүнө 1 жолу	*1 раз в неделю* Жумасына 1 жолу	*1 раз в месяц* Айына 1 жолу	*Один раз в 2-3 месяца* 2-3 айда бир жолу	*Никогда* Эч качан
a. *Рыба-меч, тунец*					
b. *Жирная рыба (сардины, сельдь, скумбрия лосось ит.д.)* Майлуу балыктар (сардины, сельдь, скумбрия лосось жб.)					
c. *Сиг, треска, пикша, камбала*					
d. *Пресноводная рыба (форель, окунь и другие) из магазина/* Тузсуз суудагы балыктар (форель, окунь), дүкөндөн сатып алынган					
e. *Пресноводная местная рыба* Тузсуз суудагы жергиликтүү балыктар.					
f. *Моллюски* /Моллюскалар					
g. *Водоросли* /Балырлар					
h. *Консервированная рыба* /Консервацияланган балыктар					

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 given the sensitivity of mercury issue for the population in Aidarcan area. Mercury mining located in the area is city-forming enterprise.

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

A lot of studies are conducted in this area from the late 90's. information about mercury contamination, social-economic status of the population and economic development of the area are available and will be used when planning actions for the community involvement.

2. Develop a communication package about the survey

Information about the project will be adapted to the target audience using available information; development of a different set of information for the local authorities and community members will be considered. Information on the survey should be easily understandable and based on scientific knowledge. The information package will explain: 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. The information sheet prepared for the survey participants and WHO information materials will be used for this purpose.

3. Ensure support from influential people

Information about the planned survey will be first communicated to local health authorities, people with authority (formal and informal) within the community (for example, head of municipalities). 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 in several ways, including through:

- developing and disseminating an information leaflet about the planned survey; this allows outreach to a wider audience but does not allow immediate answering of questions and providing clarifications;
- reaching out directly to potential survey participants (pregnant women);
- agreeing joint antenatal visits with gynaecologists and obstetricians serving the community;

5. Keep contact open during the survey implementation

Communication channels will 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 will 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 being implemented at the community level. This requires active interaction and full engagement of the local authorities in the development and implementation those measures.

Annex 5 Budget

N	Budget line/expenses	Cost per unit	Cost for budget line	The project budget	Country contribution
1	**Staff costs**				
1.1	National coordinator	50 USD per day x 50 days	2500.00	2500.00	-
1.2	Field work (staff)	laboratory analysts 25 USD per day x 50 days; Hospital staff 25 USD per women x 100 women	3770.00	3770.00	-
	Sub-total for staff costs		***6270.00***	***6270.00***	**-**
2	Communication internet/fax/ph		400.00	0	400.00
3	Printing the WHO materials		50.00	50.00	-
4	***Organization of the training for hospital staff/volunteers***				
4.1	National coordinator	50 USD per day x 6 days	500.00	500.00	-
4.2	Communication internet/fax/ph		200.00	0	200.00
4.3	Translation (questionnaires, SOPs and other relevant WHO documents)	From English into Russian – 10 USD per page x 200 pages From Russian into Kyrgyz – 10 USD per page x 20 pages From Kyrgyz and Russian into English 10 USD per page x 40 pages	2,600.00	2,400.00	200.00
4.4	Printing the questionnaires and other relevant WHO documents		50.00	50.00	
4.5	Rent for a meeting room	cost per hour/number of hours (125 USD per hour/ 8 hours)	1,000.00	-	1,000.00
4.6	Meal (coffee breaks, lunch)	cost number of participants x 20persons x 12 USD	240.00	240.00	-
4.7	Travel of the meeting participants	20 persons x 81.6 USD	1,632.00	1,632.00	-
	Total for the WS		***6,632.00***	***4,872.00***	***1,800.00***
5	Travel	1 person travel from research team for training	80.00	80.00	-
6	Translation from and to English	From English into Russian – 10 USD per pagex200 pages From Russian into Kyrgyz – 10 USD per page x 20 pages From Kyrgyz and Russian into English 10 USD per page x 40 pages	2600.00	2400.00	200.00
7	Travel	Bishkek-Osh-Bishkek 230 USD x 3	3370.00	3370.00	-

