

PEER REVIEW COMMENTS ON

**Second National Report on Biochemical Indicators of Diet and
Nutrition in the U.S. Population**

REPORT

APRIL 2011

**Comments Received from
Peer Reviewer #1**

GENERAL QUESTIONS:

1. **Are the report objectives clearly stated and appropriate?**
Yes (X) No () Unsure ()

Why?

2. **Is the overall report design appropriate for the report objectives?**
Yes (X) No () Unsure ()

Why?

The authors should be lauded for the expansion of more than doubling the biochemical indicators detailed in this report compared to the one released in 2008.

The overall design of the report provides extensive detail about the biochemical data presented. The overviews for indicators covered in the report including physiological function, health effects, intake recommendations, methods for assessing the indicators and specific methods used for collection in NHANES provide a comprehensive picture and invaluable reference.

While the detail of data in the many data tables is excellent, of unique value is the selected observations and highlights section with inclusion of figures to illustrate major trends and health policy/concerns-related results. If time allows, expanding the highlights sections of the chapters would be welcome. The knowledge and expertise of CDC's National Center for Environmental Health serves as a critical resource to accurately summarize these data.

To assure that users can quickly find data tables or figures, I would suggest adding a listing of all tables and figures with corresponding page numbers in either the Table of Contents or the Appendix.

3. **Are the methods and analyses appropriate for the report objectives?**
Yes () No () Unsure (X)

Why?

While my research background is not in biochemistry, I feel I am not qualified to judge the report on the methods used. However, the description and rich referencing in the report leads a reader such as me to have confidence in the methods used. Further, references and methods used are comprehensively referenced so further investigation/evaluation is possible of the methodologies employed.

4. **Were the data analyzed in such a way to address appropriately the objectives of the report?**
Yes () No () Unsure (X)

Why?

I refer to my response in item 3.

5. **Are the report results presented and interpreted appropriately and completely?**
Yes (X) No () Unsure ()

Why?

I answer yes overall but offer a comment on Chapters 2 and 3.

Chapter 2. Fat-Soluble Vitamins & Nutrients. In the Highlights section describing Figure H.2.a., the statement that low dietary intake of vitamin E without widespread manifestation of deficiency suggest the need for further evaluations to determine whether improve estimates (either in dietary intake or nutrient composition) are necessary is well-appreciated. However, it is probable that the Estimated Average Requirement (EAR) for vitamin E may also need further evaluation. The dietary intake method used in NHANES, the Automated Multiple Pass Method (AMPM) has been validated for energy intake on a sample of 524 adults using the doubly labelled water technique. The results of that study show that reported energy intake using the AMPM was 11% less than total energy expenditure (<http://ddr.nal.usda.gov/dspace/handle/10113/21951>). This level of underreporting does not compensate to the disconnect between >95% of the population having adequate serum concentrations of vitamin E and 93% of the population consuming less than the EAR for vitamin E.

Chapter 3. Very minor comment--In most of the figures presented, I noticed an order to the subgroups as listed in the x axis, based on what I believe is sample size from small to large. Figure H.3.d. changes that order with Mexican Americans and Non-Hispanic whites reversed.

6. **Are the report conclusions and recommendations appropriate and complete?**
Yes (X) No () Unsure ()

Why?

7. **Are there any overall comments on the manuscript? (How does the Report contribute to public health in ways not already noted? What persons/groups, in addition to those listed, will be interested in this Report? What channels of communication should be used to disseminate this Report?)**

Congratulations on a wonderful report. It will be an invaluable document in monitoring dietary and nutritonal status.

Others that may be interested in the report: I would suggest that the National Collaboration for Childhood Obesity Research would be interested in this report. Their website: <http://www.nccor.org/index.html>.

