Giant Mine Remediation Project

Health Effects Monitoring Program

RESEARCH PLAN

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1. Title of Plan

Health Effects Monitoring Program in Ndilo, Dettah and Yellowknife

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3. Summary

The purpose of the Health Effects Monitoring Program is to establish a current baseline of contaminant exposure, and possible health effects in Ndilo, Dettah, and Yellowknife, and then continue to monitor the population throughout the Giant Mine Remediation Project. The monitoring program will focus on arsenic and other chemicals of potential concern (COPC) including antimony, cadmium, lead, manganese, and vanadium which might result from the remediation project activities. Interviews and sample collection will begin in the fall 2017 with approximately one thousand participants from age 6 to 79 and Elders, from Ndilo, Dettah, and Yellowknife. Sample collection will continue in the spring 2018 with another one thousand participants from age 3 to 79 and Elders, for a total of approximately two thousand. The participation age was lowered to 3 years of age in the spring to complement the Canadian Health Measures Survey, and to increase the potential number of children participants in the study.

Residents of Yellowknife will be randomly selected from the City of Yellowknife housing list. Members from the Yellowknives Dene First Nation (Yellowknives Dene) and North Slave Métis Alliance (NSMA) will participate on a voluntary basis. Each participant will be asked to complete a lifestyle and food frequency questionnaire, and provide samples of toenail clippings, and urine for contaminant testing. Members of the Yellowknives Dene First Nation members will also be asked to answer a medical history questionnaire and undergo a brief medical exam by a registered nurse. Participants will also be asked to provide a sample of their saliva, taken with a buccal swab on the inside of their cheek, to test for 20 specific genes that are known to interact with arsenic. Analysis of these specific genes and the single nucleotide polymorphisms associated with them will provide insight on how the genetic makeup of study participants may affect their interaction with arsenic. Studies have shown that some ethnicities may metabolize arsenic more efficiently.

In addition, all participants will be asked to provide consent to have their medical records reviewed for the past five years. Precautions will be put in place to protect participant's privacy. A follow-up study with youth participants (ages 3 to 17 at the time of data collection in 2017-2018) will be invited to participate in a follow-up study in 2022. A follow-up study for all participants, including adults is planned for 2027-2028.

4. Objectives

The overall objective is to design and implement a broad health effects biomonitoring program for the population of Yellowknife, Ndilo, and Dettah focusing on arsenic and other COPC such as antimony, cadmium, lead, manganese, and vanadium which might result from the Giant Mine Remediation Project. As well as to complement the Human Health and Ecological Risk Assessment (HHERA) study. Both studies are required by the Environmental Assessment Measure #9, and together they will provide a comprehensive overview of the levels of contaminants currently present in the human population as well as the environment.

Specific Objectives (*updated March 2019*)

a) Collect biological samples of toenail clippings, urine, and saliva from consenting participants from representative Yellowknife residents, YKDFN, and the NSMA populations as baseline parameters for an on-going monitoring program for population reference arsenic levels.
b) Analyse collected samples to characterize COPC exposure (particularly arsenic) within the population and draw comparisons with the Canadian general population (CHMS, 2013).
c) Investigate any associations between COPC concentrations, particularly arsenic, within the population and observed or reported health outcomes within that same population.
d) Explore results sharing with other related studies to understand sources of contaminant exposure and health interactions (e.g. Human Health and Ecological Risk Assessment, GNWT ENR fish monitoring of Northern Pike and Lake Whitefish).
e) Coordinate with the communication team (uOttawa & INAC, with additional input from HEMPAC) to develop and implement an effective communication plan.
f) Establish a biobank (a secure -80 freezer located at the uOttawa campus) to archive collected urine and toenail samples for future reference.
g) Establish a detailed protocol including a set of benchmarks for the future on-going monitoring program.
h) Coordinate with the communication team (uOttawa, CIRNAC, GMOB, with additional input from HEMPAC) to develop and implement a Youth Outreach Plan.

5. Background

Giant mine is an inactive gold mine located within the boundary of the City of Yellowknife where it was in operation from 1948 to 2004. Gold was extracted from arsenopyrite ores through a

roasting process that generated a toxic by-product called arsenic trioxide. Despite the mine's closure, there are still currently 237,000 tonnes of arsenic trioxide dust stored in 15 underground chambers, along with 4 large tailing ponds. Water is treated onsite to ensure it is within approved limits prior to discharge into Baker Creek and eventually into Yellowknife Bay. The mine has been regarded as one of the most contaminated sites in Canada, with $1 billion remediation costs (*Spring Report of the Commissioner of the Environment and Sustainable Development*, 2012). For its first 10 years of operation from 1948 to 1958, an estimated 20,000 tonnes of arsenic trioxide dust was released every year without any filtration. Following reports of arsenic poisoning in the 1950s, a baghouse filtration system was installed in 1958 to filter and store the arsenic trioxide in underground chambers (Sandlos and Keeling, 2012). Although Giant Mine is no longer in operation, there are concerns of contamination due to a list of chemicals of potential concern including arsenic, antimony, cadmium, lead, manganese, and vanadium from the site via surface runoff and groundwater migration (Stantec, 2015).

To address the issue, the Giant Mine Remediation Project was established. The project was approved by the Mackenzie Valley Environmental Impact Review Board. The project is subject to 26 measures aimed at preventing significant adverse impacts on the environment and to mitigate public concern.

- Measure #9 Stated:

  The Developer will work with other federal and territorial departments as necessary to design and implement a broad health effects monitoring program in Ndilo, Dettah and Yellowknife focusing on arsenic and any other contaminants in people which might result from this Project. This will include studies of baseline health effects of these contaminants and ongoing periodic monitoring. This will be designed with input from: Health Canada, GNWT Health and Social Services and the Yellowknife medical community; and The Yellowknives Dene and other potentially affected communities. The organization conducting the monitoring will provide regular plain language explanations of the monitoring results in terms that are understandable to lay people and communicate this to potentially affected communities in a culturally appropriate manner.

The proposed project addresses Measure #9 by conducting a broad health effects biomonitoring program of combined cohort and longitudinal design. The aim is to investigate the impact and exposure of the Contaminants of Potential Concern, particularly arsenic, on the Ndilo, Dettah, and Yellowknife population. As such, the Health Effects Monitoring Program will be long-term, monitoring the level of COPC within humans as the remediation project progresses - (two years commencing September 2017, a follow-up study in 2022/23, and another follow-up study in 2027/28 - see Section 3 Summary for more details).

Chemicals of potential concern including arsenic, antimony, cadmium, lead, manganese and vanadium were selected based on the screening exercise conducted in the concurrent Human

Health and Ecological Risk Assessment (HHERA) study by CanNorth. Since arsenic is the major contaminant at the Giant Mine site, this program will investigate the body burden of arsenic and its potential associations with health effects. The program will also measure concentrations of cadmium and lead in the collected urine samples and compare results to the most recent individual guidance values, with final results and interpretation shared with the participants. Concentrations of antimony, manganese, and vanadium will also be measured in urine samples but no interpretation or action will be taken. Results for these three metals will be used for baseline monitoring only as there are no clear and consistent individual guidance values currently available.

A. Arsenic

Arsenic is a naturally occurring metalloid in the earth's crust (Abdul et al., 2015). It exists in the environment in organic and inorganic forms. The organic forms are arsenocholine and arsenobetaine. Inorganic arsenic naturally occurs as pentavalent arsenate, As^{5+} or As (V), and trivalent arsenite, As^{3+} or As (III). Forms of organic arsenic is found in nature and is generally considered not harmful while inorganic arsenic is toxic. Trivalent arsenite is much more toxic than pentavalent arsenate.

The predominant route of arsenic exposure is via ingestion where it is absorbed in the small intestines and distributed throughout the body relatively quickly via blood. Arsenic metabolism occurs through a series of reductions and methylations converting the original arsenical to less toxic metabolites: Monomethylarsonic acid (MMA) and Dimethylarsinic acid (DMA). However, the process is often incomplete as inorganic arsenic species and its metabolites are found in urine (Health Canada, 2013). Arsenite is generally thought to be the most toxic form of arsenic species. However, in recent studies, MMA(III) is found to be 20 times more cytotoxic in human cells than

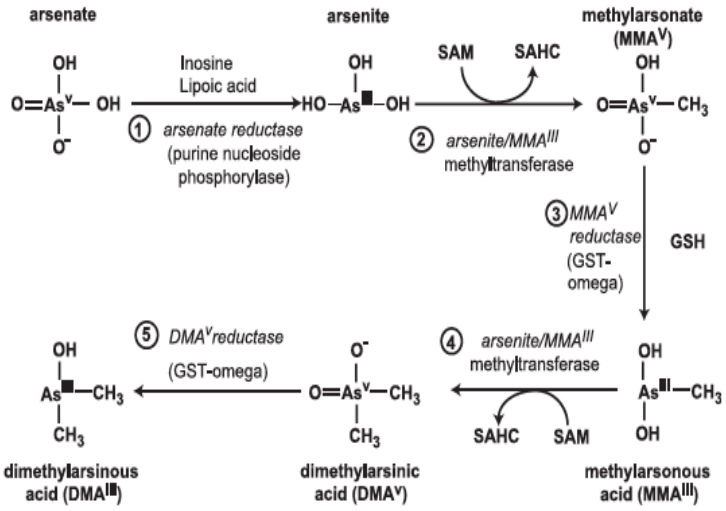


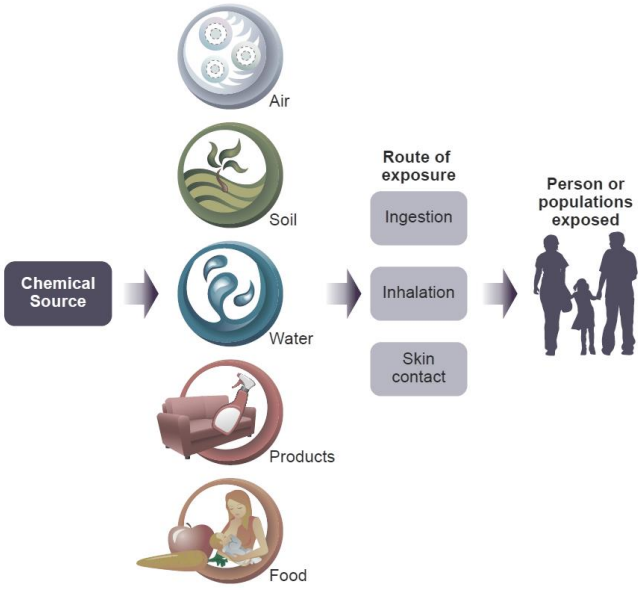
Fig 1. Arsenic biotransformation in human. Retrieved from Aposhian et al., 2004
SAM: S-adenosylmethionine
SAHC: S-adenosylhomocysteine

As (III) (Bredfeldt et al., 2006; Styblo et al., 2002). Trivalent methylated arsenic species MMA (III) and DMA (III)) produce an increased level of DNA damage compared to As (III) (Kligerman et al., 2003; Mass et al., 2001). Numerous animal studies have also been conducted that linked MMA to the incidence of cancers (ATSDR, 2007). However, to date there are no established reference values for MMA and DMA concentrations in human. A high percentage of MMA in urine often reflects metabolic inefficiencies (Gomez-Rubio et al., 2012).

Due to the differences in toxicity of different species, looking at the profile of arsenic species within humans via speciation gives a better idea of toxicity rather than just looking at total arsenic.

Arsenic exerts its toxicity by interacting with a diverse range of mechanisms thus generating numerous adverse health outcomes. Acute arsenic exposure in high concentrations can result in death, while low dose acute exposure causes nausea and vomiting, stomach irritation, diarrhea, decreased counts of red and white blood cells, abnormal heart rhythm, damage to blood vessels, a sensation of "pins and needles", as well as numbness in extremities.

Chronic exposure of relatively moderate to high doses of inorganic arsenic has been associated with diseases involving the integumentary, cardiovascular, neurological, hepatic, renal, and immune systems. A hallmark symptom of chronic arsenic toxicity is distinctive skin lesions on the extremities. Arsenic is also associated with diseases like diabetes and a variety of cancers. The International Agency for Research on Cancer (IARC) has determined that inorganic arsenic is carcinogenic to humans based on numerous studies and therefore, classified arsenic as a Group I Carcinogenic Chemical (IARC, 2012, 2017). Also, see Appendix 1 for arsenic-associated diseases and symptoms.



CHMS (2013)

Chemical compounds are present everywhere in the environment, exposing people daily. They are in water, foods, soils, air, and everyday products. They may enter our bodies through routes of exposure like ingestion, inhalation, and skin contact. For arsenic, the main route of exposure is via ingestion of drinking water and food, whether from natural arsenic sources or anthropogenic activities. Exposure through inhalation and skin contact is also possible but to a much lesser extent. Exposure through inhalation is more of a factor in terms of occupational exposure. Arsenic is poorly absorbed in the skin thus it is the least common route of exposure.

In Canada, high concentrations of arsenic in drinking water are relatively uncommon; high levels of arsenic exposure are usually from anthropogenic sources or diets (Health Canada, 2006; Elliott and Lindegger, 2009). Dietary exposure is especially relevant for First Nations and Métis populations where they hunt, fish, and harvest from local waters and lands (CINE, 1998). Traditional food is not only important for healthy diets, but it also enriches the spiritual and cultural values of the community. Traditional food diets have consistently shown to be of higher benefit, in terms of nutritional value, than of risks from chemical contamination (Chan et l., 2012, 2014 & 2016). Therefore, it is important to consider these benefits when assessing the risk of dietary exposure.

Despite daily exposure to chemical substances, harmful effects are unlikely to arise when exposure is within safe limits (Appendix 2). Adverse effects may be a concern when arsenic concentrations in soil or water are above such guideline limits, or biomarkers exceed values considered safe by the World Health Organization. Daily exposure to arsenic above safe limits may lead to chronic arsenic toxicity and subsequent arsenic-induced diseases as described above.

Chemical exposure can be assessed externally by measuring the levels of chemicals in environmental sources or internally by measuring chemical levels within the body by the use of biomarkers through a biomonitoring program. The former has currently been completed by the Human Health and Ecological Risk Assessment (HHERA) lead by Dr. Harriet Phillips and CanNorth. Environmental samples of water, sediment, soil, dust particles, and food were measured for arsenic, and other COPC. Data was used to estimate exposure levels, and to characterize the human health risk. This study proposes the latter - a Health Effects Monitoring Program. The potential impact of arsenic on the human health will be evaluated by measuring it within the body, and by studying the associations, specifically arsenic, with possible health effects. See Appendix 2 for environmental guidelines. It is anticipated that data from both studies, HHERA and the Health Effects Monitoring Program, will provide communities, and local government and organizations up to date, and comprehensive information on the levels of contaminants found in and around the Giant mine site.

B. About Biomonitoring

Biomonitoring is the measurement of a chemical compound and/or its by-products within the body. It is a tool used to assess internal concentrations of a chemical. In recent years, arsenic has been

measured in numerous studies and biomonitoring programs around the world such as Canada (Normandin et al. 2014), the US (Calderon et al. 2013), Europe (Cubadda et al. 2015), Latin America (McClintock et al. 2012) and Bangladesh (Argos et al., 2010). In North America, nationwide biomonitoring programs have been implemented such as the National Health and Nutrition Examination Survey (NHANES) in the US and the Canadian Health Measures Survey (CHMS) and the First Nations Biomonitoring Initiative (FNBI) in Canada. The CHMS is a national direct measures survey led by Statistics Canada aimed at collecting representative data from the 10 provinces concerning the general health of Canadians. A component of the survey is human biomonitoring of environmental chemicals, which consists of baseline data of selected chemicals, arsenic included, in Canadians. The arsenic data from the CHMS will be useful for comparisons with the data of this proposed monitoring program. The CHMS did not include First Nations living on reserve; this data gap was addressed by the FNBI, which was a national biomonitoring survey of 15 First Nations communities across Canada (Wuttke et al. 2013). The levels in the Yellowknife population can be compared with the Canadian general population and to the First Nations living on reserve. Biomonitoring programs have also been implemented on a more local basis. For example, there is an ongoing biomonitoring study conducted by Dr. Brian Laird in the DehCho region. A fish monitoring program testing Northern Pike and Lake Whitefish from local lakes, headed by the Government of Northwest Territories, Department of Environment and Natural Resources. As well as the Trail Lead Task Force that has been implemented for over 25 years in Trail, BC (Trail Area Health and Environment Committee, 2014). The town is home to a large lead-zinc smelter operation, which has been linked to high rates of childhood lead poisoning. A program was implemented to monitor and improve air quality as well as lead exposure in children. The program is seen as a successful model to follow. Considerations to the Trail program were made when designing this proposed study, as recommended by the Review Board in Suggestion #9 from the Environmental Assessment.

C. About Biomarkers

Biomarkers will be used to measure population and individuals' exposure to arsenic. Biomarkers are quantifiable indicators reflecting a biological state or process, which can be measured and detected in parts of the body. In terms of biomonitoring, biomarkers provide information about the activity or presence of the chemical of interest within the body. Some common biomarkers used in health studies and medicine are blood, urine, hair, nails, and breast milk. A number of biological and behavioural factors including sex, sources of drinking water supply, smoking, and frequency of fish consumption (Calderon et al. 2013) and genetic factors, such as the arsenic (III) methyltransferase (AS3MT) polymorphism (Hernández et al. 2014) have been shown to modify the levels of the biomarkers. Biomarkers may be classified in three main categories - Exposure, Effect, and Susceptibility.

(i) Biomarkers of Exposure

Biomarkers of *exposure* indicate the internal dose of the chemical present in the body, which reflects how much an individual has been exposed to a certain chemical. Several biomarkers have been shown to be useful indicators of arsenic exposure (Appendix 3). They are arsenic concentration in blood, urine, hair, and nail (finger and toenail). Samples of these biomarkers are taken and measured for the chemicals in question, which give an indication of the exposure level.