		times Osh-Bishkek 115 USD x 1 time Rent a car for travel around the region – 965 USD Accommodation costs: 40 USD per day x 5 days x 2 persons x 4 times			
8	Consumables (for hair sampling)		300.00	300.00	-
9	Urine, creatinine test	cost per a sample (5.20) x number of samples (250)	1300.00	1300.00	
10	Other costs (custom tax, etc.)		218.00	218.00	-
		TOTAL	**20,810.00**	**18,810.00**	**2,000.00**

Annex 6 Material Transfer Agreement

This Material Transfer Agreement ("Agreement"), effective as of the 12th July, 2017 (the "Effective Date"), is by and between Dr. Ainash Sharshenova and Ms. Kulbaram Arzygulova (Scientific and Production Centre for Preventive Medicine, SPCPM) located in Bishkek, Kyrgyz Republic ("Provider") and Ms. Kateřina Šebková, Ph.D., M.A., Director of the National Centre for Toxic Compounds and Stockholm Convention Regional Centre, Masaryk University, located in Brno, Czech Republic ("Recipient").

Provider and Recipient acknowledge that this Material Transfer Agreement is made pursuant to an epidemiological study sponsored by WHO, under the Human Biomonitoring Survey for Assessment of Prenatal Exposure to Mercury which will be governed by separate agreements ("Head Agreement"). Provider is willing to provide Recipient with certain research materials for analysis by Recipient, subject to the terms and conditions set forth in this Agreement. Each of Provider and Recipient, including their respective employers, Colleague scientists (as the case may be), may be referred to in this Agreement as a "Party" or collectively as the "Parties."

1. This Agreement applies to the transfer of urine, blood and hair samples from research participants.

2. No right or license is granted with respect to the Materials except as expressly set forth in this Agreement. The transfer of the Materials constitutes a limited, revocable, non-exclusive, non-transferable, non-sublicensable license to internally use the Materials and any accompanying information solely for Recipient's research purposes of mercury determinations. Materials shall not be used in humans nor to generate, modify, or supplement other materials for use in humans, including for the purpose of diagnostic testing.

3. The Materials are licensed, not sold, to Recipient for use only under the terms of this Agreement. Recipient shall use reasonable efforts to provide a secure location for the Materials and accompanying information on its premises, and shall make reasonable efforts to maintain the Materials in specified storage conditions.

4. The Materials will be used as described herein, only by Colleague Scientists who are under the Recipient's control and who shall be bound by the terms and conditions of this Agreement. Recipient shall not transfer, sublicense, lease, or assign its rights to access and use of the Materials to any non-Recipient personnel without prior written consent from Provider.

5. Any use of the Materials not expressly permitted in this Agreement is prohibited. Recipient shall not, and shall not allow or authorize a third party to reverse engineer the Materials.

6. Recipient shall use the Materials in compliance with all laws, governmental regulations and guidelines.

7. The Materials are being provided to Recipient without cost.

8. Recipient and Colleague Scientists shall maintain confidential the Materials and any information marked "confidential" (being referred to herein as "Confidential Information"). The inadvertent failure by provider to designate, label or mark disclosed information as "Confidential

Information'' shall not prevent the information from constituting Confidential Information if a reasonable person would believe the Information to be confidential information of the provider given the nature of the information and the circumstances of disclosure. The Recipient agrees not to transfer or in any way disclose the Materials and /or the Confidential information to a third party without prior consent of the Provider. However the foregoing obligations of confidentiality shall not apply to information that:

- was legally known to the Recipient prior to the date of disclosure to the Recipient by the Provider.
- is or becomes publicly available prior through no fault of the Recipient;
- has been disclosed to the Recipient by a third party on a non-confidential basis and without breaching any contractual, confidential or fiduciary obligation or any law; and
- is independently developed by the Recipient as demonstrated by documentary evidence.

