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Documentation for Laboratory Results

Laboratory 6 - Heavy Metals

(1) Documentation File Date – March 17, 2005

(2) Documentation File Name – Laboratory 6 HM- Urinary Barium, Beryllium, Cadmium, Cobalt, Cesium, Molybdenum, Lead, Platinum, Antimony, Thallium, Tungsten, and Uranium

(3) Survey Years Included in this File Release – 2001–2002

(4) Component Description

4.1 Urinary Barium, Beryllium, Cadmium, Cobalt, Cesium, Molybdenum, Lead, Platinum, Antimony, Thallium, Tungsten, and Uranium

Trace metals have been associated with adverse health effects in occupational studies or laboratory studies, but have not been monitored in general population groups.

Information on levels of exposure to these compounds is essential to determine the need for regulatory mechanisms to reduce the levels of hazardous pollutants to which the general population is exposed and to establish population-based reference intervals for several potentially toxic metals.

(5) Sample Description:

5.1 Eligible Sample

Participants aged 6 years and older who met the subsample requirements and who did not meet any of the exclusion criteria composed the eligible sample.

(6) Description of the Laboratory Methodology

6.1 Urinary Barium, Beryllium, Cadmium, Cobalt, Cesium, Molybdenum, Lead, Platinum, Antimony, Thallium, Tungsten and Uranium

Inductively coupled plasma-mass spectrometry (ICP-MS) is a multi-element analytical technique.[1] Liquid samples are introduced into the ICP through a nebulizer and spray chamber carried by a flowing argon stream. By coupling radio frequency power into flowing argon, a plasma is created in which the predominant species are positive argon ions and electrons. The sample passes through a region of the plasma with a temperature of 6000–8000 K. The thermal energy atomizes the sample and then ionizes the atoms. The ions, along with the argon, enter the mass spectrometer through the interface that separates the ICP, which operates at atmospheric pressure, from the mass spectrometer, which operates

at a pressure of 10^{-6} torr. The mass spectrometer permits detection of ions at each mass in rapid sequence, allowing individual isotopes of an element to be determined. Electrical 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. A total of 15 elements, including Be, Mn, Co, Ni, Mo, Sn, Sb, Cs, Ba, W, Pt, Tl, and Pb are measured in urine by ICP-MS based on the method by Kevin J. Mulligan et al.[2] Urine samples are diluted 1+9 with 2% v/v double-distilled concentrated nitric acid (GFS Chemicals Inc., Columbus, OH) containing both iridium and rhodium for multi-internal standardization. This procedure may be used for all 15 elements or subsets of the 15 elements.

This method is used to achieve rapid and accurate quantification of multiple elements of toxicological and nutritional interest. The method is sensitive enough to be used to rapidly screen urine specimens from subjects suspected of exposure to a number of important toxic elements or to evaluate environmental or other non-occupational exposure to these same elements.

6.2 ***Special note regarding urine cadmium***

Urine cadmium levels are corrected for interference from molybdenum oxide. The variable name for the corrected cadmium levels is URDUCD. The formula for the correction is:

URDUCD = URXUCD – [(0.00175* URXUMO) – 0.0136]

where URXUCD is the original value for the cadmium result.

Corrected values that are less than zero are recoded to equal zero. If the result for urine molybdenum is missing, then the result for the corrected cadmium result is also missing.

The corrected data set also includes a variable URDUCDLC to indicate which results were below the limit of detection. For results below the limit of detection, the corrected value was calculated using the detection limit for urinary cadmium divided by the square root of two (value = 0.04).