Most of the arsenic in the body is ingested through food and water. Arsenic enters the body through absorption in the GI tract, travelling via blood and exiting via urine. Its appearance in blood and urine through its time in the body provide two plausible biomarkers. Ingested arsenic and its metabolites are cleared in the blood in a matter of hours and excreted into urine in a couple of days. Urine is the biomarker most frequently used for measuring arsenic exposure. Arsenic in nails is a plausible biomarker for arsenic because the nails contain keratin: arsenic is known to interact with thiol (-SH) groups in different proteins thus they tend to deposit in keratin-rich tissues.

As a general rule, urinary and blood concentrations act as biomarkers of recent exposure, while fingernail and toenail levels reflect longer-term exposure. Arsenic stays in urine for up to 3-4 days and is cleared from blood within 2-3 hours (Adair et al., 2005). Therefore they reflect a short period of exposure. Nails typically reflect an exposure of 2-3 months and toenails reflect a longer exposure of 1-12 months prior to clipping as toenails grow more slowly (Slotnick & Nriagu, 2006).

For this program, the chosen biomarkers will be toenail and urine. The biomarkers were chosen for their accessibility, non-invasive nature, and validity. Past studies (Appendix 4) have evaluated the validity of the chosen biomarkers, finding significant correlations between their concentrations and environmental exposure concentrations such as in drinking water (Karagas et al., 2000; Calderon et al., 2013; Cottingham et al., 2013), household dust (Wilhelm et al., 2005; Hinwood et al., 2003; Subhani et al., 2015), soil (Wilhelm et al., 2005; Hinwood et al., 2003) and diet (MacIntosh et al., 1997). Past studies have also found significant associations between the chosen biomarkers and disease risk (e.g. Argos et al., 2014). Blood is excluded from this monitoring program due to its invasive nature, which is not ideal given the size and the age ranges of the target population. Toenails may be preferred over fingernails for measuring internal arsenic dose. They grow more slowly thereby reflecting a longer exposure period, and they are less exposed to outdoor contaminants (e.g. dust, soil) compared to hair or fingernails, and therefore less likely to contain exogenous concentrations which may interfere with measuring the internal dose.

Another advantage of the chosen biomarkers (urine and toenails) is that speciation techniques may be used to distinguish between the different arsenic species present in the biomarker medium. The arsenic forms that may be detected in biomarkers via speciation are: total arsenic, organic arsenic (arsenocholine and arsenobetaine), arsenite (As (III)), arsenate (As (V)), MMA (III), MMA (V), DMA (III), and DMA (V). As discussed, toxicity varies among arsenicals. Total arsenic concentration is not always indicative of arsenic toxicity, as some species like organic arsenic are found in nature and are considered not be toxic. Urinary arsenic profile is typically 10-30%

inorganic As, 10-20% MMA, and 60-80% DMA (Marchiset Ferlay et al., 2012; Navas-Acien et al., 2009). Speciation may indicate whether urinary profiles of study participants are below or above average levels.

It is important to note that the biomarkers used (urine or nails) are indicative of relatively recent exposure (from days to months), not historical exposure. There is a legacy of contamination from the Giant Mine, as well as other local gold mines, therefore the community is concerned with their exposure history. However, within project limits, there are no feasible ways to look at historical exposure at the individual level. Current results from the monitoring program may be compared to the results from older studies, such as the 1977 Task Force Report on Arsenic, at the population level, and using qualitative as opposed to quantitative analysis.

(ii) Biomarkers of Effect

Biomarkers of *effect* reflect the effects of the chemicals in question on a biological system. While biomarkers of exposure are used to see whether a chemical is in the body, biomarkers of effect indicate whether it is affecting the body. They may be molecular, reflecting effects on chemical processes, or a health indicator or symptoms, reflecting a pathological response. Arsenic interacts with a diverse set of cellular mechanisms, resulting in numerous health and molecular effects. There are two main biomarkers of effect chosen for this monitoring program: 1) blood pressure and urinary CC16, and 2) kidney injury and urinary KIM-1.

CC16, also known as club (formerly Clara) secretory protein, is one of the 20 proteins secreted by club cells in the alveolar epithelium of the lung. It has been observed to have anti-inflammatory and anti-toxicant properties. CC16 has been linked to environmental exposures as there have been observed increases in circulating levels of CC16 following acute environmental exposures (e.g. smoking, firefighting) perhaps due to epithelial damage to the lungs (Beamer et al., 2016). Arsenic exposure also impacts the lung function of children with possible lasting effects. A recent longitudinal-cohort study linked lower CC16 levels of those at 6 years old with decreased lung function by age 16 (Guerra et at., 2015). Arsenic has been linked to both increased risk of respiratory diseases and altered CC16 levels. Past studies have correlated decreased levels of club cell secretory protein (CC16) in adults with arsenic exposure. A study conducted in Bangladesh observed an inverse correlation between urinary arsenic and CC16 concentrations among participants with skin lesions. It was also observed that among adults with high arsenic drinking water exposure, those without skin lesions but reduced lung function were found to have lower levels of circulating CC16 (Parvez et al., 2008). For children, early life or in-utero exposure to arsenic has been associated with greater risks of infant lower respiratory tract illnesses and decreased lung function in both childhood and later on in life. Early arsenic exposure may be a predisposing factors for adult asthma and COPD (Chronic Obstructive Pulmonary Disease). A recent study by Beamer et al. (2016) looked at CC16 levels in children in relation to arsenic. They observed negative associations between urinary CC16 levels in children and environmental arsenic exposure concentrations, particularly in yard soil. In recent years, CC16 has emerged as a novel

biomarker for arsenic-induced respiratory illness. It has the potential to be a predictive indicator of early respiratory impairments.

KIM-1 is a transmembrane glycoprotein expressed by the kidney proximal tubular epithelial cells early after injury, followed by cleavage of its ectodomain into the urine (Vaidya et al., 2010). KIM-1 is involved in kidney repair after AKI, promoting the clearance of apoptotic cells (Ichimura et al., 2008). Chronic KIM-1 induction however, has been shown to be maladaptive and promotes fibrosis (Ferenbach and Bonventre, 2015) and this correlates with the persistent induction and excretion of KIM-1 in variety of inflammatory and fibrotic pathogeneses in the kidney (van Timmeren et al., 2007). In environmental settings, KIM-1 has demonstrated to be more sensitive than N-acetyl-β-D-glucosaminidase and β2 microglobulin for the detection of kidney injury induced by chronic cadmium exposure (Prozialeck et al., 2007 and Ruangyuttikarn et al., 2013). A recent study conducted on 83 children in Mexico found that arsenic exposure was significantly associated with urinary KIM-1 (Cardenas-Gonazalez et al. 2016). KIM-1 might serve as a sensitive biomarker to evaluate kidney injury in children.

For the purpose of this monitoring program, urinary samples will be analyzed for CC16 levels and KIM-1 levels for children only. Adults will not be included since these biomarkers are affected by smoking, and the smoking rate among the adult population in Yellowknife is considered high.

(iii) Biomarkers of Susceptibility

Biomarkers of *susceptibility* reflect the biological, often genetic differences between individuals that impact their susceptibility towards the effects of a chemical exposure. Genetic differences within individuals have been found to impact differences in responses to biological and metabolic processes. Some individuals are more susceptible or resilient to diseases due to their genetic makeup. Genetic polymorphisms are variations occurring at a specific location in a genome which is observed to an appreciable degree in a population. They often serve as genetic markers where patterns of polymorphic variation may reflect one's ancestry. They are a tool to understand heritability from our ancestors which have generated small differential responses to biological processes or disease.

Genetic polymorphisms may occur as sequences or even single nucleotides. The latter is referred to as single nucleotide polymorphism (SNP). For arsenic, several SNPs have been identified to be associated with arsenic, specifically metabolism of arsenic (Appendix 5). Numerous studies have looked at the effects of polymorphisms in the genes relating to arsenic (III) methyltransferase (AS3MT) and glutathione S-transferase (GST) which are two enzymes involved in arsenic metabolism (Agusa et al., 2012; Chung et al., 2008; Engstrom et al., 2001; Fujihara et al., 2009; Lindberg et al., 2007; Pierce et al., 2012). A study by Gomze-Rubio et al. (2012) looked at AS3MT polymorphisms in a population and observed %MMA was inversely correlated with genetic markers of indigenous American ancestry and the polymorphisms in question. Such results suggested that indigenous American ancestry is associated with efficiency of arsenic methylation. There are approximately 50 identified SNPs of 10 genes associated with how the body handles

arsenic. Analysis of polymorphisms will provide indications on how the genetic makeup of the study participants may affect their interaction with arsenic. Studies have shown that some ethnicities may metabolize arsenic more efficiently.

In this study, genetic polymorphisms will be analyzed in participants' DNA samples obtained by a buccal swab, which is a method of DNA collection from the inside of the cheek. The final results of the saliva swabs will be presented at the population level and shared at community meetings in 2020.

D. Other Chemicals of Potential Concern (COPC)

Biomarkers of exposure (urine and toenails) will also be analyzed for other COPC (antimony, cadmium, lead, manganese and vanadium), however no biomarkers for effect or susceptibility will be included for the following metals except for arsenic.

(i) Antimony

Antimony is a metalloid element existing in various forms and oxidation states. The predominant route of exposure for antimony is through ingestion of food, and to a lesser extent water. Antimony, in the form of antimony oxide, was identified as a high-priority substance under the Chemicals Management Plan, under the *Canadian Environmental Protection Act, 1999*. However, the draft screening assessment concluded that it was neither an environmental nor a human health concern at current levels of exposure. Chronic occupational exposure (generally much higher than environmental exposure) has been linked to myocardial and pulmonary effects. For this monitoring program, urine will be used as a biomarker for antimony as urine accounts for the majority of antimony excretion.

(ii) Cadmium

Cadmium is a naturally occurring trace metal, often found in zinc ores. The predominant source of exposure for cadmium is inhalation of cigarette smoke. Breathing high levels of cadmium can cause lung damage and death. For non-smokers, the primary source of exposure is through food, although occupation may be a factor. Eating or drinking high levels of cadmium can cause stomach irritations, vomiting, and diarrhea. Long-term exposure to lower levels through air, food or water can cause kidney damage, lung damage, fragile bones, and possible increase in risk of cancers. The effects on children are still unclear. Cadmium mainly accumulates in the renal cortex and liver. Its biological half-life is about 10-12 years, thus excretion is minimal, occurring mainly via urine and feces. For this monitoring program, urine will be used as the biomarker, which has previously been established to best reflect the total body burden of cadmium.

(iii) Lead

Lead is a heavy metal occurring in various organic and inorganic forms. Due to its natural abundance, the general population is exposed to trace amounts of lead. Lead is used for the refining and manufacturing of various products such as car batteries, sheet lead, brass, bronze pipes, paints, etc. While lead exposure has been largely reduced in Canada since the 1970s, industrial emissions are a frequent source of contamination, particularly near "point sources" such as smelters or refineries. Lead exposure has been linked to numerous adverse health outcomes, with children being the most vulnerable. Effects of chronic low exposure are less evident though it has been linked to effects on the cardiovascular system, central and peripheral nervous system, kidneys and immune system. Cognitive and neurobehavioral effects in children are a major concern. Blood is the preferred biomarker for lead. For this monitoring program, urine will be used as a biomarker to evaluate lead exposure, and participants with high urine lead level will be asked to have a blood test to confirm lead exposure.

(iv) Manganese

Manganese is a natural element as well as an essential nutrient. It is regarded as one of the least toxic elements. It is used in industry predominantly for steel production. In addition to anthropogenic sources, it is found in trace amounts in all plant and animal tissue which is the main source of exposure for the general population. Manganese is associated with bone formation, cellular protection from free radical damage, and metabolism. Despite its nutritional essentiality, moderately high occupational exposure levels have been linked to neurological effects, "metal fume fever", pneumonitis and manganism. For this monitoring program, urine will be used as a biomarker to evaluate manganese exposure.

(v) Vanadium

Vanadium is a natural element often found in combined forms such as iron ores, phosphate rocks, crude oils and petroleum products. It is used mainly in industry for alloy production. Vanadium is predominantly released into the environment as vanadium oxide through industrial atmospheric emissions, most notably the burning of fossil fuels and oil. Thus, the general population is exposed daily to vanadium however the main source of exposure is through food. Health Canada has concluded that there is insufficient data for the establishment of estimated adequate intake requirements. In addition, there is also limited information regarding effects of low-level exposure. Chronic exposure has been linked to eye and respiratory irritation. For this monitoring program, urine will be used as a biomarker for vanadium exposure.

6. Methodology

A. Data Collection

This monitoring program will use three different strategies for data collection from the three population groups within the area: the Yellowknife general population, the Yellowknives Dene First Nation (Yellowknives Dene) and the North Slave Métis Alliance (NSMA).

Overall the data collection will have the following components:
(i) Sampling strategy
(ii) Recruitment
(iii) Interviews
(iv) Medical Records (general Yellowknife population and NSMA)
(v) Medical Examination (Yellowknives Dene), based on recommendations from Yellowknives Dene leadership
(vi) Samples of urine, toenail clippings, and saliva (with a buccal swab)

(i) Sampling

For the Yellowknife general population, a methodology of random sampling was developed to obtain a representative sample based on residential addresses, with assistance from Statistics Canada. Yellowknife has a population of roughly 21,183 residents, including 1,540 Yellowknives Dene, in 10 districts, with 4,749 residential units and 739 multi-residential units (i.e. apartment buildings). The sampling size of approximately 1,900 was calculated based on statistics, with the following parameters: 20% desired level of precision, 1.00 variability of the variable to be measured, 5-10% level of confidence, 80% expected response rate, and 90% occupancy rate. Following a few adjustments, the aim was to realistically recruit a total of approximately 1500 residents of Yellowknife over the next two years starting in the fall 2017 with the first 750 participants. Participants will be recruited through random selection using the City of Yellowknife housing list where houses are selected proportionally from the ten districts (Appendix 6). Up to one adult (18+) and one child (3-17) from each selected address may be randomly selected based on whose birth date is next. For multi-residential addresses, all units will be informed that they may be selected to participate, however a random sampling technique will be used where the 3rd or 6th apartment on the list may be chosen at random. Then, up to one adult and one child, if present, will further be randomly selected based on whose birth date is next.

For the Yellowknives Dene First Nation, a mixed approach sampling will be adopted as suggested by the Yellowknives Dene leadership. First, community meetings will be held to introduce the project and answer questions. Then Yellowknives Dene members will be invited to participate on a voluntary basis. The volunteers will be checked off using household maps of Ndilo and Dettah provided by the Yellowknives Dene. Secondly, if a certain demographic or household is lacking,

in order to reflect a representative sample, that demographic or household will be contacted and invited to participate in the program. It is expected to recruit 200-400 Yellowknives Dene members over two years starting in the fall 2017.

For the North Slave Métis Alliance, samples will also be collected from a group of volunteer participants as recommended by the North Slave Métis Alliance leadership. It is expected to recruit 50-100 Métis over two years starting in the fall 2017.

Participants from the Yellowknife general population who identify as Yellowknives Dene (with proof of membership) or self-identify as NSMA will be separated from the general population pool and included in the Yellowknives Dene and NSMA pool accordingly.

If the participant self-identifies as a First Nation from a Band other than Yellowknives Dene or NSMA, that participant will be included with the general Yellowknife population.

If an individual from the Yellowknife general population approaches the research team asking to participate in the program because their house was not randomly selected, that individual will be allowed to participate as a volunteer. However, results of these volunteer participants will likely not be included in the sample population representing Yellowknife residents because they were not *randomly* sampled, and therefore can introduce sampling bias.

All participants will receive their individual results in a personal letter with an explanation of what those results mean.

(ii) Recruitment

Recruitment will begin in the fall of 2017. The study will be advertised by radio, local TV, social media and flyers. A communications and engagement plan has been finalized by the University of Ottawa and INAC team with additional input from all stakeholders.

For the Yellowknife residents, invitation letters will be sent up to 860 households and apartment buildings informing the occupant(s) that they have been randomly selected to participate in the program. This number will create a buffer for households that refuse to participate, are vacant, or are disqualified based on initial screening criteria (e.g. must have lived in Yellowknife for at least 12 months). This will be followed up by research assistants contacting them to make an appointment for an on-site interview at their home. At each household, the research assistant will explain the project (e.g. people will get their personal results in a letter, information may help guide future health advisories in the City of Yellowknife), and invite an adult and a child, if present, whose birthday is coming up next to participate in the program.

For the NSMA members, letters of invitation will be sent by email informing members they are welcome to participate. This will be followed up by a research assistant contacting them to make an appointment for an on-site interview at their home at their convenience.

For the Yellowknives Dene participants, letters of invitation will be dropped off at all the houses in Ndilo and Dettah by local youth, informing members they are welcome to participate in the program. The Yellowknives Dene Research Coordinator will then follow-up with households, and set up appointments with one of the research nurses. The appointments may take place at the participant's home, or at the Wellness Centre in Ndilo or at the Goyathiko Language Centre in Dettah.

All participants will be informed about the details of the project and sign a consent before proceeding with the interview and biological sample collection (Appendix 8). Due to the slight differences in the methodology between Yellowknife residents, Yellowknives Dene, and Métis participants, a separate consent form was created for each group. In addition, a consent form was created for children 3 to 11 years old where consent will be obtained from the parents or guardians on the child's behalf. For youth participants 12 to 17 years of age, they will be provided with the adult consent form as they are deemed able to give their own consent. This practice was adopted from the protocol of the Canadian Health Measures Survey.

Each consent form contains questions related to specific components of the monitoring program to which participants have to consent to before any information or samples can be collected. The consent for the Yellowknives Dene participants will include additional questions related to completing a medical history questionnaire, and a brief medical examination by a registered nurse.