8. **Select the appropriate category below:**

(List recommended changes or reasons for not recommending)

- A. Recommend (X)
B. Recommend with Required Changes ()
C. Not Recommended ()

ADDITIONAL QUESTIONS:

1. Are there any comments on NCEH/ATSDR's peer review process? none
2. Are there any other comments?

**Comments Received from
Peer Reviewer #2**

GENERAL QUESTIONS:

1. Are the report objectives clearly stated and appropriate?

Yes () No () Unsure ()

Why? NCHS is commissioning the report of data from the National Health and Nutrition Examination Survey (NHANES) in order to make this data available to the public. In this regard, the report is addressing a need to know this information. The stated purpose is to improve our understanding of the concentrations of biochemical indicators of diet and nutrition in the general U.S. population. Health professionals such as physicians, clinicians, scientists and public health officials may use the population reference levels to determine if a group of people has an unusually high or low level of a biochemical indicator of nutrients and/or compounds. There are other stated uses of the report including tracking trends in biochemical indicator levels over time, drawing comparison of nutritional status between special population groups, and stimulating more in-depth research on the NHANES data.

2. Is the overall report design appropriate for the report objectives?

Yes () No () Unsure ()

Why? The overall design is in the form of an easy to reach and follow report. It is organized by topic area and introduced by a complete table of contents section. The design supports the objectives and facilitates the reading and understanding of the report.

Based on the objectives, there needs to be more biochemical indicators analyzed and included in the report. The most complete and comprehensive chapter is on the subject of Water-Soluble vitamins. This chapter contains a more comprehensive discussion of the three essential water-soluble vitamins listed as problematic in the food supply. Biochemical indicators include measure of compounds in blood and urine which change in relationship to the nutritional status of folate and vitamins B6 and B12. While the report does not include other water-soluble nutrients such as choline, which has recently received attention related to perinatal brain development, the coverage of the three vitamins is complete and comprehensive. Perhaps, future analyses will include other water-soluble nutrients such as choline.

The report misleads the reader by broad categories and headings. It is not a comprehensive report and the number of nutrients in a given is limited. One can find examples in each section where there is limited information. The most complete is the Fat Soluble vitamins chapter which includes data for vitamins A, D, & E, the major carotenoids in the diet, and fatty acids [data not included]. The chapter on water-soluble vitamins lists only folate, vitamins B6 B12 and C, metabolites homocysteine and methylmalonic acids. Vitamin C data is tucked in at the end of the Water Soluble vitamins chapter without being indexed in the beginning. This coupled with missing tables has made it difficult to evaluate the contents of this report effectively.

3. Are the methods and analyses appropriate for the report objectives?

Yes () No () Unsure ()

Why? The statistical analyses are quite appropriate for the report objectives. Statistical programs such as SUDAAN and SAS were used to analyze the data. The report explains and defines the statistical analyses that were used and how these methods provide the explanation of the data analyzed and reported.

The biochemical and laboratory methods used for the selected biomarkers of nutritional adequacy in the report appear also to be appropriate. Individual variability is large for some of the parameters. Therefore, one wonders whether simply looking at serum and urine will provide

sufficient information upon which to draw conclusions about nutrient status. For example, looking at serum fatty acids may not provide as much useful information as looking at red cell membrane fatty acids. How reliable is looking at urinary excretion of Isoflavones in determining status or intake? Individual variability in this area is also very large.

4. **Were the data analyzed in such a way to address appropriately the objectives of the report?**

Yes () No () Unsure ()

Why?

The data were analyzed appropriately from a statistical viewpoint.

5. **Are the report results presented and interpreted appropriately and completely?**

Yes () No () Unsure ()

Why? One cannot overlook the missing tables that were discussed in the text but not included in the report. There was no explanation as to which were missing and would be added later. There was no explanation as to why some nutrients in various categories were not included in the report. The 2010 Dietary Guidelines for Americans were recently published in which there is a list of nutrients that are of concern for the general public and various subpopulations. As a minimum, this report should include analyses of those nutrients from NHANES database.

