National Health and Nutrition Examination Survey

2017-March 2020 Data Documentation, Codebook, and Frequencies

Volatile Organic Compound (VOC) Metabolites II - Urine (P_UVOC2)

Data File: P_UVOC2.xpt

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Component Description

The NHANES program suspended field operations in March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic. As a result, data collection for the NHANES 2019-2020 cycle was not completed and the collected data are not nationally representative. Therefore, data collected from 2019 to March 2020 were combined with data from surplus urine samples from the NHANES 2017-2018 cycle to form a nationally representative sample of NHANES 2017-March 2020 pre-pandemic data. These data are available to the public. Please refer to the Analytic Notes section for more details on the use of the data.

Assessing human benzene exposure is of public health significance. Exposure is associated with leukemia and other numerous health risks (Bahadar et. al., 2014; Smith, 2010), and people may be exposed to benzene from numerous sources, including tobacco smoke (Smith, 2010; Talhout et. al., 2006), e-cigarette aerosol (Behar et. al., 2018; Pankow et. al., 2017), automobile exhaust, and industrial applications (Smith, 2010).

VOCs can be metabolized prior to urinary excretion, so VOC exposure can be assessed by measuring their urine metabolites. An analytical method was developed to measure metabolites of benzene (trans,trans-Muconic acid [URXMUCA]; N-Acetyl-S-phenyl-L-cysteine [URXPHMA]), which will greatly improve our understanding of the extent of exposure to these selected VOCs.

Eligible Sample

All examined participants aged 3 to 5 years and participants aged 6 years and older from a one-third subsample in the NHANES 2017-March 2020 pre-pandemic sample were eligible.

Description of Laboratory Methodology

This method is a quantitative procedure to measure urinary metabolites of benzene using ultra-performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry (UPLC-ESI-MS/MS). Sample preparation involves 1:10 dilution of 50 µL urine samples in ammonium formate buffer, pH 2.9. Chromatographic separation of each prepared urine specimen is achieved by using a Waters Acquity UPLC HSS fluoro-phenyl (PFP) column using a mobile phase A (0.02% formic acid) and a mobile phase B (methanol). The eluate from the column is ionized using electrospray ionization, which is used to generate and transmit ions into the mass spectrometer. Comparison of relative response factors (ratio of native analyte to stable isotope-labeled internal standard) with known standard concentrations yields individual analyte concentrations in each sample (Bhandari et. al., 2019).

The VOC Metabolites II dataset was produced by applying an improved method for measuring N-Acetyl-S-phenyl-L-cysteine (PHMA). NHANES cycle 2015-2016 and prior measured PHMA (NHANES variable URXPMA, dataset UVOC_I) in urine samples at neutral pH. Conversely, NHANES cycle 2017-March 2020 measured PHMA (NHANES variable URXPHMA) in urine samples prepared at pH 2.9. This acid treatment converts the PHMA precursor, i.e., pre-PHMA to PHMA; thus the new method quantifies both free PHMA and PHMA formed from the acid dehydration of pre-PHMA (Bhandari et. al., 2019). This new PHMA measure

more accurately assesses benzene exposure (Sterz et. al., 2010). The PHMA results reported from NHANES 2017-March 2020 pre-pandemic data (URXPHMA) should not be directly compared to PHMA (URXPMA) reported in previous NHANES analyses (Tevis et. al., 2020).

Refer to the Laboratory Method Files section for a detailed description of the laboratory methods used.

Laboratory Method Files

Urinary metabolites of Benzene, Furfural, 5-Hydroxymethylfurfural, and N-Methyl-2-pyrrolidone Laboratory Procedure Manual (2017-2018) (September 2022)

Urinary metabolites of Benzene, Furfural, 5-Hydroxymethylfurfural, and N-Methyl-2-pyrrolidone Laboratory Procedure Manual (2019-2020) (September 2022)

Laboratory Quality Assurance and Monitoring

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

Detailed instructions on specimen collection and processing are discussed in the 2017-2018 and 2019-2020 NHANES Laboratory Procedures Manuals (LPM). Vials are stored under appropriate frozen (–30°C) conditions until they are shipped to National Center for Environmental Health for testing.

The NHANES quality assurance and quality control (QA/QC) protocols meet the 1988 Clinical Laboratory Improvement Amendments mandates. Detailed QA/QC instructions are discussed in the NHANES LPM.

Mobile Examination Centers (MECs)

Laboratory team performance is monitored using several techniques. NCHS and contract consultants use a structured competency assessment evaluation during visits to evaluate both the quality of the laboratory work and the QC procedures. Each laboratory staff member is observed for equipment operation, specimen collection and preparation; testing procedures and constructive feedback are given to each staff member. Formal retraining sessions are conducted annually to ensure that required skill levels were maintained.