(iii) Interviews

All participants who provide consent will be asked to complete a Lifestyle Questionnaire (Appendix 10). The lifestyle questionnaire contains two components: general information, and exposure history (e.g. lifestyle, diet, water source, occupational history). Participants will also be asked to complete a short Food Frequency Questionnaire (FFQ) on the types and amounts of fish consumed (Appendix 11). Information of serving sizes will be collected using models. The FFQ for the Yellowknives Dene will contain additional components including the types and amounts of wild animals, wild birds, wild berries, and mushrooms consumed as suggested by the Yellowknives Dene leadership.

Sample kits will be distributed to all participants, by Research Assistants working with the Yellowknife general population and members of the North Slave Metis Alliance, and Research Nurses working with the Yellowknives Dene, to collect urine, toenail clippings, and saliva at their own time. Instruction will be provided on who to contact for sample pick-up or drop off at any of the designated locations in Yellowknife, Ndilo, and/or Dettah. Samples will be kept at each location under appropriate storage conditions: either at room temperature for saliva and toenails or in the refrigerator at 4ºC for urine – *more details under Sample Analysis*, until ready for shipping to either University of Ottawa or Génome Quebec labs, for analysis.

(iv) Medical records

In the fall 2018, the YKHEMP received permission from the Northwest Territories Health Authority to access medical records for the past 5 years of those individuals who provided their consent.

A part-time medical researcher, familiar with the Wolf EMR electronic system, was hired to collect the data on-site therefore no medical files were removed from the office. The medical researcher used specific codes for symptoms, illnesses and diseases associated with contaminant exposure, and entered the information into a secure database on a laptop that had no access to the internet. Medical record data will only be used to investigate possible associations between contaminant exposure and specific health outcomes at the population level.

The YKHEMP is a prospective cohort study therefore, while it is not feasible to link the current findings of arsenic exposure to health outcomes, the data collected in 2017 and 2018 will form a baseline to follow-up with the individuals over time and it may be possible to see exposure-health effects relationship in the future.

(v) Medical examination and medical questionnaire

In addition to having their medical records reviewed for the past 5 years, the Yellowknives Dene will also be asked to complete a medical questionnaire (Appendix 12), and a brief medical exam that will include taking a person's height, weight, and blood pressure. This additional component was added after recommendations from the Yellowknives Dene leadership.

B. Sample Analysis

(i) Toenail and Urine Analysis

Collected toenails and urine samples will be stored in a refrigerator at 4ºC at a designated location in Yellowknife before getting shipped on ice packs to a laboratory at the University of Ottawa or Génome Quebec in Montreal, for analysis. Samples will be washed and prepared accordingly then undergo speciation analysis using high performance liquid chromatography with inductively coupled plasma mass spectrometry (HPLC-ICP-MS). HPLC-ICP-MS will analyze the samples for the different arsenic species: total arsenic, As(III), As(V), MMA(III), MMA(V), DMA(III), DMA(V), arsenocholine and arsenobetaine. Urine samples will be also analyzed for other COPC including antimony, cadmium, lead, manganese, and vanadium. Urine creatinine will be measured. Concentrations of all analytes will be reported in both ng/L and ng/g creatine. A strict quality assurance/quality control program including the analysis of blank samples and standard reference materials will be followed.

In order to ensure quality of analysis, about 5% of the samples will be measured by another independent laboratory, e.g. the Centre de Toxicologie - INSPQ in Quebec that performs the analyses for the Canadian Health Measures Survey.

Biomarker analysis: A sub-sample of urine samples collected from children (age 3-17) will also be analyzed for CC16 and KIM-1 levels via ELISA (enzyme-linked immunosorbent assay).

(ii) Genetic Determinant

DNA samples, from saliva taken with buccal swabs, will be sent to Génome Québec in Montreal for sequencing of selected polymorphisms and genes related to arsenic. Genomic analysis will be only of the stated selected polymorphisms, and the information will be confidential. For this monitoring program there are around 20 genes and 50 polymorphisms that have been reported to be related to arsenic metabolism or excretion. An SNP panel will be designed with the 20 markers of interest. Individuals containing the 20 genes in their DNA may get rid of arsenic and other contaminants more efficiently from their body. Samples will undergo analysis using Agena *iPlex*® array to detect for the selected SNPs. DNA polymorphisms will be analyzed to identify susceptible groups and results will be compared with arsenic concentrations in urine and toenail samples.

C. Data Analysis

During data collection, information will be collected by interviewers on Android tablets using Open Data Kit (ODK, v1.4.14). Following the interview, research assistants and research nurses will upload completed questionnaires using internet access (usually later that same day), and the data will be uploaded to a secure server where it will be compiled, downloaded, and saved as an Excel file on a secure computer. All laboratory results for the monitoring program will be combined into the database, and all statistical tests and analyses may be performed using SPSS statistical program.

(i) Analysis of toenail and urine samples

Concentrations will be categorized by factors including age, gender, smoking, source of drinking water, frequency of fish consumption, and other traditional foods relevant to the Yellowknives Dene, BMI and, blood pressure. Descriptive statistics including the percentage above detection limit, geometric mean, arithmetic mean, minimum and maximum values will be reported. Overall results may also be compared to known literature values of arsenic concentrations to determine whether the arsenic concentrations of the Yellowknife, Yellowknives Dene and NSMA populations are normal, elevated or at risk for certain diseases (Appendix 13). Results and associated statistics for each exposure biomarker (urine and toenail) will be summarized similarly to the data of the Canadian Health Measures Survey (Appendix 14). Participants will be sorted into the same age groups as that of CHMS: 3-5, 6-11, 12-19, 20-39, 40-59 and 60-79. The biomarker concentrations of each category will be sorted into percentiles of 10^{th}, 25^{th}, 50^{th}, 75^{th},

90th and 95th. The data collected will be compared with CHMS data to see whether the arsenic levels of the Yellowknife general, Yellowknives Dene, and North Slave Metis Alliance populations differ from that of the general Canadian population. In addition, the association of arsenic concentration of the toenail and urine samples with various factors including age, gender, time lived in Yellowknife, Ndilo or Dettah, living area in Yellowknife, Ndilo or Dettah, water source, BMI, genetic determinant, etc. will be studied using regression analysis and statistical modelling.

The speciation results will also be assessed in order to understand the urinary and toenail arsenic profile of participants. %MMA, %DMA, %As(III), % As(V), % arsenocholine and % arsenobetaine will be calculated. Other descriptive statistics will also be calculated such as MMA: DMA ratio to understand the arsenic metabolism of the participants.

(ii) Analysis of genetic polymorphisms

Results from genetic analysis will be compared with speciated arsenic concentrations in urine and toenail samples, specifically %MMA and %DMA. %MMA is reflective of arsenic methylation efficiency and the body's ability to metabolize arsenic. Statistical analysis will show whether there are significant associations between the presence of selected polymorphisms and %MMA. Test of significance may suggest that selected genetic polymorphisms which are inherited may be associated with arsenic metabolic efficiencies affecting inter-individual differences.

(iii) Health outcome analysis

Statistical models will be used to estimate adjusted hazard ratios, odds ratios for selected diseases and cancers, and risk factors with arsenic exposure. In addition, results of the biological sampling (urine and toenail) may be compared to the most up to date established reference values (See Appendix 13).

D. COPC Action Plan – *last revised May 2019*

(i) Proposed plan for interpretation of results

1. Population distribution of urine concentrations of arsenic (As), cadmium (Cd), lead (Pb) will be presented by age group similar to Canadian Health Measures Survey (CHMS (2010).

2. No interpretation or action for antimony (Sb), manganese (Mn) and vanadium (V). Only use the data for baseline reference.

3. For As, Cd, Pb, we will compare the data to the Canadian populations, i.e. the 95th percentile of the combined data obtained from the latest CHMS results (CHMS (2010). Risk of population exposure will also be discussed according to the population reference values from the CHMS (95th percentile) presented in the table below.

4. For toenail concentration of As, we will compare the results to the data from Yellowknife and from other comparable populations in Canada and elsewhere in the world.

(ii) Action for elevated level of exposure to As, Cd, and Pb

All participants will receive their own data in a letter. It is expected most participants will show levels lower than the population reference levels (table below), and be informed that the risk of their current exposure to As, Cd, and Pb is low.

1. Participants with **urine inorganic Arsenic (As) exceeding the reference level of 21 ug/L** will be referred to see a nurse practitioner. They will be asked to fill out a short follow-up questionnaire. They will be provided with medical counselling and a fact sheet as suggested by the ATSDR[1a] and will have urine samples collected for re-testing. Their record will be kept with their medical file by default.

2. Participants with **urine Cadmium (Cd) exceeding the reference level of 0.68 ug/L (3-17 years old) or 1.3 ug/L (18+ years old)** will be referred to see a nurse practitioner. They will be asked to fill out a short follow-up questionnaire. They will be provided with medical counselling and a fact sheet as suggested by the ATSDR[1b] and will have urine samples collected for re-testing. Their record will be kept with their medical file by default.

3. Participants with **urine Lead (Pb) exceeding the population reference value of 1.3 ug/L (3-17 years old) or 1.9 ug/L (18+ years old)**, will be asked to see a nurse practitioner to provide a blood sample to confirm their exposure. They will also be asked to fill out a short follow-up questionnaire. Urine is not a reliable biomarker for lead exposure.

4. Blood is the most reliable biomarker for lead exposure. Participants with **blood Pb exceeding 1.5 ug/dL (3-17 years old) or 3.3 ug/dL (18+ years old)**, will be asked to see a nurse practitioner. They will be provided with medical counselling and a fact sheet as suggested by the ATSDR[1c]. Their record will be kept with their medical file by default.

5. Participants with **toenail Arsenic (As) exceeding the 80th percentile for children (3-17 years old) at 1.3 mg/Kg, and 95th percentile for adults (18+ years old)** at **0.5 mg/Kg,** will be asked to see a nurse practitioner to provide another toenail sample. The toenail

sample will be sent to a laboratory in British Columbia, to conduct a more detailed analysis using a procedure called laser ablation ICP-MS. Laser ablation will show: 1. If arsenic in toenail comes from the surface of the nail or from inside the body; and 2. peak(s) of exposure in the last 1-12 months, depending on the length of toenail clipping provided. They will also be asked to fill out a follow-up questionnaire related to exposure to soil or dust and health outcomes. mg/Kg refers to milligram of metal per kilogram of body weight.

6. All participants will be asked whether they would like us to share their personal results with their health care provider.

Table. Reference levels for the proposed metal biomonitoring study

Metal	Biomarker	Population Reference (95th percentile)	Reference
Arsenic *inorganic*	Urine	21 ug/L	CHMS (2010)
Cadmium	Urine	0.68 µg/L (3-19 years old) 1.3 ug/L (20-79 years old)	CHMS (2010)
Lead	Urine[a]	1.3 µg/L (3-19 years old) 1.9 ug/L (20-79 years old)	CHMS (2010)
Lead	Blood[b]	1.5 ug/dL (3-19 years old) 3.3 ug/dL (20-79 years old)	CHMS (2010)
Arsenic *total*	Toenail	1.3 mg/Kg (3-17 years old)[c] 0.5 mg/Kg (18+)[d]	YKHEMP 2017-2018 baseline results

[a] Urine, a less intrusive biomarker, allows us to see if the person is potentially exposed to Lead.
[b] Blood helps us to confirm a person's exposure as it is the most reliable biomarker for Lead.
[c] 1.3 mg/Kg for children is the screening level below which we found 80% of our child participants (3-17 years). Using this screening level allows us to follow-up with more children with elevated arsenic toenail levels.
[d] 0.5 mg/Kg for Adults is the screening level below which we found 95% of adult participants (18+ years).

[1]**Physician Information**

a. *Arsenic*

Clinical Assessment
Patient Treatment
Fact Sheet
Additional Resources

b. *Cadmium*

Clinical Assessment

Patient Treatment
Fact Sheet
Additional Resources

c. ***Lead***

Clinical Assessment
Patient Information
Fact Sheet
Additional Resources

E. Long-term monitoring program

The Health Effects Monitoring Program is a biomonitoring study that will assess the current body burden of toxic chemicals, or their metabolites in Ndilo, Dettah and Yellowknife population. Baseline information will be collected in the first two years of the program (fall 2017 and spring 2018).

Children participants (age 3-17 at the time of sampling) will be re-sampled in 5 years (2022/2023) because they undergo more developmental stages. The same individuals will be invited to participate in the follow-up study. Any loss of participants will be added with new randomly selected participants to make up the required sample size in each of the age and sex groups.

In 10 years, all participants will be invited to a follow-up study, including children and adults (2027/2028). It is anticipated that there will be significant loss of original participants over time. New participants will be randomly selected to make up the number size in each of the age and sex groups.

A time-series analysis will be performed on the concentrations of each participant to document temporal changes.

7. Biobank

The Advisory Committee recommended the establishment of a biobank to archive a sub-sample of urine and toenail samples collected from the participants to allow for analysis of other contaminants such as mercury (Hg) that may be of concern in the future, or when additional information on health effects becomes available.

All urine and toenail samples that have not been used for the analysis described above will be stored in a secure freezer at -80 ºC at the University of Ottawa. The samples will be coded with the ID of the participants. No genetic materials will be archived.

Samples will be stored in the Biobank until after the completion of the follow-up studies planned in 2022 for children and in 2028 for all participants. At the end of the follow-up study in 2028,

the Advisory Committee will re-evaluate the need for maintaining the Biobank.

Archived samples in the biobank will only be used for contaminant analysis upon the agreement of the Advisory Committee. All proposals to use the archived samples in the biobank will be published at the Health Effects Monitoring Program and Giant Mine project websites. Summary results of projects using biobank samples will be disseminated to the community

8. Communications

Community engagement is of utmost importance as this program will require the participation and engagement of the greater Yellowknife population, the Yellowknives Dene First Nation, and the North Slave Métis Alliance. Communication strategies will be implemented throughout the program. Communication will occur well before recruitment and commencement of the program in the fall 2017, and again in spring 2018 using a variety of communication and engagement strategies. An Engagement and Communication Plan has been developed with the aid of the Advisory Committee (HEMPAC), and Indigenous and Northern Affairs Canada (INAC).

A monitoring program of this scale and of this matter requires constant community engagement and transparency. It is important to work closely with the concerned community and explain clearly the choices being made. It is understood that some community members may be reluctant to participate in certain parts of sampling or to divulge their medical history. The consent form will clearly state that participant has the right to opt out of any portion of the project while still being able to participate in the rest of the project (e.g. refuse to give DNA sample but still give urine and/or toenail samples and fill out the questionnaire). This will ensure a better participation rate for the program as opposed to requiring participation in all components of the program.

A. Communication and Engagement Objectives

- Keep people/groups of interest informed on the goals, process, and results of the Health Effects Monitoring Program in a manner that is in plain, meaningful language using a variety of communication channels.
- Gain community perspective, expertise and advice in developing, implementing, and communicating the Health Effects Monitoring Program.
- Identify and educate potential participants.
- Generate community interest, support and involvement for the monitoring program.
- Ensure Ndilo, Dettah, and Yellowknife residents are:
    - aware that the program is occurring
    - understand what the objectives and limitations of the program are (for example, the program can only measure current levels of arsenic, there is no existing technology that will allow the program to measure past exposure)

    - know how they can participate
    - know how participants are selected and
    - are informed throughout the process of the progress and results.
- Create an atmosphere of trust to encourage feedback and to have people/organizations feel that their contributions are appreciated and validated.
- Allow for changes to the program design (prior to submitting for ethics approval) as a result of recommendations by the Health Effects Monitoring Program Advisory Committee.
- Ensure stakeholder groups have the opportunity to recommend the most effective venues to communicate information throughout the program.
- Ensure selected participants are comfortable participating in the program (safety, confidentiality, access to results).
- Address questions about impacts of arsenic in the environment on human health.
- Address perceived health risks. Prevent misinformation from circulating and causing undue panic.
- Reinforce that the Giant Mine Remediation Project is operating in an open, inclusive, and transparent manner.
- Demonstrate how this program will directly address some of the concerns raised in the Environmental Assessment process.
- Provide a venue where questions can be answered.
- Ensure questions from media and community members are addressed in a timely manner where Giant Mine Remediation Project is the lead, and direct questions to the appropriate agencies where required.

B. Key Engagement Methods

University of Ottawa will take the lead on developing the following key products for the monitoring program, with feedback from INAC and HEMPAC stakeholders:

- Brochure (English / Wiiliideh), Posters, Flyers;
- Invitation letters;
- Logo development;
- Program website;
- Public service announcements (PSAs) in local newspapers and radio stations;
- Media interviews;
- Organization of several community meetings with Yellowknives Dene and NSMA to inform about and seek volunteer participants for the monitoring program.

INAC will manage/post information and updates related to the monitoring program on:

- Giant website (English / French);
- E-newsletter; Twitter; Facebook;
- Provide support for community meetings.

9. Partnership and Involvement

To ensure the participatory nature of the program, it is critical that an advisory committee be formed that includes key stakeholders and risk managers to oversee the planning, implementation and follow up of the program. Stakeholders of the Health Effects Monitoring Program Advisory Committee (HEMPAC) include the following organizations:

- Government of Northwest Territories Department of Environment and Natural Resources
- Government of Northwest Territories Department of Health and Social Services
- Health Canada
- Indigenous and Northern Affairs Canada
- Yellowknives Dene First Nation
- North Slave Métis Alliance
- Giant Mine Oversight Board
- City of Yellowknife

The project will also enlist the help of other experts and professionals as well as part-time researchers to aid in the implementation of the project.