6. **Are the report conclusions and recommendations appropriate and complete?**

Yes () No () Unsure ()

Why? The conclusions and recommendations in the report were not found. Also not found was a section that would be most useful, i.e., an Executive Summary. There is an adequate introductory section with background information. This information prepares the reader for the analyses that are in the report.

7. **Are there any overall comments on the manuscript? (How does the Report contribute to public health in ways not already noted? What persons/groups, in addition to those listed, will be interested in this Report? What channels of communication should be used to disseminate this Report?)**

This report is very spotty and has the appearance of being hastily pulled together. Some sections are well developed and complete and others have missing information. Much more work will be needed in order to get it ready for publication.

8. **Select the appropriate category below:**

(List recommended changes or reasons for not recommending)

D. Recommend ()

E. Recommend with Required Changes (): Some of the URLs do not open appropriately and some do not open on the intended subject matter. Tables in chapters 2 and 5 are missing and will need to be included prior to publication. An explanation is needed as to why the broad chapter headings are used when there's just one nutrient analyzed. This is misleading. The chapter entitled "Trace Elements" has only a single nutrient, iodine, listed. Why not get rid of the broad heading "trace elements" in favor of simply listing "Iodine?" If that is not feasible, the author should include more than just a single trace element in this chapter. Additionally, iron is also a trace element but is listed in a separate chapter. Why not

fold the "Iron Status" chapter into the "Trace Elements" chapter? That way, it could truly be listed as the plural "Trace Elements" chapter. The report needs an Executive Summary and an overall conclusion at the end.

F. Not Recommended ()

ADDITIONAL QUESTIONS:

9. Are there any comments on NCEH/ATSDR's peer review process?

I received the report well ahead of the deadline and was given adequate time to conduct the review. The fact that there are missing data made it difficult for me to give it a thorough evaluation. The portion that is intact made for an interesting review. Still, it was very interesting reading. Thank you for the opportunity to serve as one of the peer reviewers for this report.

10. Are there any other comments?

COMMENTS ON DATA FOR PLASMA FATTY ACIDS FOR NHANES 2003-2004 AND URINE PHYTOESTROGENS FOR NHANES 2005-2006

1. Are the methods and analyses appropriate for the report objectives?

Yes (X) No () Unsure ()

Why? This report lives up to its purpose to improve our understanding of the concentrations of biochemical indicators of the diet of the general population and of selected subpopulations. The comprehensive analyses of fatty acids, Isoflavones and Lignans reveal information on many compounds and metabolites of the major compounds. These compounds serve as biomarkers of dietary intake. The methods are consistent with previously used methods and with established analytical methodology protocols. The results of analyzing of fatty acids, Isoflavones and Lignans in subpopulations provide useful insights on racial and ethnic differences in these compounds and metabolites.

2. Were the data analyzed in such a way to address appropriately the objectives of the report?

Yes (X) No () Unsure ()

Why? Statistical analyses using geometric means are appropriate to address the objectives of the report. There is consistency from one set of analyses to the next. The statistical methods are conducted to reveal the results in an understandable fashion.

3. Are results presented and interpreted appropriately and completely?

Yes (X) No () Unsure ()

Why? Results presented and interpreted nearly appropriately and completely. The one exception is with the discussion under the heading "Health Effects" of fatty acids. Concerns about maintaining the proper ratio of n-6 to n-3 fatty acids in the diet and the prevention of cardiovascular disease have pretty much been debunked. In his article: *The Omega-6/Omega-3 Ratio and Cardiovascular Disease Risk: Uses and Abuses*, Current Atherosclerosis Reports, 2006, 8:453-459, William Harris states that:

"...the n-6/n-3 Fatty Acids ratio may be of value in interpreting biomarker data and in making nutritional recommendations. Although initially appealing, there are few human

experimental and clinical trial data to support this view. This paper reviews a variety of studies that, in the aggregate, suggest that the ratio is, both on theoretical and evidential grounds, of little value. Metrics that includes the n-3 fatty acids alone, especially EPA and DHA, appear to hold the greatest promise.”

