Appendix H – Laboratory Analysis Plan

Description of Laboratory Analysis

All assays of biological specimen will be determined by the Centre de toxicologie du Québec (CTQ) of L'Institut national de santé publique du Québec (INSPQ). The laboratory is accredited under ISO 17025 and uses numerous external quality control programs, including the German External Quality Assurance Scheme (EQAS) and Centre for Disease Control's (CDC) Lead and Multi-element Proficiency Testing (LAMP). While serving as the reference laboratory for human toxicology in the province of Quebec, it also collaborates on a number of national and international biomonitoring studies such as the Canadian Health Measures Study (CHMS) and the Maternal Infant Research on Environmental Contaminants (MIREC).

Analytical Methods

The analytic method of choice for chemicals in biological fluids is dependent on the specific chemical of interest. The method chosen for a particular study balances the availability of established reference levels with sensitivity of detection and experience. Under the direction of CTQ, the current Follow-up *Evaluation of Lead Exposure in Children (under 7) in Flin Flon, Manitoba and Creighton, Saskatchewan*, uses blood samples to estimate internal exposure of study participants. The biological samples will be analyzed using inductively coupled plasma with detection by mass spectrometry (ICP-MS). The specific analytic methods to be undertaken and respective limits of quantification for each of these assays are reported in Table 1 below.

Table 1: Overview of biomarker analyses

Biomarker	***Analytic method***	***Detection limit***	***Reproducibility***
Blood lead	ICP-MS	0.001 µmol/L	~ 3% (0.3 µmol/L)

While details specific laboratory procedures are proprietary property of CTQ, the following laboratory protocols will be used in the analysis.

- Analysis of lead in blood will be conducted according to protocol *"Analytical method for the determination of metals in blood, serum or plasma by inductively coupled plasma mass spectrometry*" protocol reference number M-557.

Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a sensitive technique for the multi-element analysis of trace elements in solution. ICP-MS combines the strengths of two established technologies: 1) the ion source (or ICP), a well proven analytical tool that operates in excess of 6000 degrees Kelvin, and 2) a quadrapole mass spectrometer that acts as a detector and separates the metal elements and their isotopes so they can be individually measured.

All determinations using ICP-MS are to be conducted using the Perkin-Elmer SCIEX - ELAN 6000. Diluted urine samples are converted into an aerosol by using an argon nebulizer flow within a spray chamber. A portion of the aerosol is transported through the spray chamber and then through the central channel of the plasma, where it is raised to temperatures of 6000K by the ICP torch. The increase in temperature dries the sample to a solid and then to a gas. The thermal energy atomizes and ionizes the sample. Once inside the mass

spectrometer, the ions pass through the ion optics, then through the mass-analyzing quadrupole before being detected as they strike the surface of the detector. Signals resulting from the detection of the ions are processed into digital information that is used to indicate the intensity of the ions and subsequently the concentration of the element such as lead.

Quality Control

For each series, the control samples will be analyzed as follows:

- Calibration curve at several levels
- Reference materials
- Duplicate intra-series (a random sample analyzed 2 times in one series of analysis)
- Duplicate inter-series (a random sample analyzed 2 times on 2 different sets of analysis)
- White reactive
- Sample added (a random sample and enriched elements of interest.

Reference materials used in this study come from the programs of comparisons interlaboratory headed the Laboratory of Human Toxicology / INSPQ. These materials were validated according to pre-established protocols and complying with ISO 17025. Reference materials and certified reference materials from outside agencies recognized. When a series of tests is completed, the technologist will check the raw data generated by the device, the stability of readings and the results of reference materials. For a series to be accepted, the results of reference materials must be within 2 standard deviations of the target value. In cases where these criteria are not met, the analysis is to be repeated. In general, the coefficients of variation of results are of the order of 5% on all tests.