Analytical Laboratories

NHANES uses several methods to monitor the quality of the analyses performed by the CDC and contract laboratories. In the MEC, these methods include performing blind split samples collected during “dry run” sessions. In addition, contract laboratories randomly perform repeat testing on 2% of all specimens.

NCHS developed and distributed a QC protocol for all CDC and contract laboratories, which outlined the use of Westgard rules (Westgard, et al., 1981) when testing NHANES specimens. Progress reports containing any problems encountered during shipping or receipt of specimens, summary statistics for each control pool, QC graphs, instrument calibration, reagents, and any special considerations are submitted to NCHS quarterly. The reports are reviewed for trends or shifts in the data. The laboratories are required to explain any identified areas of concern.

All QC procedures recommended by the manufacturers were followed. Reported results for all assays meet the Division of Laboratory Sciences’ QA/QC performance criteria for accuracy and precision, similar to the Westgard rules (Caudill et al., 2008).

Data Processing and Editing

The data were reviewed. Incomplete data or improbable values were sent to the performing laboratory for confirmation.

Analytic Notes

The COVID-19 pandemic required suspension of NHANES 2019-2020 field operations in March 2020 after data were collected in 18 of the 30 survey locations in the 2019-2020 sample. Data collection was cancelled for the remaining 12 locations. Because the collected data from 18 locations were not nationally representative, these data were combined with data from surplus specimens from the previous cycle (2017-2018) to create a 2017-March 2020 pre-pandemic data file. A special weighting process was applied to the 2017-March 2020 pre-pandemic data file. The resulting sample weights in the present file should be used to calculate estimates from the combined cycles. These sample weights are not appropriate for independent analyses of the 2019-2020 data and will not yield nationally representative results for either the 2017-2018 data alone or the 2019-March 2020 data alone. Please refer to the NHANES website for additional information for the NHANES 2017-March 2020 pre-pandemic data, and for the previous 2017-2018 public use data file with specific weights for that 2-year cycle.

Refer to the 2017-2018 and 2019-2020 Laboratory Data Overviews for general information on NHANES laboratory data.

There are over 800 laboratory tests performed on NHANES participants. However, not all participants provided biospecimens or enough volume for all the tests to be performed. Additionally, availability of specimens for surplus projects is lower than for other laboratory tests performed on NHANES participants. The specimen availability can also vary by age or other population characteristics. Analysts should evaluate the extent of missing data in the dataset related to the outcome of interest as well as any predictor variables used in the analyses to determine whether additional re-weighting for item non-response is necessary.

Please refer to the NHANES Analytic Guidelines and the on-line NHANES Tutorial for details on the use of sample weights and analytic issues.

Subsample Weights

The analytes included in this dataset were measured in all examined participants aged 3-5 years, and in a one-third subsample of participants 6 years and older. Special sample weights are required to analyze these data properly. Specific sample weights for this subsample, WTVOC2PP, are included in this data file and should be used when analyzing these data. The sample weights created for this file used the examination sample weight, i.e., WTMECPRP, as the base weight. The base weight was adjusted for additional nonresponse to these lab tests and re-poststratified to the population total using sex, age, and race/ethnicity. Participants who were part of the eligible population but who did not provide a urine specimen, or did not have sufficient volume of biospecimens, or who did not give consent for their specimens to be used for future research (for 2017-2018) are included in the file but they have a sample weight assigned “0” in their records.

Demographic and Other Related Variables

The analysis of NHANES laboratory data must be conducted using the appropriate survey design and demographic variables. The NHANES 2017-March 2020 Pre-Pandemic Demographics File contains demographic data, health indicators, and other related information collected during household interviews as well as the sample design variables. The recommended procedure for variance estimation requires use of stratum and PSU variables (SDMVSTRA and SDMVPSU, respectively) in the demographic data file.

This laboratory data file can be linked to the other NHANES data files using the unique survey participant identifier (i.e., SEQN).

Starting in the 2015-2016 NHANES cycle, the variable URXUCR (urine creatinine) will not be reported in this file. URXUCR can be found in the data file titled “Albumin & Creatinine – Urine”.