- Dr. Ken Reimer of the Royal Military College as an external expert reviewer.
- Dr. Harriet Phillips of CanNorth, project lead of the Human Health and Ecological Risk Assessment.
- Bill Slater of Slater Environmental Consulting who sits on the Giant Mine Working Group.
- Sharen Roland of Génome Québec who will aid in DNA analysis.
- Rossana Manriquez and Jean Dumais of Statistics-Canada, who will aid in developing a sampling methodology.
- Dr. Susan Chatwood of the Institute for Circumpolar Health Research, who will aid in finalizing Research Agreement with the Health Authority to access medical records.

10. Highlights from Research Partnership and Data Sharing Agreement

Dr. Chan of the University of Ottawa is the principal investigator of the Health Effects Monitoring Program and is one of the main custodians of the data. Dr. Chan is responsible for collecting the information, establishing the database and conducting analyses. University of Ottawa, the home institute of Dr. Chan, will hold the intellectual property right of the data strictly for education and research purposes, including the presentation of results at scientific conferences, and publications of the results in scientific journals. Another copy of the aggregate data will be kept at the Institute for Circumpolar Health Research in Yellowknife, on a computer located in a secure room. Any

3rd parties seeking access to the Health Effects Monitoring Program data will have to go through HEMPAC for approval.

Identity of participants will be housed at University of Ottawa however another copy will be kept at another designated site. The site will be determined through further discussions with the Government of Northwest Territories Department of Health and Social Services.

11. Timeline

Preliminary work: September 2016-March 31, 2017

- Form an Advisory Committee
- Develop program Plan
- Develop budget for planning phase to funder
- Continue consultations with Yellowknives Dene and NSMA
- Develop communication and engagement plan
- Create Guiding Principles
- Develop communication materials (logo, brochure, poster)

Year 1: April 1, 2017 – March 31, 2018

- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences
- Develop communication materials (logo, brochure, website, posters, public service announcements, presentations)
- Finalize sampling plan with support from Statistics Canada
- Prepare and submit ethics application at University of Ottawa
- Prepare and submit research license application to NWT research institute
- Finalize Plan for full implementation and submit to INAC for funding
- Recruit contract staff (research assistants, nurses, other)
- Publicize the project
- Choose participants
- Host community meetings
- WAVE 1 data collection of saliva, toenail clippings, and urine.
- Coordinate sample collection, storage, transfer/transportation and analysis
- Coordinate data collection and synthesis

Year 2: April 1, 2018 –March 31, 2019

- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences;

- Submit ethics renewal
- Submit research license renewal
- Conduct data/sample analysis;
- Prepare progress report
- Report results to 1st year participants
- Recruit contract staff
- Publicize the project
- Host community meetings
- WAVE 2 data collection of saliva, toenail clippings, and urine.
- Coordinate sample collection, storage, transfer/transportation and analysis
- Coordinate data collection and synthesis

Year 3: April 1, 2019 – March 31, 2020

- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences
- Submit ethics renewal
- Submit research licence renewal
- Conduct data/sample analysis
- Report results to Waves 1 and 2 participants
- Prepare final technical report
- Prepare communication materials
- Host community meetings, share population-level results
- Develop communication/intervention plan

Year 4: April 1, 2020 – March 31, 2021

- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences
- Submit ethics renewal
- Submit research licence renewal
- Coordinate the development and dissemination of all reports
- Prepare communication materials
- Host community meetings, share updated population-level results, as necessary
- Prepare and finalize an ongoing health effects monitoring program plan
- Plan for re-sampling of children participants, ages 3-17

Year 5: April 2021 – March 31, 2022

- Re-sample children/youth, 3 to 17 years of age

- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences
- Submit ethics renewal
- Submit research licence renewal
- Recruit contract staff
- Publicize the project
- Host community meetings
- Collect data/samples
- Coordinate sample collection, storage, transfer/transportation and analysis
- Coordinate data collection and synthesis

Year 10: 2027/2028

- Re-sample all participants, adults and children
- Coordinate and chair monthly teleconferences with the Advisory Committee; provide agendas, and maintain formal records of decisions of all meetings and teleconferences
- Submit ethics renewal
- Submit research licence renewal
- Recruit contract staff
- Publicize the project
- Host community meetings
- Collect data/samples
- Coordinate sample collection, storage, transfer/transportation and analysis
- Coordinate data collection and synthesis
- Discuss the future of the program with the HEMPAC

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Appendix 1: Symptoms and diseases associated with chronic arsenic toxicity

Cancers
Skin cancer: Squamous cell carcinoma (CC), Bowen's disease, Basal Cell Carcinoma, combined skin cancer
Liver cancer
Kidney and Bladder cancers (transitional Cell Carcinoma of bladder)
Prostate
Lung cancer (with inhalation and ingestion)
Myelogenous leukemia, Hodgkin's disease
Respiratory
Sore throat and irritated lungs (with inhalation of As)
Decreased lung function (by spirometry)
Bronchitis, Bronchiectasis, Bronchopneumonia
Cardiovascular
Atherosclerosis, thickening and vascular occlusion of blood vessels
Hypertension
Gangrene of the feet "Blackfoot disease" (Taiwan)
Reynaud's, Acrocyanosis
Prolonged QT interval and Toursades de Pointes
Ischemic heart disease
Blood and Lymphatics
Anemia
Pancytopenia
Leukopenia
Gastrointestinal
Liver disorders
Non-cirrhotic portal hypertension with bleeding esophageal varices, Splenomegaly, Hypersplenism– in those taking Fowler's solution
Nausea, Vomiting, Diarrhea, Abdominal pain
Renal
Kidney dysfunction (with ingestion of methyl As in animals)

Bladder damage (with ingestion of methyl As in animals)
Endocrine
Diabetes mellitus
Neurological
Peripheral sensory neuropathy
Peripheral motor neuropathy: wrist drop, foot drop, altered reflexes; histology findings: dying-back axonopathy and demyelination
Asymmetric bilateral phrenic neuropathy
Headache
Confusion and cognitive impairment
Encephalopathy
Dermatological
Hyperkeratotic lesions (“wart-like”)
Hyperkeratosis of the skin (palms and soles)
Hyper- or hypo-pigmentation
Mees’ lines (transverse white lines on nails)
Specific effects in children and reproduction
Cognitive impairment (reduced IQ)
Possible neurobehavioral disorders
Increased mortality in young adults with exposure during gestation and early childhood
Low birth weight, Fetal malformation, Fetal death (stillbirth, miscarriage), Preterm birth: animal studies, high inorganic As dose

Appendix 2: Arsenic environmental guidelines

Government/Agency	Guideline Limit	Exposure/Biomarker	Reference
Bangladesh, China, India, Cambodia, Laos, Myanmar, Nepal and Pakistan	50 μg/L	Drinking Water	Argos et al. (2012)
WHO, US, Canada	10 μg/L	Drinking Water	Rojas et al. 2015; Paul & Giri, 2015
ANZECC/NH&MRC	100 μg/g	Soil	Hinwood et al. (2003)
WHO	1 μg/g	Hair	Mazumder (2000)
WHO	1.1 μg/g	Nail	Mazumder (2000)
WHO	50 μg/L	Urine	Mazumder (2000)

Appendix 3: Biomarkers of arsenic exposure

Analyte	Medium	Advantages	Disadvantages
Total arsenic	Blood	Internal dose	Invasive, short half-life
Total arsenic	Urine	Non-invasive sample, less variability	When total arsenic is quantified, including non-toxic (organic) forms of arsenic, difficult to interpret from a health risk perspective
As^{III}	Urine	Non-invasive sample; biomarker of exposure to inorganic As	
As^{V}	Urine	"	
MMA	Urine	"	Occurs following exposure to non-toxic forms of arsenic
DMA	Urine	"	"
Arsenocholine	Urine	Non-invasive sample	"
Arsenobetaine	Urine	Non-invasive sample	"
Arsenic	Hair	Non-invasive sample, indicative of integrated exposure	Susceptible to external contamination
Arsenic	Nails	Non-invasive sample, indicative of integrated exposure	Susceptible to external contamination

(Summit Toxicology, 2016)

Appendix 4: Summary of past studies investigating the association of environmental arsenic exposures and arsenic in different biological samples

Biomarker	Exposure Measure	Exposure Concentration	Biomarker Concentration	Association	Study Size (n)	Subjects	Location	Health Outcomes	Study
Fingernail	Drinking Water	0.25 µg/L	Mean= 0.3513 µg/g Range= 0.0537–2.8062 µg/g	NA	63	Mean age 31.8 years; 21 women, 42 men	Leicester	NA	Brima et al. (2006)
Fingernail	Drinking Water	248 µg/L (SD= ± 59 µg/L)	Mean= 7.32 µg/g (SD=6.48) Range= 2.14-40.25 µg/g Control: Mean=0.19 µg/g Range= 0.11 µg/g–0.30 µg/g	Between drinking water and nail concentration of exposure group: r^2=0.68 (p=0.029)	47	Residents in an As-endemic region drinking As-contaminated water ~ 3–10 yrs.	West Bengal, India	NA	Mandal et al. (2003)
Fingernail	Drinking Water	Mean= 0.89 µg/g	M: Mean= 1.397 µg/g ±0.09 (SD=0.686) F: Mean= 2.034 µg/g ±0.19 (SD= 1.872)	M: r=0.53 (p=0.01) F: r=0.72 (p=0.01)	M: 25 F:26	Residents of As endemic area with ages ranging from 5-72, mean age 46 y.o. whom have developed arsenicosis during past 25 yrs.	West Bengal, India	NA	Rakib et al. (2013)
Fingernail	Dust	Mean= 8.3825 µg/g	Mean= 1.31 µg/g	p= 0.03	20	Adults	Pakistan	NA	Subhani et al. (2015)
Fingernail	Dust in industrial setting	Mean= 9.78 µg/g (SD=2.76) Median= 9.68 µg/g Range= 5.00-13.46 µg/g	Mean=2.50 µg/g (SD=1.75) Median= 2.07 µg/g Range=0.01-5.23 µg/g	NA	11	Local industrial Residents	Pakistan	Cancinogenic risk: 1.0E–04	Subhani et al. (2015)
Fingernail	Dust in rural setting	Mean= 6.95 µg/g (SD=2.05) Median= 6.08 µg/g	Mean=1.12 µg/g (SD=0.52) Median= 1.09 µg/g Range=0.55-2.02 µg/g	NA	9	Local rural residents	Pakistan	Cancinogenic risk: 6.9E–05	Subhani et al. (2015)

		Range= 5.74-11.03 µg/g							
Fingernail	Dust in urban setting	Mean= 7.59 µg/g (SD=1.56) Median= 7.64 µg/g Range= 5.11-9.37 µg/g	Mean=0.88 µg/g (SD=1.11) Median= 0.56 µg/g Range=0.16-2.83 µg/g	NA	10	Local urban residents	Pakistan	Cancinogenic risk: 8.2E–05	Subhani et al. (2015)
Fingernail	Household dust	11.6 µg/g	Mean= 0.10 µg/g Range= <0.01-2.94 µg/g	R= 0.299 (P<0.001)	209	Residents living nearby of a coal-burning power plant w/ high As emissions	Prievidza District, Slovakia	Non-melanoma skin carcinoma	Wilhelm et al. (2005)
Fingernail	Soil	0.26 µg/g	GM= 0.10 µg/g Range= <0.01-2.94 µg/g	R= 0.232 (P<0.001)	207	Residents living nearby of a coal-burning power plant w/ high As emissions	Prievidza District, Slovakia	Non-melanoma skin carcinoma	Wilhelm et al. (2005)
Fingernail	Drinking Water	Mean= 153 ± 40 µg/L Range=0.21-943 µg/L	Mean= 1.90 ± 0.20 Range= 0.20-6.5 µg/g	r = 0.74, p < 0.0001	70	Residents of an area with arsenic-rich ground waters,	Cambodia	No clinical manifestation of Arsenicosis	Gault et al. (2008)
Toenail	Drinking Water	Mean=89 ppb (SD=±6) Range=3-2100 ppb	HG-AFS: Range=BDL-12 ppm NAA: Range=BDL-16 ppm	HG-AFS:adj-r^2=0.3557 NAA: adj-r^2=0.3922 (p<0.0001)	95	Residents >45 y.o. whom have lived in the area for >20 yrs.	County in Nevada	NA	Adair et al. (2006)
Toenail	Soil	Exposed: Mean= 0.204-9.025 µg/g Control: Mean= <0.02 µg/g	Exposed: GM= 5.406 µg/g Range=0.858-25.981 µg/g Control: GM=0.122 µg/g Range= 0.073-0.273 µg/g	r = 0.60, p < 0.001	Exposed: 8 Control: 9	Exposed: Residents living near to a former As mine, Devon, UK Control: residents from Nottinghamshire, UK, with no anticipated As exposure	Devon and Nottinhamshire, UK	NA	Button et al. (2009)
Toenail	Drinking Water	89 µg/L (SD=± 6) 20-1200 µg/L	Mean total nail As=1.062 µg/g GM= 0.625 µg/g 0.023-16.251 µg/g	NA	845	Long-term residents >45 y.o. living there continuously for >5 yrs.	County in Nevada	NA	Calderon et al. (2013)

Toenail	Drinking Water	Mean= 2.72 µg/L (SE=0.35) Median=0.30 µg/L	Mean=0.12 µg/g (SE=0.005) Median= 0.085 µg/g	NA	852	25-75 y.o. residents	New Hampshire	NA	Cottingham et al. (2013)
Toenail	Drinking Water	>10 µg/L	GM=21.7 µg/g (GSD=1.75) 8.80-55.3µg/g	R=0.55 (p<0.05)	21	Residents living in rural areas of varying env. Arsenic exposures	Across Australia	NA	Hinwood et al. (2003)
Toenail	Residential Soil	> 30 µg/g	GM=32.1 µg/g (GSD=4.13) 3.20-477µg/g	R=0.50 (p<0.05)	22	Residents living in rural areas of varying env. Arsenic exposures	Across Australia	NA	Hinwood et al. (2003)
Toenail	Water and Soil	<10 µg/L or <30 µg/g	GM=3.35 µg/g (GSD=1.73) 1.30-7.70 µg/g	NA	25	Residents living in rural areas of varying env. Arsenic exposures	Across Australia	NA	Hinwood et al. (2003)
Toenail	Water and Soil	>10 µg/L or > 30 µg/g	GM=10.4 µg/g (GSD=2.48) 1.35-104 µg/g	NA	8	Residents living in rural areas of varying env. Arsenic exposures	Across Australia	NA	Hinwood et al. (2003)
Toenail	Drinking Water	GM=0.29 µg/L (SE=0.04) Range= 0.002-66.6 µg/L	GM=0.09 µg/g (SE=0.003) Range= <0.01-0.81 µg/g	R= 0.46 (P<0.001)	208	Controls (25-74 y.o.) of a nonmelanoma-skin cancer case-control study	New Hampshire	NA	Karagas et al. (2000)
Toenail	Drinking Water	≥ 1 µg/L	NA	R=0.65 (P<0.001)	208	Controls (25-74 y.o.) of a nonmelanoma-skin cancer case-control study	New Hampshire	NA	Karagas et al. (2000)
Toenail	Drinking Water	0.002-66.66 µg/L	GM= 0.087 (SD 0.003) Range= 0.014-2.484	NA	383	Patients w/ transitional cell carcinoma of the bladder cancer	New Hampshire	Bladder cancer (OR: 2.17, 95% CI: 0.92–5.11 for >0.330 mcg/g wrt <0.06 l/g)	Karagas et al. (2004)
Toenail	Diet	10.22 µg/d (SD=6.26 µg) 0.93-104.89 µg/d	0.20 µg/g (SD=1.94 µg/g) 0.02-53.98 µg/g	R=0.33 (p=0.0001)	785 (210 F and 575M)	Participants, 30-55 y.o. of a semi-quantitative survey	Across the US	NA	MacIntosh et al. (1997)

Toenail	Drinking Water	GM= 1.2 µg/L Range= <1-17 µg/L	GM= 0.151 µg/g Range= 0.027-3.354 µg/g	Pearson's r= 0.53 (p<0.001, [0.43, 0.63])	199	Residents from 18-90	Cornwall, UK	NA	Middleton et al. (2015)
Urine	Drinking Water	0.25 µg/L	17.5 µg/g creatinine	NA	63	mean age 31.8 years; 21 women, 42 me	Leicester	NA	Brima et al. (2006)
Urine	Drinking Water	89 µg/L (SD=± 6) 20-1200 µg/L	Mean total urinary As =61.7 µg/L GM= 37.3 µg/L 0.5-856.3 µg/L	NA	904	Long-term residents >45 y.o. living there continuously for >5 yrs.	County in Nevada	NA	Calderon et al. (2013)
Urine	Household dust	11.6 µg/g	Total As GM= 6.0 µg/L iAs GM= 1.7 µg/L MMA GM=0.7 µg/L DMA GM= 2.8 µg/L	R=0.138 (P=0.080)	411	Residents with non-melanoma skin cancer and controls living nearby of a coal-burning power plant w/ high As emissions	Prievidza District, Slovakia	Non-melanoma skin carcinoma	Wilhelm et al. (2005)
Urine	Soil	0.26 µg/g	Total As GM= 6.0 µg/L iAs GM= 1.7 µg/L MMA GM=0.7 µg/L DMA GM= 2.8 µg/L	Between Soil & total As R (spearman's correlation coefficient) =0.129 (P=0.105)	411	Residents with non-melanoma skin cancer and controls living nearby of a coal-burning power plant w/ high As emissions	Prievidza District, Slovakia	Non-melanoma skin carcinoma	Wilhelm et al. (2005)

Appendix 5: Identified genetic polymorphisms (SNPs) and genes associated with Arsenic

