

National Health and Nutrition Examination Survey

2017-March 2020 Data Documentation, Codebook, and Frequencies

Ethylene Oxide (P_ETHOX)

Data File: P_ETHOX.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 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.

Ethylene Oxide

Ethylene oxide (EO) is an important industrial chemical used in making consumer and non-consumer products and is used as a gaseous sterilant for medical devices. EO has been classified as a human carcinogen (Group 1) by the International Agency for Research on Cancer (IARC). EO has been detected in exogenous sources, such as tobacco smoke, automobile exhaust, and some food (Clin Chem, 2016). EO is formed endogenously in animals and humans as a result of Cytochrome P450 2E1 (CYP2E1) mediated metabolic oxidation of ethylene. It is also formed in vivo during normal physiological processes such as methionine oxidation, lipid peroxidation, and via the metabolic activity of intestinal bacteria. Information on endogenous and exogenous EO exposure in the general population is very limited and is needed to assess potential health effects associated with this exposure and to monitor changes in exposure over time.

Eligible Sample

All examined 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 procedure describes a method to measure hemoglobin adducts of EO in human whole blood or erythrocytes. Specifically, the reaction products with the N-terminal valine of the hemoglobin protein chains (N-[2-carbamoyl ethyl] valine and N-[2-hydroxycarbamoyl-ethyl] valine EO adducts) are measured.

This method is based on the modified Edman reaction, which uses the effect of N-alkylated amino acids being able to form Edman products in neutral or alkaline conditions without changing the pH to acidic conditions required in conventional Edman reaction procedures. It was first described for N-terminal hemoglobin adducts of EO, propylene oxide, and styrene oxide and later optimized to increase yield of Edman products of these adducts. This optimized method was further refined and modified in-house to increase sensitivity and enable automation.

The procedure described here consists of 4 parts:

1. Preparation of the specimen for measurement of hemoglobin adducts EO;

2. Measurement of total hemoglobin in the sample solution used for hemoglobin adduct measurements;
3. Modified Edman reaction in the sample solution and isolation of Edman products; and
4. Analysis of Edman products by high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS) and results processing.

Because results are reported in pmol adduct per gram of hemoglobin, the amount of hemoglobin used for the modified Edman reaction needs to be known. Therefore, this procedure includes a measurement procedure for total hemoglobin. It is a commercial assay kit based on a well-established procedure commonly used in clinical chemistry. Quantitation of the EO hemoglobin adducts is performed using octapeptides with the same amino acid sequence as the N-terminal of the beta-chain of hemoglobin with EO attached at the valine.

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

Laboratory Method Files

[Ethylene Oxide Lab Procedure Manual](#) (February 2023)

[Ethylene Oxide Lab Procedure Manual](#) (February 2023)

Laboratory Quality Assurance and Monitoring

Washed-packed red blood cell 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 specimen collection and processing instructions are discussed in the [2017-2018](#) and [2019-2020](#) NHANES Laboratory Procedures Manuals (LPMs). 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 protocols (QA/QC) meet the 1988 Clinical Laboratory Improvement Amendments mandates. Detailed quality control and quality assurance instructions are discussed in the NHANES LPMs.

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 contract laboratories. In the MEC, these methods include performing blind split samples collected on “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 the 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 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 demographic data 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 Overview](#) documents 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. The specimen availability can also vary by age or other population characteristics. For example, in 2017-March 2020, approximately 76% of children aged 1-17 years who were examined in the MEC provided a blood specimen through phlebotomy, while 95% of examined adults aged 18 and older provided a blood specimen. 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 further details on the use of sample weights and other analytic issues.

Subsample Weights

EO were measured 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 are included in this data file and should be used when analyzing these data.

Demographic and Other Related Variables

The analysis of NHANES laboratory data must be conducted using the appropriate survey design and demographic variables. The [2017 – March 2020 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.

The [Fasting Questionnaire File](#) includes auxiliary information such as fasting status, the time of venipuncture, and the conditions precluding venipuncture.

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

Detection Limits

The detection limits were constant for all of the analytes in the data set. Two variables are provided for each

of these analytes. The variable named ended "LC" (ex., LBDEOALC) 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. The other variable prefixed LBX (ex., LBXEOA) provides the analytic result for that analyte. For analytes with analytic results below the lower limit of detection (ex., LBDEOALC =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 lower limit of detection (LLOD, in pmol/g Hb) for EO is:

Variable Name	Analyte Description	LLOD
LBXEOA	Ethylene Oxide	12.9

References

- 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):4094-40106.
- Clinical Chemistry Branch. Laboratory Procedure Manual for N-terminal hemoglobin adducts of Acrylamide, Glycidamide, and Ethylene Oxide. (2016) Division of Laboratory Science, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA.
- International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans, volume 96. Alcohol consumption and ethyl carbamate*. Lyon, France: IARC; 2010 Available from: <http://monographs.iarc.fr/ENG/Monographs/vol96/mono96.pdf>.
- Westgard J.O., Barry P.L., Hunt M.R., Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. *Clin Chem* (1981) 27:493-501.

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 6 YEARS - 150 YEARS

WTSAPRP - Subsample A Weights Pre-Pandemic

Variable Name: WTSAPRP
SAS Label: Subsample A Weights Pre-Pandemic
English Text: Subsample A Weights Pre-Pandemic
Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
5616.660506 to 955677.30961	Range of Values	4018	4018	
0	No Lab Result	43	4061	
.	Missing	0	4061	

LBXEOA - Ethylene Oxide (pmol/g Hb)

Variable Name: LBXEOA
SAS Label: Ethylene Oxide (pmol/g Hb)
English Text: Ethylene Oxide (pmol/g Hb)
Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
9.12 to 1460	Range of Values	3637	3637	
.	Missing	424	4061	

LBDEOALC - Ethylene Oxide comment code

Variable Name: LBDEOALC
SAS Label: Ethylene Oxide comment code
English Text: Ethylene Oxide comment code
Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	detectable result	3463	3463	
1	below detectable limit	174	3637	
.	Missing	424	4061	