Detection Limits

The detection limits were constant for the analytes in the data set. Two variables are provided for each of these analytes. The variable named ending in “LC” (ex., URDPMALC) indicates whether the result was below the limit of detection: the value “0” means that the result was at or above the limit of detection, “1”

indicates that the result was below the limit of detection. For analytes with analytic results below the lower limit of detection (ex., URDPMALC=1), an imputed fill value was placed in the analyte results field. This value is the lower limit of detection divided by the square root of 2 (LLOD/sqrt [2]). The other variable prefixed URX (ex., URXPHMA) provides the analytic result for the analyte. All data are rounded to three significant figures or three decimal places, whichever is less precise.

The lower limit of detection (LLOD, in ng/mL) for URXMUCA and URXPHMA:

Variable Name	Analyte Name	LLOD
URXMUCA	*trans, trans*-Muconic acid (ng/mL)	9.81
URXPHMA	Phenylmercapturic acid (ng/mL)	0.150

References

- Bahadar, H., Mostafalou, S. & Abdollahi, M. Current understandings and perspectives on non-cancer health effects of benzene: A global concern. Toxicol. Appl. Pharmacol. (2014) 276: 83–94.
- Behar, R. Z., Luo, W., McWhirter, K. J., Pankow, J. F. & Talbot, P. Analytical and toxicological evaluation of flavor chemicals in electronic cigarette refill fluids. Sci. Rep. (2018) 8.
- Bhandari, D. et al. Development of a UPLC-ESI-MS/MS method to measure urinary metabolites of selected VOCs: Benzene, cyanide, furfural, furfuryl alcohol, 5-hydroxymethylfurfural, and N-methyl-2-pyrrolidone. J. Chromatogr. B. (2019): 1126–1127: 121746.
- Caudill, S.P., Schleicher, R.L., Pirkle, J.L. Multi-rule quality control for the age-related eye disease study. Statist. Med. (2008) 27(20):4094-4106.
- Pankow, J. F. et al. Benzene formation in electronic cigarettes. PLoS One. (2017) 12: 1–10.
- Smith, M. T. Advances in Understanding Benzene Health Effects and Susceptibility. Annu. Rev. Public Health. (2010) 31:133-148.
- Sterz, K., Köhler, D., Schettgen, T. & Scherer, G. Enrichment and properties of urinary pre-S-phenylmercapturic acid (pre-SPMA). J. Chromatogr. B Anal. Technol. Biomed. Life Sci. (2010) 878: 2502–2505.
- Talhout, R., Opperhuizen, A. & van Amsterdam, J. G. C. Sugars as tobacco ingredient: Effects on mainstream smoke composition. Food Chem. Toxicol. (2006) 44: 1789–1798.
- Tevis, D. S. et al. Large Differences in Urinary Benzene Metabolite S-Phenylmercapturic Acid Quantitation : A Comparison of Five LC – MS-MS Methods. (2020) 00: 1–9.

Codebook and Frequencies

SEQN - Respondent sequence number

Variable Name:	SEQN
SAS Label:	Respondent sequence number
English Text:	Respondent sequence number.
Target:	Both males and females 3 YEARS - 150 YEARS

WTVOC2PP - UVOC2 Subsample Weights Pre-Pandemic

Variable Name: WTVOC2PP

SAS Label: UVOC2 Subsample Weights Pre-Pandemic

English Text: UVOC2 Special Subsample Weights Pre-Pandemic

Target: Both males and females 3 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
3224.402553 to 1023924.8166	Range of Values	3896	3896	
0	Participants 3+ years with no lab specimen	994	4890	
.	Missing	0	4890	

URXMUCA - trans, trans-Muconic acid (ng/mL)

Variable Name: URXMUCA

SAS Label: trans, trans-Muconic acid (ng/mL)

English Text: trans, trans-Muconic acid (ng/mL)

Target: Both males and females 3 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
6.94 to 15800	Range of Values	3896	3896	
.	Missing	994	4890	

URDMUCLC - trans, trans-Muconic acid comment code

Variable Name: URDMUCLC

SAS Label: trans, trans-Muconic acid comment code

English Text: trans, trans-Muconic acid comment code

Target: Both males and females 3 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	3631	3631	
1	Below lower detection limit	265	3896	
.	Missing	994	4890	

URXPHMA - Phenylmercapturic acid (ng/mL)

Variable Name: URXPHMA

SAS Label: Phenylmercapturic acid (ng/mL)

English Text: Phenylmercapturic acid (ng/mL)

Target: Both males and females 3 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.106 to 30.6	Range of Values	3896	3896	
.	Missing	994	4890	

URDPMALC - Phenylmercapturic acid comment code

Variable Name: URDPMALC

SAS Label: Phenylmercapturic acid comment code

English Text: Phenylmercapturic acid comment code

Target: Both males and females 3 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	1581	1581	
1	Below lower detection limit	2315	3896	
.	Missing	994	4890	