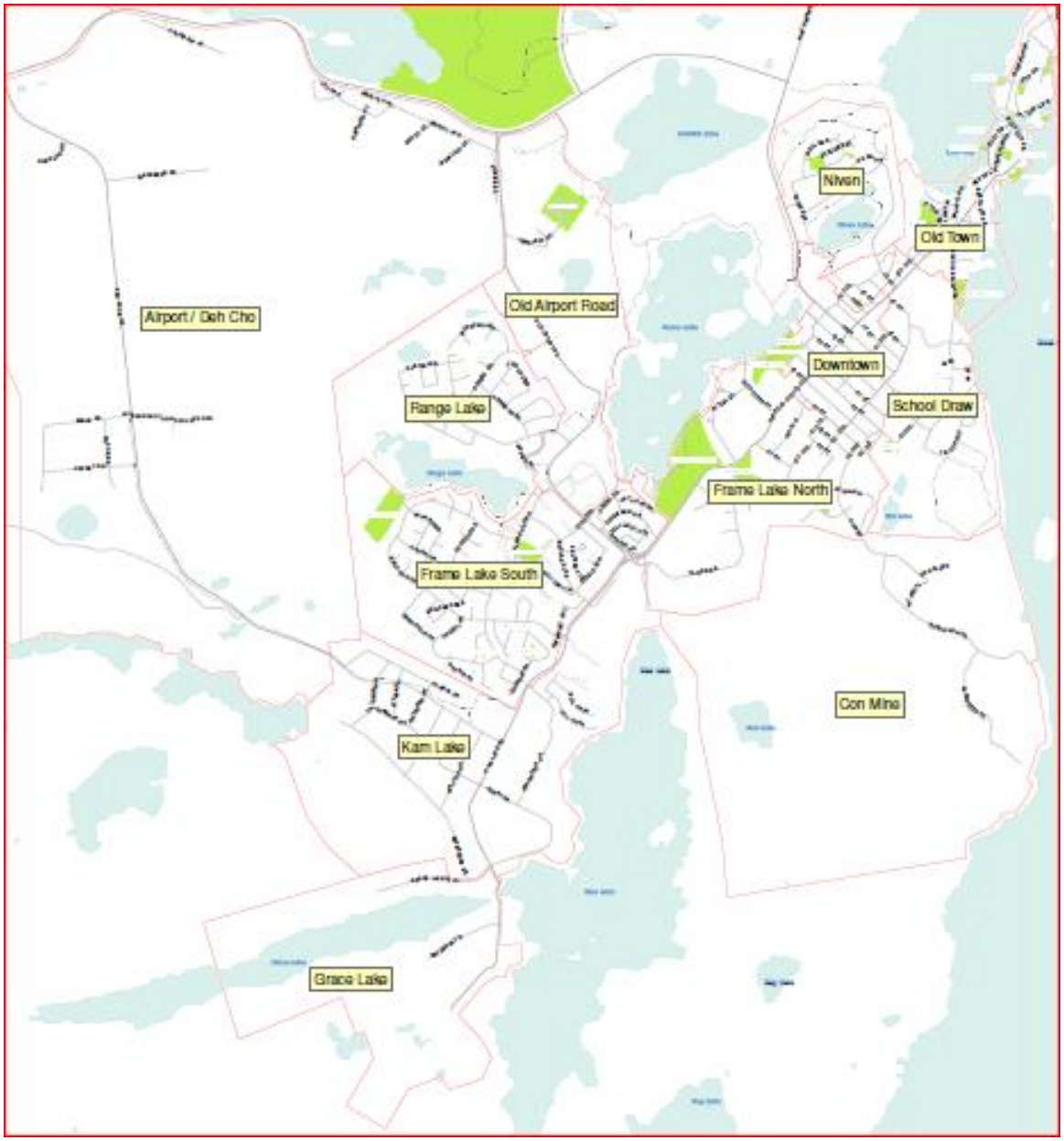
SNP	Gene	Allele/ Change	Role of Gene	Reported Effect	Reference
Asp148Glue	APE1	T to G (Asp to Glue)	DNA repair	Arsenic induced lesions	Ghosh et al. (2008)
A10209G	AS3MT	A/G	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
A27215G	AS3MT	A/G	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
A35991G	AS3MT	A/G	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
A4602G	AS3MT	A/G	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
A6144T	AS3MT	A/T	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
A9749G	AS3MT	A/G	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
C37616A	AS3MT	C/A	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
G7395A	AS3MT	G/A	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
rs11191439	AS3MT	T to C	Arsenic Metabolism	Change in % MMA	Engstrom et al. (2011)
rs11191453	AS3MT	A to G	Arsenic Metabolism	Change in % MMA	Engstrom et al. (2011)
rs3740390	AS3MT	C to T	Arsenic Metabolism	Change in % MMA	Engstrom et al. (2011)
T12390C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T12590C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T14215C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T14458/M287T	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T14458/M287T	AS3MT	T/C	Arsenic Metabolism	Increase MMA% in central European pop	Lindberg et al. (2007)
T25986C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T26790C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)

T35587C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T35587C	AS3MT	T/C	Arsenic Metabolism	Higher DMA:MMA ration in Mexican children	Meza, Gandolfi & Kilmecki (2007)
T37950C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T3963C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
T4740C	AS3MT	T/C	Arsenic Metabolism	MMA/DMA changes (Not analyzed)	Fujihara et al. (2009)
rs11191527	AS3MT (10q24.32)	A	Arsenic Metabolism	DMA%, skin lesion	Pierce et al. (2012)
rs11191659	AS3MT (10q24.32)	A	Arsenic Metabolism	MMA%, skin lesion	Pierce et al. (2012)
rs4290163	AS3MT (10q24.32)	A	Arsenic Metabolism	MMA%, skin lesion	Pierce et al. (2012)
rs4919694	AS3MT (10q24.32)	G	Arsenic Metabolism	MMA%, skin lesion	Pierce et al. (2012)
rs9527	AS3MT (10q24.32)	A	Arsenic Metabolism	DMA %, skin lesion	Pierce et al. (2012)
Lys751Gln	ERCC2	A to C (Lys→Gln)	DNA repair	Increased keratosis	Banerjee et al. (2007)
rs11509438	GST01	G to A (Glu→Lys)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)
rs11509439	GST01	C to T (Ala→Val)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)
rs15032	GST01	C to A (Thr→Asn)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)
rs156697	GST01	A to G (Asn→Asp)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)

rs4925	GST01	C to A (Ala→Asp)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)
rs56204475	GST01	Agg to del (Glu→del)	Reduction activity in Arsenic metabolism	Lower urinary concentration of As(V) and %iAs for heterozygous. Also higher M/I value	Agusa et al. (2010)
NA	GSTM1	Gene Deletion (Null)	Reduction activity in Arsenic metabolism	Wildtype had higher urinary DMA% in Vietnamese subjects	Agusa et al. (2010)
NA	GSTM1	Gene Deletion (Null)	Reduction activity in Arsenic metabolism	Subjects with >1 GSTM1 allele had sig higher risk of As-induced lesions	Ghosh et al. (2006)
Ile105Val	GSTP1	A to G (Ile→Val)	Reduction activity in Arsenic metabolism	*GG* genotype associated with greater odds of skin lesions compared to *AA* genotype	Ghosh et al. (2008)
rs1695	GSTP1	A to G (Ile to Val)	Reduction activity in Arsenic metabolism	Heterozygote *GSTP1* had a higher metabolic capacity from iAs to MMA but not for As(V) to As(III) in Vietnamese subjects	Agusa et al. (2010)
NA	GSTT1	Gene Deletion (Null)	Reduction activity in Arsenic metabolism	None observed in study	Agusa et al. (2010)
NA	GSTT1	Gene Deletion (Null)	Reduction activity in Arsenic metabolism	Homozygous wildtype associated with increased odds in skin lesions compared to null type in Bangladeshi subjects.	McCarty et al. (2007)
codon 31	p21	C to A (Ser→Arg)	Cyclin kinase inhibitor	Arg/Arg genotype had increased urothelial carcinoma risk	Chung et al. (2008)
16bp Intron 3	p53	G to A	Guardian of the genome, role in oxidative stress pathway	Increased keratosis	Chaudhuri et al. (2006)
Arg72Pro	p53	G to C	Guardian of the genome, role in oxidative stress pathway	Increased keratosis	Chaudhuri et al. (2006)
Gly51Ser	PNP	G to A (Gly→Ser)	Arsenate reductase	Arsenicism	Chaudhuri et al. (2008)

His20His	PNP	C to T	Arsenate reductase	Arsenicism	Chaudhuri et al. (2008)
Pro57Pro	PNP	C to T	Arsenate reductase	Arsenicism	Chaudhuri et al. (2008)
rs23591	XPD/ERCC2	G to A (As to Asn)	DNA repair	Increased rash of Skin Lesions	Lin et al. (2010)
rs35931	XPD/ERCC2	A to C (Lys→Gln)	DNA repair	Increased rash of Skin Lesions	Lin et al. (2010)
Arg194Trp/ rs1799782	XRCC1	C to T (Arg→Trip)	DNA repair	None observed in study	Fujihara et al. (2016)
Arg280His/ rs25489	XRCC1	G to A (Arg→His)	DNA repair	None observed in study	Fujihara et al. (2016)
Arg399Gln/ rs25487	XRCC1	G to A	DNA repair	Higher urinary iAs%	Fujihara et al. (2016)
Pro206Pro/ rs915927	XRCC1	A to G	DNA repair	AA genotype had higher MMA% and DMA:MMA ratio than AG genotype	Fujihara et al. (2016)
T241M	XRCC3	C to T (Met→Thr)	DNA repair	Presence of >1 Met allele was protective towards skin lesions, peripheral neuropathy and conjunctivitis	Kundu et al. (2011)

Appendix 6: Map of Yellowknife with residential districts



Ref: Map provided by the City of Yellowknife, July 2017

Appendix 7: Map of Yellowknife, Ndilo and Dettah

Appendix 8: Consent Forms

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Département de Biologie | **Department of Biology**
30 Marie Curie, Ottawa, ON K1N 6N5
ON Canada K1N 6N5
Tel: (613) 562-5800 x6349

Consent Form
YKDFN (13+ years)

Title of study: Health Effects Monitoring Program

Invitation to Participate: You are invited to participate in the Health Effects Monitoring Program as part of the Giant Mine Remediation Project. This study is led by Dr. Laurie Chan of the University of Ottawa. Funding is provided through Indigenous and Northern Affairs Canada.

Purpose of the Study: The purpose of the Health Effects Monitoring Program is to establish current baseline levels of contaminants, and examine possible health effects among residents in Ndilo, Dettah, and Yellowknife in the Northwest Territories, before remediation work begins. Then, during remediation, new monitoring results will be compared to the baseline to ensure participants' arsenic levels are not increasing because of work being done at Giant Mine. The monitoring program will focus on arsenic, and other Contaminants of Potential Concern (COPC) such as cadmium, lead, manganese, antimony and vanadium which may be released as a result of the remediation project.

Participation: If you agree to participate, a nurse will conduct a 60–minute interview to complete a short lifestyle questionnaire, and a food frequency questionnaire on a variety of wild fish, animals, birds, and berries consumed. In addition, the nurse will complete a medical history questionnaire, and conduct a brief medical examination that will include weighing, measuring height, and taking blood pressure. We will ask you to provide some toenail samples, a urine sample collected in the morning, and a saliva sample taken with a buccal swab from the inside of your cheek. Toenail and urine samples will be sent to the laboratory to test for arsenic and other metals of concern. The buccal swab will be used to test whether you have or do not have 20 specific genes that can help you to get rid of arsenic more efficiently from your body.

You will also be asked for permission to access your medical files for the past 5 years. We will investigate whether you have experienced symptoms related to arsenic or other contaminant exposure. This information will be coded with our study ID number.

Risks: There is no physical harm anticipated for participating in the monitoring program. Some of the questions in the Lifestyle Questionnaire are sensitive and personal, and you may feel uncomfortable. You don't have to answer all questions. You may also feel anxious about the type and amount of contaminants we may find in your body. You will receive your results with interpretation in a personal letter within a few months of data collection. A nurse of the research team will also be available to meet with you to explain your result, in case you had elevated levels of contaminants, the nurse will work with you to lower your exposure, and conduct further testing if necessary (i.e. blood test to confirm high exceedance).

Benefits: You will have the opportunity to find out whether you have been exposed to arsenic and other metals of concern. At the same time your participation will contribute to the understanding of arsenic exposure and its health effects in Ndilo, Dettah and Yellowknife.

Confidentiality and anonymity: All information you provide will be kept strictly confidential and will never be publicly attached to your name. You will receive your results with interpretation in a personal letter.

Conservation of data: The data collected (questionnaires, toenails, urine and saliva) will be kept in a secure manner (in a computer in a secure room at the University of Ottawa) until completion of the program. The Principal Investigator, along with research students, Janet Cheung and Dr. Rajendra Parajuli, will have access to the data. The data will only be used for the purpose of this study. A copy of the master database shall be provided to the Institute for Circumpolar Health Research, and kept in a secure manner, once data collection is complete.

Gift: You will receive a grocery gift card in the amount of $50 to thank you for taking the time to participate in the study.

Voluntary Participation: Your participation is voluntary. You are under no obligation to participate. If you choose to participate, you can withdraw from the study at any time and/or refuse to answer any questions without suffering any negative consequences. If you choose to withdraw, all information and data you have provided will be destroyed or returned to you on request. No samples of toenails, urine or saliva will be collected without your permission.

Who can I talk to if I have questions or problems?
The local research assistant will answer any questions you may have about this program or you may contact the following project team member at any time in the future.

Collect calls will be accepted.

Research Supervisor:
Dr. Laurie Chan
Professor and Canada Research Chair in Toxicology and Environmental Health
University of Ottawa, Faculty of Biology
Tel: 613-562-5800 ext. 7116
Email: laurie.chan@uottawa.ca

Yellowknife Contact:
Elizabeth Liske
Community Project Coordinator
Cell: 867-445-1574
Work: 873-8951 ext. 1011
Email: elizabethl@ykdene.com

If you have any questions regarding the ethical conduct of this study, you may contact:

Protocol Officer for Ethics in Research,
University of Ottawa, Tabaret Hall,
550 Cumberland Street, Room 154,
Ottawa, ON K1N 6N5
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Email: ethics@uottawa.ca

There are two copies of the consent form of which one will be kept by Dr. Chan.

Your decision to participate in the Health Effects Monitoring Program is completely up to you. You are free to withdraw from the program at any time, and you can choose not to answer any questions you don't feel comfortable answering.

By signing this form, I agree that:

1.	I understand that I am being asked to participate in a Health Effects Monitoring Program that will focus on Arsenic and other contaminants of primary concern for the Giant Mine Remediation Project.	Yes	No
2.	I understand that I have the right to not participate, to refuse to answer a question and the right to stop at any time.	Yes	No
3.	I understand that I can ask any questions related to the study at any time.	Yes	No
4.	I understand that my personal information will be kept confidential.	Yes	No
5.	I agree to give urine sample and be informed of the result.	Yes	No
6.	I agree to give toenail sample and be informed of the result.	Yes	No
7.	I agree to give saliva sample and be informed of the result.	Yes	No
8.	I agree to complete a medical history and undergo a brief medical examination by a nurse.	Yes	No
9.	I agree to have my medical file reviewed for the past 5 years.	Yes	No
10.	A follow-up study is planned in 5 to 10 years. I agree to be contacted again to be invited to participate in the follow up study.	Yes	No
11.	I agree to keep my samples in a biobank until the end of the study.	Yes	No
12.	I hereby consent to participate in the study.	Yes	No

Name of participant _____

Date of Birth (day/month/year) _____

_____ _____

Signature Date (day/month/year)

Telephone number _____

Participant's mailing address (for returning results of sample analysis):

_____

_____

Name of person who obtained consent

_____ _____

Signature Date (day/month/year)

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Université d'Ottawa | University of Ottawa
Département de Biologie | **Department of Biology**
30 Marie Curie, Ottawa, ON K1N 6N5
ON Canada K1N 6N5
Tel: (613) 562-5800 x6349

Consent Form
Yellowknife residents (13 -79 years)

Title of study: Health Effects Monitoring Program

Invitation to Participate: You have been randomly selected to participate in the Health Effects Monitoring Program as part of the Giant Mine Remediation Project. This study is led by Dr. Laurie Chan of the University of Ottawa. Funding is provided through Indigenous and Northern Affairs Canada.

Purpose of the Study: The purpose of the Health Effects Monitoring Program is to establish current baseline levels of contaminants, and examine possible health effects among residents in Ndilo, Dettah, and Yellowknife in the Northwest Territories, before remediation work begins. Then, during remediation, new monitoring results will be compared to the baseline to ensure participants' arsenic levels are not increasing because of work being done at Giant Mine. The monitoring program will focus on arsenic, and other Contaminants of Potential Concern (COPC) such as cadmium, lead, manganese, antimony and vanadium which may be released as a result of the remediation project.

Participation: If you agree to participate, we will conduct a 30–minute interview to complete a short lifestyle questionnaire, and a food frequency questionnaire on a variety of wild fish consumed. We will ask you to provide some toenail samples, a urine sample collected in the morning, and a saliva sample taken with a buccal swab from the inside of your cheek. Toenail and urine samples will be sent to the laboratory to test for arsenic and other metals of concern. The buccal swab will be used to test whether you have or do not have 20 specific genes that can help you to get rid of arsenic more efficiently from your body.

You will also be asked for permission to access your medical file for the past 5 years. We will investigate whether you have experienced symptoms related to arsenic or other contaminant exposure. This information will be coded with our study ID number.

Risks: There is no physical harm anticipated for participating in the monitoring program. Some of the questions in the Lifestyle Questionnaire are sensitive and personal, and you may feel uncomfortable. You don't have to answer all questions. You may also feel anxious about the type and amount of contaminants we may find in your body. You will receive your results with interpretation in a personal letter within a few months of data collection. A nurse of the research team will also be available to meet with you to explain your result, in case you had elevated levels of contaminants, the nurse will work with you to lower your exposure, and conduct further testing if necessary (i.e. blood test to confirm high exceedance).