9. The Recipient may disclose Confidential Information if, and solely to the extent, such is required to be disclosed by the Recipient to comply with applicable laws or governmental regulations including pursuant to a court order or a valid administrative subpoena, provided that Recipient (a) notifies the Provider within fourteen (14) business days before the execution of such order and (b) cooperates reasonably with Provider's efforts to contest or limit the scope of such order.

10. Provider and Recipient agree that any publication of the results of Research conducted using the Materials are subject to the confidentiality obligations of Section 8 and Head Agreement.

11. All rights, title, and interest to and in the data and results arising from or related to the Research conducted by Recipient are the exclusive property of the Principal Investigators and Co-investigators and its ownership and intellectual property shall be governed by Head Agreement. Recipient shall deliver a copy of any data and results to Provider and Provider shall be allowed to keep copies of any data and results, and shall be allowed to utilize the data and results for its internal use.

12. THE MATERIALS ARE BEING PROVIDED TO AND ACCEPTED BY RECIPIENT WITHOUT ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED.

13. In no event shall Provider or his employers be liable for any use of the Materials by Recipient and / or his colleague Scientists in his institution, or for any claim, liability, cost, expense, damage, deficiency, loss or obligation, of any kind or nature (including, without limitation, reasonable attorneys' fees and other costs and expenses of defense), that may arise from or in connection with this Agreement or the use, handling, storage, or disposition of the Materials. Recipient agrees to indemnify, defend with counsel acceptable to Provide, and hold harmless Provider and Provider's employers from any and all Claims.

14. Any notices required to be given hereunder shall be addressed as follows:

If to Provider: Dr. Ainash Sharshenova and Ms. Kulbaram Arzygulova, Scientific and Production Centre for Preventive Medicine (SPCPM), Bishkek, Kyrgyz Republic

If to Recipient:
Ms. Kateřina Šebková, Ph.D., M.A., Director of the National Centre for Toxic Compounds and Stockholm Convention Regional Centre, Masaryk University, (RECETOX), Brno, Czech Republic.

15. This Agreement shall be effective as of the Effective Date and shall continue until the earlier of two (2) years from the Effective Date or the completion of Recipient's research. In addition, either party may terminate this Agreement (a) upon thirty (30) days written notice to the other party or (b) by written mutual Agreement.

16. Upon termination or expiration of this Agreement, all license(s) to the Materials granted under this Agreement shall cease, the Recipient shall indicate to Provider in writing within forty-five (45) days after termination or expiration of this agreement that the Materials have been properly disposed of in accordance with applicable laws and regulation governing the disposal of waste materials.

17. The Agreement replaces all previous agreements of understanding between the Parties related to the same subject matter, and may only be amended in writing by both Parties. The terms and conditions contained in nay Non-Disclosure Agreement between the Parties to this Agreement remain in full force and effect upon the execution of this Agreement.

18. Sections 2, 5, 8, 9, 11, 12, 13, and 16 shall survive any termination or expiration of this Agreement to the extent necessary to accomplish the purposes set forth herein.

IN WITNESS WHEREOF, the Parties have caused their duly authorized officers to execute this Agreement as of dates indicated below.

PROVIDER:
Scientific and Production Centre for Preventive Medicine (SPCPM), Bishkek, Kyrgyz Republic

1. Dr. Ainash Sharshenova, 2. Ms. Kulbaram Arzygulova

Signature: …… Signature: ……

Date: Date:

RECIPIENT:
Research Centre for Toxic Compounds in the Environment (RECETOX), Brno, Czech Republic

Ms Katerina Sebkova
Director of the National Centre for Toxic Compounds and Stockholm Convention Regional Centre
Masaryk University, Brno, Czech Republic.

Signature: ……

Date:____/____/2017