4. Are the conclusions and recommendations appropriate and complete?

Yes () No () Unsure ()

Why? Conclusions and recommendations are based on data interpreted in the context of authoritative reports including the 2010 Dietary guidelines for Americans and the IOM 2005 Report on Fatty Acids. In the section of Intake Recommendations for Fatty Acids, it would be preferable for the report to cite the recommendation from the Dietary Guidelines Advisory Committee Report and the 2010 DGA regarding recommended intakes of EPA and DHA rather than citing only the Am. Heart Association. The evidence-based 2010 DGA states that Moderate evidence shows that consumption of about 8 ounces/wk of a variety of seafood, which provide an average consumption of 250 mg/d of EPA and DHA is associated with reduced cardiac deaths among individuals with and without pre-existing cardiovascular disease.

5. Are there any overall comments on the data analysis and presentation?

Overall, the data look good. The analyses reveal a good bit of new information about population and subpopulations. The first-time NHANES data for 24 plasma fatty acids will be quite useful to the scientific community and researchers in interpreting these biomarkers in relationship to disease risks. Data on subpopulations will also prove to be useful. There were patterns of consistency with regard to some of the variables measured. Plasma concentrations of long-chain omega-3 fatty acids, EPA and DHA, showed racial and ethnic differences where Mexican Americans had lower levels compared to Non-Hispanic Blacks and Whites. The expansion of NHANES data to include fatty acids and Isoflavones will add a new dimension and enhance our understanding of biomarkers for various chronic disease risks.

**Comments Received from
Peer Reviewer #3**

GENERAL QUESTIONS:

1. **Are the report objectives clearly stated and appropriate?**
Yes () No () Unsure (x)

Why?

I think it would be preferable to have an actual heading called "Objectives of this report". One of the objectives appears simply to be to provide data ("Addressing data needs"). The other set of objectives is provided under "Public Health Uses". Perhaps these could be subheadings.

2. **Is the overall report design appropriate for the report objectives?**
Yes (x) No () Unsure ()

Why?

3. **Are the methods and analyses appropriate for the report objectives?**
Yes () No () Unsure (x)

Why?

1. The report states that "a geometric mean provides a better estimate of central tendency for data distributions with a long tail at the upper end of the distribution...." But long tails at either end can distort the estimate. Perhaps this statement should be modified?

2. Not all biochemical indicators are skew. One that usually is not skew is serum vitamin C. Log-transforming it actually introduces skewness that wasn't there before, and drags down rather than dragging up the mean. This could itself provide a distorted picture of the central tendency. For vitamin C, for example, the geometric mean for Total 6+ Years is 46.2 umol/L, while the median is 56.3, a huge difference.

Since you probably prefer to be consistent, you may not want to change use of geometric mean for specific indicators. However, I suggest you consider adding a sentence in some of the relevant indicators (specifically including vitamin C) to point out that for this indicator the median is a better estimate of central tendency than geometric mean due to the fact that log-transforming introduced rather than removed skewness.

4. **Were the data analyzed in such a way to address appropriately the objectives of the report?**
Yes () No (x) Unsure ()

Why?

I'm actually going to say 'no' on this one, to indicate the strength of my concern on this issue.

1. For a number of these indicators, use of vitamin/mineral supplements is the single most important factor influencing serum concentrations. I realize you don't want to get into interpretation or modeling, etc., but I think not presenting some data by vitamin-mineral supplement use greatly weakens the usefulness of the data for at least one of your stated

objectives, “Assessing the effectiveness of public health efforts to improve diet and nutritional status” Improvements in dietary intake can be masked by vitamin supplement use. And we can see that in many cases African Americans have poorer nutrient status than whites, but our resulting public health efforts to promote better dietary intake will be off base if a large part of the ethnic differences result from differences in supplement use rather than dietary intake.

Observations that are likely to have been influenced by vitamin/mineral supplement use: a) U-shaped curve by age (older people take more such supplements than e.g. adolescents and young adults. See B vitamins; b) lower concentrations in men (women take more such supplements than men); lower concentrations in African Americans and Hispanics (supplement use is less common in these groups).