Benefits: You will have the opportunity to find out whether you have been exposed to arsenic and other metals of concern. At the same time your participation will contribute to the understanding of arsenic exposure and its health effects in Yellowknife, Ndilo and Dettah.

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Gift: You will receive a grocery gift card in the amount of $50 to thank you for taking the time to participate in the study.

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3.	I understand that I can ask any questions related to the study at any time.	Yes	No
4.	I understand that my personal information will be kept confidential.	Yes	No
5.	I agree to give urine sample and be informed of the result.	Yes	No
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7.	I agree to give saliva sample and be informed of the result.	Yes	No
8.	I agree to have my medical file reviewed for the past 5 years.	Yes	No
9.	A follow-up study is planned in 5 to 10 years. I agree to be contacted again to be invited to participate in the follow up study.	Yes	No
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Name of participant _____

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Tel: (613) 562-5800 x6349

Consent Form
NSMA (13+ years)

Title of study: Health Effects Monitoring Program

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2.	I understand that I have the right to not participate, to refuse to answer a question and the right to stop at any time.	Yes	No
3.	I understand that I can ask any questions related to the study at any time.	Yes	No
4.	I understand that my personal information will be kept confidential.	Yes	No
5.	I agree to give urine sample and be informed of the result.	Yes	No
6.	I agree to give toenail sample and be informed of the result.	Yes	No
7.	I agree to give saliva sample and be informed of the result.	Yes	No
8.	I agree to have my medical file reviewed for the past 5 years.	Yes	No
9.	A follow-up study is planned in 5 to 10 years. I agree to be contacted again to be invited to participate in the follow up study.	Yes	No
10.	I agree to keep my samples in a biobank until the end of the study.	Yes	No
11.	I hereby consent to participate in the study.	Yes	No

Name of participant _____

Date of Birth (day/month/year) _____

_____ _____

Signature Date (day/month/year)

Telephone number _____

Participant's mailing address (for returning results of sample analysis):

_____

_____

Name of person who obtained consent

_____ _____

Signature Date (day/month/year)

uOttawa

Université d'Ottawa | University of Ottawa
Département de Biologie | **Department of Biology**
30 Marie Curie, Ottawa, ON K1N 6N5
ON Canada K1N 6N5
Tel: (613) 562-5800 x6349

Consent Form
YK, NSMA (Child 3-12)

Title of study: Health Effects Monitoring Program

Invitation to Participate: Your child is being asked to participate in the Health Effects Monitoring Program as part of the Giant Mine Remediation Project. This study is led by Dr. Laurie Chan of the University of Ottawa. Funding is provided through Indigenous and Northern Affairs Canada.

Purpose of the Study: The purpose of the Health Effects Monitoring Program is to establish current baseline levels of contaminants, and examine possible health effects among residents in Ndilo, Dettah, and Yellowknife in the Northwest Territories, before remediation work begins. Then, during remediation, new monitoring results will be compared to the baseline to ensure participants' arsenic levels are not increasing because of work being done at Giant Mine. The monitoring program will focus on arsenic, and other Contaminants of Potential Concern (COPC) such as cadmium, lead, manganese, antimony and vanadium which may be released as a result of the remediation project.

Participation: If you agree to have your child participate, we will conduct a 30–minute interview to ask you to complete a short lifestyle questionnaire, and a food frequency questionnaire on a variety of wild fish your child consumed. We will ask your child to provide some toenail samples, a urine sample collected in the morning, and a saliva sample taken with a buccal swab from the inside of your child's cheek. Toenail and urine samples will be sent to the laboratory to test for arsenic and other metals of concern. The buccal swab will be used to test whether your child has or does not have 20 specific genes that can help them to get rid of arsenic more efficiently from your body.

You will also be asked for permission to access your child's medical files for the past 5 years. We will investigate whether your child has experienced symptoms related to arsenic or other contaminant exposure. This information will be coded with our study ID number.

Risks: There is no physical harm anticipated for your child to participate in the monitoring program. Some of the questions in the Lifestyle Questionnaire are sensitive and personal, and you may feel uncomfortable. You don't have to answer all questions. You may also feel anxious about the type and amount of contaminants we may find in your body. You will receive your results with interpretation in a personal letter within a few months of data collection. A nurse of the research team will also be available to meet with you to explain your result, in case you had elevated levels of contaminants, the nurse will work with you to lower your exposure, and conduct further testing if necessary (i.e. blood test to confirm high exceedance).

Benefits: You will have the opportunity to find out whether your child has been exposed to arsenic and other metals of concern. At the same time your child's participation will contribute to the understanding of arsenic exposure and its health effects in Yellowknife, Ndilo and Dettah.

Confidentiality and anonymity: All information you provide on behalf of your child will be kept strictly confidential and will never be publicly attached to his or her name. You will receive your child's results with interpretation in a personal letter.

Conservation of data: The data collected (questionnaires, toenails, urine and saliva) will be kept in a secure manner (in a computer in a secure room at the University of Ottawa) until completion of the program. The Principal Investigator, along with research students, Janet Cheung and Dr. Rajendra Parajuli, will have access to the data. The data will only be used for the purpose of this study. A copy of the master database shall be provided to the Institute for Circumpolar Health Research, and kept in a secure manner, once data collection is complete.

Gift: You will receive a grocery gift card in the amount of $50 to thank you for taking the time to answer questions on your child's behalf. In addition, your child will receive a little toy to thank them for taking the time to participate in the study.

Voluntary Participation: Your participation is voluntary. You are under no obligation to have your child participate. If you choose to have your child participate, you can withdraw your child from the study at any time and/or refuse to answer any questions without suffering any negative consequences. If you choose to withdraw your child, all information and data you have provided will be destroyed or returned to you on request. No samples of toenails, urine or saliva will be collected from your child without your permission.

Who can I talk to if I have questions or problems?
The local research assistant will answer any questions you may have about this program or you may contact the following project team member at any time in the future.

Collect calls will be accepted.

Research Supervisor:
Dr. Laurie Chan
Professor and Canada Research Chair in Toxicology and Environmental Health
University of Ottawa, Faculty of Biology
Tel: 613-562-5800 ext. 7116
Email: laurie.chan@uottawa.ca

Yellowknife Contact:
Elizabeth Liske
Community Project Coordinator
Cell: 867-445-1574
Work: 873-8951 ext. 1011
Email: elizabethl@ykdene.com

If you have any questions regarding the ethical conduct of this study, you may contact:

Protocol Officer for Ethics in Research,
University of Ottawa, Tabaret Hall,
550 Cumberland Street, Room 154,
Ottawa, ON K1N 6N5
Tel: (613) 562-5387
Email: ethics@uottawa.ca

There are two copies of the consent form of which one will be kept by Dr. Chan.

Your decision to have your child participate in the Health Effects Monitoring Program is completely up to you. You are free to withdraw your child from the program at any time, and you can choose not to answer any questions you don't feel comfortable answering.

By signing this form, I agree that:

1.	I understand that my child is being asked to participate in a Health Effects Monitoring Program that will focus on Arsenic and other contaminants of primary concern for the Giant Mine Remediation Project.	Yes	No
2.	I understand that I have the right to have my child not participate, to refuse to answer a question and the right to stop at any time.	Yes	No
3.	I understand that I can ask any questions related to the study at any time.	Yes	No
4.	I understand that my child's personal information will be kept confidential.	Yes	No
5.	I agree for my child to give urine sample and be informed of the result.	Yes	No
6.	I agree for my child to give toenail sample and be informed of the result.	Yes	No
7.	I agree for my child to give saliva sample and be informed of the result.	Yes	No
8.	I agree to have my child's medical file reviewed for the past 5 years.	Yes	No
9.	A follow-up study is planned in 5 to 10 years. I agree to be contacted again to have my child participate in the follow up study.	Yes	No
10.	I agree to keep my child's samples in a biobank until the end of the study.	Yes	No
11.	I hereby consent for my child to participate in the study.	Yes	No

I agree for my child to participate in the Health Effects Monitoring Program. My signature means that I have the legal authority to sign for the child.

Name of child _____ Date of Birth (day/month/year) _____

_____ _____

Name of parent or legal guardian Signature of parent or legal guardian

_____

Date (day/month/year)

Telephone number _____

Participant's mailing address (for returning results of sample analysis):

_____

Name of person who obtained consent

_____ _____

Signature Date (day/month/year)

uOttawa

Université d'Ottawa | University of Ottawa
Département de Biologie | **Department of Biology**
30 Marie Curie, Ottawa, ON K1N 6N5
ON Canada K1N 6N5
Tel: (613) 562-5800 x6349

Consent Form
YKDFN (Child 3-12)

Title of study: Health Effects Monitoring Program

Invitation to Participate: Your child is being asked to participate in the Health Effects Monitoring Program as part of the Giant Mine Remediation Project. This study is led by Dr. Laurie Chan of the University of Ottawa. Funding is provided through Indigenous and Northern Affairs Canada.

Purpose of the Study: The purpose of the Health Effects Monitoring Program is to establish current baseline levels of contaminants, and examine possible health effects among residents in Ndilo, Dettah, and Yellowknife in the Northwest Territories, before remediation work begins. Then, during remediation, new monitoring results will be compared to the baseline to ensure participants' arsenic levels are not increasing because of work being done at Giant Mine. The monitoring program will focus on arsenic, and other Contaminants of Potential Concern (COPC) such as cadmium, lead, manganese, antimony and vanadium which may be released as a result of the remediation project.

Participation: If you agree to have your child participate, a nurse will conduct a 60–minute interview to complete a short lifestyle questionnaire, and a food frequency questionnaire on a variety of wild fish your child consumed. In addition, the nurse will complete a medical history questionnaire, and conduct a brief medical examination that will include weighing, measuring height, and taking blood pressure. We will ask your child to provide some toenail samples, a urine sample collected in the morning, and a saliva sample taken with a buccal swab from the inside of your child's cheek. Toenail and urine samples will be sent to the laboratory to test for arsenic and other metals of concern. The buccal swab will be used to test whether your child has or does not have 20 specific genes that can help them to get rid of arsenic more efficiently from your body.

You will also be asked for permission to access your child's medical files for the past 5 years. We will investigate whether your child has experienced symptoms related to arsenic or other contaminant exposure. This information will be coded with our study ID number.

Risks: There is no physical harm anticipated for your child to participate in the monitoring program. Some of the questions in the Lifestyle Questionnaire are sensitive and personal, and you may feel uncomfortable. You don't have to answer all questions. You may also feel anxious about the type and amount of contaminants we may find in your body. You will receive your results with interpretation in a personal letter within a few months of data collection. A nurse of the research team will also be available to meet with you to explain your result, in case you had elevated levels of contaminants, the nurse will work with you to lower your exposure, and conduct further testing if necessary (i.e. blood test to confirm high exceedance).

Benefits: You will have the opportunity to find out whether your child has been exposed to arsenic and other metals of concern. At the same time your child's participation will contribute to the understanding of arsenic exposure and its health effects in Yellowknife, Ndilo and Dettah.

Confidentiality and anonymity: All information you provide on behalf of your child will be kept strictly confidential and will never be publicly attached to his or her name. You will receive your child's results with interpretation in a personal letter.

Conservation of data: The data collected (questionnaires, toenails, urine and saliva) will be kept in a secure manner (in a computer in a secure room at the University of Ottawa) until completion of the program. The Principal Investigator, along with research students, Janet Cheung and Dr. Rajendra Parajuli, will have access to the data. The data will only be used for the purpose of this study. A copy of the master database shall be provided to the Institute for Circumpolar Health Research, and kept in a secure manner, once data collection is complete.

Gift: You will receive a grocery gift card in the amount of $50 to thank you for taking the time to answer questions on your child's behalf. In addition, your child will receive a little toy to thank them for taking the time to participate in the study.

Voluntary Participation: Your participation is voluntary. You are under no obligation to have your child participate. If you choose to have your child participate, you can withdraw your child from the study at any time and/or refuse to answer any questions without suffering any negative consequences. If you choose to withdraw your child, all information and data you have provided will be destroyed or returned to you on request. No samples of toenails, urine or saliva will be collected from your child without your permission.

Who can I talk to if I have questions or problems?
The local research assistant will answer any questions you may have about this program or you may contact the following project team member at any time in the future.

Collect calls will be accepted.

Research Supervisor:
Dr. Laurie Chan
Professor and Canada Research Chair in Toxicology and Environmental Health
University of Ottawa, Faculty of Biology
Tel: 613-562-5800 ext. 7116
Email: laurie.chan@uottawa.ca

Yellowknife Contact:
Elizabeth Liske
Community Project Coordinator
Cell: 867-445-1574
Work: 873-8951 ext. 1011
Email: elizabethl@ykdene.com

If you have any questions regarding the ethical conduct of this study, you may contact:

Protocol Officer for Ethics in Research,
University of Ottawa, Tabaret Hall,
550 Cumberland Street, Room 154,
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There are two copies of the consent form of which one will be kept by Dr. Chan.

Your decision to have your child participate in the Health Effects Monitoring Program is completely up to you. You are free to withdraw your child from the program at any time, and you can choose not to answer any questions you don't feel comfortable answering.

By signing this form, I agree that:

1.	I understand that my child is being asked to participate in a Health Effects Monitoring Program that will focus on Arsenic and other contaminants of primary concern for the Giant Mine Remediation Project.	Yes	No
2.	I understand that I have the right to have my child not participate, to refuse to answer a question and the right to stop at any time.	Yes	No
3.	I understand that I can ask any questions related to the study at any time.	Yes	No
4.	I understand that my child's personal information will be kept confidential.	Yes	No
5.	I agree for my child to give urine sample and be informed of the result.	Yes	No
6.	I agree for my child to give toenail sample and be informed of the result.	Yes	No
7.	I agree for my child to give saliva sample and be informed of the result.	Yes	No
8.	I agree to complete a medical history on behalf of my child and have them undergo a brief medical examination by a nurse.	Yes	No
9.	I agree to have my child's medical file reviewed for the past 5 years.	Yes	No
10.	A follow-up study is planned in 5 to 10 years. I agree to be contacted again to have my child participate in the follow up study.	Yes	No
11.	I agree to keep my child's samples in a biobank until the end of the study.	Yes	No
12.	I hereby consent for my child to participate in the study.	Yes	No

I agree for my child to participate in the Health Effects Monitoring Program. My signature means that I have the legal authority to sign for the child.

Name of child _____ Date of Birth (day/month/year) _____

_____ _____

Name of parent or legal guardian Signature of parent or legal guardian

_____

Date (day/month/year)

Telephone number _____

Participant's mailing address (for returning results of sample analysis):

_____

Name of person who obtained consent

_____ _____

Signature Date (day/month/year)

Appendix 9: Assent Forms

Assent Form (YK-NSMA Child 3-12)

Hi. My name is *[your name]*. I'm a Research Assistant or Research Nurse with the Health Effects Monitoring Program. This program will test to see if you have certain metals in your body. It's OK for us to have some metals inside our body but not too much as that can make us sick. Right now, I'm trying to learn about adults and children living in Yellowknife and find out if they are healthy. I would like to ask you to help me by being in the study, but before I do, I want to explain what will happen if you decide to help me.

I will ask you to provide some of your toenails, urine and saliva by swabbing the inside of your cheek with a Q-tip. I will ask your mother or father to answer some questions about your health, your home life and about the foods that you eat. By being in the study, you will help me find out how much metals are in your body. Then, next year your parents will receive a letter with your personal results.

Your classmates or teacher will not know what your results are. When I tell other people about the study, I will not use your name, and no one will be able to tell who I'm talking about.

Your *[mom/dad]* says it is okay for you to be in the study. But if you don't want to be in the study, you don't have to be. It is up to you to decide. I won't be upset, and no one else will be upset if you don't want to participate. If you want to be in the study now but change your mind later, that's okay. You can stop at any time. If there is anything you don't understand you should tell me so I can explain it to you.

You can ask me questions about the study. If you have a question later that you don't think of now, you can call me or ask your parents to call or send me an email.

Do you have any questions for me now?

Would you like to be in the study, answer some questions and provide some samples?

Yes	No

Name of Child: _____

Parental Permission on File: ☐ Yes ☐ No

Child's Voluntary Response to Participation: ☐ Yes ☐ No

Signature of Researcher: _____ **Date:** _____

Assent Form (YKDFN Child 3-12)

Hi. My name is *[nurse's name]*. I'm a nurse with the Health Effects Monitoring Program. This program will test to see if you have certain metals in your body. It's OK for us to have some metals inside our body but not too much as that can make us sick. Right now, I'm trying to learn about adults and children living in Yellowknife and find out if they are healthy. I would like to ask you to help me by being in the study, but before I do, I want to explain what will happen if you decide to help me.

I will ask you to provide some of your toenails, urine and saliva by swabbing the inside of your cheek with a Q-tip. I will also measure your height, see how much you weigh and take your blood pressure. None of these procedures will hurt you. I will also ask your mother or father to answer some questions about your health, your home life and about the foods that you eat. By being in the study, you will help me find out how much metals are in your body. Then, next year your parents will receive a letter with your personal results.

Your classmates or teacher will not know what your results are. When I tell other people about my study, I will not use your name, and no one will be able to tell who I'm talking about.

Your *[mom/dad]* says it is okay for you to be in my study. But if you don't want to be in the study, you don't have to be. It is up to you to decide. I won't be upset, and no one else will be upset, if you don't want to participate. If you want to be in the study now but change your mind later, that's okay. You can stop at any time. If there is anything you don't understand you should tell me so I can explain it to you.

You can ask me questions about the study. If you have a question later that you don't think of now, you can call me or ask your parents to call or send me an email.

Do you have any questions for me now?

Would you like to be in the study, answer some questions, take your measurements, and blood pressure, and provide some samples?

