COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

Issue

1. During the Horizon Scanning session in February 2010 the Committee requested information about The National Health and Nutrition Examination Survey carried out in the US. This paper provides an introduction to the surveys and an overview of the use of the data from the surveys. The Committee is invited to suggest what further information they would like to review.

Introduction

2. The National Health and Nutrition Examination Survey (NHANES) is a major program of the National Center for Health Statistics (NCHS). It is part of the Centers for Disease Control and Prevention (CDC) which has responsibility for producing vital and health statistics for the United States of America.

3. Information on the survey content for NHANES III (the last time bound survey) and the current NHANES rolling survey are attached at Annexes A and B respectively.

4. Initial searches have been carried out to obtain information on how the NHANES data has been used. The search strategy and results are presented at Annex C

Background

5. NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The program began in the early 1960s and has been conducted as a series of surveys focusing on different population groups and/or health topics. It is unique in so far as it combines structured interviews and physical examinations.

6. The survey examines a nationally representative sample of approximately 5,000 individuals each year. These individuals are located in counties across the United States; an average of 15 counties are/have been visited each year. With the exception of the NHANES I Epidemiologic Follow up Study (NHEFS), the survey is a single point in time sample with no overlap occurring between the sampled populations in successive surveys. Individuals in the survey population are advised of any irregularities that require a follow
up visit with a health professional; however the survey does not attempt to follow the progress of these individuals.

7. The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions. The examination component consists of medical, dental, and physiological measurements, as well as laboratory tests administered by trained medical personnel.

8. Information from NHANES is made available through an extensive series of publications and articles in scientific and technical journals. Survey data are made available to researchers throughout the world via the internet and on CD-ROMs. Serum, urine and blood samples are also available to researchers on request.

Data collected from the NHANES

9. A number of historical datasets are available for researchers. The NHANES I & II datasets both cover a 4 year period, with the NHANES III dataset covering a 6 year period. Since 1999, when the survey became a continuous program, datasets have been released annually.

10. NHANES I was conducted between 1971 and 1975 on a sample of approximately 32,000 individuals aged between 1 and 74 years of age. The NHANES I study sample was selected so that certain population groups thought to be at high risk of malnutrition (persons with low incomes, preschool children, women of childbearing age, and the elderly) were oversampled at preset rates. Adjusted sampling weights were then computed in order to try and closely reflect the wider population of the United States.

11. Information for all examined individuals in NHANES I was obtained by means of:

- a household interview
- a general medical history
- a 24–hour dietary intake recall interview
- a food frequency interview
- a food program questionnaire
- a general medical examination
- dental, dermatological and ophthalmological examinations
- anthropometric measurement
- hand-wrist x-rays (of those ages 1-17 only)
- haematological, blood chemistry, and urological laboratory determinations

In addition to the data gained from all examined individuals by means of the above questionnaires, procedures and measurements, the following data were also gathered on a subsample of adults aged 25-74:

- a medical history supplement
- supplementary questionnaires concerning arthritis, respiratory and cardiovascular conditions (when applicable)
• a health care needs questionnaire
• a general well-being questionnaire
• an extended medical examination
• x-rays of the chest and hip and knee joints
• audiometry
• electrocardiography
• goniometry
• spirometry
• pulmonary diffusion and tuberculin tests

12. The NHANES I Epidemiologic Follow up Study (NHEFS) was designed to investigate the relationships between clinical, nutritional, and behavioural factors assessed in the first National Health and Nutrition Examination Survey. The NHEFS cohort includes all persons 25-74 years of age who completed a medical examination at NHANES I in 1971-75 (n = 14,407). It is comprised of a series of four follow-up studies. The first wave of data collection was conducted for all members of the NHEFS cohort from 1982 through 1984. It included tracing the cohort; conducting personal interviews with subjects or their proxies; measuring pulse rate, weight, and blood pressure of surviving participants; collecting hospital and nursing home records of overnight stays; and collecting death certificates of decedents.

13. Continued follow-up of the NHEFS population was conducted in 1986, 1987, and 1992 using the same design and data collection procedures developed in the 1982-84 NHEFS, with the exception that a 30-minute computer-assisted telephone interview was administered rather than a personal interview; and no physical measurements were taken. The 1986 NHEFS was conducted for members of the NHEFS cohort who were 55-74 years of age at their baseline examination and not known to be deceased at the 1982-84 NHEFS (n = 3,980). The 1987 NHEFS was conducted for the entire nondeceased NHEFS cohort (n = 11,750). The fourth wave of data collection, the 1992 NHEFS, includes the entire nondeceased NHEFS cohort (n = 11,195). Tracing and data-collection rates in the NHEFS have been very high. Ninety-six percent of the study population has been successfully traced at some point through the 1992 follow-up. Tracing rates for each completed wave ranged from 90 to 94 percent and interview rates ranged from 91 to 96 percent of those traced.