I know you don't want to greatly multiply the number of tables or to give too much space and emphasis to something that is not age-sex-race, but I think my concern could be handled fairly simply and minimally, as follows. For the figures that present graphs by age (e.g., Figure 1.1.a), just add one more pair of figures, on the same page: users of vitamin-mineral supplements, non-users of vitamin-mineral supplements. This wouldn't increase the number of pages, and would provide very valuable information to aid in the interpretation of the gender and race-ethnicity graphs and tables.

This observation applies mainly to water-soluble indicators and to iron indicators. And for purposes of this concern, I am specifically referring to vitamin-mineral supplements, not 'supplements' in general. So I'm talking about multivitamin/mineral supplements, and single supplements of A, B, C, D, E and iron.

2. I consider that the first line in tables (e.g., in Table 1.1.a.1), that represents the whole population aged 1 year and older (or in some tables 6 & older), is uninformative. I use tables like these all the time, and I never even look at that line because it isn't useful. I think it would be MUCH preferable to instead have two summary lines, 1-19 years and 20 and older. Because of their smaller bodies, children almost always have higher nutrient concentrations. Including them in a summary line with adults provides no real information about typical status of “the population”.

Similarly, in the same table and tables like it, including children in with adults in the race/ethnicity lines may give misleading information about race-ethnic differences. We need to be able to compare how children are doing and how adults are doing. In addition, Mexican Americans and non-Hispanic Blacks tend to have a higher proportion of their populations as children. Unless the sample-weighting already takes care of this, this could result in higher-appearing concentrations of nutrients in Mexican American and non-Hispanic Blacks than would be seen if only their adult concentrations were shown. It's not clear to me whether or not sample-weighting already takes care of this, but if not, I would urge again that the race-ethnicity lines be split into 1-19 and 20+ years.

3. The vitamin D section reports the prevalence of both 'at risk for deficiency' and 'at risk for inadequacy'. In addition, Figure H.2.c presents the prevalence by ethnicity of those two levels of potential risk. In contrast, the vitamin C section reports that there are two previously-defined levels, 'deficiency' and 'low', but reports on the prevalence of only one of those. I would urge that the two levels in vitamin C be handled as they were in vitamin D, and that prevalence of both be reported in the General Observations and Highlights, and particularly that both levels be shown in figure H.1.e as they are shown in H.2.c. We don't have much scurvy in this country, but we do have a lot of 'at risk of inadequate' levels of vitamin C.

4. See comment above re skewness.

5. **Are the report results presented and interpreted appropriately and completely?**
Yes () No () Unsure (x)

Why?

We were emailed detailed tables and figures for the fat-soluble vitamins/nutrients section. However, my book was missing comparable detailed tables and figures for Iron status, Trace elements, Isoflavones, and acrylamide. I assume that the same sets of tables found for the water-soluble and fat-soluble vitamins/nutrients will be presented for the other sections? I'm sure this was intended, as otherwise this publication will be much less valuable.

6. **Are the report conclusions and recommendations appropriate and complete?**
Yes () No () Unsure (x)

Why?

I didn't see a conclusions/recommendations section, either overall or for specific biochemical indicators.

7. **Are there any overall comments on the manuscript? (How does the Report contribute to public health in ways not already noted? What persons/groups, in addition to those listed, will be interested in this Report? What channels of communication should be used to disseminate this Report?)**

The Report is very well written, and will be a very important contribution to understanding about concentrations of these indicators.

8. **Select the appropriate category below:**

(List recommended changes or reasons for not recommending)

G. Recommend ()

H. Recommend with Required Changes (x)

Obviously these are not "required" changes. They are strongly recommended.

I. Not Recommended ()

ADDITIONAL QUESTIONS:

1. **Are there any comments on NCEH/ATSDR's peer review process?**

2. Are there any other comments?

*Typo, last line of paragraph “Biochemical Indicators and Methods”: ‘functional indicator OF folate....’