Yes	No

Name of Child: _____

Parental Permission on File: ☐ Yes ☐ No

Child's Voluntary Response to Participation: ☐ Yes ☐ No

Signature of Researcher: _____ **Date:** _____

Appendix 10: Lifestyle Questionnaire

Pre-Interview Screening Questions

Have you lived in Yellowknife for more than a year? ☐ Yes ☐ No
If no, end survey and thank them for their time as they do not meet the criteria.

Are you an Indigenous member? ☐ No
☐ Yellowknives Dene First Nation
☐ North Slave Métis
☐ Other, specify _____

Participant ID #_____
First Name _____
Last Name _____
Address _____
Postal Code _____
District in which participants home is located:
☐ Range Lake
☐ Frame Lake South
☐ Frame Lake North
☐ Kam Lake
☐ Grace Lake
☐ Con Mine
☐ School Draw
☐ Old Town
☐ Niven
☐ Ndilo
☐ Dettah

PERSONAL INFORMATION

1. a) How old are you? _____
   Enter the answer to the nearest year. Enter 99 if they refuse to answer, and then the survey will end.
   b) What is your date of birth?
   Day _____
   Enter a number between 1 and 31
   Month _____
   Year _____
2. Gender: ☐ M ☐ F ☐ Other

3. A) How many years have you lived in Yellowknife? _____ *Enter answer in years to the nearest whole number.*

   B) How many adults (18 and over) who live in this house lived in Yellowknife for at least one year?

   _____ Record Gender: e.g. 1M, 1F _____

   C) How many children (6-11 years old) living in this house lived in Yellowknife for at least one year?

   _____ Record Gender: e.g. 2M, 1F _____

   D) How many children (12-18 years old) living in this house lived in Yellowknife for at least one year?

   _____ Record Gender: e.g. 2M, 3F _____

NSMA and general Yellowknife resident-specific questions:

How tall are you? _____ (feet, inches)
How much do you weigh? _____ (pounds)

Questionnaire continues for everyone:

For female participants only,

4. Are you pregnant? ☐ Yes ☐ No
5. Are you breastfeeding? ☐ Yes ☐ No

EXPOSURE HISTORY

6. a) Do you currently smoke cigarettes or other tobacco products? ☐ Yes ☐ No

IF Yes:

b) How many cigarettes do you smoke per day? _____

c) How many years have you been smoking? _____

IF No:

d) Did you previously smoke cigarettes or other tobacco products? ☐ Yes ☐ No

e) How many cigarettes did you smoke per day? _____

f) How many years did you smoke? _____

7. What is your main water source for drinking and cooking? ☐ Public water supply (municipal/truck water)
   ☐ Private well or spring
   ☐ Bottled Water
   ☐ Ground Water
   ☐ Raw water (eg river, lake, snow)

8. How many cups of water do you drink per day on average? (Including water used to make coffee/tea, soup. etc. Do not include water in prepared food) _____

9. Do you filter your water, for example with a Brita, or have a filtration system in your home?
☐ Yes ☐ No

10. a) Do you drink water directly from lakes or rivers? ☐ Yes ☐ No
b) Which lakes and rivers do you drink from? ☐ Yellowknife Bay
☐ Yellowknife River
☐ Akaticho Bay
☐ Vee Lake
☐ Walsh Lake
☐ Duck Lake
☐ Banting Lake
☐ Other, please specify _____

11. a) Do you use the nearby waters for other activities such as swimming, playing bathing, etc.?
☐ Yes ☐ No

b) How often do you use the waters recreationally? ☐ More than once a week
☐ Weekly
☐ Monthly
☐ Once every 6 months
☐ Once a year

c) Which waters do you use recreationally? ☐ Yellowknife Bay
☐ Back Bay
☐ Long Lake
☐ Frame Lake
☐ Jackfish Lake
☐ Kam Lake
☐ Akaticho Bay
☐ Vee Lake
☐ Walsh Lake
☐ Duck Lake
☐ Banting Lake
☐ Other, please specify _____

12. a) Do you hunt? ☐ Yes ☐ No

b) If yes to (a), what do you hunt? ☐ Big Game (eg Moose, caribou, bear, etc.)
☐ Small Game (eg Rabbit, beaver, muskrat, etc.)
☐ Birds (eg spruce hen, duck, mallard, geese, etc.)
☐ Other, please specify _____

13. a) Do you eat wild meat? ☐ Yes ☐ No
b) If yes to (a), what kind of meat? ☐ Big Game (eg Moose, caribou, bear, etc.)
☐ Small Game (eg Rabbit, beaver, muskrat, etc.)
☐ Birds (eg spruce hens, ducks, mallards, geese, etc.)
☐ Other, please specify _____

14. a) Do you fish? ☐ Yes ☐ No
b) Where do you fish? ☐ Yellowknife Bay
☐ Back Bay
☐ Long Lake
☐ Frame Lake
☐ Jackfish Lake
☐ Kam Lake
☐ Akaticho Bay
☐ Vee Lake
☐ Walsh Lake
☐ Duck Lake
☐ Banting Lake
☐ Grace Lake
☐ Lower Martin Lake
☐ Other, please specify _____

15. When was your last locally harvested fish meal? ☐ past 3 days
☐ past week
☐ past month
☐ past 6 months
☐ past year
☐ More than a year ago/ Never

16. Do consume locally grown food vegetables and herbs (eg community or home garden)?
☐ Yes ☐ No

17. a. Do you eat locally collected wild berries? ☐ Yes ☐ No
b. Do you eat wild mushrooms? ☐ Yes ☐ No
c. Do you chew spruce gum? ☐ Yes ☐ No
d. Do you apply wild harvest plants on your body? ☐ Yes ☐ No

18. How often do you consume the following foods:

Type of product	At least once per day	At least once per week	At least once per month	Less than once per month	None
a. Fish from store	0	0	0	0	0
b. Shellfish from store (shrimp, lobster, scallops)	0	0	0	0	0
c. Seaweed (including sushi)	0	0	0	0	0
d. Rice and rice products from store	0	0	0	0	0
e. Locally grown rice	0	0	0	0	0

19. a) Do you currently work for the Giant Mine Remediation Project? ☐ Yes ☐ No
    b) Do you work underground in the mines and chambers? ☐ Yes ☐ No
    c) Do you work an administrative or non-mine position (eg office, canteen, custodial service)? ☐ Yes ☐ No
    d) How long have you been working with the Giant Mine Remediation Project? _____

20. a) Have you previously worked at Giant Mine? ☐ Yes ☐ No
    b) Did you work in the roaster, smelter or mill? ☐ Yes ☐ No
    c) Did you work an administrative or non-mine position (eg office, canteen, custodial service)? ☐ Yes ☐ No
    d) How long did you work at Giant Mine? _____

21. a) Have you previously work for Con Mine? ☐ Yes ☐ No
    b) Did you work in the roaster, smelter or mill? ☐ Yes ☐ No
    c) Did you work an administrative or non-mine position (eg office, canteen, custodial service)? ☐ Yes ☐ No
    d) How long did you work at Con Mine: _____

22. Do you or have you worked in the any of the following industries? (Check all that apply)

Industry Type	Never	Currently	Formerly
a. Mining/Smelting (eg copper, lead, cobalt, gold, zinc, silver)	0	0	0
b. Coal Mine/Refinery	0	0	0
c. Saw Mill	0	0	0

d. Diamond Mine	O	O	O
e. Mine remediation other than Giant Mine	O	O	O
f. Armed Forces	O	O	O
g. Glass Manufacturing Industry	O	O	O
h. Cotton fields/orchards	O	O	O
i. Electronics Manufacturing	O	O	O
j. Carpentry (wood cutting)	O	O	O
k. Firefighting	O	O	O
l. Construction (quarry pit, road operations, hurling gravel etc)	O	O	O
m. Mechanic (engine oil, etc)			

23. Do you or have you worked with the following (occupationally and recreationally)?

	Yes	No	Unknown/Can't Recall
a. Wood preservatives	O	O	O
b. Chemical fertilizers	O	O	O
c. Lab/Chemical reagents	O	O	O
d. Pesticides	O	O	O
e. Agricultural chemicals	O	O	O
f. Paints/thinners/Solvents	O	O	O
g. Rat poison	O	O	O

23. a) Were you tested for arsenic in the past in Yellowknife? **O** Yes **O** No

b) If yes, do you still have your result? **O** Yes **O** No

IF yes to 23a, explain to the participant that we are looking into archived content from NWT and ask whether they consent to having us look at their results from past studies (If available). If they agree, have them sign the NWT Archive Consent form. Explain clearly to the participant that we are not sure if their results will be at the NWT Archives but your consent will allow us to check and share the result with you if we should find it.

Thank you for your time and participation.

Appendix 11: Food Frequency Questionnaire

WILD FISH CONSUMPTION

1. a) In the past 12 months, have you eaten any Whitefish? ☐ Yes ☐No
   If answered Yes above, please answer the following:

   b) In the Summer (June-Aug), how many days did you eat Whitefish? _____

   In the Spring (Apr-May), how many days did you eat Whitefish? _____

   In the Winter (Nov-Mar), how many days did you eat Whitefish? _____

   In the Fall (Sept-Oct), how many days did you eat Whitefish? _____

   c) On the days when you ate Whitefish, how much did you usually eat? (*Refer to visual guide*)
   (i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J
   (ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
   ☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

2. a) In the past 12 months, have you eaten any Lake Trout? ☐Yes ☐No
   If answered Yes above, please answer the following:

   b) In the Summer (June-Aug), how many days did you eat Lake Trout? _____

   In the Spring (Apr-May), how many days did you eat Lake Trout? _____

   In the Winter (Nov-Mar), how many days did you eat Lake Trout? _____

   In the Fall (Sept-Oct), how many days did you eat Lake Trout? _____

   c) On the days when you ate Lake Trout, how much did you usually eat? (*Refer to visual guide*)
   (i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J
   (ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
   ☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

3. a) In the past 12 months, have you eaten any Northern Pike (Jackfish)? ☐Yes ☐No
   If answered Yes above, please answer the following:

   b) In the Summer (June-Aug), how many days did you eat Northern Pike? _____

   In the Spring (Apr-May), how many days did you eat Northern Pike? _____

   In the Winter (Nov-Mar), how many days did you eat Northern Pike? _____

In the Fall (Sept-Oct), how many days did you eat Northern Pike? _____

c) On the days when you ate Northern Pike (Jackfish), how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10 ☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

4. a) In the past 12 months, have you eaten any Burbot (Louche) liver? ☐ Yes ☐No

If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Burbot liver? _____

In the Spring (Apr-May), how many days did you eat Burbot liver? _____

In the Winter (Nov-Mar), how many days did you eat Burbot liver? _____

In the Fall (Sept-Oct), how many days did you eat Burbot liver? _____

c) On the days when you ate Burbot liver, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10 ☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

5. a) In the past 12 months, have you eaten any Burbot (Louche)? ☐ Yes ☐No

If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Burbot? _____

In the Spring (Apr-May), how many days did you eat Burbot? _____

In the Winter (Nov-Mar), how many days did you eat Burbot? _____

In the Fall (Sept-Oct), how many days did you eat Burbot? _____

c) On the days when you ate Burbot, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10 ☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

6. a) In the past 12 months, have you eaten any Connie (Inconnu)? ☐ Yes ☐ No

If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Connie? _____

In the Spring (Apr-May), how many days did you eat Connie? _____

In the Winter (Nov-Mar), how many days did you eat Connie? _____

In the Fall (Sept-Oct), how many days did you eat Connie? _____

c) On the days when you ate Connie (Inconnu), how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10 ☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

7. a) In the past 12 months, have you eaten any Pickerel (Walleye)? ☐Yes ☐No

If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Pickerel? _____

In the Spring (Apr-May), how many days did you eat Pickerel? _____

In the Winter (Nov-Mar), how many days did you eat Pickerel? _____

In the Fall (Sept-Oct), how many days did you eat Pickerel? _____

c) On the days when you ate Pickerel (Walleye), how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10 ☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

8. a) In the past 12 months, have you eaten any Grayling (Bluefish)? ☐Yes ☐No

If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Grayling? _____

In the Spring (Apr-May), how many days did you eat Grayling? _____

In the Winter (Nov-Mar), how many days did you eat Grayling? _____

In the Fall (Sept-Oct), how many days did you eat Grayling? _____

c) On the days when you ate Grayling (Bluefish), how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

9. a) In the past 12 months, have you eaten any Longnose Sucker? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Longnose Sucker? _____

In the Spring (Apr-May), how many days did you eat Longnose Sucker? _____

In the Winter (Nov-Mar), how many days did you eat Longnose Sucker? _____

In the Fall (Sept-Oct), how many days did you eat Longnose Sucker? _____

c) On the days when you ate Longnose Sucker, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

Thank you for your time and participation.

Questionnaire continues for Yellowknives Dene

LAND ANIMAL CONSUMPTION

10. a) In the past 12 months, have you eaten any Woodland Caribou? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Woodland Caribou _____

In the Spring (Apr-May), how many days did you eat Woodland Caribou? _____

In the Winter (Nov-Mar), how many days did you eat Woodland Caribou? _____

In the Fall (Sept-Oct), how many days did you eat Woodland Caribou? _____

c) On the days when you ate Woodland Caribou, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

11. a) In the past 12 months, have you eaten any Barrenland Caribou? ☐Yes ☐No
If answered Yes above, please answer the following:

b)In the Summer (June-Aug), how many days did you eat Barrenland Caribou _____

In the Spring (Apr-May), how many days did you eat Barrenland Caribou? _____

In the Winter (Nov-Mar), how many days did you eat Barrenland Caribou? _____

In the Fall (Sept-Oct), how many days did you eat Barrenland Caribou? _____

c) On the days when you ate Barrenland Caribou, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

12. a) In the past 12 months, have you eaten any Moose? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Moose? _____

In the Spring (Apr-May), how many days did you eat Moose? _____

In the Winter (Nov-Mar), how many days did you eat Moose? _____

In the Fall (Sept-Oct), how many days did you eat Moose? _____

c) On the days when you ate Moose, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

13. a) In the past 12 months, have you eaten any Rabbit? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Rabbit? _____

In the Spring (Apr-May), how many days did you eat Rabbit? _____

In the Winter (Nov-Mar), how many days did you eat Rabbit? _____

In the Fall (Sept-Oct), how many days did you eat Rabbit? _____

c) On the days when you ate Rabbit, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

14. a) In the past 12 months, have you eaten any Beaver? ☐ Yes ☐ No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Beaver? _____

In the Spring (Apr-May), how many days did you eat Beaver? _____

In the Winter (Nov-Mar), how many days did you eat Beaver? _____

In the Fall (Sept-Oct), how many days did you eat Beaver? _____

c) On the days when you ate Beaver, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

15. a) In the past 12 months, have you eaten any Muskrat? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Muskrat? _____

In the Spring (Apr-May), how many days did you eat Muskrat? _____

In the Winter (Nov-Mar), how many days did you eat Muskrat? _____

In the Fall (Sept-Oct), how many days did you eat Muskrat? _____

c) On the days when you ate Muskrat, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10

☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

16. a) In the past 12 months, have you eaten any Porcupine? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Porcupine? _____

In the Spring (Apr-May), how many days did you eat Porcupine? _____

In the Winter (Nov-Mar), how many days did you eat Porcupine? _____

In the Fall (Sept-Oct), how many days did you eat Porcupine? _____

c) On the days when you ate Porcupine, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

17. a) In the past 12 months, have you eaten any Bear? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Bear? _____

In the Spring (Apr-May), how many days did you eat Bear? _____

In the Winter (Nov-Mar), how many days did you eat Bear? _____

In the Fall (Sept-Oct), how many days did you eat Bear? _____

c) On the days when you ate Bear, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

BIRD CONSUMPTION

18. a) In the past 12 months, have you eaten any Spruce Hen/Grouse? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Spruce Hen/Grouse? _____

In the Spring (Apr-May), how many days did you eat Spruce Hen/Grouse? _____

In the Winter (Nov-Mar), how many days did you eat Spruce Hen/Grouse? _____

In the Fall (Sept-Oct), how many days did you eat Spruce Hen/Grouse? _____

c) On the days when you ate Spruce Hen/Grouse, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

19. a) In the past 12 months, have you eaten any Ptarmigan? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Ptarmigan? _____

In the Spring (Apr-May), how many days did you eat Ptarmigan? _____

In the Winter (Nov-Mar), how many days did you eat Ptarmigan? _____

In the Fall (Sept-Oct), how many days did you eat Ptarmigan? _____

c) On the days when you ate Ptarmigan, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐Γ01 ☐Γ02 ☐Γ03 ☐Γ04 ☐Γ05 ☐Γ06 ☐Γ07 ☐Γ08 ☐Γ09 ☐Γ10
☐Γ11 ☐Γ12 ☐Γ13 ☐Γ14 ☐Γ15 ☐Γ16

20. a) In the past 12 months, have you eaten any Ducks? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Ducks? _____

In the Spring (Apr-May), how many days did you eat Ducks? _____

In the Winter (Nov-Mar), how many days did you eat Ducks? _____

In the Fall (Sept-Oct), how many days did you eat Ducks? _____

c) On the days when you ate Ducks, how much did you usually eat? (*Refer to visual guide*)

(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J

(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

21. a) In the past 12 months, have you eaten any Canada Goose? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Canada Goose? _____

In the Spring (Apr-May), how many days did you eat Canada Goose? _____

In the Winter (Nov-Mar), how many days did you eat Canada Goose? _____

In the Fall (Sept-Oct), how many days did you eat Canada Goose? _____

c) On the days when you ate Canada Goose, how much did you usually eat? (*Refer to visual guide*)
(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J
(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

22. a) In the past 12 months, have you eaten any Snow Goose? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Snow Goose? _____