14. The NHEFS public use data files are divided into the following four components:
   • Vital and Tracing Status Data - The 1992 Vital and Tracing Status contains tracing, vital status, and demographic data for all 14,407 subjects for each wave of data collection
   • Interview Data - The 1982-84, 1986, 1987, and 1992 Interview data contain information collected from the subject and proxy interviews conducted during each follow-up period. When merged together, these files provide a complete follow-up history for each subject from baseline through the last completed interview
Health Care Facility Stay Data - The 1982-84, 1986, 1987, and 1992 Health Care Facility Stay data contain information collected during each follow-up period regarding overnight stays in health care facilities, including diagnostic and summary information abstracted from hospital and nursing home records. Supplemental Health Care Facility Stay data is used to provide information on overnight facility stays that occurred outside the reported follow-up period. When these five Health Care Facility Stay data files are merged together, they provide a history of all reported hospitalizations and institutionalizations from baseline through 1992.

Mortality Data - The 1992 Mortality Data contains death certificate information collected during each follow-up period coded according to ICD-9 multiple-cause-of-death procedures for all 4,497 decedents identified through 1992.

15. NHANES II was undertaken between 1976 and 1980 on a sample of 27,801 individuals aged between 6 months and 74 years of age. Of this sample, 25,286 people were interviewed and 20,322 were examined. As with NHANES I, children and persons classified as living at or below the poverty level were assumed to be at special risk of having nutritional problems, so they were sampled at rates substantially higher than their proportions in the general population. And again as with the previous survey, adjusted sampling weights were computed in order to try and closely reflect the wider population of the United States.

16. Information for all examined individuals in NHANES II was obtained by means of:

- a household interview
- a general medical history
- a 24–hour dietary intake recall interview
- a food frequency interview
- a dietary supplement questionnaire
- a medication/vitamin usage questionnaire
- a coronary heart disease questionnaire
- a general medical examination
- spirometry test
- electrocardiogram
- audiometry test
- anthropometric measurement
- allergy tests
- cervical, lumbar, spine and chest X-ray
- haematological, blood chemistry, and urological laboratory determinations

17. NHANES III was conducted between 1988 and 1994 and contains data for 33,994 individuals aged 2 months and over. A total of 89 survey locations were visited, 44 between 1988 and 1991 and 45 between 1991 and 1994. The goals of the NHANES III included the need for precise descriptive
information on the health status of selected population groups of the United States and required that these groups be sampled in large proportions to ensure the precision of the information. Children aged 2 months to 5 years and persons 60 years of age and over comprised two of these groups. Children in this age group represent about 23 percent of the NHANES III sample but only 9 percent of the U.S. population.

Information for examined individuals in NHANES III was obtained by means of:

- a household interview
- a general medical history
- a 24–hour dietary intake questionnaire
- a food frequency interview
- a dietary supplement questionnaire
- a medication/vitamin usage questionnaire
- a coronary heart disease questionnaire
- a general medical examination
- a dental health examination
- an eye examination (including fundus photography)
- a general hearing test
- spirometry test
- electrocardiogram
- central nervous system test
- audiometry test
- bone density test
- hand and knee radiography
- gall bladder ultrasound
- anthropometric measurement
- allergy tests
- RNA/DNA extraction
- haematological, blood chemistry, and urological laboratory determinations

18. Serum, urine and limited plasma samples were collected and stored as part of the NHANES III. These samples are made available to researchers on submission and approval of the details of their proposal.

19. Anonymised genetic data sets from the NHANES III are available to researchers on request. Restricted access genetic data and DNA samples are also made available to researchers although any analyses must be performed at either the Research Data Center at the National Center for Health Statistics in Hyattsville, Maryland or the Research Data Center on the CDC campus in Atlanta, Georgia. There is a fee to use either service.