*Typo?: in Water-soluble write-up, I've usually seen it shown as “radio-protein binding” rather than “radio protein-binding”. This would also mean “non-radio-protein binding”.

*Typo, Caption for figure H.2.c.

COMMENTS ON DATA FOR PLASMA FATTY ACIDS FOR NHANES 2003-2004 AND URINE PHYTOESTROGENS FOR NHANES 2005-2006

My comments concern primarily the chapter on Plasma Fatty Acids and most specifically the introduction to the chapter. The introduction to the chapter on fatty acids is very well written. There can be no criticism of the English composition – it is superb.

However, a great deal of space in the “Health Effects” section - too much, much too much - is devoted to essential fatty acids and to **Eicosapentaenoic Acid** (EPA or also icosapentaenoic acid) and Docosahexaenoic acid (DHA) both of which are referred to as omega-3 fatty acids. That is the focus is on everything except what is central to diet and CHD risk – saturated fatty acids. First of all, if Americans have a nutritional deficiency problem it is not essential fatty acid deficiency. Second, I would like to suggest that as far as CVD risk and prevention is concerned more focus should be given to saturated fatty acids and most especially to the two fatty acids in the diet responsible for raising serum cholesterol levels, i.e. Myristic and Palmitic Acids.

There is a wonderful review article on the effects of diet on serum lipids and lipoproteins. It is a bit old but it is still very useful and informative. It is: Grundy SM and Denke MA. Dietary Influences on Serum Lipids and Lipoproteins. J Lipid Research 1990;31:1149-1172. As the authors discuss, the central tenant of “Diet Heart” is and remains the lowering of saturated fatty acid and dietary cholesterol intake. Omega-3 fatty acids, I believe, are a side issue.

Reading the “Introduction” of this chapter one comes away with the impression that essential fatty acids and omega-3 fatty acids have supplanted saturated fatty acids in importance to CHD prevention. The shorter chain saturated fatty acids, as shown long ago by Keys et al and Hegstead et al, are the ones which raised blood levels of total cholesterol. As mentioned above they are the C14 (Myristic) and C16 (Palmitic) saturated fatty acids.

In the “Health Effects” section there is also an attempt to describe the differential cholesterol raising effects of saturated, PUFA and MUFA. The best way to describe their effects is to present the equations for predicting effects of diet on serum total cholesterol. The two oldest and most recognized are those developed by Keys et al and Hegsted et al (Please see Table 1 Grudy and Denke):

TABLE 1. Equations for predicting effects of diet on total serum cholesterol

Equation of Keys et al. (21)

$$\Delta \text{Cholesterol (mg/dl)} = 2.7\Delta S - 1.35\Delta P + 1.5\Delta C^{1/2} \text{ mg/1000 cal-day}$$

Equation of Hegsted et al. (22)

$$\Delta \text{Cholesterol (mg/dl)} = 2.16\Delta S - 1.65\Delta P + 0.068\Delta C_{\text{mg/day}}$$

Where S = saturated fatty acids (% of total calories); P = poly-unsaturated fatty acids (% of total calories); C = dietary cholesterol.

Both groups show that the short chain saturated fatty acids (c12-c16) raise total cholesterol levels while Stearic acid (c18) does not. MUFA were not included in their equations because they felt MUFA were

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neutral in their impact on serum total cholesterol levels.

More recently, articles by Mensink et al and Yu et al have conducted meta analyses to examine the predictive capabilities of individual fatty acids (attached). Based on their analyses it seems as though the cholesterol lowering effect of PUFA may be smaller than originally thought and as proposed in the equations from Keys and Hegsted. In addition, there is some data in the more recent papers to suggest that MUFA may indeed lower serum total cholesterol levels.