In the Spring (Apr-May), how many days did you eat Snow Goose? _____

In the Winter (Nov-Mar), how many days did you eat Snow Goose? _____

In the Fall (Sept-Oct), how many days did you eat Snow Goose? _____

c) On the days when you ate Snow Goose, how much did you usually eat? (*Refer to visual guide*)
(i) Flat size: ☐OV-XS ☐OV-S ☐OV-M ☐OV-L ☐OV-XL ☐OV-J
(ii) Thickness: ☐T01 ☐T02 ☐T03 ☐T04 ☐T05 ☐T06 ☐T07 ☐T08 ☐T09 ☐T10
☐T11 ☐T12 ☐T13 ☐T14 ☐T15 ☐T16

PLANTS

23. a) In the past 12 months, have you drank any Labrador Tea? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you drink Labrador Tea? _____

In the Spring (Apr-May), how many days did you drink Labrador Tea? _____

In the Winter (Nov-Mar), how many days did you drink Labrador Tea? _____

In the Fall (Sept-Oct), how many days did you drink Labrador Tea? _____

c) On the days when you drank Labrador Tea, how much did you usually drink? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

24. a) In the past 12 months, have you eaten any Low bush (Grey) Blueberries? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Low bush Blueberries? _____

In the Spring (Apr-May), how many days did you eat Low bush Blueberries? _____

In the Winter (Nov-Mar), how many days did you eat Low bush Blueberries? _____

In the Fall (Sept-Oct), how many days did you eat Low bush Blueberries? _____

c) On the days when you ate Low bush (Grey) Blueberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

25. a) In the past 12 months, have you eaten any High bush (Black) Blueberries? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat High bush Blueberries? _____

In the Spring (Apr-May), how many days did you eat High bush Blueberries? _____

In the Winter (Nov-Mar), how many days did you eat High bush Blueberries? _____

In the Fall (Sept-Oct), how many days did you eat High bush Blueberries? _____

c) On the days when you ate High bush (Black) Blueberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

26. a) In the past 12 months, have you eaten any Cranberries? ☐ Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Cranberries? _____

In the Spring (Apr-May), how many days did you eat Cranberries? _____

In the Winter (Nov-Mar), how many days did you eat Cranberries? _____

In the Fall (Sept-Oct), how many days did you eat Cranberries? _____

c) On the days when you ate Cranberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

27. a) In the past 12 months, have you eaten any Gooseberries (Green)? ☐ Yes ☐ No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Gooseberries (Green)? _____

In the Spring (Apr-May), how many days did you eat Gooseberries (Green)? _____

In the Winter (Nov-Mar), how many days did you eat Gooseberries (Green)? _____

In the Fall (Sept-Oct), how many days did you eat Gooseberries (Green)? _____

c) On the days when you ate Gooseberries (Green), how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

28. a) In the past 12 months, have you eaten any Gooseberries (Purple)? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Gooseberries (Purple)? _____

In the Spring (Apr-May), how many days did you eat Gooseberries (Purple)? _____

In the Winter (Nov-Mar), how many days did you eat Gooseberries (Purple)? _____

In the Fall (Sept-Oct), how many days did you eat Gooseberries (Purple)? _____

c) On the days when you ate Gooseberries (Purple), how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

29. a) In the past 12 months, have you eaten any Blackberries? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Blackberries? _____

In the Spring (Apr-May), how many days did you eat Blackberries? _____

In the Winter (Nov-Mar), how many days did you eat Blackberries? _____

In the Fall (Sept-Oct), how many days did you eat Blackberries? _____

c) On the days when you ate Blackberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

30. a) In the past 12 months, have you eaten any Wild Raspberries? ☐Yes ☐No
If answered Yes above, please answer the following:

b)In the Summer (June-Aug), how many days did you eat Wild Raspberries? _____

In the Spring (Apr-May), how many days did you eat Wild Raspberries? _____

In the Winter (Nov-Mar), how many days did you eat Wild Raspberries? _____

In the Fall (Sept-Oct), how many days did you eat Wild Raspberries? _____

c) On the days when you ate Wild Raspberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

31. a) In the past 12 months, have you eaten any Wild Strawberries? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Wild Strawberries? _____

In the Spring (Apr-May), how many days did you eat Wild Strawberries? _____

In the Winter (Nov-Mar), how many days did you eat Wild Strawberries? _____

In the Fall (Sept-Oct), how many days did you eat Wild Strawberries? _____

c) On the days when you ate Wild Strawberries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

32. a) In the past 12 months, have you eaten any Cloud Berries (Knuckleberries)? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Cloud Berries (Knuckleberries)?
_____

In the Spring (Apr-May), how many days did you eat Cloud Berries (Knuckleberries)? _____

In the Winter (Nov-Mar), how many days did you eat Cloud Berries (Knuckleberries)? _____

In the Fall (Sept-Oct), how many days did you eat Cloud Berries (Knuckleberries)? _____

c) On the days when you ate Cloud Berries (Knuckleberries), how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

33. a) In the past 12 months, have you eaten any Red Currants? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Red Currants? _____

In the Spring (Apr-May), how many days did you eat Red Currants? _____

In the Winter (Nov-Mar), how many days did you eat Red Currants? _____

In the Fall (Sept-Oct), how many days did you eat Red Currants? _____

c) On the days when you ate Red Currants, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

34. a) In the past 12 months, have you eaten any Black Currants? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Black Currants? _____

In the Spring (Apr-May), how many days did you eat Black Currants? _____

In the Winter (Nov-Mar), how many days did you eat Black Currants? _____

In the Fall (Sept-Oct), how many days did you eat Black Currants? _____

c) On the days when you ate Black Currants, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

35. a) In the past 12 months, have you eaten any Saskatoon Berries? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Saskatoon Berries? _____

In the Spring (Apr-May), how many days did you eat Saskatoon Berries? _____

In the Winter (Nov-Mar), how many days did you eat Saskatoon Berries? _____

In the Fall (Sept-Oct), how many days did you eat Saskatoon Berries? _____

c) On the days when you ate Saskatoon Berries, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

36. a) In the past 12 months, have you eaten any Rosehips? ☐Yes☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Rosehips? _____

In the Spring (Apr-May), how many days did you eat Rosehips? _____

In the Winter (Nov-Mar), how many days did you eat Rosehips? _____

In the Fall (Sept-Oct), how many days did you eat Rosehips? _____

c) On the days when you ate Rosehips, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

37. a) In the past 12 months, have you eaten any Wild Peppermint? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Wild Peppermint? _____

In the Spring (Apr-May), how many days did you eat Wild Peppermint? _____

In the Winter (Nov-Mar), how many days did you eat Wild Peppermint? _____

In the Fall (Sept-Oct), how many days did you eat Wild Peppermint? _____

c) On the days when you ate Wild Peppermint, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

38. a) In the past 12 months, have you eaten any wild mushrooms? ☐Yes☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat wild mushrooms? _____

In the Spring (Apr-May), how many days did you eat wild mushrooms? _____

In the Winter (Nov-Mar), how many days did you eat wild mushrooms? _____

In the Fall (Sept-Oct), how many days did you eat wild mushrooms? _____

c) On the days when you ate wild mushrooms, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

39. a) In the past 12 months, have you eaten any Wild Greens? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Wild Greens? _____

In the Spring (Apr-May), how many days did you eat Wild Greens? _____

In the Winter (Nov-Mar), how many days did you eat Wild Greens? _____

In the Fall (Sept-Oct), how many days did you eat Wild Greens? _____

c) On the days when you ate Wild Greens, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

40. a) In the past 12 months, have you eaten any Wild Onions? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Wild Onions? _____

In the Spring (Apr-May), how many days did you eat Wild Onions? _____

In the Winter (Nov-Mar), how many days did you eat Wild Onions? _____

In the Fall (Sept-Oct), how many days did you eat Wild Onions? _____

c) On the days when you ate Wild Onions, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

41. a) In the past 12 months, have you eaten any Wild Rhubarb? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Wild Rhubarb? _____

In the Spring (Apr-May), how many days did you eat Wild Rhubarb? _____

In the Winter (Nov-Mar), how many days did you eat Wild Rhubarb? _____

In the Fall (Sept-Oct), how many days did you eat Wild Rhubarb? _____

c) On the days when you ate Wild Rhubarb, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

42. a) In the past 12 months, have you chewed any Spruce Gum? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you chew Spruce Gum? _____

In the Spring (Apr-May), how many days did you chew Spruce Gum? _____

In the Winter (Nov-Mar), how many days did you chew Spruce Gum? _____

In the Fall (Sept-Oct), how many days did you chew Spruce Gum? _____

c) On the days when you chewed Spruce Gum, how much did you usually chew? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

43. a) In the past 12 months, have you eaten any Birch Sap? ☐Yes ☐No
If answered Yes above, please answer the following:

b) In the Summer (June-Aug), how many days did you eat Birch Sap? _____

In the Spring (Apr-May), how many days did you eat Birch Sap? _____

In the Winter (Nov-Mar), how many days did you eat Birch Sap? _____

In the Fall (Sept-Oct), how many days did you eat Birch Sap? _____

c) On the days when you ate Birch Sap, how much did you usually eat? (*Refer to visual guide*)

☐ ¼ Mug ☐½ Mug ☐ ¾ Mug ☐1 Mug ☐1 ½ Mugs ☐1 ¾ Mugs ☐2 Mugs

Thank you for your time and participation.

Appendix 12: Medical History Questionnaire (YKDFN)

MEDICAL HISTORY

Now we have a series of questions to ask about your health.

1. a) Are you currently taking medication? Yes ☐ No ☐
   b) If yes, please list and state reason.

Medication	Yes	No
Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD) ***Peptic ulcers and GORD; such as proton pump inhibitors (PPIs)***	0	0
Beta-blocking agents ***High blood pressure, heart failure, angina (chest pain)***	0	0
Ace inhibitors, plain ***Heart failure, high blood pressure***	0	0
Liquid-modifying agents, plain ***High cholesterol; such as statins***	0	0
Systemic use hormonal contraceptives ***Pregnancy prevention; such as oral and patch contraceptives***	0	0
Estrogens ***Manage menopausal symptoms/type of hormone replacement therapy (HRT)***	0	0
Thyroid ***Low thyroid function (Hypothyroidism)***	0	0
Other analgesics and anti-pyretics ***Pain; prevention of stroke/heart attack***	0	0
Anti-depressants ***Mood disorders and depression; such as anti-depressants including serotonin reuptake inhibitors***	0	0
ADHD psycho-stimulants and nootropics ***Symptoms related to attention deficit and hyperactivity disorder (ADHD)***	0	0
Adrenergics, inhalants ***Treatment of asthma, chronic bronchitis, emphysema, etc.; brocodilators***	0	0

c) Enter any other relevant details _____

Have you experienced any of the following symptoms? (Check all that apply)

2. *Dermatological*

Have you been diagnosed or suffer from dermatological (skin conditions)? ☐ Yes ☐No

If yes, I am now going to read through a series of dermatological (skin) conditions and I would like you to tell me if you have experienced any of them.

a. Hyperkeratosis ("Thickening of the skin") ☐ Yes ☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

b) Hyperkeratotic lesions ("wart-like" lesions, corns") ☐ Yes ☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

c) Hyperpigmentation/Melanosis (Dark skin patches) ☐ Yes ☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

d) Hypopigmentation (Light skin patches) ☐ Yes ☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

e) Leucomelanosis (Spotted pigmentation) ☐ Yes☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

f) Mees' Lines (White lines across nails) ☐ Yes ☐No
Where on your body
When did it start? (*Enter year)* _____
Where on your body did it occur?
☐ Head and neck
☐ Arms or hands
☐ Trunk
☐ Groin
☐ Legs or feet
Is it ongoing? ☐ Yes ☐No
When did it end? *(Enter year)* _____
Any other details of note _____

3. *Respiratory*

Have you been diagnosed or suffer from respiratory (breathing) conditions? ☐ Yes ☐No

If yes, I am now going to read through a series of respiratory (breathing) conditions and I would like you to tell me if you have experienced any of them.

a) Chronic cough ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

b) Chronic bronchitis ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

c) Chest sounds in lungs ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

d) Conjunctival congestion ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

e) Difficult or laboured breathing ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

f) Cough hemoptysis (coughing up blood) ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

g) Pulmonary edema

☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

4. *Cardiovascular*

Have you been diagnosed or suffer from cardiovascular (heart) conditions? ☐ Yes ☐No

If yes, I am now going to read through a series of cardiovascular (heart) conditions and I would like you to tell me if you have experienced any of them.

a) Artherosclerosis ☐ Yes ☐No

When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

b) Hypertension ☐ Yes ☐No

When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

c) Ischemic Heart Disease ☐ Yes ☐No

When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

d) Angina ☐ Yes ☐No

When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

e) Myocardial infraction (heart attack)

☐ Yes ☐No

When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

f) Arrythmia

☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

g) Blackfoot Disease (Foot gangrene)

☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

h) Peripheral Arterial/Vascular Disease

☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

i) Raynaud's disease (some areas of your body, such as your fingers and toes, feel numb and cold in response to cold temperatures or stress)

5. *Hematological*

Have you been diagnosed or suffer from hematological (blood) conditions? ☐ Yes ☐No

If yes, I am now going to read through a series of hematological (blood) conditions and I would like you to tell me if you have experienced any of them

a) Iron deficiency Anemia (Pernicious Anemia)
When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

b) Aplastic Anemia
When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

c) Abnormal bone marrow
When was it diagnosed? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

6. *Hepatic, Renal*

Have you been diagnosed or suffer from liver or kidney conditions? ☐ Yes ☐No

If yes, I am now going to read through a series of liver or kidney conditions and I would like you to tell me if you have experienced any of them:

a) Hepatic jaundice

☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

b) Cirrhosis ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

c) Hepatomegaly ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

d) Ascites ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

e) Difficulty with urination or dysuria (painful urination) ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

f) Blood in urine ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

7. *Neurological*

Have you been diagnosed or suffer from brain or sensory conditions? ☐ Yes ☐No

If yes, I am now going to read through a series of brain or sensory conditions and I would like you to tell me if you have experienced any of them:

a) Migraines ☐ Yes ☐No

In the past year, approximately how many migraines have you had? _____

How bad was the worst migraine?

☐ No pain
☐ Mild pain
☐ Moderate pain
☐ Severe pain
☐ Very severe pain
☐ Worst pain imaginable

Any other details to note _____

b) Paresthesia ("Pins and needles") ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

c) Peripheral sensory neuropathy (loss of sensation in hands or feet) ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

d) Peripheral motor neuropathy (Weakness or loss of movement in hands or feet) ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

e) Muscle spasms ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

f) Loss in taste of smell ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

f) Muscle weakness or tenderness ☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

8. *Cancer*

Have you been diagnosed with cancer? ☐ Yes ☐No

I am now going to read a series of types of cancer and I would like you to tell me if you have been diagnosed with any of them:

☐ Bladder cancer
☐ Liver cancer
☐ Skin cancer
☐ Colon cancer
☐ Leukemia

When were you first diagnosed? (*Enter year)* _____

Are you currently in remission? ☐ Yes ☐No

Any other details of note _____

9. *Other*

I am now going to read through a series of various conditions and I would like you to tell me if you have experienced any of them:

a) Gastroenteritis
☐ Yes ☐No

When did it start? (*Enter year)* _____

Is it ongoing? ☐ Yes ☐No

When did it end? *(Enter year)* _____

Any other details of note _____

b) Diabetes Mellitus
What type of diabetes do you have? ☐ Type 1 ☐Type 2 ☐ Don't know

When were you diagnosed? *(Enter year*) _____

Any other details of note _____

c) Thyroid Disease
When were you diagnosed? *(Enter year*) _____

Any other details of note _____

We would now like to measure your height, and take your weight and blood pressure.

10. Height: _____ cm
Round to the nearest cm

11. Weight: _____ kg
Round to the nearest kg

12. Systolic blood pressure: _____
Diastolic blood pressure: _____

Thank you for your time and participation.

Appendix 13: Exposure guidance values for disease end points from chronic inorganic arsenic exposure

Critical Dose	Exposure Type	Endpoint	RfD	Uncertainty Factors	Reference
NOAEL: 0.009 mg/L converted to 0.0008 mg/kg-day LOAEL: 0.17 mg/L converted to 0.014 mg/kg-day	Drinking water	Hyperpigmentation, keratosis and possible vascular complications	0.0003 µg/g-day	3	EPA-IRIS (2005)
NOAEL: 0.009 mg/L converted to 0.0008 mg/kg-day	Drinking water, Soil	Dermal Effects	0.0003µg /g-day	10	ATSDR (2007)
Risk-specific exposure level ($1x10^{-4}$ cancer risk): 5.6×10^{-5} mg/kg-d	Drinking water	Lung, bladder and liver cancers	NA	NA	Health Canada Water Quality and Health Bureau (2006)
Risk-specific exposure level ($1x10^{-4}$ cancer risk): 3.3×10^{-3} mg/kg-d	Drinking water, Occupational	Bladder cancer	NA	NA	Health Canada, Foods Division (2007)
Risk-specific exposure level ($1x10^{-4}$ cancer risk): 3.3×10^{-7} mg/kg-d	Drinking water	Lung and bladder cancers	NA	NA	US EPA (2008)

RfD: Reference dose, for chronic exposure
NOAEL: No observable adverse effect level
LOAEL: Lowest observable adverse effect level
iAs: Inorganic arsenic

Appendix 14: Example of summary of data results as per CHMS

	n	% <LOD	A.M. 95%CI	G.M. 95%CI	10th 95%CI	25th 95%CI	50th 95%CI	75th 95%CI	95th 95%CI
Total, age 3-79									
3-5									
6-11									
12-19									
20-39									
40-59									
60-79									

Table will consist of arithmetic and geometric means and selected percentiles of biomarker concentrations (μg/L) for the Yellowknife population aged 3-79 years (CHMS, 2013).

% <LOD: Percentage below level of detection
A.M: Arithmetic mean
G.M: Geometric mean
CI: Confidence interval