20. Since 1999 the programme has been continuous and separate NHANES datasets have been made available each year. The study sample for the survey is selected to represent the U.S. population of all ages. To produce reliable statistics, NHANES over-samples persons 60 and older, African Americans, and Hispanics.
21. Since 1999, the diseases, medical conditions, and health indicators studied by the NHANES have included:

- anaemia
- cardiovascular disease
- diabetes
- environmental exposures
- eye diseases
- hearing loss
- infectious diseases
- kidney disease
- nutrition
- obesity
- oral health
- osteoporosis
- physical fitness and physical functioning
- reproductive history and sexual behaviour
- respiratory disease (asthma, chronic bronchitis, emphysema)
- sexually transmitted diseases
- vision

22. The laboratory components of the continuous NHANES consist of:

- venipuncture
- urine collection
- bone mineral status markers
- diabetes profile
- infectious disease profile
- oral human papilloma virus
- C-reactive protein
- thyroid profile
- standard biochemical profile
- kidney disease profile
- pregnancy test
- prostate specific antigen
- nutritional biochemistries and hematologies
- sexually transmitted disease profile
- blood lipids
- environmental health profile

23. Between 1999 and 2002 the following laboratory measures were used to determine NHANES environmental health profiles:

- blood lead
- blood cadmium
- blood mercury
- serum persistent pesticides
- serum noncoplanar polychlorinated biphenyls (PCBs)
- serum dioxins, furans, and coplanar PCBs
- serum and urine levels of phytoestrogens
- urine levels of non-persistent pesticides and metabolites
- urine heavy metals
- urine phthalates
- urine polyaromatic hydrocarbons

24. From 2003 onwards the number of chemicals assessed by NHANES to determine environmental health profiles, based on potential for human exposure, known or potential health effects from exposure and technical feasibility of measurement increased significantly. Full details of the current gamut of environmental and related chemicals measured in blood, serum and urine are attached in Annex D.

25. A limited amount of plasma and urine samples have been made available to researchers (from those participants who consented to their specimens being used for future studies) since the NHANES survey became continuous in 1999. Samples for a single year of the survey are not provided for research, any proposed research projects wishing to use the samples must have a two-year design (i.e. requests must be for 1999-2000 samples or 2001-2002, etc.). A list of completed research projects using continuous NHANES (from 1999 to 2006) stored sera is attached at Annex E.

26. Between 1999 and 2002 blood was collected and DNA was purified from consenting participants age 20 or more years from the continuous NHANES. These specimens are also available to researchers. As with the genetic and DNA data from NHANES III, anonymised genetic data sets are available to researchers on request. Restricted access genetic data and DNA samples are also made available although any analyses must be performed at either the Research Data Center at the National Center for Health Statistics in Hyattsville, Maryland or the Research Data Center on the CDC campus in Atlanta, Georgia.

Type of Studies using NHANES data

27. Two preliminary literature searches have been completed to try to assess the uptake and use of NHANES data. The first search was very broad and resulted in the identification of 16,875 papers that mention NHANES. The second search aimed to identify papers that might have made use of the NHANES data; this search returned a total of 1,453 papers. The search was further refined to identify papers and subjects that would hold more relevance to the Committee, this final search returned a total of 580 papers.

28. Table 1 (overleaf) is a summary of the 580 papers returned in the final search. It highlights the number of papers identified that used or make reference to NHANES data by subject area.
<table>
<thead>
<tr>
<th>SUBJECT AREA</th>
<th>PAPERS IDENTIFIED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies that do not relate to or use NHANES data</td>
<td>342</td>
</tr>
<tr>
<td>Adverse Health Risks &amp; Biomarkers of Adverse Health</td>
<td>78</td>
</tr>
<tr>
<td>Heavy Metals (e.g. Lead/Cadmium/Mercury/Cobalt/Zinc)</td>
<td>46</td>
</tr>
<tr>
<td>Epidemiology Studies</td>
<td>20</td>
</tr>
<tr>
<td>Dietary Patterns, Interventions, Information and Health Outcomes</td>
<td>16</td>
</tr>
<tr>
<td>Occupational Health Studies</td>
<td>15</td>
</tr>
<tr>
<td>Socioeconomic and Social Science Studies</td>
<td>14</td>
</tr>
<tr>
<td>Computational or Statistical Assessments</td>
<td>8</td>
</tr>
<tr>
<td>Pesticides, Insecticides &amp; Herbicides</td>
<td>6</td>
</tr>
<tr>
<td>Volatile organic compounds (including Alkylbenzenes)</td>
<td>5</td>
</tr>
<tr>
<td>Arsenic</td>
<td>4</td>
</tr>
<tr>
<td>Dioxins</td>
<td>4</td>
</tr>
<tr>
<td>Phthalates and BPA</td>
<td>3</td>
</tr>
<tr>
<td>Polyaromatic Hydrocarbons</td>
<td>3</td>
</tr>
<tr>
<td>Environmental Contaminants and Air Pollution</td>
<td>3</td>
</tr>
<tr>
<td>Persistent Organic Pollutants</td>
<td>2</td>
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<tr>
<td>Heterocyclic Amines and Acrylamide</td>
<td>2</td>
</tr>
<tr>
<td>PCB’s</td>
<td>2</td>
</tr>
<tr>
<td>Phytoestrogen</td>
<td>2</td>
</tr>
<tr>
<td>Assessment of uncertainty</td>
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</tr>
<tr>
<td>Trihalomethane</td>
<td>1</td>
</tr>
<tr>
<td>Mycotoxins</td>
<td>1</td>
</tr>
<tr>
<td>Dietary Nitrates, Nitrites, and Nitrosamines</td>
<td>1</td>
</tr>
<tr>
<td>Antidepressant Use</td>
<td>1</td>
</tr>
</tbody>
</table>