See below for further explanation of this correction:

6.3 Effect of Molybdenum Oxide on Urine Cadmium Results

The ICP-MS method for the determination of urine cadmium has not been corrected for a possible interference from molybdenum oxide, MoO. Because the historical Proficiency Testing (PT) results for urine Cd were well within expected ranges and no consistent bias was observed with these PT samples, including several years of challenges, it was thought that, at typical biological molybdenum levels and typical instrumental oxide levels, the interference would not be significant. Upon investigation with over 6000 NHANES samples analyzed, we were able to see a possible effect on the urine Cd results when the results for the urine Cd versus Mo concentration were plotted. This effect cannot be easily seen with a few hundred sample results. Upon further investigation, we determined that the historical NHANES urine Cd results were biased high. For example, a 1st order approximation of the effect of this interference was determined to be 0.33 µg/L (at the 50th percentile) for urine Cd without correcting for the MoO interference versus 0.19 µg/L with the correction. Therefore, we investigated how best to implement a revised analytical method to eliminate

this interference. In addition, until DLS had received and implemented some new ICP-MS technology, we could not eliminate this interference using the traditional ICP-MS technologies. We have recently implemented this new technology (Dynamic Reaction Cell technology [DRC]) and have been able to develop a revised analytical method that allows for correction of this MoO interference.

A method comparison was performed using 208 samples that included the typical range of Cd and Mo concentrations in urine. The results are shown in Figure 1, where ($Cd_{Std\ Method}$ – $Cd_{Corrected\ Method}$) is plotted versus the urine molybdenum concentration. $Cd_{Std\ Method}$ is the non-DRC method and $Cd_{Corrected\ Method}$ is the DRC method. The best fit regression line had an $r^2 = 0.81$ and is given by Equation (1):

$$(Cd_{Std\ Method} - Cd_{Corrected\ Method}) = 0.00175\ (Mo) – 0.01360 \quad (1)$$

Equation (2) is the adjustment equation used to correct the Standard Method results to the new Corrected method (the new DRC method).

$$Cd_{Corrected\ Method} = Cd_{Std\ Method} – (0.00175 * (Mo) + 0.01360\ UCD_{Corrected\ Method}$$
$$= UCd_{Std\ Method} – (0.00175 * (UMO) + 0.01360 \quad (2)$$

(7) Laboratory Quality Control and Monitoring

Urine specimens are processed, stored, and shipped to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for analysis.

Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM). Vials are stored under appropriate frozen (–20°C) conditions until they are shipped to National Center for Environmental Health for testing.

(8) Data Processing and Editing

Automated data collection procedures for the survey were introduced in NHANES 1999. In the mobile examination centers (MECs) and analytical laboratories, data for the laboratory component is recorded directly onto a computerized data collection form. The system is centrally integrated and it allows for ongoing monitoring of much of the data. While the complete blood count and pregnancy analyses are performed in the MEC laboratory, most analyses are conducted elsewhere by approximately 21 laboratories across the United States.

Guidelines have been developed that provide standards for naming variables, filling missing values, and handling missing records. NCHS staff, assisted by contract staff, has developed data-editing specifications that check data sets for valid codes, ranges, and skip pattern consistencies and examine the consistency of values between interrelated variables. Comments have been reviewed and recoded. NCHS staff verifies extremely high and low

values whenever possible, and numerous consistency checks are performed. Nonetheless, users should examine the range and frequency of values before analyzing data.

For laboratory tests with a lower detection limit, results below the lower detection limit are replaced with a value equal to the detection limit divided by the square root of two. This value has been created to help the user distinguish a nondetectable laboratory test result from a measured laboratory test result.

(9) Data Access:

All data are publicly available.

(10) Analytic Notes for Data Users:

10.1 Urinary Barium, Beryllium, Cadmium, Cobalt, Cesium, Molybdenum, Lead, Platinum, Antimony, Thallium, Tungsten, and Uranium

Measures of this urinary multi-analyte profile are assessed in participants aged 6 years and over on a randomly selected 1/3 subsample. Specific sample weights for this subsample are included in this data file and should be used when analyzing these data. **Read the Special Sample Weights for this Dataset section below before beginning analysis.**

The dataset includes 2-year and 4-year subsample weights. The 4-year weights should be used if these 2001–2002 data are combined with 1999–2000 data. The 1999–2000 data files have been updated to include the subsample 4-year weights. The recommended procedure for variance estimation requires use of stratum and PSU variables (SDMVSTRA and SDMVPSU, respectively), which are included in the demographic data file for each data release. For further information, see the NHANES Analytic Guidelines, June 2004 version at: http://www.cdc.gov/nchs/data/nhanes/nhanes_general_guidelines_june_04.pdf

(11) References

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