Finally, there is notably no reference given to the National Cholesterol Education Program's Adult Treatment Panel 3 (ATP 3) and to the dietary recommendations in ATP3 (attached). The complete version is an excellent discussion of the impact of diet on serum lipids. It provides guidelines for dietary intakes of fatty acids and cholesterol. The recommendations in ATP3 are the ones physicians follow - not Dietary Guidelines for Americans or the 2005 IOM Report - and it is therefore useful to cite them.

**Comments Received from
Peer Reviewer #4**

GENERAL QUESTIONS:

1. **Are the report objectives clearly stated and appropriate?**
Yes (X) No () Unsure ()

Why?

2. **Is the overall report design appropriate for the report objectives?**
Yes (X) No () Unsure ()

Why?

3. **Are the methods and analyses appropriate for the report objectives?**
Yes (X) No () Unsure ()

Why?

4. **Were the data analyzed in such a way to address appropriately the objectives of the report?**
Yes (X) No () Unsure ()

Why?

5. **Are the report results presented and interpreted appropriately and completely?**
Yes () No () Unsure (X)

Why? I believe that a discussion of the interpretation of the geometric mean and age-adjustment would have been useful for the reader not familiar with those statistical methods.

6. **Are the report conclusions and recommendations appropriate and complete?**
Yes (X) No () Unsure ()

Why?

7. **Are there any overall comments on the manuscript? (How does the Report contribute to public health in ways not already noted? What persons/groups, in addition to those listed, will be interested in this Report? What channels of communication should be used to disseminate this Report?)**

It is unclear to me how widely disseminated is this report. "Health US" is a known product but this report is relatively new. It is clear that this report adds a great deal not included in "Health US" but not if this report has much of an impact. I suggest that if you do not already do so that you advertise it in, say, AJCN and the EpiMonitor. Even better would be a short article in AJCN announcing the release of the 2nd edition and discussing the key findings.

8. **Select the appropriate category below:**

(List recommended changes or reasons for not recommending)

J. Recommend (). I have made a number of relatively minor suggestions which I will leave to the Editors to decide if they wish to incorporate them or not.

K. Recommend with Required Changes (X) The suggested change to the Vitamin D section is, I believe, an important change that should be made. In addition, I have made a number of other relatively minor suggestions which I will leave to the Editors to decide if they wish to incorporate them or not.

L. Not Recommended ()

ADDITIONAL QUESTIONS:

9. Are there any comments on NCEH/ATSDR's peer review process?

None, except to thank you for considering me qualified enough to act as a reviewer.

10. Are there any other comments?

Let me start with that the overall the 2nd Report is well thought out and prepared. Everyone involved with it should be proud of their work. My comments are:

General Comments;

1. I suggest that you provide a definition for a "Geometric Mean" including how they are calculated and how the back transformation is performed.
2. In addition, I suggest that you describe in detail including providing an example of how the age adjustment was performed.
3. Tables 1.1.a.1 and 1.1.a.2 are very similar are you sure you need both of them? Given that the limits of the sampling design for NHANES are at the 5th and 95th percentiles I believe that you could drop – throughout the volume – tables similar to 1.1.a.1.

Page Specific Comments:

4. "1. Water Soluble B-Vitamins: Figure H.1.c: I believe that the years for NHANES III should be 1988-94.
5. Vitamin D: I would like to suggest that the authors include data on the prevalence of persons with a serum 25(OH)D level < 40 nmol/L in Figure H.2.c. That cut-point was defined as the Estimated Average Requirement (EAR) by the recent DRI Committee on Calcium and Vitamin D. I suggest that the order of presentation in the Figure be: < 40 nmol/L, < 30 nmol/L and 30-49 nmol/L. I would use as the upper value for the last group 49 nmol/L as persons with levels of 50-75 were defined by the DRI Committee as having sufficient levels.

6. For the chapter on “Iodine” I would like to suggest that the authors consider including an additional reference which gives a very nice summary of the WHO guidelines. The citation for the article is:

Andersson M, de Benoist B, Delange F, Zupan J. *Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation.* Public Health Nutrition 2007;10(12A):1606-1611