*Table 1 – Results of the literature search undertaken to identify papers using or making reference to NHANES data.*
Questions on which the views of the Committee are sought

29. Members are invited to comment on the information provided and consider the following questions:

i. Is there any further information the Committee would like to receive with regards to the NHANES, the data generated or potential uses in epidemiological studies?

ii. Do Members have any general comments on the interpretation of results of epidemiological studies conducted with the NHANES datasets?

iii. Would Members wish to have more detailed discussion on any of the topics listed in table?

Secretariat
May 2010
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

"Plan and Operation of the Third National Health and Nutrition Examination Survey 1988-94"

This report describes the plan and operation of the third National Health and Nutrition Examination Survey (NHANES III) carried out between 1988 and 1994, consisting of two phases of equal length and sample size. Both Phase 1 and Phase 2 were random samples of the US population living in households.

This document is available from:

http://www.cdc.gov/nchs/data/series/sr_01/sr01_032.pdf

Note: For copyright reasons the papers in the Annexes are not included in the published version on the COT website. The bibliographic details of the annexed material are listed above. The documents are all in the public domain and individuals can obtain them by application to appropriate sources.

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May 2010
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

This document contains three tables that outline the examination, laboratory and questionnaire components of the NHANES rolling survey as conducted between 1999 and 2010. It also provides a glossary of terms used.

This document is available from:


Note: For copyright reasons the papers in the Annexes are not included in the published version on the COT website. The bibliographic details of the annexed material are listed above. The documents are all in the public domain and individuals can obtain them by application to appropriate sources.

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NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

Search Strategy

This Annex presents the search strategies used to obtain details of papers that have used data from NHANES. For detail of the reasoning behind the three searches, please refer to the main paper.

Secretariat
May 2010
SEARCH STRATEGY - NHANES

PubMed Search 01 – 10TH March 2010

Search Dates (From/To) – No parameters set

Search Terms – NHANES

Limits – No parameters set

Number of Papers Identified – 16,875

PubMed Search 02 – 10th March 2010

Search Dates (From/To) – No parameters set

Search Terms – NHANES AND (Epidemiologic* OR Biomarker* OR "Health Outcome")

Limits – No parameters set

Number of Papers Identified – 1,453

PubMed Search 03 – 7th April 2010

Search Dates (From/To) – No parameters set

Search Terms – NHANES AND Risk AND (Chemical* OR Exposure OR Biomarker* OR Toxic*)

Limits – No parameters set
COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

*Environmental and Related Chemicals Measured in Blood, Serum or Urine in NHANES from 2003*

This document contains a table of the chemicals either currently being measured or planned to be measured in blood, serum or urine specimens from NHANES by the Division of Laboratory Sciences (DLS), National Center for Environmental Health, CDC.

This document is available from:

http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/environmentalhealth_03.pdf

Note: For copyright reasons the papers in the Annexes are not included in the published version on the COT website. The bibliographic details of the annexed material are listed above. The documents are all in the public domain and individuals can obtain them by application to appropriate sources.

**Secretariat**

**May 2010**
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) - INTRODUCTION

Summary of Research Undertaken Using Stored Specimens from the Continuous NHANES (from 1999 onwards)

This Annex presents summary details of all the research projects that have been undertaken using stored specimens (collected between 1999 and 2006) from the continuous NHANES.

Full details can be obtained from the NHANES website:


Note: For copyright reasons the papers in the Annexes are not included in the published version on the COT website. The bibliographic details of the annexed material are listed above. The documents are all in the public domain and individuals can obtain them by application to appropriate sources.

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